

ANNUAL PUBLICATIONS

2017



**Graduate School of
Medical and Dental Sciences
Tokyo Medical and Dental University**

CONTENTS

Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

Oral Health Sciences

Oral Pathology	1
Bacterial Pathogenesis, Infection and Host Response	4
Molecular Immunology	6
Advanced Biomaterials	8
Diagnostic Oral Pathology	11
Oral Radiation Oncology	12
Oral and Maxillofacial Surgery	14
Oral and Maxillofacial Radiology	18
Anesthesiology and Clinical Physiology	21
Orofacial Pain Management	24
Pediatric Dentistry	27
Orthodontic Science	30
Cariology and Operative Dentistry	36
Fixed Prosthodontics	44
Pulp Biology and Endodontics	48
Removable Partial Prosthodontics	54
Oral Implantology and Regenerative Dental Medicine	59

Maxillofacial and Neck Reconstruction

Plastic and Reconstructive Surgery	64
Head and Neck Surgery	66
Radiation Therapeutics and Oncology	68
Maxillofacial Anatomy	70
Cognitive Neurobiology	73
Molecular Craniofacial Embryology	76
Cellular Physiological Chemistry	78
Biodesign	81
Maxillofacial Surgery	82
Maxillofacial Orthognathics	84
Maxillofacial Prosthetics	89

Bio-Matrix

Cell Biology	94
Medical Biochemistry	96
Joint Surgery and Sports Medicine	98
Biostructural Science	104
Pharmacology	106
Connective Tissue Regeneration	108
Biochemistry	110
Cell Signaling	114
Periodontology	116

Public Health

Global Health Promotion	124
Environmental Parasitology	129
Forensic Medicine	132
Health Care Management and Planning	134
Molecular Epidemiology	136
Research Development	139
Health Policy and Informatics	141
Life Sciences and Bioethics	145
Forensic Dentistry	148
Health Care Economics	151
Dental Education Development	153
Oral Health Promotion	155
Sports Medicine and Dentistry	158
Educational System in Dentistry	161

Educational Media Development	164
Insured Medical Care Management	166
Global Health Entrepreneurship	168
Gerontology and Gerodontology	
Geriatrics and Vascular Medicine	171
Rehabilitation Medicine	173
Gerodontology and Oral Rehabilitation	175
Comprehensive Patient Care	
Laboratory Medicine	181
Intensive Care Medicine	183
Liaison Psychiatry and Palliative Medicine	186
Pharmacokinetics and Pharmacodynamics	190
Medical Education Research and Development	191
Acute Critical Care and Disaster Medicine	194
Clinical Oncology	196
Dentistry for Persons with Disabilities	198
General Dentistry	200
Psychosomatic Dentistry	205
Behavioral Dentistry	208
Professional Development in Health Sciences	210
Cognitive and Behavioral Medicine	
Neuroanatomy and Cellular Neurobiology	213
Systems Neurophysiology	214
Pharmacology and Neurobiology	217
Molecular Neuroscience	219
Neuropathology	222
Ophthalmology and Visual Science	226
Otorhinolaryngology	231
Neurology and Neurological Science	233
Psychiatry and Behavioral Sciences	238
Neurosurgery	242
Endovascular Surgery	246
NCNP Brain Physiology and Pathology	248
Bio-Environmental Response	
Immune Regulation	259
Molecular Virology	262
Immunotherapeutics	265
Cellular and Environmental Biology	268
Biodefense Research	269
Pathological Cell Biology	272
Pediatrics and Developmental Biology	276
Rheumatology	290
Immunology → Refer to Immunology (page466~468)	
Dermatology	295
NCCHD Child Health and Development	298
Systemic Organ Regulation	
Human Pathology	303
Physiology and Cell Biology	307
Molecular Cellular Cardiology	310
Stem Cell Regulation	314
Molecular Pharmacology	316
Stem Cell Biology	317
Respiratory Medicine	320
Gastroenterology and Hepatology	323
Specialized Surgeries	332
Cardiovascular Medicine	336
Anesthesiology	341
Cardiovascular Surgery	343
Nephrology	347

Comprehensive Reproductive Medicine	353
Urology	359
Gastrointestinal Surgery	363
Molecular Cell Biology → Refer to Molecular Cell Biology (page463)	
Chronobiology → Refer to Developmental and Regenerative Biology (page464~465)	
Thoracic Surgery	369
Igakuken Disease-oriented Molecular Biology	371
Advanced Therapeutic Sciences	
Clinical Anatomy	376
Systems BioMedicine	380
Comprehensive Pathology	383
Molecular Oncology	385
Surgical Pathology	388
Experimental Animal Model for Human Disease	390
Signal Gene Regulation	392
Biomedical Devices and Instrumentation	
→ Refer to Biomedical Devices and Instrumentation (page440~444)	
Material Biofunctions	393
Genetic Regulation	396
Applied Gene Medicine	398
Molecular Cytogenetics	402
Hematology	404
Molecular Endocrinology and Metabolism	409
Hepatobiliary and Pancreatic Surgery	412
Orthopaedic and Spinal Surgery	416
Medical Instrument → Refer to Biomedical Information (page445)	
Biointerface Engineering → Refer to Bioelectronics (page446~450)	
Diagnostic Radiology and Nuclear Medicine	422
Disease Genomics	428
Human Genetics and Disease Diversity	431
Applied Regenerative Medicine	434
Minimally Invasive Medical Treatment	437
Life Science and Technology	
Life Science and Technology	
Biomedical Devices and Instrumentation	440
Biomedical Information	445
Bioelectronics	446
Material-Based Medical Engineering	451
Organic and Medicinal Chemistry	454
Chemical Bioscience	457
Biomechanics	460
Molecular Cell Biology	463
Developmental and Regenerative Biology	464
Immunology	466
Epigenetics	469
Medical Science Mathematics	471
Structural Biology	476
Neuroscience	478
Bio-informational Pharmacology	481
Molecular Genetics → Refer to Applied Gene Medicine (page398~401)	
Epigenetic Epidemiology	487
RIKEN Molecular and Chemical Somatology	490
Metallic Biomaterials	495
Inorganic Biomaterials	498
Organic Materials	501
Medicinal Chemistry	504
NCC Cancer Science	507
Cellular and Molecular Medicine	512
Medical and Dental Science and Technology	
Lifetime Oral Health Care Sciences	514

Oral Care for Systemic Health Support	516
Preventive Oral Health Care Sciences	518
Oral Health Science for Community Welfare	520
Oral Health Care Education	522
Basic Sciences of Oral Health Care	524
Basic Oral Health Engineering	526
Oral Biomaterials Development Engineering	528
Oral Prosthetic Engineering	531
Endowed Departments	
Department of Liver Disease Control	534
Department of Cartilage Regeneration → Refer to Joint Surgery and Sports Medicine (page98~103)	
Department of Advanced Therapeutics for GI Diseases	538
Department of Orthopaedic Research and Development → Refer to Orthopaedic and Spinal Surgery (page416~421)	
Department of Sleep Modulatory Medicine	542
Department of Joint Reconstruction → Refer to Joint Surgery and Sports Medicine (page98~103)	
Joint Research Departments	
Department of Translational Oncology	544
Advanced Technology in Medicine → Refer to Orthopaedic and Spinal Surgery (page416~421)	
Functional Joint Anatomy → Refer to Clinical Anatomy (page376~379)	
Medical Hospital	
Central Clinical Facilities	
Clinical Laboratory	546
Radiology Center → Refer to Radiation Therapeutics and Oncology (page68~69)	
Transfusion Medicine	550
General Medicine · Professional Development Center → Refer to Medical Education Research and Development (page191~193)	
Center for Cell Therapy	552
Dental Hospital	
Hospital Departments	
Cleanroom	560
Center for Development of Devices and Drugs in Dentistry	561

Oral Pathology

Professor
Tohru Ikeda

Junior Associate Professor
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Assistant Professor
Kou Kayamori

Technical Staff
Miwako Hamagaki

Graduate Students
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Yae Ohata
Akane Wada
Shoko Ishida
Maiko Tsuchiya
TEERAWONG CHANYANUCH

(1) Research

- 1) Pathology and biology associated with bone
- 2) Pathological and biological studies on oral cancers, odontogenic tumors and oral premalignant lesions
- 3) Pathological and biological studies on microenvironment associated with invasion and metastasis of cancers
- 4) Clinicopathological and diagnostic histopathological studies on oral and maxillofacial lesions

(2) Education

Lectures and microscope practice in the module “Pathology” to 3rd grade students. The Pathology module comprises two sections; General pathology and Oral pathology. Main objective of General pathology is to provide students knowledge on various diseases, which is essential to work in dental, medical and biological fields. Oral pathology provides detailed knowledge on oral diseases, which is indispensable for a dentist.

(3) Clinical Services & Other Works

Our staffs and graduate students participate in diagnostic pathology practice in the Dental Hospital, where nearly 3,000 specimens are annually submitted to laboratory investigation. Our staffs and graduate students also participate in autopsy in the Medical Hospital in cooperation with the staffs and graduate students at the Faculty of Medicine.

(4) Publications

[Original Articles]

1. Oikawa Y, Morita K, Kayamori K, Tanimoto K, Sakamoto K, Katoh H, Ishikawa S, Inazawa J, Harada H. Receptor tyrosine kinase amplification is predictive of distant metastasis in patients with oral squamous cell carcinoma *Cancer Science*. 2017.02; 108(2); 256-266
2. Nguyen CT, Okamura T, Morita K, Yamaguchi S, Harada H, Miki Y, Izumo T, Kayamori K, Yamaguchi A, Sakamoto K. LAMC2 is a predictive marker for the malignant progression of leukoplakia *Journal of Oral Pathology and Medicine*. 2017.03; 46(3); 223-231
3. Fujita, S., Ikeda, T.. The CCL2-CCR2 axis in lymph node metastasis from oral squamous cell carcinoma: an immunohistochemical study *2017.04; 75; 742-749*
4. Sakamoto, Y, Fujita, S., Adachi, M., Sakamoto, H., Naruse, T., Yanamoto, S., Ikeda, T., Umeda, M.. Carcinoma ex pleomorphic adenoma of the tongue: Difficulty in diagnosis between metastasis of breast cancer and salivary tumor *Journal of Craniofacial Surgery*. 2017.05; 28; e182-e185
5. Naruse, T., Yamashita, K., Yanamoto, S., Rokutanda, S., Matsushita, Y., Sakamoto, Y., Sakamoto, H., Ikeda, H., Ikeda, T., Asahina, I., Umeda, M.. Histopathological and immunohistochemical study in keratocystic odontogenic tumors: predictive factors of recurrence *Oncology Letters*. 2017.05; 13; 3487-3493
6. Akane Yukimori, Yu Oikawa, Kei-Ichi Morita, Chi Thi Kim Nguyen, Hiroyuki Harada, Satoshi Yamaguchi, Kou Kayamori, Akira Yamaguchi, Tohru Ikeda, Kei Sakamoto. Genetic basis of calcifying cystic odontogenic tumors. *PLoS ONE*. 2017.06; 12(6); e0180224
7. Yukimori, A., Oikawa, Y., Morita, K., Nguyen, C. T. K., Harada, H., Yamaguchi, S., Kayamori, K., Yamaguchi, A., Ikeda, T., Sakamoto, K.. Genetic basis of calcifying cystic odontogenic tumors. *Plos One*. 2017.06; 12; e0180224
8. Shohei Tomii, Takumi Akashi, Noboru Ando, Tomoki Tamura, Akira Sakurai, Asami Terada, Asuka Furukawa, Yoshimi Suzuki, Kou Kayamori, Kei Sakamoto, Hironori Ishibashi, Yoshinobu Eishi. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology*. 2017.07; 84(4); 171-183
9. Tomii S, Akashi T, Ando N, Tamura T, Sakurai A, Terada A, Furukawa A, Suzuki Y, Kayamori K, Sakamoto K, Ishibashi H, Eishi Y. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology*. 2017.07; 84(4); 171-183
10. Wanlada, S., Masita, M., Ikeda, T., Sakamoto, K.. Downregulation of Notch 1 expression in 4-nitroquinoline-1-oxide-induced precancers of mouse tongue. *The Journal of the Stomatological Society, Japan*. 2017.07; 84; 84-92
11. Nakao, Y., Yamada, S., Yanamoto, S., Tomioka, T., Naruse, T., Ikeda, T., Kurita, H., Umeda, M.. Natriuretic peptide receptor A is related to the expression of vascular endothelial growth factors A and C, and is associated with the invasion potential of tongue squamous cell carcinoma *International Journal of Oral and Maxillofacial Surgery*. 2017.08; 46; 1237-1242
12. Ikeda, T., Seki, S., Fujiwara, M, Matsuura, M., Ozaki, Y., Fujita, S., Ikeda, H., Umeda, M., Asahina, I.. Low-risk population among patients with TNM stages III and IV oral squamous cell carcinoma *Oncology Letters*. 2017.09; 14; 3711-3716
13. Yamagata Y, Tomioka H, Sakamoto K, Sato K, Harada H, Ikeda T, Kayamori K. CD163-Positive Macrophages Within the Tumor Stroma Are Associated With Lymphangiogenesis and Lymph Node Metastasis in Oral Squamous Cell Carcinoma *J Oral Maxillofac Surg*. 2017.10; 75(10); 2144-2153
14. Ohata Y, Tatsuzawa A, Ohyama Y, Ichikawa A, Mochizuki Y, Ishibashi S, Itakura Y, Sakamoto K, Ikeda T, Kitagawa M, Yamamoto K. A distinctive subgroup of oral EBV+ B-cell neoplasm with polymorphous features is potentially identical to EBV+ mucocutaneous ulcer *Human Pathology*. 2017.11; 69; 129-139

15. Yamagata Y, Tomioka H, Sakamoto K, Sato K, Harada H, Ikeda T, Kayamori K. CD163-Positive Macrophages Within the Tumor Stroma Are Associated With Lymphangiogenesis and Lymph Node Metastasis in Oral Squamous Cell Carcinoma *J Oral Maxillofac Surg.* 2017.10; 75(10); 2144-2153
16. Ohata Y, Tatsuzawa A, Ohyama Y, Ichikawa A, Mochizuki Y, Ishibashi S, Itakura Y, Sakamoto K, Ikeda T, Kitagawa M, Yamamoto K. A distinctive subgroup of oral EBV+ B-cell neoplasm with polymorphous features is potentially identical to EBV+ mucocutaneous ulcer *Human Pathology.* 2017.11; 69; 129-139
17. Yae Ohata, Anna Tatsuzawa, Yoshio Ohyama, Ayako Ichikawa, Yumi Mochizuki, Sachiko Ishibashi, Yuri Itakura, Urara Sakurai, Kei Sakamoto, Tohru Ikeda, Masanobu Kitagawa, Kouhei Yamamoto. A distinctive subgroup of oral EBV+ B-cell neoplasm with polymorphous features is potentially identical to EBV+ mucocutaneous ulcer. *Hum. Pathol.* 2017.11; 69; 129-139
18. Ozaki-Honda, Y., Seki, S., Fujiwara, M., Matsuura, M., Fujita, S., Ikeda, H., Umeda, M., Ayuse, T., Ikeda, T.. Prognostic prediction of oral squamous cell carcinoma by E-cadherin and N-cadherin expression in overall cells in tumor nests or tumor cells at the invasive front. *Cancer Microenvironment.* 2017.12; 14; 87-94
19. Rokutanda, S., Yamada, S., Kawasaki, G., Kawano, T., Yanamoto, S., Fujita, S., Ikeda, T., Umeda, M.. Solitary neurofibroma of the maxillary sinus: Report of a case *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology.* 24(201200); 237-240

[Conference Activities & Talks]

1. Uo M, Wada T, Komiya R, Harada H, Sakamoto K, Ikeda T, Yamaguchi A. Trace metallic element accumulation in the sequestrum of medication-related osteonecrosis of the jaw (MRONJ). 14th International Symposium on Applied Bioinorganic chemistry – ISABC14 June 7-10th 2017 2017.06.07 Toulouse, France
2. Ohata Y, Tsuchiya M, Hirai H, Yamaguchi S, Akashi T, Sakamoto K, Yamaguchi A, Ikeda T, Kayamori K. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. Research and Clinical Excellence Day, University of California San Francisco 2017.10.12 California San Francisco
3. T. Uchihara Correspondence information about the author T. Uchihara , M. Sango, H. Takubo, T. Komori, N. Yoshimura, C. Nohara, T. Homma, A. Wada, M. Kodama, S. Orimo, E. Isozaki, M. Kitagawa, K. Hirokawa, S. Toru. Reduced MIBG uptake under relative preservation of cardiac sympathetic nerve in four autopsy patients of CBD-tau without lewy pathology. XXIII World Congress of Neurology 2017.10.15 KYOTO

Bacterial Pathogenesis

Professor SUZUKI Toshihiko

Associate Professor

ASHIDA Hiroshi

Assistant Professor

SUZUKI Shiho

Graduate Student

OKANO Tokuju

Graduate Student

YAMAMURA Kiyonobu

Graduate Student

LEEWANANTHAWET Anongwee (Department of Periodontology)

Graduate Student

ABASS Adiza (Department of Molecular Virology)

(1) Research

Research Subjects

- 1) Molecular mechanisms of infection by pathogenic bacteria
- 2) Mechanisms of activation and regulation of inflammasomes via Nod-like receptors and caspase activation
- 3) Study of virulent genes based on comparative genomics
- 4) Relationship between persistent bacterial infection and chronic inflammatory diseases such as adipose or diabetes

(2) Lectures & Courses

Purpose of Education

The aim of our laboratory in the graduate course is to understand molecular mechanism of pathogen infection and host immune responses. Students also learn planning of research, experiments and methods for evaluating.

(3) Publications

[Original Articles]

1. Noboru Nakasone, Yasunori Ogura, Naomi Higa, Claudia Toma, Yukiko Koizumi, Toshihiko Suzuki, Tetsu Yamashiro. Hot-PBS extract of *Vibrio vulnificus* induces NF- κ B activation *Electronic J. Biol.* 2017;
2. Yohei Yamaguchi, Tomoko Kurita-Ochiai, Ryoki Kobayashi, Toshihiko Suzuki, Tomohiro Ando. Regulation of the NLRP3 inflammasome in *Porphyromonas gingivalis*-accelerated periodontal disease. *Inflamm. Res.* 2017.01; 66(1); 59-65
3. Ayumi Saeki, Toshihiko Suzuki, Akira Hasebe, Ryouyusuke Kamezaki, Mari Fujita, Futoshi Nakazawa, Ken-ichiro Shibata. Activation of nucleotide-binding domain-like receptor containing protein 3 inflammasome in dendritic cells and macrophages by *Streptococcus sanguinis*. *Cell. Microbiol.* 2017.03; 19(3);

4. Noboru Nakasone, Naomi Higa, Claudia Toma, Yasunori Ogura, Toshihiko Suzuki, Tetsu Yamashiro. Epigallocatechin gallate inhibits the type III secretion system of Gram-negative enteropathogenic bacteria under model conditions. *FEMS Microbiol. Lett.* 2017.07; 364(13);

[Books etc]

1. Ashida Hiroshi, Toshihiko Suzuki, Chihiro Sasakawa. *Antibiotics and Chemotherapy* . Iyaku Journal-sha , 2017.01
2. Hiroshi Ashida, Shiho Suzuki, Toshihiko Suzuki. *The Cell*. New Science, 2017.12

[Misc]

1. Hiroshi Ashida, Chihiro Sasakawa. Bacterial E3 ligase effectors exploit host ubiquitin systems. *Curr. Opin. Microbiol.* 2017.02; 35; 16-22

[Conference Activities & Talks]

1. Claudia Toma, Takayoshi Yamaguchi, Naomi Higa, Arina Matsumoto, Nobuhiko Okura, Noboru Nakasone, Toshihiko Suzuki, Tetsu Yamashiro. Interaction of virulent *Leptospira interrogans* with renal epithelial cells. The 90th Annual Meeting of Japanese Society for Bacteriology 2017.03.20 Sendai
2. Ayumi Saeki, Masahiro Sugiyama, Akira Hasebe, Toshihiko Suzuki, Ken-ichiro Shibata. Activation of IL-1beta production in macrophages by mycoplasmal lipoproteins. The 84th Hokkaido Chapter Meeting of Japanese Society for Bacteriology 2017.08.26 Sapporo
3. Tokuju Okano, Toshihiko Suzuki. Activation of inflammasome by *Porphyromonas gingivalis* in hypoxic condition. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17 Matsumoto
4. Ayumi Saeki, Akira Hasebe, Toshihiko Suzuki, Ken-ichiro Shibata . Activation of inflammasome by mycoplasmal lipoproteins . The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17 Matsumoto
5. Hiroshi Ashida, Toshihiko Suzuki, Chihiro Sasakawa. Establishment and analysis of murine infection model for development of vaccine and drug against bacterial infection. ConBio 2017; Consortium of Biological Science 2017 2017.12.06 Kobe
6. Shiho Suzuki, Toshihiko Suzuki. The microbial-host interaction that drive the activation of the Nlr4 inflammasome in *Shigella*-infected macrophages. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai
7. Toshihiko Suzuki. Pathogen infection and host responses. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Tatsukuni Ohno
Adjunct instructor	Hiroshi Kiyono Takeshi Azuma
Graduate Students (Doctor)	Hirunwidchayarat Worawalun(~ Sept.) Nadya Niken Adiba(~ Sept.) Naoto Nishii(Oral and Maxillofacial Surgery) Xia Yulong Furusawa Emi(Pediatric Dentistry) Katou Hiroshi(Maxillofacial Surgery) Yang Yue Kashima Yoshihisa(Oral and Maxillofacial Surgery)(Apr. ~) Ao Xiang(Pulp Biology and Endodontics)(Apr. ~) Wongtim Keeratika(Oct. ~) Tachinami Hidetake(University of Toyama)
Research Student	Jin Xin(~ Sept.)

(1) Research

Research Subjects

- 1) Mechanisms of immune responses in oral diseases
- 2) Studies on lymphocyte functional molecules
- 3) Immunotherapy by molecular targeting

(2) Lectures & Courses

Purpose of Education

Main objective of Molecular Immunology in the graduate course is to understand and study how the immune system works for biological defense. Students also learn immunopathology and immunophysiology of systemic and organ-specific immune diseases and how the immune diseases control and regulate.

(3) Publications

[Original Articles]

1. Kang S, Zhang C, Ohno T, Azuma M. Unique B7-H1 expression on masticatory mucosae in the oral cavity and trans-coinhibition by B7-H1-expressing keratinocytes regulating CD4⁺ T-cell-mediated mucosal tissue

- inflammation. *Mucosal Immunol.* 2017.05; 10(3); 650-660
2. Ohno T, Kondo Y, Zhang C, Kang S, Azuma M. Immune checkpoint molecule, VISTA regulates T cell-mediated skin inflammatory responses. *J Invest Dermatol.* 2017.06; 137(6); 1384-1386
 3. Wallberg M, Recino A, Phillips J, Howie D, Vienne M, Paluch C, Azuma M, Wong FS, Waldmann H, Cooke A. Anti-CD3 treatment up-regulates programmed cell death protein-1 expression on activated effector T cells and severely impairs their inflammatory capacity. *Immunology.* 2017.06; 151(2); 248-260
 4. De Riva A, Wallberg M, Ronchi F, Coulson R, Sage A, Thorne L, Goodfellow L, McCoy K, Azuma M, Cooke A, Busch R. Regulation of type 1 diabetes development and B-cell activation in nonobese diabetic mice by early life exposure to a diabetogenic environment. *Plos One.* 2017.08; 12(8); e0181964
 5. Hirunwidchayarat W, Furusawa E, Kang S, Ohno T, Takeuchi S, Rungsiyanont S, Azuma M. Site-specific regulation of oral mucosa-recruiting CD8⁺ T cells in a mouse contact allergy model. *Biochem Biophys Res Commun.* 2017.09; 490(4); 1294-1300
 6. Nadya NA, Tezuka H, Ohteki T, Matsuda S, Azuma M, Nagai S. PI3K-Akt pathway enhances the differentiation of interleukin-27-induced type 1 regulatory T cells. *Immunology.* 2017.11; 152(3); 507-516
 7. Sugita J, Asada Y, Ishida W, Iwamoto S, Sudo K, Suto H, Matsunaga T, Fukuda K, Fukushima A, Yokoi N, Ohno T, Azuma M, Ebihara N, Saito H, Kubo M, Nakae S, Matsuda A. Contributions of interleukin-33 and TSLP in a papain-soaked contact lens-induced mouse conjunctival inflammation model. *Immun Inflamm Dis.* 2017.12; 5(4); 515-525
 8. Swangphon P, Pientong C, Sunthamala N, Bumrunghai S, Azuma M, Kleebkaow P, Tangsirawatthana T, Sangkomkamhang U, Kongyingyoes B, Ekalaksananan T. Correlation of circulating CD64⁺/CD63⁺ monocyte ratio and stroma/peri-tumoral CD163⁺ monocyte density with human papillomavirus infected cervical lesion severity. *Cancer Microenvironment.* 2017.12; 10(1-3); 77-85

Advanced Biomaterials

Professor UO Motohiro
Assistant Professor WADA Takahiro
Graduate Student CHAIAMORNSUP Patcharanun
Graduate Student Kang Donghoon (Pulp Biology and Endodontics)
Graduate Student KOMIYA Ruri (Oral and Maxillofacial Surgery)
Graduate Student KOYAMA Akihiro (Orthodontic Science)
Graduate Student KINJO Rio (Sports Medicine and Dentistry)
Graduate Student Serif Adel (Pulp Biology and Endodontics)

(1) Research

1. Analysis of Dental and biomedical materials and biological tissue using the synchrotron radiation.
Research is aimed to apply the new analysis method using synchrotron radiation for the estimation of various properties of the dental and biomedical materials.
2. Development of the functional dental and biomedical materials using glass and ceramics.
Research is aimed to develop and evaluate the new glass and ceramics based materials as the dental and biomedical materials, e.g. composite resins, glass ionomer cements, dental porcelains and zirconia ceramics.

(2) Education

1. Lecture of unit “Biomaterials and Dental Materials”
A series of lectures on the “science on biomaterials”, “properties of dental and biomedical materials”, “application of dental materials” will be taught through the lecture and practice.
2. Lecture of unit “Advanced Biomaterials” (graduate school)
Evaluation methods of various dental and biomedical materials will be taught.

(3) Publications

[Original Articles]

1. Hua Huang, Takahiro Wada, Hiroko Ariga, Satoru Takakusagi, Kiyotaka Asakura, Yasuhiro Iwasawa. Controlling the Inhomogeneity of Solid Catalysts at the Mesoscopic Scale Chemical Physics Letters. 2017.01; 683; 18-21
2. Naoyoshi Murata, Takahiro Wada, Takuya Suzuki, Shingo Mukai, Hiromitsu Uehara, Hiroaki Nitani, Yasuhiro Niwa, Kiyotaka Asakura, Yasuhiro Iwasawa. High temperature cell for *in-situ* fluorescence XAFS and characterization of Pt-SnO₂ thin film catalyst for gas sensor Journal of the Japanese Society for Synchrotron Radiation Research. 2017.01; 30(1); 21-26
3. Keiki Nakamura, Hidenori Hamba, Syozi Nakashima, Alireza Sadr, Toru Nikaido, Masakazu Oikawa, Motohiro Uo, Junji Tagami. Effects of experimental pastes containing surface pre-reacted glass ionomer fillers on inhibition of enamel demineralization. Dent Mater J. 2017.03;

4. Motohiro Uo, Takahiro Wada, Kiyotaka Asakura. Structural analysis of strontium in human teeth treated with surface pre-reacted glass-ionomer filler eluate by using extended X-ray absorption fine structure analysis *Dental Materials Journal*. 2017.03; 36(2); 214-221
5. Qiuyi Yuan, Satoru Takakusagi, Yuki Wakisaka, Yohei Uemura, Takahiro Wada, Hiroko Ariga, Kiyotaka Asakura. Polarization-dependent Total Reflection Fluorescence X-ray Absorption Fine Structure (PTRF-XAFS) Studies on the Structure of a Pt Monolayer on Au(111) Prepared by the Surface-limited Redox Replacement Reaction *Chemistry Letters*. 2017.06; 46(8); 1250-1253
6. Tanimoto H., Akiba N., Nakamura T., Zhao H., Suzuki H., Uno A., Uo M., Minakuchi S.. An objective estimation of the removability of three home reliners *Dental Materials Journal*. 2017.06; 36(3); 309-318
7. Hiraishi Noriko, Wada Takahiro, Kimijima Ken'ichi, Masao Kimura, Uo Motohiro, Tagami Junji. Analysis of silver compounds in reaction products of silver diamine fluoride, an anticaries agent, with bovine tooth *Photon Factory Activity Report 2016*. 2017.07; 34;
8. Yuki Wakisaka, Yuya Iwasaki, Hiromitsu Uehara, Shingo Mukai, Daiki Kido, Satoru Takakusagi, Yohei Uemura, Takahiro Wada, Qiuyi Yuan, Oki Sekizawa, Tomoya Uruga, Yasuhiro Iwasawa, Kiyotaka Asakura. Approach to Highly Sensitive XAFS by Means of Bent Crystal Laue Analyzers *Journal of The Surface Science Society of Japan*. 2017.08; 38(8); 378-383
9. Shirako T, Churei H, Wada T, Uo M, Ueno T. Establishment of experimental models to evaluate the effectiveness of dental trauma splints *Dent Mater J*. 2017.11; 36(6); 731-739
10. Maekawa m, Koyama A, Ozaki S, Shima Y, Kanno Z, Doi H, Hanawa T, Wada T, Uo M, Ono T. Comparison of 3-point bending property of rectangular low-stress hysteresis Ni-Ti orthodontic wires with different cross-sectional dimensions 2017.11; 36(6); 470-477
11. Shirako Takahiro, Churei Hiroshi, Wada Takahiro, Uo Motohiro, Ueno Toshiaki. Establishment of experimental models to evaluate the effectiveness of dental trauma splints *DENTAL MATERIALS JOURNAL*. 2017.12; 36(6); 731-739

[Misc]

1. Motohiro Uo. Glasses for Dental Materials 2017.11; 24; 410-414

[Conference Activities & Talks]

1. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Uo M, Minakuchi S. Crystallographic analysis of alumina sandblasted highly translucent dental zirconia. 95th General Session and Exhibition of the IADR 2017.03 San Francisco
2. Sai Khan Lyann, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Masaomi Ikeda, Junji Tagami. Adsorption behavior of phosphoric functional monomers to 3Y-TZP surface. IADR/AADR/CADR GENERAL SESSION & EXHIBITION 2017.03.02 San Francisco, California, USA
3. Yuki Wakisaka, Hiromitsu Uehara, Daiki Kido, Tadashi Ohba, Qiuyi Yuan, Shigo Mukai, Yuya Iwasaki, Satoru Takakusagi, Yohei Uemura, Toshihiko Yokoyama, Takahiro Wada, Motohiro Uo, Oki Sekizawa, Tomoya Uruga, Yasuhiro Iwasawa, Kiyotaka Asakura. Back-illuminated XAFS measurement with low concentration by means of BCLA. 2017.03.14
4. A. Takahashi, T. Takagaki, T. Nikaido, M. Ikeda, T. Wada, M. Uo, J. Tagami. Effect of phosphoric acid cleaning for saliva contaminated zirconia ceramics. IADR/AADR/CADR GENERAL SESSION & EXHIBITION 2017.03.22 San Francisco, California, USA
5. Yuki Wakisaka, Hiromitsu Uehara, Daiki Kido, Tadashi Ohba, Qiuyi Yuan, Shingo Mukai, Yuya Iwasaki, Satoru Takakusagi, Yohei Uemura, Toshihiko Yokoyama, Takahiro Wada, Motohiro Uo, Oki Sekizawa, Tomoya Uruga, Yasuhiro Iwasawa, Kiyotaka Asakura. In-situ XAFS measurement of low concentration Pt/HOPG by means of bent crystal Laue analyzer. 2017 International Workshop on Electrified Interfaces for Energy Conversions (EIC2017) 2017.05.19 Kanagawa, Japan

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7. Motohiro Uo, Takahiro Wada, Ruri Komiya, Hiroyuki Harada, Kei Sakamoto, Tohru Ikeda, Akira Yamaguchi. Trace metallic element accumulation in the sequestrum of medication-related osteonecrosis of the jaw (MRONJ). 14th International Symposium on Applied Bioinorganic chemistry – ISABC14 2017.06.07 Toulouse, France
8. Kang D, Wada T, Uo M, Okiji T. Evaluation of mechanical and rheological properties of the clay added calcium silicate cement. The 146th Meeting of The Japanese Society of Conservative Dentistry 2017.06.08 Link Station Hall Aomori
9. Takahiro Wada, Churei Hiroshi, Toshiaki Ueno, Motohiro Uo. Shock-absorbing property of face guard made by a carbon-fiber reinforced thermoplastic. 2017.06.18
10. Polarization-dependent total reflection in-situ XAFS of polycrystalline Pt thin film surface. 2017.08.17
11. Yoshida Y, Churei H, Wada T, Takeuchi H, Uo M, Ueno T. Antibacterial performance of mouthguard material incorporated with silver-nanoparticles-embedded EVA masterbatch. 105th FDI Annual World Dental Congress 2017.08.29 Madrid, Spain
12. Wada Takahiro, Churei Hiroshi, Yokose Mako, Takayanagi Haruka, Iwasaki Naohiko, Ueno Toshiaki, Takahashi Hidekazu, Uo Motohiro. Evaluation of the Mechanical Properties of a Faceguard Made of Fiber-Reinforced Thermoplastics. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya, Japan
13. Tanabe G, Hata T, Tun PS, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards.. The 2017 ADM Annual Meeting 2017.10.07 Nuremberg
14. Motohiro Uo, Takahiro Wada, Yosuke Akiba. Detection of dental alloy derived elements contained in tissues of oral lichen planus using synchrotron radiation fluorescence X-ray analysis. 2017.10.14
15. Effect of surface treatment agent on lamination bonding strength of mouth guard sheet materials. 2017.10.14
16. Yusuke Yamamoto, Naohiko Iwasaki, Patcharanun Chaiamornsop, Tetsuya Suzuki. Effects of load on machinability of composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Toki Messe, Niigata city
17. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Mechanical property and microstructural analysis of an ion-releasing S-PRG filler contained cement. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.15 Niigata
18. Kang D, Wada T, Uo M, Okiji T. The study for the improvement of compressive strength and operability of the synthesized calcium silicate cement. The 70th Meeting of The Japanese Society for Dental Materials and Devices 2017.10.15 Niigata
19. Yuan Qiuyi, Takakusagi Satoru, Wakisaka Yuki, Uemura Yohei, Wada Takahiro, Ariga Hiroko, Kiyotaka Asakura. An Investigation into the Stoichiometry of Galvanic Displacement Reaction Using XAFS. The 8th International Symposium on Surface Science (ISSS-8) 2017.10.22 Tsukuba, Ibaraki, Japan
20. Y. Wakisaka, H. Uehara, D. Kido, T. Ohba, Q. Yuan, S. Mukai, Y. Iwasaki, S. Takakusagi, Y. Uemura, T. Yokoyama, T. Wada, M. Uo, O. Sekizawa, T. Uruga, Y. Iwasawa, K. Asakura.. Back-illuminated XAFS measurement with the use of BCLA for low concentration Pt/HOPG under electrochemical conditions. International Symposium on Novel Energy Nanomaterials, Catalysts and Surfaces for Future Earth - Material Research, Characterization and Imaging by In situ/Operando XAFS and X-ray Techniques 2017.10.28 Tokyo, Japan
21. Shimizu H, Inokoshi M, Takagaki T, Uo M, Minakuchi S. Bonding effectiveness of 4META/MMA-TBB resin to surface-treated highly translucent dental zirconia. The 36th Annual Meeting of Japan Society for Adhesive Dentistry 2017.11.26 Tokyo

Diagnostic Oral Pathology

Associate Professor: Toshiyuki IZUMO
Visiting Lecturer: Yasuo YAGISHITA, Yasumasa MORI
Hospital Staff: Rei TOHYAMA,
Yuuichi YAMADA, Kiyoko NAGUMO,
Kana NANBA, Akiko ASANO,
Mayuko MINAMI, Yukiko Kuroki,
Kou YANAI, Yuuta TAKAHASHI

(1) Outline

Diagnostic oral pathology is a branch of pathology which studies human pathology, and aims at practice and development of the oral science as clinical medicine. The main object is to bring up graduate students and post-doctoral residents for pathology specialist to the great oral pathologists through the lecture of surgical pathology and pathology diagnosis and research instruction of oral and general diseases for the time being.

(2) Research

Research Subjects

- 1) Surgical pathology of oral cancer.
- 2) New diagnostic approach and reconstruction of oral diseases.

(3) Clinical Services & Other Works

Diagnostic oral pathology is playing three roles, pathological diagnosis (3,400 cases in a year), clinical laboratory (215,000 tests in a year) which consist of hematological, biochemical, bacteriological, physiological and pathological parts, and blood transfusion (100 cases in a year) in the dental hospital.

Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA
Clinical Fellow	Tatuaki GOTOU (~March)
	Shota SHIMIZU
Graduate Students	Hiroyuki ONOZATO
	Nisha GOWRI MANILA
	Sirimanas JIARANUCHART
	Hisao HONMA
	Hitomi NOJIMA
Adjunct Instructor	Tatuaki GOTO (April)

(1) Outline

Main objective of this branch is to provide opportunities to study radiation oncology for oral cancer and translational research for radiosensitization of oral cancer.

(2) Research

- 1) Visualization of tumor radioresponse by molecular imaging
- 2) Mechanism of DNA damage response
- 3) Radioresistant signal transduction pathways
- 4) Radiotherapy for oral cancer

(3) Education

Oral Radiation Oncology is a branch of radiation oncology dealing with basic radiobiology, translational research, and radiotherapy for oral cancer. Main objective of this branch in the graduate course is to provide opportunities to study biological strategies for radiosensitization, development of radiosensitizers, molecular mechanism of tumor radioresistance, the state of the art technology of radiotherapy, and basis of individualized radiotherapy depending on each student's research projects.

(4) Lectures & Courses

The educational policy is to cultivate researchers to be able to extract problems and to work out solutions to them.

(5) Clinical Services & Other Works

Oral Radiation Oncology clinic provides radiotherapeutic treatment for head and neck cancer patients, especially brachytherapy for oral cancer, in cooperation with Diagnostic and Therapeutic Radiology clinic in the Medical Hospital.

(6) Clinical Performances

We are performing brachytherapy for oral cancer, which is now the only treatment modality without surgical excision, as a center institution in Japan.

(7) Publications**[Original Articles]**

1. Ozaki Y, Watanabe H, Kaida A, Miura M, Nakagawa K, Toda K, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole-body radiation exposure from brachytherapy for oral cancer using Monte Carlo simulation. *Journal of Radiation Research*. 2017.02; 58(4); 523-528
2. Yusuke Onozato, Atsushi Kaida, Hiroyuki Harada, Masahiko Miura. Radiosensitivity of quiescent and proliferating cells grown as multicellular tumor spheroids. *Cancer Sci*. 2017.04; 108(4); 704-712
3. Oba A, Shimada S, Akiyama Y, Nishikawaji T, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Asahara H, Kaida A, Miura M, Tanabe M, Tanaka S . ARID2 modulates DNA damage response in human hepatocellular carcinoma cells *Journal of Hepatology*. 2017.05; 66(5); 942-951
4. Sato M, Saitoh Y, Takayama T, Omata T, Watanabe H, Yoshimura R, Miura M.. Remote radioactive seed-loading device for permanent brachytherapy of oral cancer with Au-198 grains. *Robomech Journal*. 2017.09; 4; 23
5. Atsushi Kaida, Hiroshi Watanabe, Kazuma Toda, Keiko Yuasa-Nakagawa, Ryoichi Yoshimura, Masahiko Miura. Effects of dose rate on early and late complications in low dose rate brachytherapy for mobile tongue carcinoma using Ir-192 sources. *Oral Radiol*. 2017.09; 33(3); 187-192

[Conference Activities & Talks]

1. Atsushi KAIDA. Effects of tumor microenvironments on cell cycle kinetics following X-irradiation. TMDU Intractable Disease (Cancer) Unit Overseas training Seminar Young Researchers (Soo chow Uniiversity) 2017.02.22 Soo chow, China
2. Masahiko Miura. Oral Cancer and brachytherapy. The 39th Annual Scientific Conference on Dental Research 2017.04.04 Ho Chi Minh City, Vietnam
3. Katarzyna A. Inoue, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura, Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. FASEB Conference 2017.07.09 Lisbon, Portugal
4. Masahiko Miura. Redistribution revisited by visualizing cell cycle. 1st International Symposium on Radiation Therapeutics and Biology 2017.11.01 Shenzhen, China
5. Nisha Gowri Manila, Atsushi Kaida, Masahiko Miura. Insulin-like growth factor I receptor (IGF-IR) regulates radiation-induced G2/M checkpoint by controlling Chk1 localization in HeLa cells. TMDU Intractable Disease(Cancer) Unit Workshops for Young Researchers 2017.11.06 Tokyo
6. Atsushi Kaida, Yusuke Onozato, Masahiko Miura. Determining radiosensitivity of quiescent and proliferating tumor cells irradiated under different tumor microenvironments. 33th International Symposium of Radiation Biology Center, Kyoto University 2017.12.05 Kyoto

Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA
Associate Professor Eriko MARUKAWA
Junior Associate Professor Fumihiko TSUSHIMA
Assistant Professor Hiroaki SHIMAMOTO, Hirofumi TOMIOKA,
Hideaki HIRAI, Kae TANAKA, Takeshi KUROSHIMA

Graduate Student
Naoto NISHII, Sirimanas JIARANUCHART, Shuhei FUKUDA,
Ruri KOMIYA, Yoshihisa KASHIMA, Hitomi NOJIMA, Misaki YOKOKAWA,
Naoya KINOSHITA, Yuuki TAKAGAWA, Aoi KANEKO, Yuma ISHIDA,
Shintaro SAKAKITANI, Yoshimitu SATO, Misako TANAKA, Hiroaki SHIMONO
Kaho Takada, Shohei YANAGISAWA, Takuya KOMIYAMA, Cuong TRAN MINH

(1) Outline

Purpose of Education

The program is designed for acquiring the broad knowledge and basic skills of oral and maxillofacial surgery, mainly concerning the diagnostic procedure, treatment technique and the perioperative patient care. Also throughout the professional education, we promote the system in which each graduate student can select his or her special field in the full scope of oral and maxillofacial surgery in the future.

Research Subjects

- 1) Development of multidisciplinary treatment of oral cancer.
- 2) Clinical study on sentinel node navigation surgery for oral cancer.
- 3) Study on molecular markers for lymph node metastasis of oral cancer.
- 4) Clinical study on maxillomandibular skeletal and dental changes after orthognatic surgery.
- 5) Study on neurosensory disturbances using the heat flux technique.
- 6) Multidisciplinary treatment of temporomandibular disorders.
- 7) Clinical and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 8) Development of multidisciplinary treatment of oral mucosal diseases.

Clinical Services

The Oral and Maxillofacial Surgery Clinic examines yearly more than 6,200 new patients with various diseases arising in oral and maxillofacial regions. The clinic has diplomat of the Japanese Society of Oral and Maxillofacial Surgeons and accepts many referrals from dentists and medical doctors. We provide a full range of services including extractions, removal of wisdom teeth and management of facial trauma, jawbone defect, facial deformity, temporomandibular joint disease, cleft lip and palate, oral mucosal disease, and benign and malignant tumors. The special outpatient clinics are organized by the specialists to offer the best service, especially for patients with malignant tumor, temporomandibular joint disease, cleft lip and palate, facial deformity and oral mucosal disease which need high degree of specialty and long term follow up. We also prepare some groups for inpatients with an emphasis on specialties, to provide the recent and advanced treatment.

(2) Publications**[Original Articles]**

1. Takahara N, Kabasawa Y, Sato M, Tetsumura A, Kurabayashi T, Omura K. MRI Changes of temporomandibular joint following mandibular setback using sagittal split ramus osteotomy with rigid fixation The Journal of Craniomandibular & Sleep Practice. 2017.01; 35(11); 38-45
2. Kaneko MK, Nakamura T, Honma R, Ogasawara S, Fujii Y, Abe S, Takagi M, Harada H, Suzuki H, Nishioka Y, Kato Y. Development and characterization of anti-glycopeptide monoclonal antibodies against human podoplanin using glycan-deficient cell lines generated by CRISPR/Cas and TALEN Cancer Medicine. 2017.01; 6(2); 382-396
3. Oikawa Y, Morita K, Kayamori K, Tanimoto K, Sakamoto K, Katoh H, Ishikawa S, Inazawa J, Harada H. Receptor tyrosine kinase amplification is predictive of distant metastasis in patients with oral squamous cell carcinoma Cancer Science. 2017.02; 108(2); 256-266
4. Shimada Y, Nakagawa Y, Ide K, Sato I, Hagiwara S, Yamada H, Kawasaki Y, Maruoka Y. Clinical importance of elimination of potential dental focal infection before the first cycle of chemotherapy in patients with hematologic malignancy. Support Care Cancer. 2017.02;
5. Lam PD, Kuribayashi A, Sakamoto J, Nakamura S, Harada H, Kurabayashi T. Imaging findings of childhood B-cell lymphoblastic lymphoma in the mental region: a case report. Dentomaxillofacial Radiology. 2017.03; 46(3); 20160313
6. Nguyen CT, Okamura T, Morita K, Yamaguchi S, Harada H, Miki Y, Izumo T, Kayamori K, Yamaguchi A, Sakamoto K. LAMC2 is a predictive marker for the malignant progression of leukoplakia Journal of Oral Pathology and Medicine. 2017.03; 46(3); 223-231
7. Onozato Y, Kaida A, Harada H, Miura M. Radiosensitivity of quiescent and proliferating cells grown as multicellular tumor spheroids Cancer Science. 2017.04;
8. Akane Yukimori, Yu Oikawa, Kei-Ichi Morita, Chi Thi Kim Nguyen, Hiroyuki Harada, Satoshi Yamaguchi, Kou Kayamori, Akira Yamaguchi, Tohru Ikeda, Kei Sakamoto. Genetic basis of calcifying cystic odontogenic tumors. PLoS ONE. 2017.06; 12(6); e0180224
9. Hihara H, Kanetaka H, Kanno A, Koeda S, Nakasato N, Kawashima R, Sasaki K. Evaluating age-related change in lip somatosensation using somatosensory evoked magnetic fields PLOS One. 2017.06; 12(6);
10. Mochizuki Y, Harada H, Shimamoto H, Tomioka H, Hirai H. Multiple Free Flap Reconstructions of Head and Neck Defects Due to Oral Cancer Plast Reconstr Surg Glob Open. 2017.06; 5(6);
11. Shimamoto H, Oikawa Y, Osako T, Hirai H, Mochizuki Y, Tanaka K, Tomioka H, Harada H. Neck failure after elective neck dissection in patients with oral squamous cell carcinoma Oral Surg Oral Med Oral Pathol Oral Radiol. 2017.07; 124(1); 32-36
12. Itai S, Fujii Y, Kaneko MK, Yamada S, Nakamura T, Yanaka M, Saidoh N, Chang YW, Handa S, Takahashi M, Suzuki H, Harada H, Kato Y. H2Mab-77 is a sensitive and specific anti-HER2 monoclonal antibody against breast cancer Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.08;
13. Kaneko MK, Kunita A, Yamada S, Nakamura T, Yanaka M, Saidoh N, Chang YW, Handa S, Ogasawara S, Ohishi T, Abe S, Itai S, Harada H, Kawada M, Nishioka Y, Fukayama M, Kato Y. Anti-Podocalyxin Antibody chPcMab-47 Exerts Antitumor Activity in Mouse Xenograft Models of Colorectal Adenocarcinomas Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.08;
14. Nakano T, Ogasawara S, Tanaka T, Hozumi Y, Mizuno S, Satoh E, Sakane F, Okada N, Taketomi A, Honma R, Nakamura T, Saidoh N, Yanaka M, Itai S, Handa S, Chang YW, Yamada S, Kaneko MK, Kato Y, Goto K. DaMab-2: Anti-Human DGK Monoclonal Antibody for immunocytochemistry Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.08;
15. Ngansom S, Nakamura S, Kabasawa Y, Harada H, Tohyama R, Kurabayashi T. Imaging findings of intraosseous traumatic neuroma of the mandible Oral Radiology. 2017.09;
16. Sato M, Harada H, Nagata C, Suzuki K. A case of Ectomesenchymal Chondromyxoid Tumor on the tongue Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2017.09;

17. Hirai H, Tomioka H, Mochizuki Y, Oikawa Y, Tsushima F, Harada H. Clinical Course of Oral Squamous Cell Carcinoma in Patients on Immunosuppressant and Glucocorticoid Therapy J Oral Maxillofac Surg. 2017.09; 75(9);
18. Takahara N, Nakagawa S, Sumikura K, Kabasawa Y, Sakamoto I, Harada H. Association of TMJ pain according to magnetic resonance imaging findings in TMD patients J Oral Maxillofac Surg. 2017.09; 75(9); 1848-1855
19. Sakamoto J, Kotaki S, Nakamura S, Sumikura K, Harada H, Kurabayashi T. A Case of Ghost Cell Odontogenic Carcinoma in the Maxilla Shika Hoshasen. 2017.10; 57(1); 57-59
20. Itai S, Kaneko MK, Fujii Y, Yamada S, Nakamura T, Yanaka M, Saidoh N, Handa S, Chang YW, Suzuki H, Harada H, Kato Y. Development of EMab-51, a Sensitive and Specific Anti-EGFR Monoclonal Antibody in Western Blot and Immunohistochemistry Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.10;
21. Itai S, Yamada S, Kaneko MK, Harada H, Kato Y. Immunohistochemical Analysis Using Antipodocalyxin Monoclonal Antibody PcMab-47 Demonstrates Podocalyxin Expression in Oral Squamous Cell Carcinomas Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.10;
22. Yamada S, Itai S, Nakamura T, Yanaka M, Saidoh N, Chang YW, Handa S, Harada H, Kagawa Y, Ichii O, Konnai S, Kaneko MK, Kato Y. PMab-52: Specific and Sensitive Monoclonal Antibody Against Cat Podoplanin for Immunohistochemistry Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.10;
23. Itai S, Fujii Y, Nakamura T, Chang YW, Yanaka M, Saidoh N, Handa S, Suzuki H, Harada H, Yamada S, Kaneko MK, Kato Y. Establishment of CMab-43, a Sensitive and Specific Anti-CD133 Monoclonal Antibody, for Immunohistochemistry Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.10;
24. Yamagata Y, Tomioka H, Sakamoto K, Sato K, Harada H, Ikeda T, Kayamori K. CD163-Positive Macrophages Within the Tumor Stroma Are Associated With Lymphangiogenesis and Lymph Node Metastasis in Oral Squamous Cell Carcinoma J Oral Maxillofac Surg. 2017.10; 75(10); 2144-2153
25. Ohata Y, Tatsuzawa A, Ohyama Y, Ichikawa A, Mochizuki Y, Ishibashi S, Itakura Y, Sakamoto K, Ikeda T, Kitagawa M, Yamamoto K. A distinctive subgroup of oral EBV+ B-cell neoplasm with polymorphous features is potentially identical to EBV+ mucocutaneous ulcer Human Pathology. 2017.11; 69; 129-139
26. Itai S, Yamada S, Kaneko MK, Harada H, Kagawa Y, Konnai S, Kato Y. Expression of cat podoplanin in feline squamous cell carcinomas Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.11;
27. Itai S, Yamada S, Kaneko MK, Chang YW, Harada, H, Kato Y. Establishment of EMab-134, a sensitive and specific anti-epidermal growth factor receptor monoclonal antibody for detecting squamous cell carcinoma cells of the oral cavity Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.11;
28. Yamada S, Itai S, Nakamura T, Chang YW, Harada H, Suzuki H, Kaneko MK, Kato Y. Establishment of H2Mab-119, an Anti-Human Epidermal Growth Factor Receptor 2 Monoclonal Antibody, Against Pancreatic Cancer Monoclonal Antibodies in Immunodiagnosis and Immunotherapy. 2017.11;
29. Takemoto T, Kabasawa Y, Higuchi Y, Tabata Y, Aoki K, Tamura Y, Harada H. Combination of the RANKL-binding peptide W9 and bFGF induces ectopic bone regeneration in the rat calvarial defect mode Dental, Oral and Craniofacial Research. 2017.12; 4(3); 2-7
30. Koki Hobo, Kanako Noritake, Masayo Sunaga, Tomoe Miyoshi, Ridan Cao, Hiroshi Nitta, Yuji Kabasawa, Atsuhiko Kinoshita. Effects of an interactive simulation material for clinical dentistry on knowledge acquisition and memory retention in dental residents. J. Med. Dent. Sci.. 2017.12; 64(4); 43-52

[Conference Activities & Talks]

1. Miyazaki H, Wada Y, Tanaka K, Harada H, Asamura S. Treatment strategies for oral vascular anomalies: Approaches to massive lesions using intralesional laser photocoagulation. European Congress of Laser Dentistry, March 30-April 1 2017. 2017.03.30 Plovdiv
2. Uo M, Wada T, Komiya R, Harada H, Sakamoto K, Ikeda T, Yamaguchi A. Trace metallic element accumulation in the sequestrum of medication-related osteonecrosis of the jaw (MRONJ). 14th International Symposium on Applied Bioinorganic chemistry – ISABC14 June 7-10th 2017 2017.06.07 Toulouse, France
3. Shimada Y, Kawasaki Y, Ide K, Sato I, Hagiwara S, Yamada H, Maruoka Y. Differential diagnosis of fever in patients with hematologic malignancy receiving chemotherapy: A retrospective cohort study in Japan. 99th the American Association of Oral and Maxillofacial Surgeons(AAOMS) Annual Meeting Oct 9-14th 2017 2017.10.09 San Francisco
4. Systemic administration of low dose TLR7 agonist augments antitumor responses in the PD-1 checkpoint blockade-resistant and regulatory T cell-dominant murine tumor models. 2017.12.12

Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI

Associate Professor: Hiroshi WATANABE

Junior Associate Professor: Naoto OHBAYASHI, Norio YOSHINO

Assistant Professor: Akemi TETSUMURA, Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO

Hospital Staff: Yoshikazu NOMURA, Mamiko FUJIKURA

Graduate Student: Shinya KOTAKI, Ngamsom SUPAK, Hiroko ISHII, Noriko SUZUKI,

Chutamas DEEPHO, Tran Thi Xuan LAN, Sakurako ASAI, Wamasing PEERAPONG

Secretary: Izumi MOTOHASHI

(1) Research

- 1) Diagnosis of maxillofacial diseases by CT, MRI and PET imaging
- 2) Advantages of cone-beam CT for clinical dentistry
- 3) Development of high resolution MRI technology.
- 4) Novel MRI techniques for TMJ disorders.
- 5) Factors determining radioresistance of oral and maxillofacial cancers.

(2) Lectures & Courses

Oral and maxillofacial radiology is a branch of dental science which deals with the effective application of radiation energy to the diagnosis and treatment of oral and maxillofacial diseases. Main objective of oral and maxillofacial radiology in the graduate course is to provide students opportunity to study advanced imaging modalities including digital imaging, cone-beam CT, multi-detector row CT and MRI, and also to study image processing and image analysis technology. Students are also taught on basic radiation oncology and its related laboratory technology depending on their research project.

(3) Clinical Services & Other Works

Oral and maxillofacial radiology clinic provides a full spectrum of imaging examinations and diagnosis, including CT and MRI. Non-invasive, interventional radiology for patients with salivary gland stone is also performed in the clinic.

(4) Publications

[Original Articles]

1. Takahara N, Kabasawa Y, Sato M, Tetsumura A, Kurabayashi T, Omura K. MRI Changes of temporomandibular joint following mandibular setback using sagittal split ramus osteotomy with rigid fixation The Journal of Craniomandibular & Sleep Practice. 2017.01; 35(11); 38-45
2. Ozaki Y, Watanabe H, Kaida A, Miura M, Nakagawa K, Toda K, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole-body radiation exposure from brachytherapy for oral cancer using Monte Carlo simulation. Journal of Radiation Research. 2017.02; 58(4); 523-528

3. Watanabe H, Kuribayashi A, Sumi Y, Kurabayashi T. Resolution characteristics of optical coherence tomography for dental use. *Dentomaxillofacial Radiology*. 2017.03; 46(3); 20160358
4. Deepho C, Watanabe H, Kotaki S, Sakamoto J, Sumi Y, Kurabayashi T. Utility of fusion volumetric images from computed tomography and magnetic resonance imaging for localizing the mandibular canal. *Dentomaxillofacial Radiology*. 2017.03; 46(3); 20160383
5. Lam PD, Kuribayashi A, Sakamoto J, Nakamura S, Harada H, Kurabayashi T. Imaging findings of childhood B-cell lymphoblastic lymphoma in the mental region: a case report. *Dentomaxillofacial Radiology*. 2017.03; 46(3); 20160313
6. Chie Watanabe, Junichiro Wada, Koji Mizutani, Hiroshi Watanabe, Noriyuki Wakabayashi. Chronological grey scale changes in supporting alveolar bone by removable partial denture placement on patients with periodontal disease: A 6-month follow-up study using digital subtraction analysis. *J Dent*. 2017.05; 63; 8-13
7. Toriihara A, Nakadate M, Nakamura S, Kubota K, Tateishi U. Seventy FDG-PET/CT cases in which nuclear medicine physicians suspected lymphoma: how reliable are we? *Asia Ocean Journal Nuclear Medicine Biology*. 2017.05; 5(2); 95-103
8. Ngamsom S, Nakamura S, Sakamoto J, Kotaki S, Tetsumura A, Kurabayashi T. The intravoxel incoherent motion MRI of lateral pterygoid muscle: a quantitative analysis in patients with temporomandibular joint disorders *Dentomaxillofacial Radiology*. 2017.07; 46(5); 20160424
9. Nguyen Ho Quynh Anh, Yamazaki Yoko, Yoshino Norio, Taira Masato, Kurabayashi Tohru, Shimada Masahiko. Altered Grey Matter Volume in Trigeminal Neuralgia *The Journal of the Stomatological Society* . 2017.07; 84(2); 73-83
10. Sato M, Saitoh Y, Takayama T, Omata T, Watanabe H, Yoshimura R, Miura M.. Remote radioactive seed-loading device for permanent brachytherapy of oral cancer with Au-198 grains. *Robomech Journal*. 2017.09; 4; 23
11. Atsushi Kaida, Hiroshi Watanabe, Kazuma Toda, Keiko Yuasa-Nakagawa, Ryoichi Yoshimura, Masahiko Miura. Effects of dose rate on early and late complications in low dose rate brachytherapy for mobile tongue carcinoma using Ir-192 sources. *Oral Radiol*. 2017.09; 33(3); 187-192

[Conference Activities & Talks]

1. Ngamsom S, Nakamura S, Sakamoto J, Kotaki S, Kurabayashi T. The Intravoxel Incoherent Motion MRI of Lateral Pterygoid Muscle: A Quantitative Analysis in Patients with Temporomandibular Joint Disorders. *European Congress of Radiology 2017* 2017.03 Vienna, Austria
2. Quynh Anh Nguyen Ho, Y. Yamazaki, H. Imura, N. Yoshino, M. Taira, T. Kurabayashi, M. Shimada. Trigeminal Neuropathy and Brain Plasticity. *IADR/AADR/CADR General Session & Exhibition 2017.03.22 USA, San Francisco*
3. Watanabe H, Kuribayashi A, Sumi Y, Kurabayashi T. Developing a chart device for measuring spatial resolution of optical coherence tomography for dental use. *The 21th International Congress of Dent-Maxillofacial Radiology 2017.04.27 Kaohsiung, Taiwan*
4. N. Ohbayashi, S. Asai, T. Sakaino, Y. Harada, M. Izawa, Y. Okumura, T. Kurabayashi. Comparison of Patient Entrance Dose of Intraoral X-ray Unit using TMDU Dental Hospital to Japanese Diagnostic Level . *58th academic meeting and 14th general meeting of Japanese Society for Oral and Maxillofacial Radiology 2017.06.02 Kagoshima City*
5. Watanabe C, Wada J, Mizutani K, Watanabe H, Katsuki A, Wakabayashi N. Chronological effects of removable partial denture placement on periodontally compromised abutment teeth: A digital subtraction analysis. *The 126th Scientific Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama*
6. Ozawa E, Ozawa T, Omori H, Shimazaki K, Kurabayashi T, Ono T. The influence of orthodontic appliance-derived artifacts on MR angiography. *The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo*

7. Reiko Hoshi, Akemi Tetsumura, Satoshi Yamaguti. Relationship between hypesthesia of the inferior alveolar nerve after mandibular cystectomy and preoperative imaging findings on panoramic X-ray films and CT scan. The 62nd Congress of the Japanese Society of Oral and Maxillofacial Surgeon 2017.10.20 Kyoto
8. Kurabayashi T. Special lecture: Imaging of odontogenic tumors and cysts. The 1st Japan-Korea International Conference of Oral and Maxillofacial Radiology 2017.11.25 Naha
9. Yamada I, Yoshino N, Hikishima K, Sakamoto J, Oikawa Y, Harada H, Kurabayashi T, Saida Y, Tateishi U, Izumo T, Asahina S. Oral Carcinoma: Clinical evaluation using diffusion kurtosis imaging and its correlation with histopathologic findings. The 103rd Scientific Assembly and Annual Meeting of the Radiological Society of North America 2017.11.26 Chicago

[Awards & Honors]

1. Hiroshi Watanabe. Excellence in Research 2016, Tokyo Medical and Dental University, Faculty of Dentistry, 2017.02
2. Deepho Chutamas. The first prize in presentation., The Stomatological Society, Japan., 2017.11

Anesthesiology and Clinical Physiology

Professor

Haruhisa Fukayama

Associate Professor

Ryo Wakita

Junior Associate Professor

Keiko Abe (~ Sep) ,

Tomoka Matsumura (Feb ~)

Assistant Professors

Tomoyuki Miyamoto,

Tomoka Matsumura (~ Jan)

Yukiko Baba (Apr ~)

Hospital Staffs

Kotomi Uchinuma (Apr ~)

Hidetaka Murata(Apr ~)

Tunataka Abo

Takutoshi Inoue(Apr ~)

Kouichirou Ozawa (Apr ~)

Sayaka Asano (Apr ~)

Graduate Students

Chihiro Suzuki,

Kaeko Araki,

Takaya Ito,

Yuu Satou,

Keiko Abe (Apr ~)

Research Students

Keita Niimi(Apr ~),

Moegi Toyomaki(Apr ~),

Advanced Clinical Training

Feng Yu Pin (~ Jun)

Secretary

Natsu Sato

(1) Outline

For safety and comfortable dentistry for both patients and dentists, educations, researches and clinical practices are performed in the department. Education includes basics and practices of local and general anesthesia, sedation, monitoring (monitored anesthesia care, MAC) in addition to cardio-pulmonary resuscitation, or, basic life support during dental treatment. Our researches are consisted of basic and clinical trials for the purposes. Many cases give us many chances to keep the patients safe and comfortable during local and general anesthesia. Local groups, such as dental associations, are welcomed to promote safe and comfortable dental treatments.

(2) Research

- 1) Non-invasive drug delivery system
- 2) New methods for local anesthesia in dentistry
- 3) Neuropathic pain in oral and maxillofacial regions
- 4) Diffuse noxious inhibitory control or controlled pain modulation
- 5) Sedation for dentistry

(3) Education

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

(4) Lectures & Courses

Anesthesia and anesthesiology for dentistry, which are not only local anesthesia but also general anesthesia are given to the both under and post graduate students. Lectures and trainings are consisted of local and general anesthesia, sedation and cardio-pulmonary-resuscitation (CPR), or, basic life support (BLS). For local anesthesia, the students learn mechanism of local anesthesia, local anesthetics, techniques and local and systemic complications due to local anesthesia. Physiology, biochemistry and pharmacology are also provided for general anesthesia which includes possible mechanism of general anesthesia, anesthetics, muscle relaxants and what are used for general anesthesia. They also acquire the techniques of topical, infiltration and conduction anesthesia, nitrous oxide inhalation sedation and basic life support.

(5) Clinical Services & Other Works

Safe medical and perioperative managements are given to the patients of our ambulatory anesthesia service which has more than 2,000 cases per year and the central operation rooms which has 750 cases per year. Some difficult cases are referred to our hospital because of many clinical experiences.

Several cases that need emergency care also supported by our department. ER members are sometimes called in the medical hospital.

Local groups like dental associations often ask us to hold some lectures, trainings, workshops for safe dental treatment. These proposals are welcomed by our staffs. When intravenous sedation cases are introduced, some responsible staff is sent to their own clinic.

(6) Clinical Performances

Any patient is welcomed, especially patients of oral surgery and implant operation who need special care using general anesthesia and sedation.

Referred patients from open practitioners are also accepted for safe and comfortable dental treatment.

(7) Publications

[Original Articles]

1. Ikeda Y, Funayama T, Fukayama H, Okubo Y, Suzuki H. Modafinil enhances altering-related brain activity in attention networks *Psychopharmacology*. 2017.04; 234; 2077-2089
2. Tsunataka Abo, Tomoyuki Miyamoto, Takutoshi Inoue, Kazumasa Kubota, Keiko Abe, Kanji Doushita, Haruhisa Fukuyama. Anesthetic Management of a Patient with Human Immunodeficiency Virus (HIV)

Undergoing a Sagittal Split Ramus Osteotomy (SSRO). *Journal of Japan Dental Society Anesthesiology*. 2017.04; 45(2); 214-216

3. Kotomi Ota, Tomoyuki Miyamoto, Kazumasa Kubota, Haruhisa Fukayama. Management during Tooth Extraction of a Patient with Glanzmann's Thrombasthenia. *Journal of Japan Dental Society Anesthesiology*. 2017.04; 45(2); 178-180
4. Medications in 5,699 medically compromised elderly dental patients *Japanese Journal of Gerodontology*. 2017.09; 32(2); 257-258
5. Kubota K, Miyamoto T, Ota K, Fukayama H, Minakuchi S. Anesthetic management of a patient with benign tracheal tumor identified at induction of general anesthesia *Journal of Clinical Anesthesia*. 2017.12; 43; 66-67

[Conference Activities & Talks]

1. Haruhisa Fukayama. Tips for local anesthesia in dentistry. 36th Myanmar Dental Conference & 167th FDI-MDA joint Educational Meeting 2017.01.20 Yangon, Myanmar
2. A case report of the systemic management by clear sight system ® and transthoracic echocardiogram during dental treatment in a patient with dilated cardiomyopathy. 2017.03.03
3. Kazumasa Kubota, Shunsuke Minakuchi, Haruhisa Fukuyama. Anesthetic Management for a Patient Diagnosed with Chronic Kidney Disease Scheduled for Transplanted of Scapular Osteocutaneous Flap Harvest. The 28th Annual Meeting of Japanese Society of Gerodontology 2017.06.15 Nagoya
4. Ohwatari T, Takahashi K, Kyosaka Y, Inokoshi M, Inoue M, Minakuchi S, Fukayama H, Shimoyama K. Medications in 5,699 medically compromised elderly dental patients. 2017.06.16 Nagoya
5. Yukiko Baba, Hisa Okumura, Junko Kobayashi, Haruhisa Fukayama. A case in which ventilation failure is considered to be caused by bronchospasm immediately after intubation. 2017.06.24
6. Ryo Wakita. The effect on cardiac function of adrenaline in local anesthesia. 8th Mandaley Dental Conference 2017.07.23 Mandaley
7. Haruhisa Fukayama. Dental Emergencies during treatment. 8th Mandalay Dental Conference 2017 2017.07.23 Mandalay, Myanmar
8. The survey on dental-treatments under intravenous sedation in the clinic for patients with disabilities at the dental association. 2017.10.28
9. Dental treatment in a patient with hypertrophic obstructive cardiomyopathy. 2017.10.28
10. Stressors due to dental treatment caused a high fever in a patient with intellectual developmental disorder: a case report . 2017.10.28

Orofacial Pain Management

Professor	Masahiko SHIMADA
Junior Associate Professor	Akira NISHIYAMA
Assistant Professor	Yoko YAMAZAKI
Hospital Staff	Hiroko KIMURA, Ryouko KURUSU, Hiroko IMURA, Masako TOBE, Hiroyuki ISHIYAMA, Maya SAKAMOTO, Ryoko KURISU
Graduate Student	Akitoshi HOSODA, Kaori TUKAGOSHI, Rena NAKAYAMA, Nguyen Ho QUYNH ANH, Ngan Nguyen, Liang Shanshan, KAY THWE YE MIN SOE

(1) Outline

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

(2) Research

Main research subjects of orofacial pain management is to establish the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders , in particular, is to elucidate the mechanism of pain, neuropathic pain, temporomandibular disorders.

- 1)New Treatment methods for neuropathic pain
- 2)Analyses of abnormal orofacila pain
- 3)Study on Biological Response to Dental Interventions
- 4)Analyses and new treatment of dysgeusia
- 5)Development of multidimensional evaluation system for etiological factors of TMD
- 6)Influence of patients' psychosomatic factors for TMD
- 7)Sleep bruxism: its etiology, influence and treatment
- 8)Effectiveness of physiological therapy for TMD
- 9)Mechanisms of occlusal discomfort

(3) Education

Purpose of education for students and residents in this course is to provide an opportunity to learn basic knowledge on diagnostic and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area. In special course for graduate students, main objective of orofacial pain management is to learn the diagnosis and treatment of the disease with a pain, abnormal sensation, sensory paralysis, abnormal movement, motor paralysis and temporomandibular disorders in the orofacial area, in particular, mechanism of pain, neuropathic pain, temporomandibular disorders, and we instruct statistical techniques especially with the multi variate analysis by using clinical data acquired from patients with temporomandibular disorders (TMD).

(4) Clinical Services & Other Works

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the pheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

(5) Clinical Performances

Orofacial Pain Clinic is concerned with the the pain, abnormal sensation, sensory paralysis, abnormal movement, and motor paralysis in the orofacial area and management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the pheripheral nerves including acupuncture and psychotherapies. Temporomandibular joint clinic provides diagnosis and treatment for diseases and disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

(6) Publications**[Original Articles]**

1. Yoko Yamazaki, Maya Sakamoto, Hiroko Imura, Masahiko Shimada. Pre-Trigeminal Neuralgia Similar to Atypical Odontalgia: A Case Report *Journal of Pain & Relief*. 2017.05; 63(3); 291
2. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Meiyo Tamaoka, Yasunari Miyazaki, Kenji Fueki, Noriyuki Wakabayashi. Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial *J Prosthodont Res.*. 2017.07; 61(3); 259-267
3. Nguyen Ho Quynh Anh, Yamazaki Yoko, Yoshino Norio, Taira Masato, Kurabayashi Tohru, Shimada Masahiko. Altered Grey Matter Volume in Trigeminal Neuralgia *The Journal of the Stomatological Society* . 2017.07; 84(2); 73-83
4. Rena Nakayama, Akira Nishiyama and Masahiko Shimada. Creating a Quality of Life Index for Patients with Temporomandibular Disorders *Int J Dent Oral Health* . 2017.09; 3(5);
5. Tsukagoshi K., Nishiyama A., Shimada M.. Association between Symptoms of Temporomandibular Disorders and Duration of Computer Use in a Working Population in Japan *Int J Dent Oral Health*. 2017.10; 3(5); open access
6. Suzuki K, Kokai S, Uesugi S, Nishiyama A, Ono T. Evaluation of the laterality of the tissue oxygen saturation of masticatory muscles in subjects with facial asymmetry *Orthodontic Waves*. 2017.12; 76(4); 232-237
7. Nakayama R., Nishiyama A., Matsuda C., Nakayama Y., Hakuta C., Shimada M.. Oral health status of hospitalized amyotrophic lateral sclerosis patients *Acta Odontologica Scandinavica*. 2017.12; 76; open access

[Books etc]

1. Masahiko Shimada, Yoshiki Sugiyama et al. *Oral and Maxillofacial Surgery*. ISHIYAKU PUBLISHERS, INC., 2017.09 (ISBN : 978-4-263-45806-8)

[Conference Activities & Talks]

1. Quynh Anh Nguyen Ho, Y. Yamazaki, H. Imura, N. Yoshino, M. Taira, T. Kurabayashi, M. Shimada. Trigeminal Neuropathy and Brain Plasticity. IADR/AADR/CADR General Session & Exhibition 2017.03.22 USA, San Francisco

2. Suzuki K, Kokai S, Uesugi S, Nishiyama A, Ono T. Evaluation of the laterality of the tissue oxygen saturation of masticatory muscles in subjects with facial asymmetry. The 93rd congress of the European Orthodontic Society 2017.06.05 Montreux, Switzerland
3. Masahiko Shimada. Orofacial Pain Management in Japan. The 1st China-Japan Friendship Oral Medicine Symposium 2017.06.10 Beijing

Pediatric Dentistry

Associate Professor
Michiyo MIYASHIN

Assistant Professor
Yoshiaki HASHIMOTO, Mizuho MOTEGI,
Satoko KAKINO, Tomoki UEHARA

Clinical Professor
Keiichi TAKEI

Adjunct Lecturer
Mitsuko INOUE, Hitoyata SHIMOKAWA, Masayo ONO
Hiroaki NAGAI, Nobutaka ISOGAWA,
Asuri jayawarudeina, Naoko UEHARA,
Makiko TAKASHI, Natsumi TSUCHIHASHI

Hospital staff
Atsushi OISHI, Kanae WADA, Taki KEKIYA,
Kuniomi NAKAMURA(Apr. ~), Kenichi MIURA(Apr. ~)

Graduate Student
Kuniomi NAKAMURA(~ Mar.), GANBOLD Khongorzul(~ Sep.),
Erika KUBOTA, IJBARA Manhal M.A.,
ZUMULAITI Shaokelati, WIT Yee Wint, Satomi FURUSAWA,
Shigeki NAGAIHIRO, Rika KODAMA(Apr. ~),
Manami TAKENOSHITA(Apr. ~)
Amrita Widyagarini Subagyo(Oct. ~)

Research Student
Chika INOHARA, Ayano INOUE(Apr. ~),
Yuko SEKI(Apr. ~), Yui SEKIDO(Apr. ~),
Kenichi MIURA(~ Mar.)

fellowship
GANBOLD Khongorzul(Oct. ~),

Enrolled dentist
Yui SEKIDO(~ Mar.), Mana KATAOKA(~ Mar.)

(1) Outline

The Department of Pediatric Dentistry was founded in 1955, as the first in Japan. Pediatric dentistry is a subject of clinical dentistry that deal with education and research of not only developmental oral health sciences but also

prevention and treatment methods of the diseases which disturb oro-facial growth and development of children.

(2) Research

Research Subjects

- 1) Physiological and biological studies on the stomatognathic function of children
- 2) Studies on the development and developmental disturbance of the teeth
- 3) Studies on the growth and development of the maxillofacial cranium and the dentition
- 4) Development of new Endodontics and Traumatology for deciduous and immature permanent teeth
- 5) Basic research on clinical pediatric dentistry

(3) Education

Lecture subjects

Pediatric dentistry, Oral pediatrics

(4) Lectures & Courses

The main objective of pediatric dentistry in this graduate course is to provide students an opportunity to study the theory and the method for the guidance of the oro-facial growth and development and for the diagnosis, prevention and treatment of diseases and malfunctions which disturb the oro-facial growth and development during the period of childhood.

Oral pediatrics is a subject of clinical dentistry that deal with education and research of not only maintenance and promotion of the oral health for growing children but also prevention and treatment methods of diseases and malfunctions which disturb oral health of growing children. The main objective of oral pediatrics in this graduate course is to provide students an opportunity to understand that a child is a living body with mental, physical, and physiological characteristics which are different from those of adults and to study the pathogenesis, prevention, and treatment of the particular oral diseases in childhood. Students are also taught the theory and the method of ongoing health care that is necessary for maintaining and promoting oral health from infant to adult. In addition, they are taught the clinical significance and importance of the behavioral management of child patients and the necessity and importance of understanding and cooperation of the parents to it.

(5) Clinical Services & Other Works

The pediatric dentistry clinic in the department of oro-facial development and function provides the comprehensive dental treatment for a child while growing.

(6) Clinical Performances

The examination, diagnosis, and treatment of the oral diseases and the oral abnormalities are performed in the clinic. In addition, health guidance, preventive measures, and the long-term oral health management by the periodical checking system are carried out, in order to keep and promote oral health from infant to adult.

(7) Publications

[Original Articles]

1. Kazuhiro Kohata, Soichiro Itoh, Naohiro Horiuchi, Taro Yoshioka, Kimihiro Yamashita. Influences of osteoarthritis and osteoporosis on the electrical properties of human bones as in vivo electrets produced due to Wolff's law *Bio-Medical Materials and Engineering*. 2017.01; 28(1); 65-74
2. Wada K, Kanazawa H, Kudo M, Kindaichi J, Miyashin M . Management of developmental enamel defects in the primary dentition. *Journal of Oral Science*. 2017.01; 59(3); 457-460

3. Oishi A. Intentional replantation with retrograde root canal filling for transverse root fracture accompanied by periodontal-endodontic disease in an immature incisor: a case report and 4 years of follow-up. *Journal of Clinical Pediatric Dentistry*. 2017.05; 41(3); 187-192
4. Nakamura K, Oishi A, Uehara T, Wada K, Miyashin M. Healing after experimental luxation and intra-alveolar root fracture in immature rat teeth. *Pediatric Dental Journal*. 2017.09; 27(3); 128-136
5. Hirunwidchayarat W, Furusawa E, Kang S, Ohno T, Takeuchi S, Rungsiyanont S, Azuma M. Site-specific regulation of oral mucosa-recruiting CD8⁺ T cells in a mouse contact allergy model. *Biochem Biophys Res Commun*. 2017.09; 490(4); 1294-1300
6. Ganbold K, Kakino S, Ikeda H, Miyashin M. Human pulpal blood flow in different root formation stages measured with Transmitted-light plethysmography. *Archives of Oral Biology*. 2017.11; 83; 327-333
7. Yuji Sugawara, Kohsuke Imai, Ayako Kashimada, Kengo Moriyama, Shimpei Baba, Ryuta Nishikomori, Mizuho Motegi, Yasuo Takeuchi, Tomohiro Morio. Autoinflammatory phenotypes in Aicardi-Goutières syndrome with interferon upregulation and serological autoimmune features *J. Allergy Clin. Immunol*. 2017.11;

[Books etc]

1. Miiyashin M. Handbook of Dental trauma in Children . Genso-sya , 2017.12 (ISBN : 978-4-86209-066-9 C2047)

[Conference Activities & Talks]

1. Koyama T, Kakino S, Matsuura Y. Photoacoustic Imaging of Hidden Dental Caries by Using a Fiber-Based Probing System. Biomedical Imaging and Optical Sensing Conference (BISC) 2017.04.19 Yokohama
2. Uehara T, Nagahiro S, Uehara M, Kubota E, Furusawa E, Miyashin M. Findings from clinical reports of pulpotomies in primary teeth-a literature review. 2017.05.25 Kitakyusyu
3. Iwashita T, Suzuki T, Ichinose K, Akiyama K, Sekiya T, Miyashin M, Takei K.. Questionnaire of feeding behavior of children at nursery school in Yamanashi (3)Factor Analysis. The 55Th Conference of Japanese Society of Pediatric Dentistry 2017.05.25 Kitakyusyu
4. Koyama T, Kakino S, Matsuura Y. Ex-vivo photoacoustic imaging of hidden dental caries. 2017.09.25 Tokyo
5. Iwashita T, Suzuki T, Ichinose K, Akiyama K, Sekiya T, Miyashin M, Takei K. Questionnaire of feeding behavior of children at nursery school in Yamanashi (4)Qualitative Research with SCAT. The 32nd Japanese Society of Pediatric Dentistry, Kanto Branch 2017.10.01 Matsudo
6. Kakino S, Ganbold K, Uehara T, Inoue A, Ikeda H, Jayawardena A, Miyashin M. Pulpal circulation measurement of the luxated young permanent teeth with abnormal root formation using TLP. 8th Conference of Asian International Association of Dental Traumatology 2017.11.17 Bangkok, Thailand
7. Miyashin M. Intentional tooth replantation for traumatized teeth in children. The 8Th Conference of Asian International Association of Dental Traumatology 2017.11.18 Bangkok, Thailand
8. Ijbara M, Wada K, Miyashin M. Enamel Microcracks Induced by Simulated Occlusal Wear in Mature, Immature and Deciduous Teeth. the 65th Annual Meeting of JADR 2017.11.19 Tokyo

[Works]

1. Michiyo Miyashin : Natural root canal model of children, Educational Materials, 2013.04 - Now

[Others]

1. 2017.04
<http://www.sakaiku.jp/column/health/2017/012964.html>

Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zuisei KANNO, Jun HOSOMICHI
Assistant Professor	Kazuo SHIMAZAKI, Ippei WATARI, Satoshi KOKAI (-Mar), Ikuo YONEMITSU Takayoshi ISHIDA, Risa USUMI (Dec-)
Project Assistant Professor	Risa USUMI (Sep-Nov)
Project Assistant Professor (Institute of Global Affairs Administrative Division)	Yuji ISHIDA (-Mar)
Dental Resident	Yuji ISHIDA (Apr-), Naoki SHIBUTANI (-Mar), Yasuhiro SHIMIZU (-Mar) Risa USUMI(-Aug), Chiho KATO, Hidemasa OKIHARA, Yuhei IKEDA Syunsuke UESUGI (Apr-)
Graduate Students	Yasunori ABE (-Mar), Yukano FUKUSHIMA (-Mar), Yuki KASAHARA (-Mar) Karin Harumi UCHIMA KOECKLIN (-Mar), Jin-Gyu AN, Takuya OGAWA, Iku SHIBATA Akemi KANAGUCHI (-Sep), Velusamy PAVETHY NATH (-Sep), Eri SAITO Kayo KIMURA, Yuta NAKAI, Kenzo WATAKABE Erusu NIN, Huan TANG, Roody BEAUBOEUF Edward CHO, Masamu INOUE, Erika OZAWA Moe SATO, Kasumi HATANNO, Keiko FUKINO Shin-Sheng Yang, Lu ZHAO, Thi kim Uyen DONG Yuta UCHIKAWA, Akihiro KOYAMA, Kim Sun-min Phyo Thura Aung, Ryo KIMURA (Apr-), Shahriar Mohd Shams (Apr-), Haixin HONG (Apr-) Lekvijittada Kochakorn (Jun-), Anindya K Gunarso (Oct-)
Graduate School Research Students	Hiroko OMORI, Toshihiro IMAMURA, Minami MIYASAKA (-Mar) Mutsumi MIYAZAKI (-Mar), Asuka OKITO (-Mar) Ayako KIRII(-Mar), Syusuke UESUGI (-Mar), Shuji OISHI, Soma KITA Yoichiro KUMA, Tomomi SAKAGUCHI, Hiroyuki YAMAGUCHI Mio MAKIGUCHI, Tomonari MATSUMURA, Junpei SUZUKI Kyohei YAMADA, Misako KOKETSU, Takahiro SHIMAMINE Katsuhiko SUZUKI, Mirei HAGIWARA, Chiho SATOKAWA Asuka MANABE, Shuntaro SAWAZAKI, Masako KAWADA Takashi TANAKA, Shunya HORIUCHI, Shams SHAHRIAR MOHD (-Mar) Haixin HONG (-Mar), Shuko ARAI (Apr-), Kai LI (Oct-)
Visiting Research Scholars	Velusamy PAVETHY NATH (Oct-)

(1) Outline

Orthodontic Science is one of the dental sciences which propose to control the craniofacial growth and development in equilibrium with the whole body, and also deals with the prevention and/or treatment of malocclusion and related disorders, by which the alteration of maxillofacial function with aging could be kept to the most suitable condition.

(2) Research

Research Subjects

- 1) Biomechanical study of occlusion
- 2) Studies on biological response and functional adaptation followed by orthodontic and occlusal stimulation
- 3) Clinical application of autotransplantation in orthodontic treatment
- 4) Studies on interrelation between malocclusion and temporomandibular joint
- 5) Studies on occlusion and age-related changes in cranio-maxillofacial morphology and function
- 6) Studies on interrelation between cranio-maxillofacial complex and whole body
- 7) Development of mechanics and materials for orthodontic treatment
- 8) Pathophysiological studies on sleep and breathing disorders
- 9) Studies on interrelation between breathing and body function

(3) Education

Subjects of Education:

Orthodontic Science, Pathophysiology for Malocclusion, Biology for Functional Adaptation

(4) Lectures & Courses

Orthodontic Science

- 1) To explain the unhealthy physiological condition of malocclusion and deepen the scientific basis for orthodontic treatment.
- 2) To understand the biological reaction and adaptation of occlusal tissues to mechanical stresses such as occlusal force or orthodontic force, and also the changes with aging.
- 3) To explain the art for controlling the morphologic and functional problems of occlusion in orthodontic treatment, from the view points of biomaterials and biomechanics.
- 4) To enlighten the social dentistry for the needs and demands of orthodontic treatment.

Pathophysiology for Malocclusion

To understand the alteration of occlusal function and morphology with aging, and to explain the pathological condition of malocclusion from the viewpoint of physiology, biomechanics, biology and sociology.

Biology for Functional Adaptation

To understand the procedure of biological reaction and adaptation of occlusal system to the orthodontic stimuli, including the influence of aging, and to provide the control of the surroundings of the occlusal system.

(5) Clinical Services & Other Works

Clinical Services

In the field of practical orthodontic, with the development of materials and treatment techniques, we have taken initiatives in two big turning points at all time. Namely, one is the Direct Bonding System which has made it possible to attach brackets directly to the teeth surface without orthodontic metal bands. Another is the development of Super-Elastic Ti-Ni Alloy Wire, and following Improved Super-Elastic Ti-Ni Alloy Wire. With these new wires, we have provided an epoch-making orthodontic technique, where teeth could be moved more efficiently and safely with light continuous forces, and in consequences, the limits for teeth movement are expanded and the treatment outcomes are also improved. On the other hand, in order to determine the scientific basis for the needs of orthodontic treatment, we are engaging in the study of pathophysiology of malocclusion, and these research results are getting feedback to the orthodontic practices as soon as possible to stimulate the development of new treatment protocols.

Students in the graduate course not only pursue their scientific researches but also being educated in accordance with our curriculum for the post-graduated clinical program. In this program, we aim to bring up the leading persons of next generation who have highly specialized knowledge and skills of orthodontics as well as prominent minds of clinical researches.

(6) Clinical Performances

Highlights of Clinical Services

- 1) Orthodontic treatments by using Improved Super-Elastic Ti-Ni Alloy Wire
- 2) Comprehensive Orthodontic Treatments

With the cooperation of related field, we provide comprehensive treatments for those patients with cleft lips and palates and other congenital anomalies, jaw deformities, maxillofacial functional disorders, periodontal diseases, impacted teeth, autotransplantation combined cases, and usages of implant anchorages.

(7) Publications

[Original Articles]

1. Uchima Koecklin KH, Hiranuma M, Kato C, Funaki Y, Kataguchi T, Yabushita T, Kokai S, Ono T. Unilateral nasal obstruction during later growth periods affects craniofacial muscles in rats. *Front Physiol.* 2017.01; 7(669); 1-10
2. Abe Y, Kato C, Uchima Koecklin KH, Okihara H, Ishida T, Fujita K, Yabushita T, Kokai S, Ono T. Unilateral nasal obstruction affects motor representation development within the face primary motor cortex in growing rats. *J Appl Physiol.* 2017.01; 122(6); 1494-1503
3. Hosomichi J, Kuma Y, Oishi S, Nagai H, Maeda H, Usumi-Fujita R, Shimizu Y, Kaneko S, Shitano C, Suzuki J, Yoshida K, Ono T. Intermittent hypoxia causes mandibular growth retardation and macroglossia in growing rats. *Am J Orthod Dentofacial Orthop.* 2017.02; 151(2); 363-371
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6. Yamaguchi H, Ishida Y, Hosomichi J, Suzuki J, Usumi-Fujita R, Shimizu Y, Kaneko S, Ono T. A new approach to transfect NF- κ B decoy oligodeoxynucleotides into the periodontal tissue using the ultrasound-microbubble method. *Int J Oral Sci.* 2017.06; 9(2); 80-86
7. Manabe A, Ishida T, Yoon HS, Yang SS, Kanda E, Ono T. Differential changes in the adenoids and tonsils in Japanese children and teenagers: A cross-sectional study *Sci Rep.* 2017.08; 29(1); 9734
8. Fukushima-Nakayama Y, Ono T, Hayashi M, Inoue M, Wake H, Ono T, Nakashima T. Reduced Mastication Impairs Memory Function *J Dent Res.* 2017.08; 96(9); 1058-1066
9. Uesugi S, Kokai S, Kanno Z, Ono T. Prognosis of primary and secondary insertions of orthodontic miniscrews: What we have learned from 500 implants *Am J Orthod Dentofacial Orthop.* 2017.08; 152(2); 224-231
10. Matsumura T, Ishida Y, Kawabe A, Ono T. Quantitative analysis of the relationship between maxillary incisors and the incisive canal by cone-beam computed tomography in an adult Japanese population *Prog Orthod.* 2017.08; 18(1); 24
11. Ishida Y, Ono T. Nonsurgical treatment of an adult with a skeletal Class II gummy smile using zygomatic temporary anchorage devices and improved superelastic nickel-titanium alloy wires *Am J Orthod Dentofacial Orthop.* 2017.11; 152(5); 693-705
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15. Suzuki K, Kokai S, Uesugi S, Nishiyama A, Ono T. Evaluation of the laterality of the tissue oxygen saturation of masticatory muscles in subjects with facial asymmetry *Orthodontic Waves.* 2017.12; 76(4); 232-237

[Conference Activities & Talks]

1. Hosomichi J, Suzuki T, Shibutani N, Hatano K, Yamaguchi H, Kuma K, Kaneko S, Ono T. . Distribution of Ki67 and LGR5-positive Periodontal Cells During Tooth Movement. 2017 IADR/AADR/CADR General Session & Exhibition 2017.03.22 San Francisco, CA, USA
2. Kenzo Watakabe, Ikuo Yonemitsu, Yuhei Ikeda, Mutsumi Miyazaki, Takashi Ono. Nasal obstruction in growing rats induces morphological and histological changes in the mandible. The 39 th Annual Scientific Conference on Dental Research 2017.03.31 Ho Chi Minh city, Vietnam
3. Ren E, Watari I, Hsu J, Mizumachi-Kubono M, Inoue K, Watabe T, Ono T. Unilateral nasal obstruction effects gustatory function in rats. The 39 th Annual Scientific Conference on Dental Research 2017.03.31 Ho Chi Minh city, Vietnam
4. Yamaguchi H, Ishida Y, Hosomichi J, Suzuki J, Ono T. Transfection of NF- κ B decoy into the rodent periodontium using ultrasound-microbubble technique prevents the progression of the periodontitis. The 93rd congress of the European Orthodontic Society 2017.06.05 Montreux, Switzerland
5. Suzuki K, Kokai S, Uesugi S, Nishiyama A, Ono T. Evaluation of the laterality of the tissue oxygen saturation of masticatory muscles in subjects with facial asymmetry. The 93rd congress of the European Orthodontic Society 2017.06.05 Montreux, Switzerland
6. Ogawa T, Okihara H, Kokai S, Michikawa M, Ono T. Nasal obstruction induces memory and learning impairment and decreases the number of hippocampal neurons in growing mice. The 93rd congress of the European Orthodontic Society 2017.06.05 Montreux, Switzerland
7. Fujita K, Omura S, Imai H, Honda K, Yamashita Y, Takasu Y, Murata S, Iwai T, Shibutani N, Yonemitsu I, Shimazaki K, Ono T, Tohnai I. Making of splint in CAD/CAM method -difference from indirect method using articulator-. 27th Annual Meeting of the Japanese Society for Jaw Deformities 2017.06.15 Tokyo
8. Imai H, Omura S, Fujita K, Honda K, Yamashita Y, Takasu Y, Iwai T, Shibutani N, Yonemitsu I, Shimazaki K, Tohnai I, Ono T. Accuracy of maxillary repositioning by using CAD/CAM method and SLM technique. 27th Annual Meeting of the Japanese Society for Jaw Deformities 2017.06.15 Tokyo
9. Hoda K, Omura S, Fujita K, Imai H, Yamashita Y, Takasu Y, Murata S, Iwai T, Shibutani N, Yonemitsu I, Shimazaki K, Ono T, Tohnai I. Two-jaw surgery with CAD/CAM method -A significance of SLM technique-. 27th Annual Meeting of the Japanese Society for Jaw Deformities 2017.06.15 Tokyo
10. Watari I, Yonemitsu I, Kirii A, Koketsu M, Hagiwara M, Ozawa E, Kanaguchi-Arita A, Ono T. Pharyngeal airway changes after lower teeth distal movement using the implant anchorage. 9th World Implant Orthodontic Conference 2017.07.02 Kobe
11. Ohmori H, Midorikawa Y, Lai WJ, Kannno Z, Takemura H, Ono T. Six-axis orthodontic force evaluation of cantilever: comparison between super-elastic Ti-Ni wire and stainless steel wire. 2017.07.12 Tokyo
12. Torikai K, Kaida E, Shimazaki K, Kijima T, Satake T. Will wide subperiosteal dissection in primary cleft lip/palate surgery result in maxillary growth impairment?. 53rd French Oral&Maxillofacial society congress 2017.10.04 Marseilles, France
13. Kijima K, Torikai K, Kaida E, Shimazaki K, Sano T, Satake T. “Pullforward” method as a secondary palatoplasty for bilateral cleft lip and palate. 53rd French Oral&Maxillofacial society congress 2017.10.04 Marseilles, France

14. Hosomichi J, Maeda H, Yoichiro Kuma, Oishi S, Yoshida KI, Ono T. Differential effects of intermittent hypoxia on phenotypic and metabolic features of airway muscles in weaning- and adolescent-aged rats. World Sleep 2017 2017.10.11 Prague, Czech Republic
15. Hosomichi J, Suzuki T, Shibutani N, Hatano K, Yamaguchi H, Kuma Y, Kaneko S, Kasahara Y, Oishi S, Usumi-Fujita R, Shimizu Y, Ono T. Altered localization of Ki67 and LGR5-positive periodontal cells during tooth movement. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
16. Manabe A, Ishida T, Ono T. Differential longitudinal changes in the ratio of adenoids/tonsils to the airway in Japanese children. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
17. Saito E, Watati I, Kubono M, Kyo S, Ono T. Reduced and recovered mechanical stress on the periodontium influence the AQP5 localization in salivary gland. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
18. Ikeda Y, Ishida Y, Imamura T, Oishi S, Kita S, Kuma T, Matsumura T, Okuzawa M, Ono T. Three-dimensional CBCT analyses of the anterior tooth roots in the open bite patients. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
19. Ishida T, Manabe A, Shin -Sheng Y, Abe Y, Watakabe K, Ono T. A patient with OSA treated with Le Fort I osteotomy. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
20. Matsumoto Y, Shimizu Y, Inoue M, Ozawa E, Sato M, Hatano K, Fukino K, Okuzawa K, Sawazaki S, Kaku KEO P, Cho E, Cho R, Yan S, Ono T. Effectiveness of super-elastic Ni-Ti alloy wire in detecting and relieving teeth mobility and premature contacts. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
21. Ogawa T, Okihara H, Kokai S, Abe Y, Uchima Koecklin KH, Makiguchi M, Kato C, Yabushita T, Michikawa M, Ono T. Nasal obstruction during growth period affected Memory and learning and change of hippocampal tissue. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
22. Sakai K, Kato C, Ono T. A deep overbite case treated with dental implant restoration for the missing lower incisor. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
23. Ozawa E, Ozawa T, Omori H, Shimazaki K, Kurabayashi T, Ono T. The influence of orthodontic appliance-derived artifacts on MR angiography. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
24. Wakasugi E, Watari I, Inoue K, Kubono M, Ono T. GLP-1 related gene analysis in mouse osteoblastic MC3T3-E1 cells using next generation sequencer. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
25. Ishida Y, Imamura T, Matsumura T, Ikeda Y, Oishi S, Kuma T, Okuzawa M, Ono T. Three-dimensional CBCT analyses of the mandibular dentition in the alveolar process. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
26. Nin, E, Watari I, Kyo S, Inoue K, Kubono M, Watabe T, Ono T. Unilateral nasal obstruction effects the gustatory receptors in rats. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
27. Ozawa E, Ozawa T, Omori H, Shimazaki K, Kurabayashi T, Ono T. The influence of orthodontic appliance-derived artifacts on MR angiography. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
28. Manabe A, Ishida T, Ono T. Changes in the proportions of adenoid and tonsil size to the upper airway area in Japanese individuals: a cross-sectional study. The 65th Annual Meeting of Japanese Association for Dental Research 2017.11.18 Tokyo

[Awards & Honors]

1. Ozawa E. The 76th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2017.10
2. Yamada K. The Japanese Orthodontic Society, Best Paper Award, Japanese Orthodontic Society, 2017.10
3. Ishida T. The 76th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2017.10
4. Ozawa E. The 76th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2017.10
5. Ogawa T. The 76th Annual Meeting of the Japanese Orthodontic Society, Excellent Exhibition Award, Japanese Orthodontic Society, 2017.10

Cariology and Operative Dentistry

Professor: Junji Tagami

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Toru Nikaido, Masatoshi Nakajima

Assistant Professor: Takako Yoshikawa, Yasushi Shimada(January), Go Inoue,

Keiichi Hosaka, Tomohiro Takagaki, Rena Takahashi, Naoko Mastui(April)

Hospital Staff: Oto Aramaki(March), Naoko Matsui(March), Ayaka Chiba(March),

Takaaki Sato(September), Kento Sato(June), Yukinori Kano(April),

Juri Hayashi(April September), Takashi Hatayama(April September),

Nami Takashino(April September), Yusuke Kuno(September),

Shigeki Uchinuma(September), Akifumi Takahashi(October), Shin Rozan(October), Yuka Tsuda(November)

Specially Appointed Assistant Professor: Matin N.H.M. Khairul

JSPS Research Fellowship Noriko Hiraishi

Technical Assistant: Yuan Zhou(June)

Staff Assistant: Shiori Ogi, Takako Nakagawa

Graduate Student:

Chihiro Matsuura (~ March) , Yukinori Kano (~ March) , Yuki Naruse (~ March) ,

Juri Hayashi (~ March) , Miho Sugiura (~ March) , Yuta Sumitani (~ March) ,

Atsuko Tagami (~ March) , Keiki Nakamura (~ March) , Yukari Noda (~ March) ,

Takashi Hatayama (~ March) , Yuka Tsuda (~ March) , Yuan Zhou (~ March) ,

Nami Takashino (~ March) , Ayaka Kusanagi Sato (~ March) , Keita Taguchi (~ March) ,

Jorge Espigares(September),

Mari Okada, Junji Atomura, Akifumi Takahashi, Ayako Nakamoto, Tomoko Tabata,

Daisuke Araoka, Takuya Nakata, Thwe Zin Ei, LUONG DAO Minh Nguyet,

Amr Abdelaziz Aly Aly SAAD, SEGARRA Michelle Sunico, Wa Than Lin,

ALQARNI DHAIFALLAH ABDULLAH G, ALGHAMDI ALI GUZAN J,

KHINE Win Zan, KHIN Yupar Kyaw,

Sae Akehashi, Nao Takahashi, Yuna Kanamori, Yukina Ochiai, Kurumi Ide,

Yusuke Kuno, Yuki Ito, Shigeki Uchinuma, Daiki Nagano, Yusuke Kakiuchi,

Akira Nakane, RIMA ZAKZOUK, HALABI SOMAYAH ABDULRAHMAN A,

RUMMANI GHASSAN MAHMOOD S, ALQAHTANI ALI AWAD M,

ARAVETI SANDEEP KUMAR, HOSEA LAL RIN MUANA, SAI KHAM LYANN,

AYE KO KO, Meiken Hayashi, Shou Obayashi, Saori Muta, Kazuhide Yonekura,

Satomi Matsunaga, Shin Rozan, HESHAM HASSAN OSMAN MOHAMMED,

Yukiko Tanno, AHMED MOHAMED ABDELRAHMAN ABDOU,

MAHMOUD MOHAMED SAYED AHMED, SOE YU PAING, SWE ZIN AUNG,

QUTAIBA Y A A ALSANDI, SAN SAN MAY PHYO AUNG,

ALMASABI WALEED ABDULQADER M,

WIJETUNGA CHAMARI LASINDRA , ERICK LUZ MADRIGAL (April),

Motoi Takahashi(April), Sakiko Tsuchiya(April), Kim Seunggun(April),

Kyoko Ishikawa(April), Toyooki Kobayashi(April), Miyuki Shimizu(April),

Mayu Hasegawa(April), Shun Kobayashi(April), Nanako Ueda(April),

Misa Kashiwa(April), Saki Uchiyama(April), Yosuke Minato(April),

Yuta Baba(April), LEILA NASIRY KHANLAR (April),

VICHEVA MARTINA GEORGIEVA(April), Citra Kusumasari (October),

Min Khant Ko Ko(October), Pa Pa Kay Khine (October)

Research Student: Shinji Ogura, Mineo Kijima,

VICHEVA MARTINA GEORGIEVA (March), ERICK LUZ MADRIGAL(March),

Nooruldeen Ali Saeed (April)

(1) Outline

TMDU possesses the longest history as a national dental university in Japan. We have contributed to the progress of science and education through presenting a number of world leading graduates in the field of den-

tistry. Many of their achievements are now recognized as global standards in the field of dental research and clinical practice.

At Cariology and Operative Dentistry, we believe that the ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

Cariology and Operative Dentistry is a home to the late professor Takao Fusayama, who developed the “Caries Detector” for removal of the caries, and promoted “Total-etch technique” and other restorative techniques using adhesive resin composite for the minimally invasive caries treatment.

Our group, consisting of members of the faculty, staff and graduate students, is among the international leaders in the ongoing dental research. I would hereby like to extend an invitation to those fellows and prospect graduate students interested in perusing high-level research and gaining an insight into modern concepts to join our diverse international team of scientists.

(2) Research

1) Evaluation of dentin bonding systems

Adhesion of bonding materials to enamel, dentin and cementum of tooth are evaluated using methods such as the microshear and the microtensile bond strength tests. Factors affecting adhesion such as the region and caries state of tooth substrate, light-curing irradiation, release of fluoride from material, tooth preparation methods, root canal treatment of the tooth, etc. have been investigated. We have also focused on the difference between various adhesives system in terms of their composition, performance and bonding durability.

2) Super Enamel and Super Dentin

Using various electron microscopy techniques, we have demonstrated that resistance of enamel and dentin to acid attack could be increased in an acid-base resistant zone which was formed following the application of some self-etching dental adhesives. We proposed that the diffusion of such acidic monomers beyond the classic hybrid layer (interfacial zone) and their ion-exchange interactions with the available hydroxyapatite could result in formation of stable organic-inorganic complexes, and that the structures should be termed “super tooth”, which includes the reinforced enamel and dentin.

3) Development of OCT for establishing its clinical application

Optical coherent tomography (OCT) is a noninvasive, cross-sectional imaging system that can visualize the internal structures nondestructively and without exposure to X-ray or ionizing radiation. Our research has aimed to further develop OCT and introduce a dental OCT system that can be used to diagnose dental defects and diseases such as tooth cracking and caries.

4) Non-destructive test of adhesive restorations

We are working to establish a method for non-destructive detection of gap and secondary caries beneath composite restorations using optical coherence tomography (OCT).

5) Evaluation of polymerization behavior of light-cured resin composites

Aim to establish clinical techniques to compensate polymerization shrinkage stress of resin composite, we evaluated effect of adhesives, resin composite composition, light curing methods and cavity configuration factor(C-factor) on polymerization shrinkage stress using micro-focus X-ray computed tomography (micro-CT) and 3D visualization method.

6) Resin coating technique

Resin coating using a bonding agent and flowable composite benefits the adaptation of indirect restorations to dentin surface which is a key interface within a restoration. We have proposed that this resin coating technique should be technique of choice for placement of indirect restorations.

7) Research on optical properties of the dental structure

As a part of the OCT development project, we work on characterization of the basic optical properties such as attenuation coefficient and refractive index of dentin and enamel, and their changes following demineralization and remineralization.

8) Research on direct core build up materials

Adhesive performance to the root canal dentin by resin core build up systems has been evaluated. These materials can be used in combination with fiber posts.

9) Study on dental erosion

Erosive loss of enamel due to consumption of acidic beverages and some drugs has been evaluated using 3D focus-variation microscopy as well as profilometry.

10) Caries risk assessment

We have investigated caries risk based on the measurement of saliva buffering capacity in samples collected from patients. We have also probed the association between the pH of lesion surface and caries activity.

11) Adhesion of cariogenic bacteria to dentin surface

We have developed a model to experimentally evaluate factors affecting the ability of cariogenic bacteria such as *S.mutans* to attach to the tooth surface in the initial phase of biofilm formation.

12) Biocompatibility of resin-based dental adhesives

Immunohistochemical studies have been performed to evaluate the effects of various adhesive materials on dental pulp tissue.

13) The potential of fluoride- and/or Calcium containing materials on caries prevention

Inhibitory effects of CPP-ACP paste and fluoride on the enamel and dentin demineralization have been evaluated by the micro-focus X-ray computed tomography (micro-CT) non-destructively. We have also established a standard methodology for assessment of lesion parameters such as depth and mineral loss for micro-CT.

14) Evaluation of caries removal methods

We have evaluated the effect of caries removal method by the conventional rotary cutting instruments in comparison with new caries removal methods such as chemical removal agents, laser irradiation and abrasion on the adhesion performance and restoration success.

15) Development and evaluation of aesthetic dental materials

We have worked on optical properties and color match of the composite resins, in addition to clinical applications of tooth whitening materials .

16) Clinical research

We have created a protocol to evaluate the long-term and short-term performance of restorative materials in the patients who were admitted to the operative dentistry clinics at TMDU Dental Hospital.

(3) Education

Cariology and Operative Dentistry section offers a four-year graduate program. First-year graduate students attend lectures and seminars given in the graduate school and are expected to gain an understanding of the fundamentals about methodology and the knowledge necessary for their research. The contents of the classes given in our section include topics related to cariology and operative dentistry: caries diagnosis, biocompatibility, caries treatment and restoration, prevention and control, dental materials, new instruments and equipment. In keeping with the internationally orientated philosophy of this section, lectures are conducted in English and are open to all foreign students. First-year graduate students also undergo clinical training the procedures of modern adhesive restorations. Laboratory work, which commences in the first year, is performed under the supervision of our faculty staff. During the four-year program, several papers are required to be presented in domestic and / or international conferences and submitted to journals. The minimum requirements are completing the prescribed courses, a supervised research project and a dissertation for the degree published in a top international journal.

(4) Lectures & Courses

The ultimate goal of the oral health care programs is to provide well-being of the patients. In order to achieve this goal, besides the clinical training that we offer to the licensed graduate students, high-caliber research projects are being carried out aimed at developing, enhancing and evaluation of the materials and techniques in dentistry; particularly for adhesives, caries prevention, diagnosis and treatment, and oral health maintenance.

(5) Clinical Services & Other Works

Full-time faculty see patients in Operative Dentistry and Endodontics, and provide restoration of teeth with fillings for dental cavities, trauma and tooth wear, and root canal treatments. The faculty members supervise both pre-and postdoctoral students in the clinic.

(6) Clinical Performances

Our Operative Dentistry clinic provide restoration of teeth with fillings for dental cavities, trauma and tooth wear under Minimal intervention concept. The clinical services are based on accumulated scientific researches.

(7) Publications**[Original Articles]**

1. Wataru Komada, Tasuku Inagaki, Yoji Ueda, Satoshi Omori, Keiichi Hosaka, Junji Tagami, Hiroyuki Miura. Influence of water immersion on the mechanical properties of fiber posts. *J Prosthodont Res.* 2017.01; 61(1); 73-80
2. Ayaka Chiba, Takashi Hatayama, Kimisuke Kainose, Masatoshi Nakajima, David H Pashley, Noriyuki Wakabayashi, Junji Tagami. The influence of elastic moduli of core materials on shear stress distributions at the adhesive interface in resin built-up teeth. *Dent Mater J.* 2017.01; 36(1); 95-102
3. Atsuko Tagami, Rena Takahashi, Toru Nikaido, Junji Tagami. The effect of curing conditions on the dentin bond strength of two dual-cure resin cements. *J Prosthodont Res.* 2017.01;
4. Masami Arai, Tomohiro Takagaki, Akifumi Takahashi, Junji Tagami. The role of functional phosphoric acid ester monomers in the surface treatment of yttria-stabilized tetragonal zirconia polycrystals. *Dent Mater J.* 2017.01;
5. Noriko Hiraishi, Takahiro Maruno, Naoya Tochio, Ryohei Sono, Masayuki Otsuki, Tsutomu Takatsuka, Junji Tagami, Yuji Kobayashi. Hesperidin interaction to collagen detected by physico-chemical techniques. *Dent Mater.* 2017.01; 33(1); 33-42
6. Zhengdi He, Lingling Chen, Yasushi Shimada, Junji Tagami, Shuangchen Ruan. Evaluation of sub-surface penetration and bonding durability of self-etching primer systems to Er:YAG laser treated cervical dentin. *Dent Mater J.* 2017.01;
7. Yuan Zhou, Khairul Matin, Yasushi Shimada, Yasunori Sumi, Junji Tagami. Evaluation of resin infiltration on demineralized root surface: An in vitro study. *Dent Mater J.* 2017.01;
8. Wa Than Lin, Yuichi Kitasako, Syozi Nakashima, Junji Tagami. A comparative study of the susceptibility of cut and uncut enamel to erosive demineralization. *Dent Mater J.* 2017.01; 36(1); 48-53
9. Yuichi Kitasako, Y Sasaki, T Takagaki, A Sadr, J Tagami. Multifactorial logistic regression analysis of factors associated with the incidence of erosive tooth wear among adults at different ages in Tokyo. *Clin Oral Investig.* 2017.02;
10. Kento Sato, Keiichi Hosaka, Masahiro Takahashi, Masaomi Ikeda, Fucong Tian, Wataru Komada, Masatoshi Nakajima, Richard Foxton, Yoshihiro Nishitani, David H Pashley, Junji Tagami. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. *J Adhes Dent.* 2017.02; 19(1); 31-37
11. Taweesak Prasansuttiporn, Ornnicha Thanatvarakorn, Junji Tagami, Richard M Foxton, Masatoshi Nakajima. Bonding Durability of a Self-etch Adhesive to Normal Versus Smear-layer Deproteinized Dentin: Effect of a Reducing Agent and Plant-extract Antioxidant. *J Adhes Dent.* 2017.03; 19(3); 253-258
12. M S Segarra, Y Shimada, A Sadr, Y Sumi, J Tagami. Three-Dimensional Analysis of Enamel Crack Behavior Using Optical Coherence Tomography. *J. Dent. Res.* 2017.03; 96(3); 308-314
13. Keiki Nakamura, Hidenori Hamba, Syozi Nakashima, Alireza Sadr, Toru Nikaido, Masakazu Oikawa, Motohiro Uo, Junji Tagami. Effects of experimental pastes containing surface pre-reacted glass ionomer fillers on inhibition of enamel demineralization. *Dent Mater J.* 2017.03;
14. Ritsuko Mashiko, Go Inoue, Toru Nikaido, Junji Tagami. Morphological evaluation of artificial caries-affected dentin after applying FCP-COMPLEX. *J Oral Sci.* 2017.05;
15. Nigel B Pitts, Domenick T Zero, Phil D Marsh, Kim Ekstrand, Jane A Weintraub, Francisco Ramos-Gomez, Junji Tagami, Svante Twetman, Georgios Tsakos, Amid Ismail. Dental caries. *Nat Rev Dis Primers.* 2017.05; 3; 17030

16. Zhengdi He, Lingling Chen, Xuejuan Hu, Yasushi Shimada, Masayuki Otsuki, Junji Tagami, Shuangchen Ruan. Mechanical properties and molecular structure analysis of subsurface dentin after Er:YAG laser irradiation. *J Mech Behav Biomed Mater.* 2017.06; 74; 274-282
17. Tomoko Tabata, Yasushi Shimada, Alireza Sadr, Junji Tagami, Yasunori Sumi. Assessment of enamel cracks at adhesive cavosurface margin using three-dimensional swept-source optical coherence tomography. *J Dent.* 2017.06; 61; 28-32
18. Yuichi Kitasako, Yoshiyuk Sasaki, Tomohiro Takagaki, Alireza Sadr, Junji Tagami. Erosive Tooth Wear Among Different Tooth Types and Surfaces in Japanese Adults 15 to 89 Years Old. *Oral Health and Preventive Dentistry.* 2017.07; 15(4); 357-364
19. Yukari Noda, Masatoshi Nakajima, Masahiro Takahashi, Teerapong Mamanee, Keiichi Hosaka, Tomohiro Takagaki, Masaomi Ikeda, Richard M Foxton, Junji Tagami. The effect of five kinds of surface treatment agents on the bond strength to various ceramics with thermocycle aging. *Dent Mater J.* 2017.07;
20. Renata Bacelar-Sá, Salvatore Sauro, Gabriel Abuna, Rafael Vitti, Toru Nikaido, Junji Tagami, Glaucia Maria Bovi Ambrosano, Marcelo Giannini. Adhesion Evaluation of Dentin Sealing, Micropermeability, and Bond Strength of Current HEMA-free Adhesives to Dentin. *J Adhes Dent.* 2017.08; 1-8
21. Mashiko R, Inoue G, Nikaido T, Tagami J. Morphological evaluation of artificial caries-affected dentin after applying FCP-COMPLEX *Journal of Oral Science.* 2017.09; 59(3); 343-350
22. Rena Takahashi, Erika Ota, Keika Hoshi, Toru Naito, Yoshihiro Toyoshima, Hidemichi Yuasa, Rintaro Mori, Eishu Nango . Fluoride supplementation (with tablets, drops, lozenges or chewing gum) in pregnant women for preventing dental caries in the primary teeth of their children *Cochrane Database of Systematic Reviews.* 2017.10;
23. Saad A, Inoue G, Nikaido T, Ikeda M, MF Burrow, Tagami J. Microtensile Bond Strength of Resin-Modified Glass Ionomer Cement to Sound and Artificial Caries-Affected Root Dentin With Different Conditioning Operative Dentistry. 2017.11; 42(6); 626-635
24. Ornnicha Thanatvarakorn, Taweesak Prasansuttiporn, Suppason Thittaweerat, Richard M Foxton, Shizuko Ichinose, Junji Tagami, Keiichi Hosaka, Masatoshi Nakajima. Smear layer-deproteinizing improves bonding of one-step self-etch adhesives to dentin. *Dent Mater.* 2017.12;

[Misc]

1. Junji Tagami. Editorial: The dawn of adhesive dentistry. *J Adhes Dent.* 2017.08; 19(2); 91

[Conference Activities & Talks]

1. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Uo M, Minakuchi S. Crystallographic analysis of alumina sandblasted highly translucent dental zirconia. 95th General Session and Exhibition of the IADR 2017.03 San Francisco
2. Noda S, Kawashima N, Hashimoto K, Aramaki O, Yamamoto M, Okiji T. Dense culture conditions induced human dental pulp stem cell differentiation. 95th General Session & Exhibition of the IADR 2017.03.22 San Francisco, CA
3. John Sorensen, Juri Hayashi, Carlota Suarez, Alireza Sadr. 3D Crack Detection and Quantification in Ceramic Restorations by OCT. 95th General Session & Exhibition of the IADR 2017.03.22
4. Alireza Sadr, Juri Hayashi, Yasushi Shimada, Junji Tagami. Effects of Fiber Reinforcement on Composite Adaptation in Deep Cavities. 95th General Session & Exhibition of the IADR 2017.03.22
5. Juri Hayashi, Alireza Sadr, Tomohiro Takagaki, Tomoko Numata, Yasushi Shimada, Junji Tagami, Yasunori Sumi. 3D assessment of Bulk-fill Composites Gap Formation and Polymerization Shrinkage. 95th General Session & Exhibition of the IADR 2017.03.22
6. Amr SAAD, Go Inoue, Junji Atomura, Toru Nikaido, Junji Tagami. μ TBS of RM-GIC on demineralized root dentin with several conditioners. 95th General session & exhibition of the IADR 2017.03.22

7. Nao Takahashi, Yasushi Shimada, Minh Nguyet Luong Dao, Yasunori Sumi, Junji Tagami. Fractographic analysis of dentin-composite interface after micro-tensile bond test. 2017 IADR general session and exhibition 2017.03.24 San Francisco
8. Noriko Hiraishi, Fumiaki Hayashi, Tomohiro Takagaki, Masayuki Otsuki, Junji Tagami. Solid-state NMR Investigation on the Mineral Structure in De/re-mineralized Dentin. 95th IADR General Session 2017 2017.03.25
9. T. Yoshikawa, A. Sadr. J. Tagami. . Dye Penetration Test and Micro-CT Observation of Composite/Cavity-Wall Adaptation.. 95th, IADR 2017.03.25 San Francisco
10. Ali Alghamdi, Tomohiro TAKAGAKI, Yuki NARUSE, Toru Nikaido, Masaomi Ikeda, Junji Tagami. Influence of Time Elapsed After Alumina-Blasting on a CAD/CAM Resin-Block. 95th IADR General Session 2017 2017.03.25
11. Akifumi Takahashi, Tomohiro Takagaki, Toru Nikaido, Masaomi Ikeda, Takahiro WADA, Motohiro Uo, Junji Tagami. Effect of Phosphoric Acid Cleaning for Saliva Contaminated Zirconia Ceramics. 95th IADR General Session 2017 2017.03.25
12. Tomohiro Takagaki, Fumiaki Hayashi, Rui Guan, Noriko Hiraishi, Toru Nikaido, Junji Tagami. Adsorption Behavior of Phosphoric Functional Monomers to Y-TZP Surface. 95th IADR General Session 2017 2017.03.25
13. Sai Lyann, Tomohiro Takagaki, Toru Nikaido, Takahiro Wada, Motohiro Uo, Masaomi Ikeda, Junji Tagami.. Efficacy of Various Surface Treatments on Saliva Contaminated Lithium-disilicate Ceramics. 95th IADR General Session 2017 2017.03.25
14. Minh Nguyet Luong Dao, Alireza Sadr, Yasunori Sumi, Junji Tagami. Effects of Aging on Crack Formation Through Dentin and Composite. 95th General Session IADR 2017.03.25 San Francisco
15. Noriko Hiraishi, Yukihiko Tamura, Yusuke Tsutumi, Takao Hanawa, Jyunji Tagami. Analysis of arsenic in MTA cement and effect of glutathione on arsenic-induced toxicity on pulpal-like cells. 69th Meeting of Japanese Society for Dental Materials and Devices 2017.04.25 Tokyo
16. Noriko Hiraishi, Fumiaki Hayashi, Tomohiro Takagaki, Masayuki Otsuki, and Junji Tagami. Solid-state NMR Investigation on the Mineral Structure in De/re-mineralized Dentin. 2017 IADR/AADR/CADR General Session 2017.05.22 San Francisco, USA
17. Khin Kyaw , Noriko Hiraishi, Masayuki Otsuki, and Junji Tagami. Effect of Calcium-phosphate Toothpaste on Staining Susceptibility of Acid-eroded Enamel. 2017 IADR/AADR/CADR General Session 2017.05.22 San Francisco, USA
18. MATSUNAGA Satomi, TAKAGAKI Tomohiro, MATSUI Naoko, ARISAKA Yoshinori, TAMURA Atsushi, IKEDA Masaomi, NIKAIDO Toru, YUI Nobuhiko, TAGAMI Junji. The development of a new "reversible-adhesion" resin cement with a UV-cleavable PRX cross-linker. The 146th Meeting of the Japanese Society of Conservative Dentistry 2017.06.07 Aomori
19. HAYASHI Meiken, TAKAGAKI Tomohiro, IKEDA Masaomi, NAKASHIMA Syozi, NIKAIDO Toru, KUBO Shisei, TAGAMI Junji. CLSM observation of morphological progression of non-carious cervical lesions. The 146th Meeting of the Japanese Society of Conservative Dentistry 2017.06.07 Aomori
20. Noda S, Kawashima N, Hashimoto K, Yamamoto M, Aramaki O, Tagami J, Okiji T. Effects of culture density on stem cell properties of human dental pulp stem cells. 2017.06.08
21. Junji Tagami. Keys for the Best Bonding Performance in Various Clinical Situations. IAAD 2017 Meeting, International Academy for Adhesive Dentistry 2017.06.16 The University of Pennsylvania School of Dental Medicine
22. Junji Tagami. About composite resin restoration. 2017.06.21 Showa University
23. Tomohiro Takagaki. Predictable use of resin cement in all-ceramic cementation; science for durable bonding and esthetic result.. Hokkaido Summer Institute 2017.07.26

24. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
25. Nguyen TTT, Seki N, Moross J, Hosaka K, Sunaga M, Morio I, Kinoshita A. The effectiveness of newly developed computer-assisted simulation materials on overseas learners. The 28th SEAADE (South East Asia Association for Dental Education) Annual Scientific Meeting 2017.08.11 Taipei, Taiwan
26. Junji Tagami. Pathophysiology and treatment guidelines of Tooth Wear. 2017.08.20
27. Junji Tagami. Direct bonding strategies in various clinical situations. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.30
28. Keiichi Hosaka. Current update in adhesive systems. Thai Prosthodontic Association 2017.08.31 Bangkok
29. Meet-the-Expert(Dental materials):Dental materials. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.31
30. Junji Tagami. Is bulkfill composite reliable?. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.31
31. Ghuassan Rummani, Kurumi Ide, Masatoshi Nakajima, Junji Tagami. . The effect of cavity depth on the ultimate tensile strength of bulkfill resin coposite after long-term water immersion. . 10th World Congress of International Federation of Esthetic Dentistry 2017.09.14
32. Dhaifallah Alqarni, Keiichi Hosaka, Teerapong Mamane, Masatoshi Nakajima, Masaomi Ikeda, Junji Tagami. Effect of different surface treatments on repair uTBS of composite bonded to resin matrix after water exposure. The 10th World Congress of International Federation of Esthetic Dentistry 2017.09.14 Toyama
33. Kyaw KY, Niraishi N, Otsuki M, Tagami J . Effect of application of desensitizers before bleaching on change of tooth sgade. 10th World Congress of International Federation of Esthetic Dentistry 2017.09.14 Toyama, Japan
34. Tomohiro Takagaki. Predictable use of resin cement in all-ceramic cementation; science for durable bonding and esthetic result.. The 10th World Congress of International Federation of Esthetic Dentistry 2017.09.16 Toyama
35. Keiichi Hosaka. Bioactive technology meets MI esthetic direct composite restorations. - The present and future -. The 10th World Congress of International Federation of Esthetic Dentistry 2017.09.16 Toyama
36. Luong MND, Otsuki M, Shimada Y, Sumi Y, Tagami J. Bleaching effect of light sources with various wavelength. 10th World Congress of International Federation of Esthetic Dentistry 2017.09.17 Toyama, Japan
37. Lasindra WC, Otsuki M, Tagami J. Effect of pH on tooth bleacing action in vitro. 10th World Congress of International Federation of Esthetic Dentistry 2017.09.17 Toyama, Japan
38. Inokoshi M, Nozaki K, Takagaki T, Van Meerbeek B, Minakuchi S. Initial curing characteristics of composite cements under ceramic restorations. CED-IADR/NOF Oral Health Research Congress 2017 2017.09.22 Vienna
39. Kazuo Hirota, Rena Takahashi, Go Inoue, Junji Tagami. No Marginal Gap Around Composite Resin Restoration with Pre-Polymerized HEMA Filler. CED-IADR/NOF Oral Health Research Congress 2017.09.23 Vienna, Austria
40. Nakane A, Otsuki M, Tagami J. Change of root dentin by low-power iraditaion of Er:YAG laser. 29th Annual Meeting of Japanese Society for Laser Dentistry 2017.09.24 Niigata, Japan
41. Yoshinori Arisaka, Atsusi Tamura, Tomohiro Takagaki, Junji Tagami, Nobuhiko Yui. Synthesis of supermolecule-based photocleavable crosslinkers for smart dental materials. 70th Meeting of Japanese Society for Dental Materials and Devices 2017.10.14 Niigata

42. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Mechanical property and microstructural analysis of an ion-releasing S-PRG filler contained cement. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.15 Niigata
43. SWE ZIN AUNG, TAKAGAKI Tomohiro, IKEDA Masaomi, KOSUKE Nozaki, NIKAIDO Toru, TAGAMI Junji. The Effect of Different Light-curing Units on Degree of Conversion of Flowable Composites. The 147th Meeting of the Japanese Society of Conservative Dentistry 2017.10.26 Morioka
44. SAN SAN MAY PHYO AUNG, Tomohiro TAKAGAKI, SAI KHAM LYANN, Masaomi IKEDA, Toru NIKAIDO, Junji TAGAMI. Effect of Alumina-blasting Pressures on the Bonding Performance to Ultra/Super-translucent Zirconia Ceramics. The 147th Meeting of the Japanese Society of Conservative Dentistry 2017.10.26
45. Shin Rozan, Rena Takahashi, Toru Nikaido, Junji Tagami. The effect of resin coating technique on dentin bond strength and internal adaptation of CAD/CAM-fabricated inlays. The 147th Meeting of the Japanese Society of Conservative Dentistry 2017.10.27 Iwate, Japan
46. Takako Yoshikawa, Alireza Sadr. Light-Cured Composite Adaptation to the Cavity Wall and Polymerization Behavior Analysis using μ CT. 2017.10.27
47. Ali Alqahtani, Go Inoue, Toru Nikaido, Junji Tagami. Effect of concentrations of potassium and sodium fluoride on micro-shear bond strength and inhibition of demineralization . 147st Hozon Gakkai 2017.10.27
48. Mahmoud Sayed, Naoko Matsui, Noriko Hiraishi, Go Inoue, Toru Nikaido, Junji Tagami. Evaluation of Discoloration of Demineralized Dentin with Silver Diamine Fluoride. 147st Hozon Gakkai 2017.10.27
49. Rena Takahashi, Atsuko Tagami, Toru Nikaido, Junji Tagami. The dentin bond strength of dual-cure resin cements. Brazil-Japan Joint Research Workshop on Adhesive Dentistry 2017.11.01 Campinas, Brazil
50. Toru Nikaido. Assessment of adhesive materials for direct composite restorations.. Brazil-Japan Joint Research Workshop on Adhesive Dentistry 2017.11.01 UNICAMP, Sao Paulo, Brazil
51. Takaaki Sato, Tomohiro Takagaki, Rui Guan, Nikaido Toru, Junji Tagami. Evaluation of the enamel/bond interfaces of Multimode One-bottle Self-etching Adhesives. Brazil-Japan Joint Research Workshop on ADHESIVE DENTISTRY 2017.11.01 Brazil, Piracicaba
52. Kumagai RY, Takagaki T, Sato T, Nikaido T, Rodrigues JA, Reis AF, Tagami J. Acid-Base Resistant Zone at Adhesive Resin Cement/Enamel Interface: A Morphological Evaluation.. The 36th Meeting of Japanese Society of Adhesive Dentistry 2017.11.25 Funabori
53. Shimizu H, Inokoshi M, Takagaki T, Uo M, Minakuchi S. Bonding effectiveness of 4META/MMA-TBB resin to surface-treated highly translucent dental zirconia. The 36th Annual Meeting of Japan Society for Adhesive Dentistry 2017.11.26 Tokyo
54. Keiichi Hosaka. Direct Composite Restorations Based on Adhesive Technology. Invited Lecture 2017.12.08 Masaryk University, Brno, Czech republic

[Awards & Honors]

1. Wilmer Souder Award, The International Assosiation for Dental Research(IADR), 2017.03

Fixed Prosthodontics

Professor
Hiroyuki MIURA

Associate Professor
Kenichi YOSHIDA

Junior Associate Professor
Daizo OKADA
Wataru KOMADA

Assistant Professor
Chiharu SHIN
Shiho OTAKE
Satoshi OMORI
Reina NEMOTO

Attending Staff
Miho SATO
Tazuko MAKIYAMA
Yoko ISHIKAWA
Natsuko IWATA
Mariko KUBO
Kazuhisa FUJITA
Hideto MATSUI
Risa YAMADA
Michika MINAMIFUCHI
Ayana URABA
Bakhit Mohammed Yassin M
Paisankobrit Vibul
Rana ASANO
Ayaka SHIRASAKI
Mina TAKITA
Shiro RIKITOKU
Kai SHIBAGUCHI
Kiriko SUGANO
Kenichiro HAYASHI
Mayuko MATSUMURA
Erika SUKUMODA
Michiko NODA
Kunihiko MIZUSAWA

(1) Research

- 1)Occlusion and Mastication.(mandibular position, mandibular movement, articulator, masticatory efficiency)
- 2)Influence of mechanical stress caused by occlusal contact on stomatognathic system. (Tooth displacement, distortion of alveolar bone, occlusal contact, proximal contact etc.)
- 3)Relationship of main occluding area and occlusal contact
- 4)Research on post and core(materials, stress analysis etc.)
- 5)Clinical application of latest technology and development of new materials (CAD/CAM, Zirconia, optical impression etc.)
- 6)Influence of occlusal contact for an important prosthesis on the periodontal tissues of the antagonist.
- 7)Application of laser welding in crown and bridge restorations.
- 8)Influence of dental materials for periodontal tissues and biological body.
- 9)Functional analysis of abnormal stomatognathic function

(2) Lectures & Courses

The major subjects of the studies are occlusion of Cr-Co prostheses (fixed restoration such as crown and fixed partial denture), analysis of mandibular movement, influence of crown and periodontal tissue and its systemic affect, accuracy of manufacturing processes of crown (i.e. casting, soldering, luting and adjustment of occlusion), functional analysis of stomatognathic system and development of apatite ceramic implant. The research themes are investigated with measurement systems of mandibular movement, measuring instruments of tooth micro-displacement, electromyography, measurement apparatus of dimensional accuracy, EPMA (electron probe microanalyzer) for analyzing very small amount of dental alloy and histopathological methods. Clinical training and general lecture on prosthodontics are prepared for the graduate students in the first year. After the second year they will have special training for their research methods and experiments will be performed according to the research plan. In the last year the students will write the paper for thesis under the direction of the professor.

(3) Clinical Services & Other Works

- 1) Clinic for prosthodontics (Prosthodontics practice clinic)

This clinic is organized by clinical teams, and 4 to 8 dentists compose 1 team working in cooperation between teams. Here offers a complete range of restorative, rehabilitative, and esthetic dentistry, treatment types include since simple one teeth to complete oral rehabilitation using the latest technologies.

- 2) Clinic for dental allergy (Dental allergy clinic)

This clinic provides allergy tests test for dental alloys and dental materials on potential patients before dental treatment, besides, patients with skin and/or oral diseases histories induced by previous dental restorations. The causal allergen/s is/are identified by patch tests or if some metal restoration is allergy set on, is analyze by Electron Probe Micro Analyzer (EPMA), removing out only restoration such content allergens.

(4) Publications

[Original Articles]

1. Wataru Komada, Tasuku Inagaki, Yoji Ueda, Satoshi Omori, Keiichi Hosaka, Junji Tagami, Hiroyuki Miura. Influence of water immersion on the mechanical properties of fiber posts. *J Prosthodont Res.* 2017.01; 61(1); 73-80
2. Kyoshi Matsukawa, Reina Nemoto, Kosuke Nozaki, Mariko Kubo, Tasuku Inagaki, Keiichi Yoshida, Hiroyuki Miura. The influence of the framework thickness on surface strain of the 3-unit Zirconia resin-bonded fixed dental prostheses under the functional loading. *Asian Pacific Journal of Dentistry.* 2017.01; 17(1); 1-7
3. Siyang LUO, Daizo OKADA, Mohammed BAKHIT, Chiharu SHIN, Reiko OGURA, Hiroyuki MIURA. Stress Distribution in Cements with Different Post and Core Systems. *Asian Pacific Journal of Dentistry.* 2017.01; 17; 15-22
4. Kento Sato, Keiichi Hosaka, Masahiro Takahashi, Masaomi Ikeda, Fucong Tian, Wataru Komada, Masatoshi Nakajima, Richard Foxton, Yoshihiro Nishitani, David H Pashley, Junji Tagami. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. *J Adhes Dent.* 2017.02; 19(1); 31-37
5. Risa Yamada, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Reina Nemoto, Hiroyuki Miura, Akiko Nagai. Ag nanoparticle-coated zirconia for antibacterial prosthesis. *Mater Sci Eng C Mater Biol Appl.* 2017.09; 78; 1054-1060
6. Natsuko Iwata, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Yusuke Tsutsumi, Hiroyuki Miura, Akiko Nagai. Effects of controlled micro-/nanosurfaces on osteoblast proliferation. *J Biomed Mater Res A.* 2017.09; 105(9); 2589-2596
7. Yoko Ishikawa, Wataru Komada, Tasuku Inagaki, Reina Nemoto, Satoshi Omori, Hiroyuki Miura. The effects of post and core material combination on the surface strain of the 4-unit zirconia fixed partial denture margins. *Dent Mater J.* 2017.11; 36(6); 798-808
8. Ayana Uraba, Reina Nemoto, Kosuke Nozaki, Tasuku Inagaki, Satoshi Omori, Hiroyuki Miura. Biomechanical behavior of adhesive cement layer and periodontal tissues on the restored teeth with zirconia RBFDPs using three-kinds of framework design: 3D FEA study. *J Prosthodont Res.* 2017.11;
9. Vibul Paisankobrit, Satoshi Omori, Rie Fujita, Yoji Ueda, Reina Nemoto, Hiroyuki Miura. Effect of thickness of zirconia framework on fracture strength and fracture mode of ceria-stabilized tetragonal zirconia polycrystals/alumina ceramic restoration on resin tooth abutment. *Asian Pacific Journal of Dentistry.* 2017.12; 17(2); 31-40
10. Michika Minamifuchi, Reina Nemoto, Ayana Uraba, Satoshi Omori, Kosuke Nozaki, Hiroyuki Miura. Evaluating the optimal design of zirconia based resin-bonded fixed dental prostheses using finite element analysis. *The Journal of the Japan Academy of Digital Dentistry.* 2017.12; 7(2); 169-174
11. Mohammed Bakhit, Daizo Okada, Siyang Luo, Chiharu Shin, Reiko Ogura, Wataru Komada, Hiroyuki Miura. The stress distribution within dentin upon the use of different restoration materials *Asian Pacific Journal of Dentistry.* 2017.12; 17(2); 41-47

[Conference Activities & Talks]

1. K.Hayashi, S.Otake, S.Omori, R.Nemoto, R.Asano, S.Rikitoku, H.Miura. Bond strengths of cements to a new Pressable ceramics. *IADR 2017.03.24 San Francisco, the USA*
2. M.Matsumura, W.Komada, K.Sugano, K.Hayashi, C.Shin, S.Otake, H.Miura. Flexural strength of new pressable Lithium Disilicate Glass Ceramics. *IADR 2017.03.24 San Francisco, the USA*
3. K.Sugano, M.Matsumura, K.Hayashi, C.Shin, W.Komada, T.Inagaki, Y.Ueda, R.Fujita, H.Miura. The fitness of crowns fabricated by new dental press ceramics. *IADR 2017.03.24 San Francisco, the USA*
4. M.Minamifuchi, R.Nemoto, T.Inagaki, S.Omori, H.Miura. Influence of framework design on shear stress distribution. *The 8th Scientific Meeting of Japan Academy of Digital Dentistry 2017.04.22 Tsurumi, Kanagawa, Japan*

5. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
6. K. Nozaki, K. Fujita, N. Horiuchi, K. Yamashita, H. Miura, A. Nagai, K. Itaka. Regulation of periodontal ligament-derived cell morphology by type III collagen-coated hydroxyapatite. 2nd International Symposium on Creation of Life Innovation Materials 2017.09.30

Pulp Biology and Endodontics

Professor:

Takashi OKIJI

Associate Professor:

Mitsuhiro SUNAKAWA

Junior Associate Professor:

Hideharu IKEDA, Nobuyuki KAWASHIMA

Assistant Professor:

Arata EBIHARA, Hiroyuki MATSUMOTO, Tomoatsu KANEKO, Satoshi WATANABE, Jun KAWAMURA

Hospital Staff:

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Graduate Student:

Kazuto FURUHATA, Sailiman AIERKEN, Alamuddin BAKHIT, Miki NISHIJO, Kenrato HASHIMOTO
Donghoon KANG, Keisuke NARA, Sonoko NODA, Tomoyuki HONGO, Mayuko FUJII
Bayan RASHED, Youhei FUKUMORI, Yuki KASAHARA, Shunsuke KIMURA, Masashi KURAMOTO, Bin GU
Akira KOUNO, Yasuhiro HOSHIHARA, Keiichiro MAKI, Shinya YAMAUCHI, Thaw Dar OO, Phyo Pyai SONE
Su Yee Myo ZAW, Pyae Hein HTUN, Taro NAKATSUKASA, Hiroki MURANO, Yadanar Su PHYO, Ao XU
Aung Nyein Pyae SONE, Htoo Shwe Sin THEIN, Saleh Sherif Adel ABDELFATTAH, Zar Chi Thein ZAW

Research Student:

Tamae HASEGAWA

(1) Outline

The Department of Pulp Biology and Endodontics deals with endodontics/endodontology, and is concerned with research and clinical practice on the prevention, diagnosis and treatment of dental pulp and periapical diseases. In order to preserve and well maintain the function of the teeth in the oral cavity, it is important to understand the structural and functional features of the dental pulp and protect it carefully from noxious stimuli. However, pulp diseases, if left untreated, may progress to develop pulp necrosis and apical periodontitis, where meticulous treatment is required to eliminate infection from the complex root canal system. The goal of endodontics is to achieve long term maintenance of tooth function by the prevention and treatment of pulpal and periapical diseases.

(2) Research

- 1) Properties of oral tissue-derived mesenchymal stem cells/ Horizon of dental pulp regeneration
- 2) Crosstalk between pulpal inflammation and regeneration
- 3) Evaluation of newly developed endodontic sealers

- 4) Evaluation of endodontic technique using computational fluid dynamics(CFD)
- 5) Application of laser to endodontics
- 6) Application of optical coherence tomography
- 7) Analysis of nickel-titanium endodontic instruments
- 8) Electrophysiological approach to cell-to-cell couplings between odontoblasts
- 9) Diffusion through enamel and dentin
- 10) Lymphangiogenesis in the dental pulp
- 11) Influence of sympathetic nervous control on dentinogenesis of odontoblasts
- 12) Neuro-scientific research for dental pain
- 13) Diagnosis using CBCT & Diagnosis of vertical root fractures by analyzing reconstructed three-dimensional models obtained from CBCT images

(3) Education

The educational aim of the Department of Pulp Biology and Endodontics is to cultivate students so that they can obtain knowledge and skills required for leading scientists, researchers or practitioners of endodontics. Since recent progress of pulp biology and endodontics is remarkable, the students are educated to acquire the newest knowledge on modern endodontology and its related subjects, such as neuroscience, microbiology, molecular biology, immunology and biomaterial sciences, and are trained to master the newest technology of endodontics. All the students are asked to add new findings to the field of endodontics based on their own original research.

(4) Clinical Services & Other Works

The Department of Pulp Biology and Endodontics is in charge of the Clinic of Operative Dentistry and Endodontics in our Dental Hospital, together with the Department of Cariology & Operative Dentistry, and offers the global standard of care in the treatment of pulpal and periapical diseases to our patients. We provide clinical care in the full spectrum of endodontics including;

- Vital pulp therapies,
- Nonsurgical root canal therapies,
- Root canal retreatments,
- Endodontic microsurgeries,
- Internal tooth bleaching, and
- Post-endodontic restorations

(5) Clinical Performances

The latest development of endodontics is remarkable as seen in root canal instrumentation by super-elastic Ni-Ti rotary files, diagnosis by cone beam computed tomography, and microendodontics by using a surgical operating microscope. In particular, microendodontics has dramatically changed conventional “blind” endodontics into more predictable endodontics since it allows us to obtain accurate diagnostic information and provide precise procedures under an illuminated and magnified view. Also, we seek to provide evidence-based endodontic treatment based on our laboratory and clinical research.

(6) Publications

[Original Articles]

1. Kawashima N, Tomura J, Yokota K, Okiji T. Effect of a pH-modified low-concentration EDTA irrigant on smear layer removal and dentin demineralization *The Japanese journal of conservative dentistry*. 2017.02; 60(1); 32-39
2. Sugawara S, Shigetani Y, Kenmotsu S, Okiji T, Ohshima H. Evaluation of a new mouse model for studying dental pulpal responses to GaAlAs laser irradiation. *Journal of Oral Biosciences*. 2017.02; 59(1); 38-43
3. Tazawa K, Ikeda H, Kawashima N, Okiji T. Transient receptor potential melastatin (TRPM) 8 is expressed in freshly isolated native human odontoblasts. *Archives of Oral Biology*. 2017.03; 75; 55-61

4. Tokita D, Ebihara A, Miyara K, Okiji T. Assessment of torque and vertical force generated by torque-sensitive and time-dependent reciprocal movements of nickel-titanium rotary root canal instruments The Japanese Society of Conservative Dentistry. 2017.06; 60(3); 162-169
5. Sueyama Y, Kaneko T, Ito T, Kaneko R, Okiji T. Implantation of endothelial cells with mesenchymal stem cells accelerates dental pulp tissue regeneration/healing in pulpotomized rat molars. *Journal of Endodontics*. 2017.06; 43(6); 943-948
6. Tokita D, Ebihara A, Miyara K, Okiji T. Dynamic torsional and cyclic fracture behavior of profile rotary instruments at continuous or reciprocating rotation as visualized with high-speed digital video imaging. *Journal of Endodontics*. 2017.07; 43(8); 1337-1342
7. Tokita D, Ebihara A, Nishijo M, Miyara K, Okiji T. Dynamic torque and vertical force analysis during nickel-titanium rotary root canal preparation with different modes of reciprocal rotation. *Journal of Endodontics*. 2017.07; 43(10); 1706-1710
8. Ohkura N, Edanami N, Takeuchi R, Tohma A, Ohkura M, Yoshiba N, Yoshiba K, Ida-Yonemochi H, Ohshima H, Okiji T, Noiri Y. Effects of pulpotomy using mineral trioxide aggregate on prostaglandin transporter and receptors in rat molars. *Scientific Reports*. 2017.07; 7(1); 6870
9. Ganbold K, Kakino S, Ikeda H, Miyashin M. Human pulpal blood flow in different root formation stages measured with Transmitted-light plethysmography *Archives of Oral Biology*. 2017.08; 83(8); 327-333
10. Kawashima N, Noda S, Yamamoto M, Okiji T. Properties of dental pulp-derived mesenchymal stem cells and the effects of culture conditions. *Journal of Endodontics*. 2017.09; 43(9S); S31-S34
11. Niwano K, Okiji T, Noiri Y. Novel analysis of endodontic file manipulation using a newly developed apparatus for recording force and torque values with real-time lissajous curve display. *Journal of Dentistry and Oral Disorders*. 2017.09; 3(5); 1073
12. Ito T, Kaneko T, Sueyama Y, Kaneko R, Okiji T. Dental pulp tissue engineering of pulpotomized rat molars with bone marrow mesenchymal stem cells. *Odontology*. 2017.10; 105(4); 392-397
13. Yao K, Satake K, Watanabe S, Ebihara A, Kobayashi C, Okiji T. Effect of laser energy and tip insertion depth on the pressure generated outside the apical foramen during Er:YAG laser-activated root canal irrigation. *Photomedicine and Laser Surgery*. 2017.12; 35(12); 682-687
14. Hinata G, Yoshiba K, Han L, Edanami N, Yoshiba N, Okiji T. Bioactivity and biomineralization ability of calcium silicate-based pulp-capping materials after subcutaneous implantation. *International Endodontic Journal*. 2017.12; 50(Suppl 2); e40-e51
15. Yamamoto S, Han L, Noiri Y, Okiji T. Evaluation of the Ca ion release, pH and surface apatite formation of a prototype tricalcium silicate cement. *International Endodontic Journal*. 2017.12; 50(Suppl 2); e73-e82
16. Watanabe S, Kouno A, Hongo T, Satake K, Ide A, Yao K, Okiji T. Apical Extrusion of Irrigating Solution during Root Canal Irrigation Activated by Er:YAG Laser:Effect of Tip Insertion Depth *Journal of Japanese Society for Laser Dentistry*. 2017.12; 28(2,3); 31-35

[Books etc]

1. Glossary of Operative Dentistry. 2017.04 (ISBN : 978-4-263-45803-7)

[Conference Activities & Talks]

1. Kawashima N, Noda S, Hashimoto K, Saito M, Okiji T. Meis2 induces odonto-/osteoblastic differentiation and mineralization. 95th General Session & Exhibition of the IADR 2017.03.22 San Francisco, CA
2. Noda S, Kawashima N, Hashimoto K, Aramaki O, Yamamoto M, Okiji T. Dense culture conditions induced human dental pulp stem cell differentiation. 95th General Session & Exhibition of the IADR 2017.03.22 San Francisco, CA
3. Okiji T. Vital pulp therapy: biological basis & current concepts. Capital Medical University 2017.05.26 Beijing

4. Bin GU, Tomoatsu KANEKO, Yukiko SUEYAMA, Phyo Pyai Sone, Takashi OKIJI. Kinetic Analysis of M2 Macrophages in the Regenerative Process of Rat Engineered Pulp Tissue. The 73rd Annual Meeting of The Japanese Society of Microscopy 2017.05.31
5. Tomoatsu Kaneko, Yukiko Sueyama, Bin Gu, Takashi Okiji. Differentiation of Mesenchymal Stem Cells Implanted into Rat Pulpotomized Pulp Chambers . The 73rd Annual Meeting of The Japanese Society of Microscopy 2017.05.31
6. Kang D, Wada T, Uo M, Okiji T. Evaluation of mechanical and rheological properties of the clay added calcium silicate cement. The 146th Meeting of The Japanese Society of Conservative Dentistry 2017.06.08 Link Station Hall Aomori
7. Bin GU, Tomoatsu KANEKO, Yukiko SUEYAMA, Phyo Pyai Sone, Su Yee Myo Zaw, Takashi OKIJI. Kinetic Analysis of M2 Macrophages in the Regenerative Process of Rat Engineered Pulp Tissue. 2017.06.08
8. Kusamoto M, Kawashima N, Nozaki K, Bakhit AY, Nara K, Fujii M, Hashimoto K, Noda S, Okiji T. Mineral trioxide aggregate modulates functions of LPS-stimulated macrophages via calcium-sensing receptor. 2017.06.08
9. Noda S, Kawashima N, Hashimoto K, Yamamoto M, Aramaki O, Tagami J, Okiji T. Effects of culture density on stem cell properties of human dental pulp stem cells. 2017.06.08
10. Yamauchi S, Hoshihara Y, Hongo T, Yao K, Watanabe S, Okiji T. Removal of Mineral Trioxide Aggregate Filling Material from the Root Canal Using Er:YAG Laser Irradiation. 2017.06.08 Aomori
11. Kouno A, Hongo T, Yao K, Satake K, Watanabe S, Okiji T. Generation of apical pressure and vaporized bubbles during root canal irrigation activated by Er:YAG laser: Effect of pulse number and tip configuration. The 146th Meeting of the Japanese Society of Conservative Dentistry 2017.06.08 Aomori
12. Kimura S, Tokita D, Maki K, Nishijo M, Miyara K, Ebihara A, Okiji T. Evaluation of mechanical properties of HyFlex EDM NiTi rotary instruments . The 146rd Meeting of the Japanese Society of Conservative Dentistry 2017.06.08 Aomori
13. Maki K, Tokita D, Kimura S, Nishijo M, Miyara K, Ebihara A, Okiji T. The effect of the speed of up-and-down motion of nickel titanium rotary files on root canal shape.. The 146th Meeting of the Japanese Society of Conservative Dentistry 2017.06.09 Aomori
14. Su Yee Myo Zaw, Tomoatsu KANEKO, Bin GU, Yukiko SUEYAMA, Phyo Pyai Sone, Takashi OKIJI. Distribution of LacZ-expressing Stem Cells in Rat Engineered Pulp Tissue. 2017.07.22
15. Maki K, Tokita D, Kimura S, Nishijo M, Miyara K, Ebihara A, Okiji T. Comparative evaluation of shaping ability of different root canal preparation techniques performed by undergraduate students.. The 37th Annual Scientific Meeting of Japanese Endodontic Association 2017.07.22 Tokyo
16. Kouno A, Watanabe S, Hongo T, Yao K, Satake K, OKIJI T. Vaporized cavitation bubbles during root canal irrigation activated by Er:YAG laser : Effect of tip configuration. 2017.07.22 Tokyo
17. Kouno A, Watanabe S, Hongo T, Yao K, Satake K, Okiji T. Vaporized cavitation bubbles during root canal irrigation activated by Er:YAG laser: Effect of tip configuration. The 38th Annual Scientific Meeting of Japan Endodontic Association 2017.07.22 Tokyo
18. Nishijo M, Tokita D, Maki K, Kimura S, Miyara K, Ebihara A, Okiji T . Evaluation of screw-in forces in three types of NiTi rotary instruments for glide path preparation. The 38th Annual Scientific Meeting of Japan Endodontic Association 2017.07.22 Tokyo
19. Kasahara Y, Komatu K, Iino Y, Uraba S, Ebihara A, Okiji T. Evaluation of periapical bone defects using conventional radiography and cone-beam computed tomography . The 38th Annual Scientific Meeting of Japan Endodontic Association 2017.07.22 Tokyo
20. Distribution of LacZ-expressing Stem Cells in Rat Engineered Pulp Tissu. The 38th Annual Scientific Meeting of Japan Endodontic Association 2017.07.22

21. Ebihara A, Kawamura J, Tsuruta J, Kinoshita A, Okiji T. Preparation by students for flip teaching to preclinical practice of endodontics. The 36th annual meeting of Japanese Dental Education Association 2017.07.29 Matsumoto
22. Jun KAWAMURA, Daisuke TOKITA, Arata EBIHARA, and Takashi OKIJI. Introduction of e-learning-aided preclinical teaching of nickel -titanium rotary root canal preparation. The 36th annual meeting of Japanese Dental Education Association 2017.07.29 Matsumoto
23. Su Yee Myo Zaw, Kaneko T, Sueyama Y, Gu B, Phyo Pyai Sone, Okiji T. The fate of stem cells implanted in rat dental pulp. FDI World Dental Congress 2017.08.29 Madrid, Spain
24. Ebihara A. Vertical Root Fracture. Lecture at Himeji Dental Association 2017.09.02 Himeji
25. Fujii M, Kawashima N, Okiji T. Hypoxia inducible factor 1 alpha augments the synthesis of inflammatory mediators in lipopolysaccharide-stimulated human dental pulp cells . The 59th Annual Meeting of Japanese of Association of Oral Biology 2017.09.16 Shiojiri
26. Microendodontics. Dalian Medical University, Special lecture 2017.09.29 Dalian
27. Kang D, Wada T, Uo M, Okiji T. The study for the improvement of compressive strength and operability of the synthesized calcium silicate cement. The 70th Meeting of The Japanese Society for Dental Materials and Devices 2017.10.15 Niigata
28. Hoshihara Y, Watanabe S, Kouno A, Hongo T, Yao K, Ide A, Satake K, Okiji T. Er:YAG Laser-activated Root Canal Irrigation: Cleaning Efficacy in Regions Apart from the Laser Tip . 2017.10.26 Morioka
29. KimuraS, TokitaD, MakiK, NishijoM, MiyaraK, EbiharaA, OkijiT. Analysis of stresses developed during root canal shaping with torque-sensitive reciprocal motion: comparison between single-length technique and crown-down technique. The 147rd Meeting of the Japanese Society of Conservative Dentistry 2017.10.26 Morioka
30. Bakhit AY, Kawashima N, Hashimoto K, Noda S, Nara K, Okiji T. Strontium ranelate-evoked proliferation and mineralization of mouse dental papillae cells is mediated via calcium sensing receptor. 2017.10.27
31. Ebihara A. Application of CBCT to Endodontics. 22nd Clinical Imaging Conference, Japan Radiological Society 2017.11.12 Morioka
32. Ikeda H. Are odontoblasts pain receptor cells?. Pulp biology symposium on sensory transduction in the dental pulp 2017.11.17 Bangkok, Thailand
33. Kakino S, Ganbold K, Uehara T, Inoue A, Jayawardena A, Ikeda H, Miyashin M. Pulpal circulation measurement of the luxated young permanent teeth with abnormal root formation using TLP. The 8th conference of Asian International Association of Dental Traumatology 2017.11.18 Bangkok, Thailand
34. Gu B, Kaneko T, Sueyama Y, Su Yee Myo Zaw, Phyo Pyai Sone, Murano H, Okiji T. M1/M2 macrophage recruitment during coronal tissue-engineering in rat molars. JADR2017 2017.11.18 Tokyo
35. Phyo Pyai Sone, Kaneko T, Su Yee Myo Zaw, Sueyama Y, Gu B, Murano H, Okiji T. Nerve Fibers in Regenerative Process of Coronal Pulp Tissue Engineering. JADR2017 2017.11.18
36. Ebihara A. Vertical Root Fracture. Open lecture of Satsuki-kai, 2017 2017.11.19 Tokyo
37. Nishijo M, Ebihara A, Tokita D, Doi H, Hanawa T, Okiji T. Evaluation of selected mechanical properties of NiTi rotary glide path files manufactured from controlled memory wires. 2017.11.19 Tokyo
38. Kawashima N, Noda S, Yamamoto M, Okiji T. Hard-tissue forming properties of dental pulp derived-mesenchymal stem cells. 2017 Faculty Annual Scientific Meeting of Hong Kong University 2017.12.14 Prince Philip Dental Hospital, Hong Kong University, Hong Kong

[Awards & Honors]

1. Outstanding Reviewer Status for Archives of Oral Biology in the past two years, Archives of Oral Biology, 2017.11

[Others]

1. 2017 Marquis Who's Who Lifetime Award Winner, 2017.06

We are pleased to announce that Marquis Who's Who has selected you for our official 2017 Albert Nelson Marquis Lifetime Achievement Award. You have been selected to receive this prestigious award as a result of your hard work and dedication to your profession.

2. Co-work with Department of Biochemistry and Physiology, Mahidol University, Thailand, 2017.11
Co-work with Department of Biochemistry and Physiology, Mahidol University, Thailand

Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki

Junior associate professor - Takeshi Ueno

Assistant professors

- Ichiro Minami, Juro Wadachi, Eiko Kohno, Junnichi Wada, Natsuko Murakami, Atsushi Takaichi

Hospital staff

- Natsuki Suzuki, Yuki Arai, Yasuha Nogawa, Takeshi Ootsubo, Hideaki Inagawa, Yuka Inamochi, Kensuke Takakusaki, Yasuo Nakajima, Hitomi Matsuno, Chie Watanabe

Graduate students

- Keigo Isoshima, Keiichiro Uchikura, Hirofumi Uchida, Wang Zuo, Hisami Okawara, Kittikundecha Nuttaphon, K Zin Myint Oo, Hiroki Saito, Yuya Satokawa, Shichiri Yuka, Shizuka Suzuki, Erina Seki, Tenhaku Tan, Kazutoshi Nakamura, Tomiharu Nagayama, Gen Nabeshima, Yoko Hayashi, Hironari Hayama, Masahiro Hirasawa, Toshiki Yamazaki

(1) **Outline**

The Department of Removable Partial Prosthodontics specializes in removable partial denture treatment, which is one of the major disciplines of clinical dentistry. The department has taken the baton from the First Department of Prosthodontics and the Department of Masticatory Function Rehabilitation.

Our objectives are to enhance the art and science of removable prosthodontics for the management of various oral conditions associated with tooth loss, from a single missing tooth to a single remaining tooth, in the maxillary and/or mandibular arch.

(2) **Research**

1. Function and Physiology in Partial Denture Wearers
2. Optimization of Partial Denture Design based on Stress Analysis
3. Development and Applications of New Prosthodontic Biomaterials
4. Biology of Oral Tissues in Denture Wearers
5. Epidemiology and Education for Removable Partial Prosthodontics

(3) **Education**

School of Dentistry

Year 1

Introduction to Dentistry

Year 3

Tooth Carving

Introduction to Clinical Dentistry

Observation and assistance at clinic term I and II

Basic Occlusal Reconstruction

Introduction to Research article writing and Patent acquisition

Year 4

Research Project

Removable Partial Prosthodontics

Advanced knowledge and skill with occlusion

Experience learning of dental practice

Years 5 and 6

Case study

Dental Practice and Clinical Practicum for Comprehensive Patient Care (Clinical Internship)

School of Oral Health Care Sciences, School of Oral Health Care Sciences

Year 2 Prosthodontics

Years 3 and 4 Practice for Dental Hygiene Care

School of Oral Health Care Sciences, Course for Oral Health Engineering

Year 2 Removable Prosthodontics Technology

(4) Lectures & Courses

The Department of Removable Partial Prosthodontics offers a variety of educational courses pertaining to the specialized clinical management of tooth loss, primarily for undergraduate students at the School of Dentistry. The courses include lectures, tutorials, hands-on sessions, clinical simulations, and clinical internship instructions.

The ability to perform clinical operations on patients with tooth loss, including the skills required for medical interviews, oral examinations, diagnosis, decision making, impression making, bite registration, denture design and technology, and denture delivery and maintenance, is essential for clinical dental professionals. The objectives of our courses are to provide learning and training in contemporary removable prosthodontics and enhance the knowledge and skills of students to help them develop and flourish in their future career as dental and oral health professionals.

(5) Clinical Services & Other Works

All faculty members of the Department of Removable Partial Prosthodontics are assigned to treat patients at the Prosthodontics department in the Dental Hospital of the Tokyo Medical and Dental University. While the rate of tooth retention has increased in comparison with previously reported rates, the number of patients in need of a removable partial denture has increased. Our specialists primarily work on advanced cases that are referred from other departments and outside the hospital. The departmental mission also includes the development and application of new prosthodontic materials, their clinical trial, and the spread of novel and inventive knowledge to the community.

(6) Clinical Performances

The department specializes in removable partial prosthodontics and aims to restore missing teeth and associated oral tissues; improve physiological functions such as occlusion, mastication, swallowing, and speech; maintain normal oral sensation; and restore the original appearance of individual patients.

Treatment modalities, materials, and denture design are all based on the case history and chief complaint of the patients. The ultimate goal is to improve the oral health-related quality of life of patients.

(7) Publications

[Original Articles]

1. Akihito Uezato, Mitsuhiro Enomoto, Meiyo Tamaoka, Mizue Hobo, Shusuke Inukai, Masayuki Hideshima, Yasunari Miyazaki, Toru Nishikawa and Kazuyoshi Yagishit. Shorter sleep onset latency in patients undergoing hyperbaric oxygen treatment *Psychiatry and Clinical Neurosciences*. 2017.01; 71(1); 73-74
2. Yoshizo Matsuka, Yoshiyuki Hagiwara, Katsushi Tamaki, Hisahiro Takeuchi, Masanori Fujisawa, Takahiro Ono, Yoshihiro Tsukiyama, Kan Nagao, Kazuhiro Tsuga, Hideki Aita, Hisatomo Kondo, Kenji Fueki, Hiroaki Tsukasaki, Keisuke Nishigawa, Shogo Ozawa, Rika Kuwatsuru, Hajime Minakuchi, Toshimitsu Iinuma, Takashi Matsuura, Kanji Ishibashi, Shigehisa Fujii, Toshihiro Hirai, Keiichi Sasaki, Hirofumi Yatani, Yoshimasa Igarashi, Yuji Sato, Tetsuo Ichikawa, Tetsuo Yamamori, Takuo Kuboki, Kazuyoshi Baba, Kiyoshi Koyano, Hironobu Sato, Hideo Matsumura. Reliability and validity of the patient disability-oriented diagnostic nomenclature system for prosthetic dentistry. *J Prosthodont Res*. 2017.01; 61(1); 20-33
3. Ayaka Chiba, Takashi Hatayama, Kimisuke Kainose, Masatoshi Nakajima, David H Pashley, Noriyuki Wakabayashi, Junji Tagami. The influence of elastic moduli of core materials on shear stress distributions at the adhesive interface in resin built-up teeth. *Dent Mater J*. 2017.01; 36(1); 95-102
4. Sasipin Lauvahutanon, Maho Shiozawa, Hidekazu Takahashi, Naohiko Iwasaki, Meiko Oki, Werner J. Finger, Mansuang Arksornnukit. Discoloration of various CAD/CAM blocks after immersion in coffee *Restorative Dentistry and Endodontics*. 2017.01; 42(1); 9-18
5. Magdalini Thymi, Corine Visscher, Eiko Yoshida-Kohno, Wim Crielaard, Daniel Wismeijer, and Frank Lobbezoo.. Associations between sleep-bruxism and (peri-) implant complications: a prospective cohort study. *BDJ Open*. 2017.03; 3(17003);
6. K Fueki, E Yoshida-Kohno, N Wakabayashi. Oral health-related quality of life in patients with non-metal clasp dentures: a randomised cross-over trial. *J Oral Rehabil*. 2017.05; 44(5); 405-413
7. Chie Watanabe, Junichiro Wada, Koji Mizutani, Hiroshi Watanabe, Noriyuki Wakabayashi. Chronological grey scale changes in supporting alveolar bone by removable partial denture placement on patients with periodontal disease: A 6-month follow-up study using digital subtraction analysis. *J Dent*. 2017.05; 63; 8-13
8. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Meiyo Tamaoka, Yasunari Miyazaki, Kenji Fueki, Noriyuki Wakabayashi. Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial *J Prosthodont Res*.. 2017.07; 61(3); 259-267
9. Chie Yoshihara, Takeshi Ueno, Peng Chen, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi. Inverse response of osteoblasts and fibroblasts to growth on carbon-deposited titanium surfaces. *J. Biomed. Mater. Res. Part B Appl. Biomater*.. 2017.09;
10. Y Inamochi, K Fueki, N Usui, M Taira, N Wakabayashi. Adaptive change in chewing-related brain activity while wearing a palatal plate: an functional magnetic resonance imaging study. *J Oral Rehabil*. 2017.10; 44(10); 770-778
11. Yuka Kajima, Atsushi Takaichi, Takayuki Nakamoto, Takahiro Kimura, Nuttaphon Kittikundecha, Yusuke Tsutsumi, Naoyuki Nomura, Akira Kawasaki, Hidekazu Takahashi, Takao Hanawa, Noriyuki Wakabayashi. Effect of adding support structures for overhanging part on fatigue strength in selective laser melting. *Journal of the Mechanical Behavior of Biomedical Materials*. 2017.11; 78; 1-9
12. Yuya Satokawa, Ichiro Minami, Noriyuki Wakabayashi. Short-term changes in chewing efficiency and subjective evaluation in normal dentate subjects after insertion of oral appliances with an occlusal flat table. *J Oral Rehabil*. 2017.11; 45(2); 116-125

13. Kazuyuki Handa, Natsuko Murakami, Toshiki Yamazaki, Hidekazu Takahashi, Noriyuki Wakabayashi. The ball-on-disk cyclic wear of CAD/CAM machinable dental composite and ceramic materials *Journal of Oral Science*. 2017.12; 59(4); 589-596
14. Masahiro Hirasawa, Chiaki Tsutsumi-Arai, Kensuke Takakusaki, Toyohisa Oya, Kenji Fueki, Noriyuki Wakabayashi. Superhydrophilic co-polymer coatings on denture surfaces reduce *Candida albicans* adhesion-An in vitro study. *Arch. Oral Biol.*. 2017.12; 87; 143-150

[Misc]

1. Yuki Arai, Ryunosuke Kazama, Noriyuki Wakabayashi, Masayoshi Fukushima. Monolithic zirconia restorations for chairside single-visit dentistry 2017.02; 129(2); 342-352
2. K Fueki, K Baba. Shortened dental arch and prosthetic effect on oral health-related quality of life: a systematic review and meta-analysis. *J Oral Rehabil*. 2017.07; 44(7); 563-572
3. Wakabayashi N, Ueno T, Fueki K. Major and minor connectors as partial denture components designed to aim for multiple roles in denture function *Ann Jpn Prosthodont Soc*. 2017.07; 9(3); 205-210
4. Fueki K, Inamochi Y. Clinical evidence of non-metal clasp denture:a systematic review *Ann Jpn Prosthodont Soc*. 2017.10; 9(4); 297-302

[Conference Activities & Talks]

1. Hirasawa M, Tsutsumi C, Takakusaki K, Takahashi H, Fueki K, Wakabayashi N. Reduction of *Candida albicans* adhesion by coating of hydrophilic methacrylamide polymer on the PMMA-denture base acrylic resin. Annual Scientific Meeting of Japan Prosthodontic Society Higashi-Kanto Branch February 5, 2017, Chiba 2017.02.05 Chiba
2. Watanabe C, Wada J, Mizutani K, Watanabe H, Katsuki A, Wakabayashi N. Chronological effects of removable partial denture placement on periodontally compromised abutment teeth: A digital subtraction analysis. The 126th Scientific Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama
3. Inamochi Y, Fueki K, Usui N, Wakabayashi N. Adaptive change of oral function and brain activation in chewing with wearing palatal plate: An fMRI study. The 126 Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama, Kanagawa, Japan
4. Hayama H, Fueki K, Wadachi J, Wakabayashi N. A accuracy of digital impression by optical scanning for a mandibular partially dentate model . The 126 Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama, Kanagawa, Japan
5. Kajima Y, Takaichi A, Takahashi H, Wakabayashi N. Effects of support structure on the fatigue strength of additive fabrication. The 126th annual meeting of the Japan Prosthodontic society 2017.07.02 Yokohama
6. Junichiro Wada, Aiichiro Ao, Hideo Nara, Noriyuki Wakabayashi. A case report of patient transmitted from non-vertical stop occlusion to the occlusal condition with lower overdenture in short time . The 126th Annual Meeting of the Japan Prosthodontic Society 2017.07.02 Yokohama
7. Hirasawa M, Tsutsumi C, Takakusaki K, Satomura K, Fueki K, Wakabayashi N. Reduction of *Candida albicans* adhesion by coating of superhydrophilic co-polymer on the PMMA-denture base acrylic resin . The 100st Annual meeting of Japanese Society for Bacteriology Kanto Branch 2017.09.28 Tokyo
8. Naohiko Iwasaki, Maho Shiozawa, Yusuke Yamamoto, Tetsuya Suzuki and Hidekazu Takahashi. Relationship among Marginal Reproducibility, Machinability and Mechanical Property of Zirconia Blank for CAD/CAM System. International Conference on Materials and Systems for Sustainability 2017 (IC-MaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya University, Nagoya
9. Takaichi A, Kajima Y, Nakamoto T, Tsutsumi Y, Nomura N, Takahashi H, Hanawa T, Wakabayashi N. Effect of adding support structures for overhanging part on fatigue strength in selective laser melting. . The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata

10. Kajima Y, Takaichi A, Nakamoto T, Nuttaphon K, Nomura N, Takahashi H, Wakabayashi N, Kawasaki A. Study on the effective condition of heat treatment on the anisotropy control of selective laser melted Co-Cr alloy.. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata
11. Naohiko Iwasaki, Toru Yasue, Maho Shiozawa, Yusuke Yamamoto, Shinji Tanaka, Tetsuya Suzuki, Hidekazu Takahashi.. Mechanical properties of recent composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices, 2017.10.14 Toki Messe, Niigata city
12. Shota Hayashi, Masayuki Hideshima, Naoki Ishihara, Tomohiro Kurashima, Shusuke Inukai, Yuuko Mitsuma, Shuhei Nakamura, Toshihide Fujie, Yasunari Miyazaki, Meiyo Tamaoka. Conversion from continuous positive airway pressure therapy to oral appliance therapy for obstructive sleep apnea in Tokyo Medical and Dental University Hospitals. 16th the Japanese Academy of Dental Sleep Medicine 2017.11.04 Yamaguchi, Japan
13. Gen Nabeshima. Effect of dietary counselling with prosthetic restoration on dietary intake in partially dentate patients : a prospective study. The Stomatological Society, Japan 2017.11.20 Tokyo Medical and Dental University
14. Kazutoshi Nakamura, Ichiro Minami, Yasuha Ikawa, Junichiro Wada, Noriyuki Wakabayashi. Head position affects the direction of occlusal force during tapping movement. The 82th Annual Meeting of the Stomatological Society, Japan 2017.11.20 Tokyo
15. N Murakami. A removable partial denture supported by structurally compromised and endodontically treated abutments for a patient exhibiting high bite forces. The 21st Scientific Meeting of Japan Prosthodontic Society Tokyo branch 2017.12.02 Tokyo Dental College Suidobashi Campus
16. Hayama H, Fueki K, Wadachi J, Wakabayashi N. Trueness of digital impression by optical scanning for mandibular partially dentate models. The 21th annual meeting of Japan Prosthodontic Society Tokyo Branchi 2017.12.03 Tokyo, Japan
17. Yuya Satokawa, Ichiro Minami, Noriyuki Wakabayashi. Short-term changes in chewing efficiency and subjective evaluation in normal dentate subjects after insertion of oral appliances with an occlusal flat table. The 21st Scientific Meeting of Japan Prosthodontic Society Tokyo branch 2017.12.03 Tokyo Dental Collage
18. Isoshima Keigo, Ueno Takeshi, Hiroki Saito, Tsutsumi Yusuke, Peng Chen, Hisashi Doi, Hanawa Takao, Wakabayashi Noriyuki. Increased cellular attachment on electropositive titanium surfaces. . The 7th international conference on mechanics of biomaterials and tissues (MOBT) 2017.12.11 Waikoloa, Hawaii
19. Takeshi Ueno, Noriyuki Wakabayashi, Takahiro Ogawa.. UV pretreatment of titanium decreases intracellular ROS production in osteoblasts. . The 7th international conference on mechanics of biomaterials and tissues (MOBT) 2017.12.13 Waikoloa, Hawaii

[Awards & Honors]

1. Dentsply Sirona Merit Award, The 126th Scientific Meeting of Japan Prosthodontic Society, 2017.07
2. DENTSPLY Sirona Award, Japan Prosthodontic Society, 2017.07

Oral Implantology and Regenerative Dental Medicine

Professor and Chair Shohei KASUGAI
 Associate Professor Makoto SHIOTA
 Assistant Professor(Lecturer) Noriko TACHIKAWA, Shinji KURODA
 Assistant Professor Hidemi NAKATA

Medical Staffs:

Kazuhiro KON, Masaki FUJII, Takayuki MIYAHARA, Tokuo AKINO,
 Masahiro SHIMOGISHI, Masahiro ISHIWATA, Chiharu IMAKITA, Maiko Yamamoto

Graduate Students:

Taiji HAMADA, Masaki SHIBASAKI, Reo IKUMI, Shintaro NAKAMURA, Kenya YONEDA, MULATI Aierken, MYOE Kyaw Thet, Peng ZHANG, THIKE Aung Bobo, WULANSARI Lia Kartika, Sawako KAWAKAMI, Yuki KUWAHARA, Wataru KOZUMA, Akihiro SUZUKI, Xiaohui TIAN, Motoi MIURA, YU Mon Myint, SUN Quan, Kaori YOKOTA, Yuji MIKI, WAI Myo Maung, SUN Xiaolong, SABBAGH Afnan Ahmed, Kanpei TAKEICHI, WU Bixi, WANG Fangshou, YEE Mon Shwe, THIHA Tin Kyaw, XU Jiayun, Hiromi TANINOKUCHI, Hajime, IJIMA, Takahiro SASAKI, Daisuke YAMAMOTO, ABDULRAZZAQ Ben Eessn

Graduate Research Students:

Shuichi KOYAMA, Tadamasu YOSHIDA, Toshimitsu SHIGEMATSU, Toshihiko MORIKAWA, Kazuhiko INOUE, Takeshi WATANABE, Arihiro IWATA, Seiji OOHARA, Junya HAMAGUCHI, Dotetsu TAKONAI, Munemitsu MIYASAKA, Akihiro TAKAHASHI, Kento TAIRA, You-kyoung KIM, Mizuki SATO, Yoko OBA, Kaho TAMURA, Kazuko YOSHIMURA, WANG Tiyayue, AILI Reziwanguli

Registered Residents:

Toshifumi KOJIMA, Kensuke FUKUTOMI, Reina SHIBUYA, Aoi SAKUYAMA, Kazuhisa TSURUMI, Takahiro NAKAMURA, Soichi NAKANO, Maho AKATSUKA, Narumi SATO

Clinical Professor (Faculty of Dentistry) Hideaki KATSUYAMA
 Clinical Visiting Associate Professor Koji HAGINO
 Clinical Visiting Associate Professor Tsuneji OKADA

Adjunct Assistant Professor (Faculty of Dentistry):

Maho KON, Yuki DATE, Akiko FURUICHI, Hiroshi KOBAYASHI,
 Daisuke SATO, Shang GAO, Sawako YOKOYAMA, Ai KOBAYASHI

Adjunct Assistant Professor (Dental Hospital):

Hisatomo KONDO, Toru KANAI

(1) Outline

Prosthetic treatment with dental implants (implant treatment) is extremely effective as a treatment method for edentulous patients and this treatment has been currently practiced widely. However, there are several problems that must be solved. Most of the staffs and students are treating patients with dental implants in Dental Implant Clinic, Dental Hospital. Dental Implant Clinic has been certified as a training facility of

the Japanese Society of Oral Implantology and the Japanese Academy of Oral-Maxillofacial Implants. Due to the wide spread of implant treatments, patients suffering problems after implant treatments are increasing. Furthermore, patients with some difficulties in dental implant treatments also visit the clinic. Under these circumstances, we are conducting researches on materials and methods related to implant treatment. We are also conducting researches of bone and soft tissue regenerations related to implant treatment. We are constantly aiming for the world's top runner in clinical treatments and researches.

(2) Research

Implant treatment is currently predictable and effective; however, there are several problems that must be solved. Continuing from the previous year, we conducted the following studies.

- (1) Relationship between implants and implant supporting tissues
- (2) Adjustment of the superstructure of the implant
- (3) Method of Inspection of Implant Surrounding Tissue
- (4) Prevention and treatment of peri-implant inflammation
- (5) Development of a biocompatible implant
- (6) Development of bone and soft tissue regeneration method
- (7) Differentiation of adipose tissue-derived stem cells

The results of these studies were presented in the academic meetings and scientific journals.

(3) Education

4th grade students of Dental School: Lectures and trainings.

6th grade students of Dental School: Trainings in the clinic.

3rd grade students of Oral Health Care Course: Lectures and trainings.

Students of Graduate School of Medical and Dental Sciences: Lectures and trainings 34 35 students of doctor course in the department: Guiding researches

22 graduate research students in the department: Guiding researches

(4) Lectures & Courses

Research is always ongoing rapidly. Thus, today's common sense is likely to become insane in the future. Contents in a textbook are not always right. It is important to always think flexibly.

(5) Clinical Services & Other Works

In Dental Implant Clinic, we treated many partially or fully edentulous patients with dental implants. If soft tissue management and/or bone augmentation procedures are required, we also perform these surgeries. Number of patients in Dental Implant Clinic is increasing every year and approximately 100 patients visited every day, which is extremely over our capacities. Approximately 1,700 implants were placed in 2017. Patients with some clinical problems, who are treated in other clinics, are increasing and this is a great concern. Such patients visited our clinic and we fixed most of the problems.

(6) Clinical Performances

We are safely providing implant treatments of highly functional and aesthetic level with long-term good prognosis. We are also conducting cutting-edge clinical researches of dental implant and regenerative dental medicine.

(7) Publications**[Original Articles]**

1. Nakata Hidemi, Yamamoto Maiko, Okada Emi, Nagayama Tomoko, Miyasaka Munemitsu, Kasugai Shohei, Kuroda Shinji. Osteogenic Potential of Adipose-Derived Macrospheroids Cocultured with CD11b+ Monocytes INTERNATIONAL JOURNAL OF ORAL & MAXILLOFACIAL IMPLANTS. 2017; 32(4); E231-E240
2. Kazuhiro Kon, Makoto Shiota, Aoi Sakuyama, Maho Ozeki, Wataru Kozuma, Sawako Kawakami, Shohei Kasugai. Evaluation of the Alteration of Occlusal Distribution in Unilateral Free-End and Intermediate Missing Cases. J Oral Implantol. 2017.02; 43(1); 3-7
3. Fuchigami K, Munakata M, Kitazume T, Tachikawa N, Kasugai S, Kuroda S.. A diversity of peri-implant mucosal thickness by site. Clinical Oral Implants Research. 2017.02; 28(2); 171-176
4. Ono M, Oshima M, Ogawa M, Sonoyama W, Hara ES, Oida Y, Shinkawa S, Nakajima R, Mine A, Hayano S, Fukumoto S, Kasugai S, Yamaguchi A, Tsuji T, Kuboki T.. Practical whole-tooth restoration utilizing autologous bioengineered tooth germ transplantation in a postnatal canine model. Scientific Report. 2017.03; 7; 445222
5. Maeda H, Kobayashi H, Miyahara T, Hashimoto Y, Akiyoshi K, Kasugai S. Effects of a polysaccharide nanogel-crosslinked membrane on wound healing. Journal of Biomedical Material Research B: Applied Biomaterials . 2017.04; 105(3); 544-550
6. Nakata H, Yamamoto M, Okada E, Nagayama T, Miyasaka M, Kasugai S, Kuroda S.. Osteogenic Potential of Adipose-Derived Macrospheroids Cocultured with CD11b+ Monocytes. International Journal of Oral Maxillofacial Implant. 2017.07; 26(2); 275-283
7. Yajima N, Munakata M, Fuchigami K, Sanda M, Kasugai S.. Influence of bisphosphonates on implant failure rates and characteristics of postmenopausal woman mandibular jawbone. Journal of Oral Implantology. 2017.09;
8. Kaboosaya Boosana, Wulansari Lia Kartika, Trang Nguyen V.N., Aoki Kazuhiro, Kasugai Shohei. Ligation Period Required to Induce Periodontitis in Mice: Analysis with Micro-computed Tomography Journal of Oral Tissue Engineering. 2017.09; 15(1); 25-33
9. Boosana KABOOSAYA, Lia Kartika WULANSARI, Trang Nguyen V.N., Kazuhiro AOKI, Shohei KASUGAI. Ligation Period Required to Induce Periodontitis in Mice: Analysis with Micro-computed Tomography Journal of Oral Tissue Engineering. 2017.10; 15(1); 25-34
10. Lin DING, Peng ZHANG, Xin WANG, Jia HAO, Kazuhiro AOKI, Shinji KURODA, Shohei KASUGAI. Effect of doxycycline-treated hydroxyapatite surface on bone apposition: A histomorphometric study in murine maxillae Dental Materials Journal. 2017.11;
11. Aierken MULATI, Songtao WU, Kazuhiro AOKI, Shohei KASUGAI. Effects of Osteotomy with Drilling on Osteocytes Journal of Oral Tissue Engineering. 2017.12; 15(2); 95-101
12. Shohei Kasugai. Inflammation and bone regeneration Journal of Bio-integration. 2017.12; 7(1); 1-6
13. Nakamura Shintaro, Kon Kazuhiro, Shiota Makoto, Kawakami Sawako, Sanda Minoru, Kasugai Shohei. Efficacy of Bone Regeneration using Micro-graft Suspension of Palatal Mucosa in Rats Journal of Oral Tissue Engineering. 2017.12; 15(2); 71-78
14. Ding Lin, Zhang Peng, Kasugai Shohei. Effect of doxycycline other than an antibiotic: Stimulating bone regeneration. Journal of Bio-Integration. 2017.12; 7(1); 105-108
15. Mulati Aierken, Wu Songtao, Aoki Kazuhiro, Kasugai Shohei. Effects of Osteotomy with Drilling on Osteocytes Journal of Oral Tissue Engineering. 2017.12; 15(2); 95-101
16. Kazuhiro Kon, Makoto Shiota, Maho Ozeki, Shohei Kasugai. The effect of graft bone particle size on bone augmentation in a rabbit cranial vertical augmentation model: a microcomputed tomography study. Int J Oral Maxillofac Implants. 29(2); 402-406

[Misc]

1. Ding L, Zhang P, Kasugai S. Effect of doxycycline other than an antibiotic: Stimulating bone regeneration Journal of Bio-integration. 2017.12; 7(1); 105-108

[Conference Activities & Talks]

1. KM. Thu, D. Sato, M. Kanazawa, M. Tanoue, K. Oda, Y. Kadiliya, A. Miyayasu, M. Asami, VL. Thuy, S. Minakuchi. Single Implant Retained Mandibular Overdenture [1-IOD] in Edentulous Patient with Massive Osteotomy; A Case Report. 37th Myanmar Dental Conference 2017.01.19 Yangon, Myanmar
2. Shinji Kuroda. Anatomy and Imaging, Diagnosis and Treatment Planning . Myanmar Dental Association Basic Dental Implant Training 2017.02.18 Myanmar
3. S. Kuroda, H. Nakata, S. Kasugai. Functional and Aesthetic Recovery with Implant-Supported Removable Overdentures and Difficulty of Implant-Supported Fixed Bridges to Multi-Tooth Defects of The Jaws. The Annual Meeting of the Academy of Osseointegration 2017.03.15 Orlando, FL, USA
4. H. Nakata, S. Kuroda, M. Yamamoto, E. Okada, S. Kasugai. Clinical Approach to Peri-implantitis – A Combination Therapy with Microbial Analysis and Bone Regeneration: A Case Series. The Annual Meeting of the Academy of Osseointegration 2017.03.15 Orlando, FL, USA
5. Kasugai S. Four keys in your daily dental practice and life. Continual Educational Course by Myanmar Dental Association 2017.03.25 Summit Parkview, Yangon, Myanmar
6. Kasugai S. History of dental implant treatment. Implant design and surface modification.. FINSIA. Kyocera Exclusive Implant Seminar 2017.05.17
7. Kasugai S. Dental Implant Treatment and Regenerative Medicine: New Direction of Regenerative Medicine. Lecture in Japan Institute of Advanced Dentistry 2017.06.11 Japan Institute of Advanced Dentistry, Tokyo
8. Iwaki Maiko, Kanazawa manabu, Miyayasu Anna, Sato Daisuke, Kasugai Shohei, Minakuchi Shunsuke. Prospective study of immediate Loaded two-implants mandibular overdentures: 5-years follow up. 2017.06.30 Yokohama
9. Yuriko Komagamine, Manabu Kanazawa, Anna Miyayasu, Vo Lam. Thuy, Yuri Omura, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi. Masticatory Performance with Magnet Retained Mandibular Two Implant Overdentures. 31st ISDR-SEA 2017.08.12 Taipei International Convention Center, Chinese Taipei
10. Suzuki A, Otomaru T, Nakata H, Kon K, Kasugai S, Kuroda S. Mode analysis of two different types of fixed implant supported prosthetic devices on maxillary edentulous jaw. 47th Meeting of Japanese Society of Oral Implantology 2017.09.02 Sendai International Center
11. M. Kanazawa, M. Iwaki, D. Sato, A. Miyayasu, M. Asami, R Shimada, KM Thu, VL Thuy, S. Kasugai, S. Minakuchi. Immediate Loading of two-implant mandibular overdentures: 5-year prospective study. 17th biennial meeting of the International College of Prosthodontists 2017.09.08 Santiago, Chile
12. Y. Komagamine, M. Kanazawa, D. Sato, A. Miyayasu, M. Asami, R Shimada, KM Thu, VL Thuy, S. Kasugai, S. Minakuchi. Comparison of patient-reported outcomes between immediately and conventionally loaded mandibular two-implant overdentures: A preliminary study. 17th biennial meeting of the International College of Prosthodontists 2017.09.08 Santiago, Chile
13. Kasugai S. Materials for bone augmentation: From autogenous bone to bone substitutes. 47th Meeting of Japanese Society of Oral Implantology 2017.09.17 Sendai International Center
14. Takahashi S, Shiota M, Kon K, Akino T, Imakita C, Tagonai D, Kawakami S, Kasugai S. Stability of paired teeth of implant superstructures in long-term cases. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22 Sendai International Center
15. Tanabe K, Shiota M, Kon K, Kohzuma W, Nakata H, Kuroda S, Tachikawa N, Kasugai S. Risk factors related to the survival of remaining natural teeth in long-term clinical cases of dental implant treatment. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22 Sentai International Center

16. Tagonai D, Imakita C, Shiota M, Watanabe T, Nakata H, Kuroda S, Tachikawa N, Kasugai S . Clinical statistical survey over the past 20 years in new patients to the dental implant clinic. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22 Sendai International Center
17. Nakamura S, Kawakami S, Sanda M, Kon K, Shiota M, Kasugai S. Efficacy of bone augmentation using micro-graft suspension of rat palatal mucosa. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22 Sendai International Center
18. Miyahara T, Ootsuki M, Nakai N, Wada M, Akino T, Fujii M, Suzuki A, Kon K, Kasugai S. Decision tree of the treatment of periimplantitis. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22
19. Nakata H, Kuroda S, Yamamoto M, Kobayashi A, Kobayashi H, Ohara S, Fujii M, Kasugai S. Three clinical cases evaluated by bacterial examination after bone grafting to treat peri-implantitis. 47th Meeting of Japanese Society of Oral Implantology 2017.09.22 Sendai International Center
20. Emi Okada, Hidemi Nakata, Maiko Yamamoto, Shohei Kasugai, Shinji Kuroda. Feasibility of indirect osteoblast differentiation by liposomal clodronate. ICMaSS 2017.09.30 NAGOYA UNIVERSITY
21. Kasugai S. Bone regeneration with healing potential of the tissue. 15th Meeting of Japanese Society of Oral Tissue Engineering 2017.10.21 Osaka Dental University
22. Kasugai S. Four keys required in dental implant treatment. Celebrating Party of the Incorporation of Bio-integration Society 2017.10.28
23. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Kuroda S, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Assessment of International dental education course for clinical expertise at TMDU graduate school. 82nd Annual Meeting of the Stomatological Society 2017.11.19 Tokyo
24. Kasugai S. Six keys for long term good prognosis in dental implant treatments. Bangkok Implant Symposium 2017 (BIS2017) 2017.12.07 Royal Paragon Hall, Bangkok, Thailand
25. Kasugai S. Bone resorption in dentistry. 2017.12.09 Seiryō-Kaikan, Tokyo
26. Kasugai S. Six keys for long-term good prognosis in dental implant treatment. Biointegration Society Workshop 2017.12.16 Hakone Yumoto Fujiya Hotel, Hakone, Japan

Plastic and Reconstructive Surgery

Professor: Mutsumi Okazaki

Junior Associate Professor: Hiroki Mori

Assistant Professor (Hospital Staff): Noriko Uemura

Project Assistant Professor (Hospital Staff) : Kentaro Tanaka

Graduate Student: Aki Takada, Takuya Higashino, Tsutomu Homma, Satoshi Usami,
Mayuko Hamanaga, Nobuko Suesada

(1) Research

Basic research

1. A mechanism and prophylaxis of the post-inflammatory pigmentation
2. A scarless wound healing
3. The blood circulation study of the flap using indocyanine green
4. Donor specificity on various flaps or full thickness skin

Clinical research

1. Sensory recovery and contour prediction in the breast reconstruction
2. The algorithmic development and the evaluation of various reconstructions in the skull base reconstruction
3. The development of reconstructive method after an oral cavity / pharyngeal cancer resection - Aiming at the functional preservation
4. The classification of the symptom and static and dynamic reconstruction of the facial paralysis
5. A classification and the algorithmic development in blepharoptosis surgery
6. The objective evaluation for the ischemic limb and therapeutic strategy utilizing wound healing mechanism
7. The prospective studies about the color reproducibility of the medical tattoo in the nipple areola reconstruction

(2) Education

Plastic surgery is a specialized branch of surgery concerned with the repair of deformities and the correction of functional deficits. The specialty of plastic surgery covers a wide range of procedures, and unlike other medical specialties which concentrate on one particular area of the body, plastic surgeons are involved in the reconstruction and remolding of nearly all external body structures.

(3) Clinical Performances

We cover the whole field of plastic surgery. In particular, we deal with the following field; congenital anomaly (cleft lip and palate, microtia blepharoptosis or polydactyly etc), LASERs, cutaneous malignant tumor, skin ulcer, breast reconstruction, head and neck reconstruction, facial palsy, axillary osmidrosis.

(4) Publications**[Original Articles]**

1. Yoko Maruyama, Keita Inoue, Keita Mori, Katsuya Gorai, Ryo Shimamoto, Tetsuro Onitsuka, Hiroyoshi Iguchi, Mutsumi Okazaki, Masahiro Nakagawa. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as predictors of wound healing failure in head and neck reconstruction. *Acta Otolaryngol.* 2017.01; 137(1); 106-110
2. Runa Mihara, Hiroki Mori, Mutsumi Okazaki. Nipple Reconstruction with Dorsal Skin Provides Better Projection than Reconstruction with Abdominal or Breast Skin with Cartilage Grafting. *Aesthetic Plast Surg.* 2017.02; 41(1); 31-35
3. Satoshi Usami, Mutsumi Okazaki. Fingertip reconstruction with a posterior interosseous artery perforator flap: A minimally invasive procedure for donor and recipient sites. *J Plast Reconstr Aesthet Surg.* 2017.02; 70(2); 166-172
4. Satoshi Usami, Mutsumi Okazaki, Tomohisa Nitta, Noriko Uemura, Tsutomu Homma, Keiichi Akita. Histological investigation of common insensate flaps obtained from the hand and forearm regions for use in fingertip reconstruction. *J Plast Surg Hand Surg.* 2017.06; 51(3); 182-186
5. Tsutomu Homma, Mutsumi Okazaki, Kentaro Tanaka, Noriko Uemura. Simultaneous Surgical Treatment for Smile Dysfunction and Lagophthalmos Involving a Dual Latissimus Dorsi Flap. *Plast Reconstr Surg Glob Open.* 2017.07; 5(7); e1370
6. Kohei Nojima, Takeshi Namiki, Takaaki Hanafusa, Masahiro Yamamoto, Keiko Miura, Kentaro Tanaka, Masaru Tanaka, Hiroo Yokozeki. A case of mucoepidermoid carcinoma presenting as a subcutaneous tumour of the cheek. *Eur J Dermatol.* 2017.08; 27(4); 403-405
7. Takeshi Namiki, Kohei Nojima, Takaaki Hanafusa, Hiroki Mori, Mutsumi Okazaki, Keiko Miura, Masaru Tanaka, Hiroo Yokozeki. A case of basal cell carcinoma with a neighbouring melanocytic nevus: dermoscopic features. *Eur J Dermatol.* 2017.08; 27(4); 441-442
8. Kentaro Tanaka, Kimihiro Igari, Mitsuhiro Kishino, Satoshi Usami, Tsutomu Homma, Takahiro Toyofuku, Yoshinori Inoue, Mutsumi Okazaki. The possibility of free tissue transfer as a nutrient flap for critical ischemic foot: A case report. *Microsurgery.* 2017.09; 37(6); 694-698

[Conference Activities & Talks]

1. Usami S, Inami K. Fingertip reconstruction using posterior interosseous artery perforator flap. 9th Congress of World Society for Reconstructive Microsurgery-WSRM2017 2017.06.14 Seoul Korea
2. Tanaka Ken, Okazaki M. The Role of Microsurgery in the face of Peripheral Vascular Disease in the Diabetic Foot. 9th Congress of World Society for Reconstructive Microsurgery 2017.06.15 Seoul Korea

Head and Neck Surgery

Professor: Takahiro Asakage
Project professor: Seiji Kishimoto
Junior associate professor: Yosuke Ariizumi
Assistant professor: Yusuke Kiyokawa, Fuminori Nomura
Senior Resident: Akihisa Tasaki, Ryuhei Okada, Hiroaki Kawabe
Student: Hirofumi Fukushima, Takao Tokumaru, Masaharu Kishikawa

(1) Outline

Our department is responsible for clinical management, education and research in the field of head and neck surgery. Clinically, the Department of Head and Neck Surgery manages the tumor of extensive area of head and neck, except brain, eye and vertebra. Surgical and medical treatment of the head and neck tumors are mainly employed in our department.

(2) Research

Surgical approaches to the skull base and deep area of the face.
Surgical anatomy of the skull base.
Establishment of the standard neck dissection.
Treatment of pediatric head and neck tumors.
Chemoradiotherapy for head and neck cancers.
Clinical application of navigation system and 3D entity model surgery for skull base surgery.
Diagnosis and treatment for superficial squamous cell carcinoma of head and neck region.
Human papilloma virus infection and head and neck cancer.
Polymorphisms in alcohol metabolism genes and Head and Neck Cancers.

(3) Education

Education: Undergraduate Course

In the classes at the 3th grade of medical school, head and neck oncology are systematically lectured. Clinical practice is experienced at the 4th to 6th grade in the out-patient clinic, the ward, and operating theater.

Education :Graduate Course

Education and researches at the graduate school are focused on (1)surgery of the head and neck tumor, (2)clinical management of the patients with head and neck tumor, and (3)clinical anatomy of head and neck region.

(4) Publications**[Original Articles]**

1. Kenro Kawada, Tatsuyuki Kawano, Taro Sugimoto, Kazuya Yamaguchi, Yuudai Kawamura, Toshihiro Matsui, Masafumi Okuda, Taichi Ogo, Yuuichiro Kume, Yutaka Nakajima, Andres Mora, Takuya Okada, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Ryuhei Okada, Yusuke Kiyokawa, Fuminori Nomura, Takahiro Asakage, Ryo Shimoda, Takashi Ito. Case of Superficial Cancer Located at the Pharyngo-esophageal Junction Which Was Dissected by Endoscopic Laryngopharyngeal Surgery Combined with Endoscopic Submucosal Dissection. *Case Rep Otolaryngol.* 2017.01; 2017; 1341059
2. Hamahata A, Beppu T, Tokumaru ,et al. A Comparison of Large Soft Palate Defect Reconstruction Using the New "Tunnel Structure" and Traditional "Port Structure" Methods. *J Reconstr Microsurg.* 2017.01; 33(1); 70-76
3. Shinozaki T, Ebihara ,Beppu T,et al. Quality of life and functional status of terminally ill head and neck cancer patients: a nation-wide, prospective observational study at tertiary cancer centers in Japan. *Jpn J Clin Oncol.* . 2017.01; 47(1); 47-53
4. kawada k, Kawano T, Sugimoto T, Yamaguchi K,Kawamura Y, Matsui T, Okuda M, Ogo T,Kume Y, Nakajima Y, Andres Mora, Okada T,Hoshino A, Tokairin Y,Nakajima Y,Okada R,Kiyokawa Y,Nomura F,Asakage T,Shimoda R,Ito T. Case of Superficial Cancer Located at the Pharyngo-esophageal Junction Which Was Dissected by Endoscopic Laryngopharyngeal Surgery Combined with Endoscopic Submucosal Dissection. *Case Rep Otolaryngol.* 2017.01;
5. Watanabe Tatsuo, Kurata Takashi, Sano Kenji, Suzuki Shigeru, Kaneko Tomoki, Motobayashi Mitsuo, Shigemura Tomonari, Sumi Takuro, Koike Kenichi, Nakazawa Yozo. Dramatic Reduction in Tumor Size During 5 Months of Pazopanib Therapy in Combination With Ifosfamide, Carboplatin, and Etoposide in an Early Infant With Progressive Soft Tissue Sarcoma. *J Pediatr Hematol Oncol.* 2017.03; 39(2); 154-156
6. Yu Ohkubo, Yoshihiro Saito,Takeshi Beppu,et al. The Treatment results of definitive radiotherapy for cervical esophageal cancer: a single-institution experience *Esophagus* . 2017.05; 14; 254-261
7. Okada R, Muro S, Eguchi K, Yagi K, Nasu H, Yamaguchi K, Miwa K, Akita K . The extended bundle of the tensor veli palatini: Anatomic consideration of the dilating mechanism of the Eustachian tube. *Auris Nasus Larynx.* 2017.06;
8. Kawada K, Kawano T, Okada T, Yamaguchi K,Kawamura Y, Matsui T,Okuda M,Ogo T,Kume Y,Nakajima Y,Andres Mora,Hoshino A, Tokairin Y, Nakajima Y,Okada R,Kiyokawa Y,Nomura F,Ariizumi Y,Sugimoto T,Asakage T,Ito T. The usefulness of intra-oropharyngeal U-turm method using trans-nasal endoscopy for detecting superficial squamous cell carcinoma of the base of the tongue *J Otolaryngol ENT Res.* 2017.08; 8; 240
9. Yuki Nakajima,Takeshi Beppu,et al. Surgical Treatment for Pulmonary Metastasis of Head and Neck Cancer: Study of 58 Cases *Ana Thorac Cardiovasc Surg.* 2017.12;
10. Masahiro Kishikawa, Atsunobu Tsunoda, Yoji Tanaka, Seiji Kishimoto. Large nasopharyngeal inverted papilloma presenting with rustling tinnitus. *Am J Otolaryngol.* 35(3); 402-404

[Conference Activities & Talks]

1. Ichikura K, Yamashita A, Matsuoka S, Nakayama N, Ariizumi Y, Sumi . Stress coping skill training for patients with head and neck cancer: Interim report of a randomized controlled trial. 19th World Congress of Psycho-Oncology and Psychosocial Academy 2017.08.11 Berlin
2. Ichikura Kanako, Yamashita Aya, Matsuoka Shiho, Nakayama Nao, Ariizumi Yousuke, Sumi Takuro, Sugimoto Taro, Asakage Takahiro, Matsushima Eisuke. Stress coping skill training for patients with head and neck cancer: Interim report of a randomized controlled trial. 19th World Congress of Psycho-Oncology and Psychosocial Academy 2017.08.18 Berlin, Germany
3. Asakage T. Chairman Oral Presentation 16.Central Neck Dissection 1. 2nd Asia-Pacific Society of Thyroid Surgery Okinawa 2017.11.01 Okinawa
4. Ryuhei Okada, Masaru Yokomura, Keiji Oi, Yosuke Ariizumi, Yusuke Kiyokawa, Fuminori Nomura, Akihisa Tasaki, Yumiko Tateishi, Susumu Kirimura, Takahiro Asakage. Medullary thyroid carcinoma detected based on elevated serum procalcitonin levels: A case report. 2nd Congress of Asia-Pacific Society of Thyroid Surgery 2017.11.02

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura

Lecturers Kazuma Toda

Research Associates Keiko Nakagawa, Mio Kojima

Hospital Staff members Takuya Nagano(~ Mar.), Ryoko Suzuki(Nov. ~),

(1) Outline

At the Department of Radiation Therapeutics and Oncology, clinical services, research, and education related to radiotherapy for all cancers are undertaken.

(2) Research

Mainly clinical research related to radiotherapy is performed.

(3) Education

Lectures are given to medical students or graduate students, and clinical clerkship is organized. After the students enter our department, comprehensive training is provided at both our department and the Department of Diagnostic Radiology and Nuclear Medicine for 3 years, since the certified radiologist exam is common.

Our department holds a radiation oncology seminar for students and residents with the Department of Radiation Oncology of Juntendo University and Showa University.

Lectures for medical students or graduate students, and clinical clerkship are performed.

(4) Lectures & Courses

Our department teaches students and residents about cancer therapy from the radiation oncologist's perspective.

Every student/resident of this department aims to be a certified radiation oncologist.

(5) Clinical Services & Other Works

All the staff members are engaged in performing external beam radiation therapy or high-dose-rate or low-dose-rate brachytherapy in the hospital.

A total of 596 patients, including 132 head and neck cancer patients, 126 urological cancer patients, 90 breast cancer patients, 64 lung cancer patients, and 53 esophageal cancer patients, were treated by external beam radiotherapy at our hospital in 2015. Moreover, high-dose-rate brachytherapy was performed in 51 patients with uterine cancer, and low-dose-rate brachytherapy in 58 patients with oral cancer, and in 19 patients with prostate cancer.

(6) Clinical Performances

Our department specializes in low-dose-rate brachytherapy for oral cancer patients.

(7) Publications**[Original Articles]**

1. Ozaki Y, Watanabe H, Kaida A, Miura M, Nakagawa K, Toda K, Yoshimura R, Sumi Y, Kurabayashi T. Estimation of whole-body radiation exposure from brachytherapy for oral cancer using Monte Carlo simulation. *Journal of Radiation Research*. 2017.02; 58(4); 523-528
2. Sato M, Saitoh Y, Takayama T, Omata T, Watanabe H, Yoshimura R, Miura M. Remote radioactive seed-loading device for permanent brachytherapy of oral cancer with Au-198 grains. *Robomech Journal*. 2017.09; 4; 23
3. Atsushi Kaida, Hiroshi Watanabe, Kazuma Toda, Keiko Yuasa-Nakagawa, Ryoichi Yoshimura, Masahiko Miura. Effects of dose rate on early and late complications in low dose rate brachytherapy for mobile tongue carcinoma using Ir-192 sources. *Oral Radiol*. 2017.09; 33(3); 187-192

[Conference Activities & Talks]

1. Kazuma Toda, Akira Toriihara, Keiko Nakagawa, Mio Kojima, Takuya Nagano, Ukihide Tateishi, Ryoichi Yoshimura. Time Dependency of Volume-Based Metabolic Parameters Obtained by Dual-Time-Point TOF-PET/CT for Head and Neck Squamous Cell Cancer. ASTRO 59th annual meeting 2017.09.26 San Diego
2. Kazuma Toda, Ryo-ichi Yoshimura, Mio Kojima, Keiko Nakagawa, Ryouko Suzuki. Changes of Volume-Based Metabolic Parameters in PET/CT of Head and Neck Cancer. The 30th annual meeting of Japanese Society for Radiation Oncology 2017.11.18

Maxillofacial Anatomy

Professor	Shunichi SHIBATA
Assistant Professor	Shun-ichi SHIKANO
Graduate Student	Masato Takahashi
Graduate Student	Maki Hasegawa
Graduate Student	Shota Kusaka
Lecturer	Rei Sato
PD	Chiho Watanabe

(1) Outline

Maxillofacial anatomy section is engaged in lecture and practical course of gross anatomy and dental anatomy in undergraduate school. In graduate school, this section is engaged in morphological studies of hard tissues such as tooth, bone and cartilage.

(2) Research

Research Subjects

- 1) Structural features of mandibular condylar cartilage.
- 2) Mechanism of epithelial attachment of junctional epithelium in human gingiva.
- 3) Comparative histology and embryology of teeth.
- 4) Observation on the structural features of oral mucous
- 5) Anatomical names of the structures of human skeletal system.
- 6) Hyaluronan synthesis in tooth germ.
- 7) Studies on regeneration of jaw bone.
- 8) Structural features of dental pulp and extracellular matrix

(3) Education

In Undergraduate school

Lecture for 2nd degree students: Human structure I, II, Dental anatomy, Neuroanatomy,
Practical course for 2nd degree students: Gross Anatomy, Neuroanatomy, Dental Anatomy
Lecture and practical course for 5th degree students: Clinical craniofacial anatomy

In Graduate school

Lecture, seminar and practical course to understand the function of various oral organs in a morphological viewpoint, and to evaluate various vital phenomenon encountered in medical practice.

(4) Lectures & Courses

The main purpose of education in undergraduate school is to understand human structure and function from the viewpoints of gross anatomy. In line with this purpose, we execute lectures of systematic anatomy (osteology, myology, neurology, angiology, splanchnology) and topographic anatomy (craniofacial anatomy). To understand three-dimensional structures of human body, we execute practical course of human gross anatomy

after completing lectures. In the practical course, we make an effort to make students understand ethics as dental students to be bright future dentist.

The main purpose of education in graduate school is to understand various vital phenomenon, which we encounter in research fields of basic and clinical sciences, from the viewpoints of morphology. In lectures, we teach various techniques to investigate structural features from the standpoints of light and electron microscopy, organ and tissue culture, and molecular biology.

(5) Publications

[Original Articles]

1. Kim JH, Jin ZW, Shibata S, Murakami G, Rodriguez-Vazquez JF, Cho BH. Fetal development of human oral epithelial pearls with special reference to their stage-dependent changes in distribution *Cleft Palate and Craniofacial Journal*. 2017.05; 54(3); 295-303
2. Shibata S, Jin ZW, Jin Y, Zhao P, Murakami G. Immunohistochemistry for matrix proteins in newly formed mandibular condylar cartilage in a human fetus *Anatomy & Physiology*. 2017.07; 7(3); 262
3. Obara N, Suzuki Y, Irie K, Shibata S. Expression of planar cell polarity genes during mouse tooth development *Archives of rap Biology*. 2017.11; 83; 85-91

[Books etc]

1. Dental Outlook Special Issue 2017 New Paradigm for Dental Medicine Its Future and Our Dreams The 23rd General Meeting of the Japanese Association for Dental Science. Ishiyaku Publishers, Inc., 2017.05

[Misc]

1. Shunichi SHibata. Anatomy of teeth, jaw bone and oral cavity 2017.07; 37(7); 626-639

[Conference Activities & Talks]

1. Shibata S. Structural features of tooth germ after accelerate mineralization in organ culture system . 2017 International Frontier meeting of Craniofacial and Oral Science 2017.02.11 Japan Women' s University, Tokyo Japan
2. High-Frequency Pulsed Low-Level Diode Laser Therapy Accelerates Wound Healing of Tooth Extraction Socket. High-Frequency Pulsed Low-Level Diode Laser Therapy Accelerates Wound Healing of Tooth Extraction Socket. The 95th General Session & Exhibition of the IADR 2017.03.25 SAN FRANCISCO, CALIF, USA
3. Shibata S. Structural features of developing mandibular condylar cartilage. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.16
4. Takahashi M, Kusaka S, Shibata S. Expression of MMPs and TIMPs in the developing condylar cartilage of fetal mouse mandible.. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17
5. Shibata S, Takahashi M, Kusaka S, Fujikawa K. Spacial relationship between poster part of Meckel's cartilage and genial bone in postnatal mice. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17
6. Teramoto A, Akiyama A, Yakahashi Y, Kadota-Watanabe C, Ito Y, Higashihori N, Suzuki S, Ohbayashi N, Kurabayashi T, Moriyama K. Study on the morphological correlations between tongue and oral cavity by using silicon impression method. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
7. Higashihori N, Hikita R, Kadota-Watanabe C, Akiyama S, Takahashi Y, Ito Y, Moriyama K. Variations of respiratory function for mandibular prognathism patients treated by surgical orthodontics: comparison between subjective/objective evaluations. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido

8. Takahashi Y, Higashihori N, Funahashi K, Matsumura K, Ito Y, Uezono M, Kadota-Watanabe C, Hikita R, Suzuki S, Moriyama K. Analysis of perioral soft tissue movements during speech in skeletal Class II facial deformity patients. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
9. Shibata S, Takahashi M, Fujikawa K. Gonial bone development with reference to reduction of Meckel's cartilage. JADR 65th annual meeting 2017.11.19 Showa University, Tokyo
10. Fujikawa K, Nakamura M, Shibata S. Expression patterns of Syndecan family in the developing fetal mouse mandibular condylar cartilage. JADR 65th annual meeting 2017.11.19 Showa University, Tokyo
11. Wu Y Y, Kadota-Watanabe C, Ogawa T, Moriyama K. Establishment of a Novel Murine Model of Temporomandibular Joint Osteoarthritis. The 30th Taiwan Association of Orthodontists Annual Meeting 2017.12.09 Kaohsiung, Taiwan

Cognitive Neurobiology

Professor: Masato Taira
Assistant Professor: Narumi Katsuyama
Assistant Professor: Nobuo Usui
Staff Assistant: Takako Kishida
JSPS Research Fellow: Rui Watanabe
Graduate Student:
Eriko Kikuchi(Tachi)
Yuko Imai
Yoko Kono
Kazuya Watanabe
Maki Okada
Hiroaki Tanaka
Takuaki Tani
Research Student:
Yuri Kim
Hitoshi Nanjo
Adjunct Lecturer:
Hisayuki Ojima
Akiko Yamashita
Saneyuki Mizutani

(1) Outline

Higher brain functions have been studied in this laboratory. To explore the individual functions listed below, functional MRI, psychological or psychophysical approach, and traditional electrophysiological recordings together with animal training are applied to animal models such as non-human primates and rodents as well as to human. Our goal is to clarify how perceptual mechanisms underlying higher brain functions are described by the neuronal activity pattern and how cortical wide connectivity is interacted while brain is judging, decision making, extracting biological meanings of sounds including languages.

(2) Research

1. Neural Mechanisms of control of motor behavior.

Research is aimed at understanding the brain mechanisms of execution and control of the motion and behavior of animals and human.

2. Neuronal mechanisms for perception and cognition.

Research is aimed at understanding the brain mechanisms of perception and cognition of objects through vision and tactile senses of animals and human.

3. Processing of natural sounds in auditory cortex

Research is aimed at understanding the brain mechanisms of hearing and vocalization of animals.

(3) Education

1. Lectures of unit "Functions of Nervous Systems I (Introduction to Neurophysiology, Motor Functions)"
Basic knowledge of neurophysiology will be lectured as an introduction together with the motor functions.
2. Lectures of unit "Functions of Nervous Systems II (Perception, Emotion, Instinct, Sleep, Higher functions)".
A series of lectures will be taught on functions of the sensation, perception, and motion as well as the neural mechanisms of higher brain functions.
3. Lectures of unit "Homeostatic Functions for Life Support".
Lectures will be taught on the structure of the autonomic nervous system and its regulatory mechanisms in the circulation, respiration, digestion/absorption, humor/body temperature, metabolism, excretion, and internal secretion/reproduction.
4. Lectures of unit "Oral Physiology"
Lectures will be taught on the structure and function of various somatosensory organs in the oral cavity. Neural regulations of mastication and deglutition as well as the secretion mechanism of saliva will also be learned.
5. Unit of "Practice of Physiology"
The purpose of the practice is to learn about the physiological mechanisms underlying the normal functions of human body through experiments. The goal is to master the basic experimental procedures, and to experience how to capture and analyze the data in order to draw conclusions.

(4) Lectures & Courses

Students are expected to be voluntarily involved in research activity. Brain is an extremely complicated organ in terms of its morphology and functions. Learning of textbook knowledge is mandatory and is followed by capturing up-to-date scientific information through reading published articles. Once the overview of the field in which graduates/undergraduate students are interested in is completed, they will start to be engaged in on-going research topics under the tutelage of laboratory staff. Through this process, students are encouraged to associate their own research interests with the on-going research topics and will learn practically how data can be captured, rearranged and analyzed through real experiments.

(5) Publications

[Original Articles]

1. Akiko Kamada, Nobuo Usui, Daisuke Yoshino. Relation between impression evaluation and choice behavior for merchandise (2) : An examination of the mere exposure effect. *Bulletin of Human Science*. 2017.03; (38); 121-127
2. M Kubota, S Sugimoto, Y Hosokawa, H Ojima, J Horikawa. Auditory-visual integration in fields of the auditory cortex. *Hear. Res.* 2017.03; 346; 25-33
3. Yamamoto K, Tabei K, Katsuyama N, Taira M, Kitamura K. Brain activity in patients with unilateral sensorineural hearing loss during auditory perception in noisy environments. *Journal of Medical and Dental Sciences*. 2017.03; 64(1); 19-26
4. J Horikawa, H Ojima. Cortical Activation Patterns Evoked by Temporally Asymmetric Sounds and Their Modulation by Learning. *eNeuro*. 2017.05; 4(2);
5. Michiue T, Yamamoto T, Yasuoka Y, Goto T, Ikeda T, Nagura K, Nakayama T, Taira M, Kinoshita T. High variability of expression profiles of homeologous genes for Wnt, Hh, Notch, and Hippo signaling pathways in *Xenopus laevis*. *Dev Biol.* 2017.06; 426(2); 270-290
6. Nguyen Ho Quynh Anh, Yamazaki Yoko, Yoshino Norio, Taira Masato, Kurabayashi Tohru, Shimada Masahiko. Altered Grey Matter Volume in Trigeminal Neuralgia *The Journal of the Stomatological Society* . 2017.07; 84(2); 73-83
7. Y Inamochi, K Fueki, N Usui, M Taira, N Wakabayashi. Adaptive change in chewing-related brain activity while wearing a palatal plate: an functional magnetic resonance imaging study. *J Oral Rehabil*. 2017.10; 44(10); 770-778

8. Rui Watanabe, Takahiro Higuchi, Yoshiaki Kikuchi, Masato Taira. Visuomotor effects of body part movements presented in the first-person perspective on imitative behavior. *Hum Brain Mapp.* 2017.12; 38(12); 6218-6229

[Misc]

1. Taira M. Interface between brain and outside. *BRAIN and NERVE.* 2017.04; 69(4); 339-345

[Conference Activities & Talks]

1. Inamochi Y, Fueki K, Usui N, Wakabayashi N. Adaptive change of oral function and brain activation in chewing with wearing palatal plate: An fMRI study. The 126 Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama, Kanagawa, Japan
2. Juri Fujiwara, Philippe Tobler, Ken-Ichiro Tsutsui, Masato Taira, Yoshikazu Ugawa, Satoshi Eifuku. Neural mechanisms underlying self-consistency in social behavior. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.20 Chiba, Chiba
3. Kamada A, Usui N, Yoshino D. An examination of disappearance of the mere exposure effect by using Go/No-go task. The 81st Annual Convention of the Japanese Psychological Association 2017.09.22 Kurume, Fukuoka
4. Ikeda A, Miyamoto J, Usui N, Taira M, Moriyama K. Effect of chewing on appetite regulation system:A cognitive psychological study using visual food stimuli. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo, Hokkaido
5. Juri Fujiwara, Philippe N. Tobler, Ken-Ichiro Tsutsui, Masato Taira, Yoshikazu Ugawa, Satoshi Eifuku. Neural mechanisms underlying self-consistency in social behavior. Society for Neuroscience 2017 Annual Meeting 2017.11.12 Washington, DC, USA

Molecular Craniofacial Embryology

Staffs and Students

Professor

Sachiko ISEKI

Associate Professor

Masa-Aki IKEDA

Tenure Track Assistant Professor

Masaki TAKECHI

Part-time lecturers

Shumpei YAMADA

Youichirou NINOMIYA

Visiting Researcher

Toshiko FURUTERA

Graduate Students

CHAROENLARP Ponkawee

MYA Nandar

Norisuke YOKOYAMA

Erika KUBOTA (Pedodontics)

XIAOHUI Tian (Oral Implantology and Regenerative

Dental Medicine)

RAJENDRAN Arun kumar

Takahiko YAMADA (Maxillofacial Surgery)

VU HOANG Tri

Manami TAKENOSHITA (Pedodontics)

Rika TAKEUCHI (Jikei Medical University)

NAMANGKALAKUL Worachat (10月-)

(1) Research

- 1) Molecular mechanisms of mammalian craniofacial development
- 2) Application of developmental mechanisms to regenerative medicine
- 3) Identification of tissue stem cells in craniofacial region and molecular mechanism of the mechanism of their stemness
- 4) Regulation of gene expression in cell growth and differentiation
- 5) Modulating endochondral ossification of mesenchymal stem cells for bone regeneration

(2) Publications

[Original Articles]

1. Amin M.B., Miura M. Uddin M.K., Islam M.J., Yoshida N., Iseki S., Kume T. Trainor P.A., Saitsu H. Kazushi Aoto.. Foxc2CreERT2 knock-in mice mark stage-specific Foxc2-expressing cells during mouse organogenesis. *Congenital Anomalies*. 2017.01; 57(1); 24-31
2. Kriangkrai R., Chareonvit S., Iseki S., Limwong V.. Pretreatment Effect of Folic Acid on 13-Cis-RA-Induced Cellular Damage of Developing Midfacial Processes in Cultured Rat Embryos. *The Open Dentistry Journal* . 2017.03; 11; 200-221
3. Nobuo Tsuchida, Masa-Aki Ikeda, T oshizumu I shino, Michele Grieco, Giancarlo Vecchio. FUCA1 is induced by wild-type p53 and expressed at different levels in thyroid cancers depending on p53 status. *Int. J. Oncol.*. 2017.06; 50(6); 2043-2048

4. Furutera, T., Takechi, M. (Co-first, Corresponding author), Kitazawa, T., Takei, J., Yamada, T., Vu Hoang, T., Rijli, F. M., Kurihara, H., Kuratani, S., Iseki, S.. Differing contributions of the first and second pharyngeal arches to tympanic membrane formation in the mouse and chick. *Development*. 2017.09; 144(18); 3315-3324
5. Sivashanmugam A, Charoenlarp P, Deepthi S, Rajendran A, Nair SV, Iseki S, Jayakumar R.. Injectable Shear-Thinning CaSO₄/FGF-18-Incorporated Chitin-PLGA Hydrogel Enhances Bone Regeneration in Mice Cranial Bone Defect Model. *ACS Appl Mater Interfaces*. *ACS Applied Materials & Interfaces*. 2017.12; 9(49); 42639-42652

[Misc]

1. Charoenlarp P., Arun Kumar R., Iseki S.. Role of Fibroblast Growth Factors in bone regeneration. *Inflammation and Regeneration*. 2017.08; 37; 10

[Conference Activities & Talks]

1. Rajendran AK, Arisaka Y, Yui N, Iseki S.. Regulation of Osteogenic Differentiation by Utilizing Supramolecular Mobility of Polyrotaxanes for the Treatment of Craniosynostosis.. The 13th Craniosynostosis meeting 2017.07.08 Ishikawa Ongakudo
2. Charoenlarp P, Fujihara R, Rajendran AK, Nakahama K, Sasaki Y, Akiyoshi K, Iseki S. The effects of RGD modification of porous NanoClik hybrid gel carrier for growth factors on healing of calvarial bone defect.. The 38th Annual Meeting of the Japanese Society of Inflammation and Regeneration 2017.07.18 Osaka International Convention Center
3. Mya N, Takechi M, Okuhara S, Furutera T, Kume T, Iseki S. Understanding the role of Foxc1 transcription factor in the development of cranial base.. The 57th Annual Meeting of the Japanese Teratology Society 2017.08.26 Faculty of Science and Engineering, Waseda University
4. ZHAO L, KEO P, MATSUMOTO Y, ISEKI S, ONO T. Effects of orthodontic force on root development in rats. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
5. Yokoyama N, Takechi M, Iseki S. Expression analysis of typeX collagen in osteoblasts of mouse and chick fetuses. ConBio2017 2017.12.06 Kobe Convention Center

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama
Assistant Professor Yasuhiro Yoshimatsu
Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masao Saito

Research Student : Hong Ding Liu
: Syun Nishihara
: Hiroki Kuwahara
: Syuhei Fukuda
: Hirohito Miki

(1) Outline

In our Lab, we study the role of cell-communication in bone remodeling, cancer and vascular calcification using various techniques, for example, cell culture, molecular biology and mutant mice.

(2) Research

Research Subjects

- 1, Cell-cell communication and cell functions
- 2, Bone remodeling and cell communications
- 3, Cancer and cell communications
- 4, Mechanism of vascular calcification

(3) Education

For undergraduate students. We have some class in biological chemistry for the second grader.

For graduate students. These students can choose the one of themes in our lab. They have to attend meetings and seminars in our Lab.

(4) Lectures & Courses

Undergraduate students should understand basic biochemistry and physiology under healthy/diseased conditions.

Graduate students are expected to solve the problems by themselves. However, appropriate suggestions will be given by at least three supervisors whenever you want.

(5) Publications**[Original Articles]**

1. Yuichi Akatsu, Yasuhiro Yoshimatsu, Taishi Tomizawa, Kazuki Takahashi, Akihiro Katsura, Kohei Miyazono, Tetsuro Watabe. Dual targeting of vascular endothelial growth factor and bone morphogenetic protein-9/10 impairs tumor growth through inhibition of angiogenesis. *Cancer Sci.* 2017.01; 108(1); 151-155
2. Rie Norita, Yasuhiro Suzuki, Yutaka Furutani, Kazuki Takahashi, Yasuhiro Yoshimatsu, Katarzyna A Podyma-Inoue, Tetsuro Watabe, Yasufumi Sato. Vasohibin-2 is required for epithelial-mesenchymal transition of ovarian cancer cells by modulating transforming growth factor- β signaling. *Cancer Sci.* 2017.03; 108(3); 419-426
3. Kosei Shinohara, Takeshi Yoshida, Hongding Liu, Shizuko Ichinose, Tomoka Ishida, Ken-Ichi Nakahama, Natsuko Nagaoka, Muka Moriyama, Ikuo Morita, Kyoko Ohno-Matsui. Establishment of novel therapy to reduce progression of myopia in rats with experimental myopia by fibroblast transplantation on sclera. *J Tissue Eng Regen Med.* 2017.04;
4. Tsuyoshi Matsuura, Shizuko Ichinose, Masako Akiyama, Yuki Kasahara, Noriko Tachikawa, Ken-Ichi Nakahama. Involvement of CX3CL1 in the Migration of Osteoclast Precursors Across Osteoblast Layer Stimulated by Interleukin-1 β . *J. Cell. Physiol.* 2017.07; 232(7); 1739-1745
5. Ishida T, Yoshida T, Shinohara K1, Cao K, Nakahama K, Morita I, Ohno-Matsui K. Potential role of sirtuin 1 in Müller glial cells in mice choroidal neovascularization *PLoS One.* 2017.09; 12(9);
6. Takahiro Sato, Masako Akiyama, Ken-Ichi Nakahama, Shujiro Seo, Masamichi Watanabe, Jin Tatsuzaki, Ikuo Morita. A novel mode of stimulating platelet formation activity in megakaryocytes with peanut skin extract. *J Nat Med.* 2017.10;
7. Syun Nishihara, Mami Ikeda, Hitoshi Ozawa, Masako Akiyama, Satoshi Yamaguchi, Ken-Ichi Nakahama. Role of cAMP in phenotypic changes of osteoblasts. *Biochem. Biophys. Res. Commun.* 2017.11;

[Misc]

1. Yasuhiro Yoshimatsu. Molecular mechanisms governing the formation and maintenance of lymphatic vessels and lymph nodes *Experimental Medicine.* 2017.01; 387-396

[Conference Activities & Talks]

1. Yasuhiro Yoshimatsu. Transcription Factors and Signals that Regulate Lymphatic Vessel Formation. 2017.02.16 Sapporo
2. Katarzyna Anna Inoue, Kazuki Takahashi, Takumi Matsuda, Chihiro Takao, Yasuhiro Yoshimatsu and Tetsuro Watabe. Role of TGF- β in the invasiveness of oral carcinoma cells. Joint Symposium of Immunology and Pathological Biochemistry Units 2017.03.08 Tokyo
3. Yasuhiro Yoshimatsu. The role of a network of signaling cascades and transcription factors in the maintenance of endothelial identity. Joint Symposium of Immunology and Pathological Biochemistry Units at TMDU 2017.03.08 Bukyo-ku, Tokyo
4. Yasuhiro Yoshimatsu. Molecular mechanisms by which platelet-derived growth factor signals regulate lymphatic vessel formation. The 41st Annual Meeting of The Japanese Society of Lymphology 2017.06.02 Kagoshima, Kagoshima
5. Yasuhiro Yoshimatsu. ELK3 is a functional regulator of Prox1 in lymphatic endothelial cells. Lymphatic Forum 2017 2017.06.08 The Thorne Auditorium, Northwestern University, Chicago
6. Katarzyna A. Inoue, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura and Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. FASEB Conference "TGF-B Superfamily: Signaling in Development and Disease" 2017.07.10

7. Yasuhiro Yoshimatsu. The role of a network of signaling cascades and transcription factors in endothelial homeostatic maintenance. The 5th Matsumoto Lymphology Conference 2017.08.19
8. Katarzyna A. Inoue, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Miki Yokoyama and Tet-suro Watabe. Exosomes secreted by oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. ConBio2017 2017.12.06 Kobe, Japan
9. Syun Nishihara, Mami Ikeda, Hitoshi Ozawa. Masako Akiyama, Satoshi Yamaguchi, Ken-ichi Nakahama . Role of cAMP in phenotypic changes of osteoblasts. ConBio2017 2017.12.06 Kobe Port island
10. Asuka OKITO, Masako Akiyama, Jun HOSOMICHI, Takashi ONO, Ken-ichi NAKAHAMA. Mechanism for transcriptional regulation of osteopontin in osteoblasts. ConBio2017 2017.12.07 Kobe Port island

Biodesign

Professor Kazuo TAKAKUDA
Assistant Professor Hisashi DOI
Mari YUASA
Research Assistants Shukan OKANO
Hiroyuki MASUNO
Noriko NAKAISHI
Graduate Students (Doctoral coarse)
Hiroki IKEDA, Hiroyuki KUSABA,
Hisaya NOMATA, Eiko MARUKAWA

(1) Outline

Biodesign division started in 1951 at establishment of the dental materials research institute as one of the constituting department. Since then, the division changed its name from the department of machinery, the department of precision machinery, the division of mechanics, and the division of biodesign as the institute continued reorganization till the present form of the Institute of Biomaterials and Bioengineering. Although our research work was originally concentrated to cutting tool for dentistry, we are now investigating mechanics of living tissues and biomaterials, biomechanical compatibility of tissues and artificial materials, and the development of artificial organs bearing the mechanical functions in living bodies.

(2) Education

Basic-Clinical Borderless Education

Maxillofacial Surgery

Junior Associate Professor: Satoshi YAMAGUCHI

Assistant Professor: Hiroyuki YOSHITAKE, Yasuyuki MICHI, Kouichi NAKAKUKI, Keiiti MORITA

Hospital Staff: Kunihiro MYO, Nobuyoshi TOMOMATSU, Tomomi SAKUMA, Ryouyusuke NAGAOKA, Jun SUMINO, Chika MIURA, Madhiko KOSUGI, (from April) Tomoki KANEMARU, Mari SIBATA, Kentaro SUGIYAMA, Natsuko HONDA, Mayuko MARUIWA, Mana TAKAGI

Graduate Student: Reiko HOSHI, Syun NISHIHARA, Erina TONOUCHI, Takasuke INADA, Durugu-nn BATBO-RUDO, Eri SONE, Narumi OSIBE, Keiichihiro NAKAZATO, Hiroshi KATO, Takahiko YAMADA, Yusun KIMU, Katuya HYODO, Daisuke YAMAMOTO, (from April) Eri SIBATA

Student: Tizuko KOMURO, Tkahiro KIKUTI, Sinya KOUSAKA, Souiti ROKUSIMA, (from April)

Emeritus Professor: Teruo AMAGASA

Clinical professor: Masashi YAMASHIRO

Part-time Lecturer: Kazuki HASEGAWA, Hiroyuki WAKE, Fumiaki SATO, Junichi ISHII, Eizi FUZII, Akiko KOBAYASHI, Yutaka SATO, Yasushi NIINAKA, Takao WATANABE, Testuo SUZUKI, Masayuki YAMANE, Takashi MISHIMAGI, Kazuto KUROHARA, Katuya AIKOU, Yosio OYAMA, Shigehiro ABE, Miho MIZUTANI, Yasuhiro KURASAWA, Chieko MICHIKAWA

(1) Research

Research Subjects

- 1) Head and Neck Surgery: Innovation of management patients with benign and malignant tumors and cysts in oral and facial region.
- 2) Reconstructive Surgery: Developing method of correcting jaw, facial bone and facial soft tissue trouble left as the result of removal of disease or previous trauma.
- 3) Correction of Birth Defects: Improving surgically correction of birth defects of the face and skull, including cleft lip and palate.
- 4) Dentofacial Deformities and Orthognathic Surgery: Development of new surgical techniques to improving reconstruct and realign the upper and lower jaws.
- 5) Temporomandibular Joint Disorders: Renewing skills in the diagnosis and treatment due to temporomandibular joint problem.
- 6) Oral Mucosa Disease: Creation new method with light and color for diagnosis of oral mucosa disease, including leukoplakia and cancer.

(2) Lectures & Courses

Oral and maxillofacial surgery is a surgical specialty involving the diagnosis, surgical treatment and management of defects and injures related to the function and aesthetics of the face and jaws. In order to practice the full scope of the specialty, oral and maxillofacial surgeons are required education in dentistry, medicine and surgery for regional requirement.

(3) Clinical Performances

Clinical Services

- 1) Diagnosis, removing and reconstruction of jaw, oral or facial tumor or cyst.
- 2) Diagnosis and treatment of cleft lip and palate.

- 3) Treatment of jaw aligned with orthognathic surgery.
- 4) Therapy of temporomandibular disorder with or without temporomandibular joint surgery.
- 5) Diagnosis and treatment of oral mucosa disease.
- 6) Treatment of inflammation in the region jaw and facial trauma.
- 7) Extraction tooth including wisdom tooth.

(4) Publications

[Original Articles]

1. Yae Ohata, Maiko Tsuchiya, Hideaki Hirai, Satoshi Yamaguchi, Takumi Akashi, Kei Sakamoto, Akira Yamaguchi, Tohru Ikeda, Kou Kayamori. Leukemia inhibitory factor produced by fibroblasts within tumor stroma participates in invasion of oral squamous cell carcinoma. PLoS ONE. 2018.02; 13(2); e0191865
2. Takasuke Inada, Atsushi Tamura, Masahiko Terauchi, Satoshi Yamaguchi, Nobuhiko Yui . A silencing-mediated enhancement of osteogenic differentiation by supramolecular ternary siRNA polyplexes comprising biocleavable cationic polyrotaxanes and anionic fusogenic peptides Biomaterials Science. 2018.02; 6(2); 440-550

[Conference Activities & Talks]

1. NAKAZATO Keiichiro, UZAWA Narikazu, KAYAMORI Kou, TSUCHIYA Maiko, WATANABE Hiroshi, SUMINO Jun, MICHI Yasuyuki, YAMAGUCHI Satoshi. The Change of Metabolic Control Mechanism in the Development and Progress of the Tongue Carcinoma. 2018.01.25 Niigata, Japan

Maxillofacial Orthognathics

Professor	Keiji MORIYAMA
Associate Professor	Shoichi SUZUKI
Junior Associate Professor	Takuya OGAWA
Assistant Professor	Michiko TSUJI, Norihisa HIGASHIHORI, Jun MIYAMOTO, Yukiho KOBAYASHI, Yosuke ITO
Clinical Fellow	Rina HIKITA, Yuko YASUDA, Kenji OGURA, Yuki TAKAHASHI, Naoki KOUDA, Kohei YAHIRO
Post-doctoral Fellow	Chiho KADOTA, Masayoshi UEZONO
Graduate Student	Akitsu IKEDA, Taizo HIRATSUKA, Miyu ARAKI, Takeshi OGASAWARA, Hiroyuki KAMIMOTO, Kyoko HIRABAYASHI, Kenta FUNAHASHI, Hideyuki YOSHIKAWA, Aung Bhone Myat, Wu Yu Yun, Kaori KADOWAKI, Soonhwa KANG, Sayuri SAITO, Hidekazu MATSUMOTO, Takayuki MIYAZAKI, Teramoto Iida Airy, Nay Myo Min Swe, Phyo Thiha, Nanase IGARASHI, Yumi INAGAKI, Masaki INOUE, Yoshiya KAISAKA, Yuki NIKI, Thili HLA Myint, Pooktuantong Ornnicha, Teekavanich Chutimont, Badrakhkhoo Nomin Dulguun
Graduate International Research Student	Naomi YAMAMOTO, Sakiko AKIYAMA, Takuya ASAMI, Ayumi SHOJI, Entei RIN, Rie KINOSHITA, Ruriko NAKAMURA, Syuhei AKIYAMA, Megumi ARIMURA, Asuka TAMURA, Cheng Shih-Wei Eric, Yuri BABA, Kenjiro MATSUMURA, Yukiko KINOSHITA, Chisato TOMINAGA, Daichi HAYAKA, Lin Tun Oo, Thili HLA Myint, Yuki NAKAZAWA, Sahori MATSUNO, Misato HANDA
Visiting Research Scholar	Lisa R.Amir
Part-time Lecturer	Tatsuo KAWAMOTO, Naoto SUDA, Takafumi SUSAMI, Tamiko TERASHIMA, Yoshiyuki KATO, Yasuo ISHIWATA, Yoshiyuki BABA, Toshimoto TENGAN, Masahiko YOKOZEKI, Shigetoshi HIYAMA, Shigeki TAKAHASHI, Hiroki FUKUOKA, Junichi TAKADA, Ryo MARUOKA

(1) Research

- 1) Basic and clinical studies of cleft lip and/or palate and other congenital craniofacial conditions
- 2) Morphological and physiological studies of facial deformity

- 3) Physiological study about control mechanism of stomatognathic function
- 4) Functional MRI study in the craniofacial region
- 5) Clarify the factors of malocclusion with epidemiological technique

(2) Education

The goal of the program of Maxillofacial Orthognathics is to provide information related to craniofacial growth and development, and stomatognathic function in order to develop basic knowledge and skills for the treatment of the patients with a wide variety of malocclusion. It also provides valuable information of diagnosis and treatment planning for orthodontic and orthognathic therapies of the patients with jaw deformities and congenital craniofacial anomalies.

Comprehensive care by a team of specialists including maxillofacial surgeons, orthodontists, speech therapists etc. is needed for the treatment of the patients with cleft lip and palate and other craniofacial anomalies. The Graduate Program provides the clinical education of orthodontics as a part of the multi-disciplinary approach for such patients.

(3) Clinical Performances

In the Clinic, we treat a large number of patients presenting a variety of malocclusions to be assigned to group practice in order to gain valuable experience in diagnosis, treatment planning, orthodontic therapy, and patient management. Especially for patients born with cleft lip and/or palate and who need craniofacial and orthognathic surgery, we have clinical meetings and conferences for the comprehensive care through a team approach with maxillofacial surgeons, maxillofacial prosthodontists and speech therapists. We also provide supportive counseling to families who have members with congenital anomalies before the treatment.

(4) Publications

[Original Articles]

1. Yahiro K, Higashihori N, Moriyama K. Histone methyltransferase Setdb1 is indispensable for Meckel's cartilage development. *Biochemical and Biophysical Research Communications*. 2017.01; 482(4); 883-888
2. Koda N, Sato T, Shinohara M, Ichinose S, Ito Y, Nakamichi R, Kayama T, Suzuki H, Moriyama K, Asahara H. The transcription factor mohawk homeobox regulates homeostasis of the periodontal ligament. *Development*. 2017.01; 144(2); 313-320
3. Ikeda M, Miyamoto JJ, Takada JJ, Moriyama K. Association between 3-dimensional mandibular morphology and condylar movement in subjects with mandibular asymmetry. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2017.02; 151(2); 324-334
4. Sawada H, Ogawa T, Kataoka K, Baba Y, Moriyama K. Measurement of Distraction Force in Cleft Lip and Palate Patients During Le Fort I Maxillary Advancement With Rigid External Distraction. *Journal of Craniofacial Surgery*. 2017.03; 28(2); 406-412
5. Shiga M, Ogawa T, Ekprachayakoon I, Moriyama K. Orthodontic Treatment and Long-Term Management of a Patient With Marfan Syndrome. *The Cleft Palate-Craniofacial Journal*. 2017.05; 54(3); 358-367
6. Inagaki Y, Abe M, Inaki R, Zong L, Suenaga H, Abe T, Hoshi K. A Case of Systemic Infection Caused by *Streptococcus pyogenes* Oral Infection in an Edentulous Patient *Diseases*. 2017.08; 5(3); 17
7. Araki M, Yasuda Y, Ogawa T, Tumurkhuu T, Ganburged G, Bazar A, Fujiwara T, Moriyama K. Associations between Malocclusion and Oral Health-Related Quality of Life among Mongolian Adolescents. *International Journal of Environmental Research and Public Health*. 2017.08; 14(8); pii: E902
8. Shoji-Matsunaga A, Ono T, Hayashi M, Takayanagi H, Moriyama K, Nakashima T. Osteocyte regulation of orthodontic force-mediated tooth movement via RANKL expression. *Scientific Reports*. 2017.08; 7(1); 8753

9. Higashihori N, Lehnertz B, Sampaio A, Underhill T M, Rossi F, Richman J M . Methyltransferase G9A Regulates Osteogenesis via Twist Gene Repression. *Journal of Dental Research*. 2017.09; 96(10); 1136-1144
10. Aida J, Matsuyama Y, Tabuchi T, Komazaki Y, Tsuboya T, Kato T, Osaka K, Fujiwara T. Trajectory of social inequalities in the treatment of dental caries among preschool children in Japan. *Community Dentistry and Oral Epidemiology*. 2017.10; 45(5); 407-412
11. Ogasawara T, Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama K. Shape Optimization of Bone-Bonding Subperiosteal Devices with Finite Element Analysis *BioMed Research International*. 2017.11; 2017; 3609062
12. Veistinen LK, Mustonen T, Hasan MR, Takatalo M, Kobayashi Y, Kesper DA, Vortkamp A, Rice DP. Regulation of Calvarial Osteogenesis by Concomitant De-repression of GLI3 and Activation of IHH Targets. *Frontiers in Physiology*. 2017.12; 8; 1036

[Books etc]

1. Kobayashi Y, Duarte C, Moriyama K. Biomarkers in Bone Disease. Part of the series Biomarkers in Disease: Methods, Discoveries and Applications. Springer, 2017.07 (ISBN : 978-94-007-7692-0)

[Conference Activities & Talks]

1. Komazaki Y, Ogawa T, Kataoka K, Baba Y, Moriyama K. Postoperative changes of the maxilla after distraction osteogenesis in cleft palate patients - Comparison between internal device and external device. 13th International Cleft Congress 2017.02.08 Chennai,India
2. Ogawa T. Maxillary distraction osteogenesis in CLP patients with severe maxillary deficiency: Methodology, timing and long term follow up. 13th International Cleft Congress 2017.02.08 Chennai,India
3. Miyamoto J, Tamura A, Ogura K, Ogawa T, Morita K, Moriyama K. A case of UCLP treated by maxillary distraction osteogenesis in late stage of pubertal growth. The 41st Annual Meeting of Japanese Cleft Palate Association 2017.05.18 Tokyo
4. Uezono M, Ogawa T, Yamaguchi S, Moriyama K. Orthodontic treatment of a Beckwith-Widemann syndrome patient with glossectomy. The 41st Annual Meeting of Japanese Cleft Palate Association 2017.05.18 Tokyo
5. Ogawa T, Handa M, Uezono M, Komazaki Y, Tsuji M, Moriyama K. A survey of orthodontic treatment of rare disease with cleft lip and/or palate. The 41st Annual Meeting of Japanese Cleft Palate Association 2017.05.18 Tokyo
6. Kikuchi M, Sato T, Shirosaki Y, Aizawa M, Kadowaki K, Uezono M, Moriyama K, Takakuda K. Hydroxyapatite/collagen bone-like nanocomposite for medical applications (Invited) . 12th Pacific Rim Conference on Ceramic and Glass Technology 2017.05.21 Hawaii, USA
7. Moriyama K. Orthodontic Treatment in a Super-aging Society in Japan. The 15th National Scientific Conference of the Dental Faculty Consortium of Thailand 2017.07.19 Phitsanulok, Thailand
8. Moriyama K. Soft Tissue Consideration in Treatment of Dentoskeletal Discrepancy Cases. 2017 International Orthodontic Conference and the 16th Annual Session of Chinese Orthodontic Society 2017.09.17 Shanghai,China
9. Takahashi Y, Higashihori N, Funahashi K, Matsumura K, Ito Y, Uezono M, Kadota-Watanabe C, Hikita R, Suzuki S, Moriyama K. Analysis of perioral soft tissue movements during speech in skeletal Class II facial deformity patients. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
10. Ogura K, Kobayashi Y, Hikita R, Syoji A, Tsuji M, Moriyama K. Analysis of palatal morphology of craniosynostosis patients: Comparison between apert syndrome and crouzon syndrome. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido

11. Yahiro K, Higashiori N, Moriyama K. The effects of histone methyltransferase Setdb1 on Meckel's cartilage development via BMP signals. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
12. Teramoto A, Akiyama A, Yakahashi Y, Kadota-Watanabe C, Ito Y, Higashiori N, Suzuki S, Ohbayashi N, Kurabayashi T, Moriyama K. Study on the morphological correlations between tongue and oral cavity by using silicon impression method. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
13. Ikeda A, Miyamoto J, Usui N, Taira M, Moriyama K. Effect of chewing on appetite regulation system: A cognitive psychological study using visual food stimuli. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
14. Higashiori N, Hikita R, Kadota-Watanabe C, Akiyama S, Takahashi Y, Ito Y, Moriyama K. Variations of respiratory function for mandibular prognathism patients treated by surgical orthodontics: comparison between subjective/objective evaluations. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
15. Hayakawa D, Koda N, Takahashi Y, Kang S, Matsumoto H, Naymyo M, Tsuji M, Kobayashi Y, Moriyama K. Craniofacial characteristics and general symptoms of Stickler syndrome and Robin sequence patients. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
16. Kinoshita Y, Takahashi Y, Koda N, Saito S, Miyazaki T, Phyo T, Tsuji M, Kobayashi Y, Moriyama K. Characteristics of oral symptoms of Stickler syndrome patients. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18
17. Hiratsuka T, Takakuda K, Kikuchi M, Uezono M, Suzuki S, Moriyama K. Osteolytic changes associated with HAp/Col-induced rapid subperiosteal ossification on the base bone. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
18. Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. Development of novel coating method for hydroxyapatite/collagen nanocomposite to apply orthodontic anchorage devices. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
19. Ogawa T, Yamagushi S, Moriyama K. Surgical orthodontic treatment for a unilateral anterior crossbite case using maxillary dentoalveolar distraction osteogenesis. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
20. Ito Y, Higashiori N, Kanazawa M, Kabasawa Y, Moriyama K. Surgical orthodontic treatment of skeletal Class III malocclusion with occlusal support in molar regions. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
21. Tominaga C, Koda N, Takahashi Y, Kadowaki K, Ogura K, Tsuji M, Kobayashi Y, Moriyama K. A case report of a Stickler syndrome patient who presented condylar hypertrophy after growing spurt. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
22. Shoji A, Higashiori N, Lin W, Tsuji M, Moriyama K. Diagnosis and treatment for impacted upper canines from an orthodontic viewpoint. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
23. Lin W, Tsuji M, Shoji A, Higashiori N, Moriyama K. Clinical statistical investigation on orthodontic patients with impacted teeth at TMDU for the past 10 years. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Hokkaido
24. Miyamoto J. New evaluation of oral function via blood flow measurement -in patients with lip incompetence-. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico
25. Miyamoto J. Human brain activity related to oral function. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico
26. Moriyama K. Orthodontic Treatment for Adolescent Patients with Mandibular Prognathism. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico

27. Moriyama K. An orthodontic perspective of long-term care for cleft lip and palate and its related congenital anomalies patients. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico
28. Moriyama K. Some Considerations in Orthodontic Treatment for Class III Patients. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico
29. Moriyama K. Non-surgical and Surgical Orthodontic Treatment for Adult Patients with Mandibular Prognathism.. XXV International Congress of the Academia Mexicana de Ortodoncia 2017.11.16 Mexico City, Mexico
30. Araki M, Yasuda Y, Ogawa T, Tumurkhuu T, Ganburged G, Bazar A, Fujiwara T, Moriyama K. Association of malocclusion on oral health-related quality of life in Mongolian adolescents. The 65th Annual Meeting of Japanese Association for Dental Research. 2017.11.18 Tokyo
31. Wu Y Y, Kadota-Watanabe C, Ogawa T, Moriyama K. Establishment of a Novel Murine Model of Temporomandibular Joint Osteoarthritis. The 30th Taiwan Association of Orthodontists Annual Meeting 2017.12.09 Kaohsiung, Taiwan

Maxillofacial Prosthetics

2017 April

Professor
TANIGUCHI Hisashi

Junior Associate Professor
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Part-time Special Student
WATANABE Mao
ZHANG Manjin
LIU Rongguang

Speech-Language-Hearing Therapist
MIBU Michiko

(1) Outline

Department of Maxillofacial Prosthetic is the special unit of the prosthodontic and/or prosthetic treatment for patients with defects in oral and/or maxillofacial regions. The main objective of this course is to provide students with opportunity to gain sound understanding of the restoration of functional and esthetic disorders of oral and/or maxillofacial areas that are caused by congenital developmental or acquired diseases by means of the high-advanced dental and medical cares.

(2) Research

Our department is the special unit for the prosthodontic treatment for patients with congenital or acquired defects in head and neck regions. The main goal of the research is to establish a novel theory and feedback it to the clinic to improve the quality of life of each patient. In this respect, we are focusing on several projects.

Diagnosis of functional impairment in patients with a maxillofacial defect

Treatments for functional rehabilitation of patients with a maxillofacial defect

Masticatory evaluation in patients with a maxillofacial defect

Speech evaluation in patients with a maxillofacial defect

Development of new materials for facial prosthesis

(3) Publications

[Original Articles]

1. Yeerken Y, Otomaru T, Kamarudin KH, Sumita YI, Said M, Munakata M, Kasugai S, Taniguchi H. Prosthodontic rehabilitation of a mandibulectomy patient with an implant-retained overdenture: A clinical report. *Open Journal of Clinical and Medical Case Reports*. 2017.02; 1218
2. Chikai M, Kamiyanagi A, Kimura K, Seki Y, Endo H, Sumita YI, Taniguchi H, Ino S. Pilot study on an acoustic measurements system of the swallowing function using an acoustic-emissions microphone. *Journal of Advanced Computational Intelligence and Intelligent Informatics*. 2017.03; 21(2); 293-300
3. Elbashti ME, Hattori M, Patzelt SBM, Schulze D, Sumita YI, Taniguchi H. Feasibility and accuracy of digitizing edentulous maxillectomy defects: A comparative study. *International Journal of Prosthodontics* . 2017.04; 30(2); 147-149
4. Yeerken Y, Otomaru T, Said M, Li N, Taniguchi H. Applicability of the CIELAB and CIEDE2000 formulae for detection of colour changes in colour-changeable chewing gum for evaluating masticatory function. *Journal of Clinical and Diagnostic Research*. 2017.04; 11(4); 119-123
5. Sumita YI, Hattori M, Elbashti ME, Taniguchi H. Orientation of handle for successful prosthetic treatment in patients with an anatomic compromise after a maxillectomy. *Journal of Prosthodontic Dentistry*. 2017.05; 117(5); 694-696
6. Said M, Otomaru T, Sumita YI, Leung KCM, Khan Z, Taniguchi T. Systematic review of literature: functional outcomes of implant-prosthetic treatment in patients with surgical resection for oral cavity tumors. *Journal of Investigative and Clinical Dentistry*. 2017.05; 8(2); e12207
7. Kamiyanagi A, Sumita YI, Chikai M, Kimura K, Seki Y, Ino S, Taniguchi H. Evaluation of swallowing sound using a throat microphone with an AE sensor in patients wearing palatal augmentation prosthesis. *Journal of Advanced Computational Intelligence and Intelligent Informatics*. 2017.05; 21(3); 573-580
8. Yanagi A, Murase M, Sumita YI, Taniguchi H. Investigation of nutritional status using the Mini Nutritional Assessment-Short Form and analysis of the relevant factors in patients with head and neck tumour. *Gerodontology*. 2017.06; 34(2); 227-231
9. Sumita YI, Hattori M, Oki M, Yoshi S, Takahashi H, Iwasaki N, Taniguchi H. Viscoelastic Properties of Experimental Facial Prosthetic Silicone Materials - Effects of Thixotropic Agent and Polymerization Conditions - 2017.06; 40(1); 1-6

10. Said M, Otomaru T, Yeerken Y, Taniguchi H. Masticatory function and oral health-related quality of life in patients after partial maxillectomies with closed or open defects. *J Prosthet Dent.* 2017.07; 118(1); 108-112
11. Sumita YI. Consideration of the soft tissue can brush up routine dental examination. *Ann Jpn Prosthodont Soc.* 2017.07; 9; 169-174
12. Aswehlee AM, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Geometric evaluation of the effect of prosthetic rehabilitation on the facial appearance of mandibulectomy patients: a preliminary study. *Int J Prosthodont.* 2017.08; 30(5); 455-457
13. Elbashti ME. Welcome to IJMP, a new journal with new value. *Int J Maxillofac Prosthetics.* 2017.08; 1(1); 1
14. Elbashti ME, Ashwehlee AM, Zaggut A, Hattori M, Sumita YI, Taniguchi H. The role of digital technology in overseas maxillofacial prosthetic collaboration; a model of future collaboration. *Libyan Dent J.* 2017.08; 7(1); 1-7
15. Sumita YI. Key points to success in maxillofacial prosthetic treatment. *Ann Jpn Prosthodontic Soc.* 2017.10; 9(4); 339-344
16. Suzuki A, Otomaru T, Taniguchi H, Hoshiai T, Nakata H, Oki M, Shinozuka O, Kasugai S, Kuroda S. A modal analysis of fixed implant supported prosthetic device of the six abutments placed in edentulous maxilla Jpn. *J. Maxillofac. Impl.* 2017.12; 16(4); 275-283
17. Aswehlee A, Elbashti ME, Hattori M, Sumita YI, Taniguchi H. Geometrical evaluation of the effect of prosthetic rehabilitation on the facial appearance of mandibulectomy patients: A preliminary study *International Journal of Prosthodontics.* 2017.12; accepted;
18. Elbashti ME, Aswehlee A, Sumita YI, Hattori M, Taniguchi H. The role of portable documentation format in three-dimensional interactive visualization in maxillofacial prosthetics *International Journal of Prosthodontics.* 2017.12; accepted;
19. Li N, Otomaru T, Taniguchi H. Sleep quality in long-term survivors of head and neck cancer: preliminary findings. *Supportive Care in Cancer.* 2017.12; 25(12); 3741-3748
20. Aswehlee A, Hattori M, Elbashti ME, Sumita YI, Taniguchi H. Geometric evaluation of the effect of prosthetic rehabilitation on facial asymmetry in patients with unilateral maxillectomy. *International Journal of Prosthodontics.* 2017.12; accepted;
21. Li N, Otomaru T, Said M, Kanazaki A, Yeerken Y, Taniguchi H. Factors associated with sleep quality in maxillectomy patients. *International Journal of Prosthodontics.* 2017.12; accepted;
22. Elbashti ME, Sumita YI, Hattori M, Aswehlee AM, Taniguchi H. Digitized speech characteristics in patients with maxillectomy defects. *J Prosthodont.* 2017.12; accepted;
23. Kamarudin KH, Hattori M, Sumita YI, Taniguchi H. A chairside technique to add customized anterior acrylic resin teeth to a surgical obturator. *J Prosthet Dent.* 2017.12; accepted;

[Conference Activities & Talks]

1. Haraguchi M, Tachikawa N, Sumita YI, Taniguchi H. Prosthetic rehabilitation for 3 patients with bilateral cleft lip and palate. The 41st annual meeting of Japanese Cleft Palate Association 2017.05.19 Tokyo (Japan)
2. Otomaru T, Sumita YI, Hatano N, Haraguchi M, Murase M, Kanazaki A, Taniguchi H. Prosthetic treatment in a left cleft lip and palate patient with fistula; A case report. The 41st annual meeting of Japanese Cleft Palate Association 2017.05.19 Tokyo (Japan)
3. Morita K, Mibu M, Otomaru T, Shimazaki K, Ogawa T, Tachikawa N, Miyashin m, Ono T, Moriyama K, Taniguchi H, Harada H. Oral and Maxillofacial Malformation Clinic of Tokyo Medical and Dental University Dental Hospital. 2017.05.19 Tokyo(Japan)

4. Elbashti ME, Aswehlee A, Hattori M, Sumita YI, Taniguchi H. Effect of prosthetic rehabilitation on geometrical face asymmetry in mandibulectomy patients. 6th Triennial Congress of Advancing Digital Technology in Head and Neck Reconstruction 2017.05.31 Amiens (France)
5. Elbashti ME, Aswehlee A, Sumita YI, Hattori M, Taniguchi H. The role of portable documentation format in three-dimensional interactive visualization in maxillofacial prosthetics. 6th Triennial Congress of Advancing Digital Technology in Head and Neck Reconstruction 2017.05.31 Amiens (France)
6. Aswehlee A, Hattori M, Elbashti M, Sumita YI, Taniguchi H. Geometrical evaluation of prosthetic rehabilitation effect on facial asymmetry of unilateral maxillectomy patients. The 34th annual meeting of Japanese Academy of Maxillofacial Prosthetics 2017.06.02 Tokyo (Japan)
7. Murase M, Sumita YI, Taniguchi H. A case report of functional rehabilitation by maxillofacial prosthesis for the multiple disabilities patient after total glossectomy. The 34th annual meeting of Japanese Academy of Maxillofacial Prosthetics 2017.06.02 Tokyo (Japan)
8. Watanabe M, Otomaru T, Li N, Hideshima M, Taniguchi H. Clinical follow-up of obstructive sleep apnea applied with an oral appliance in a patient with maxillectomy. The 34th annual meeting of Japanese Academy of Maxillofacial Prosthetics 2017.06.03 Tokyo(Japan)
9. Haraguchi M, Tachikawa N, Michi Y, Harada H, Sumita YI, Taniguchi H. The different outcome of dental implant treatment in 3 segmental mandibulectomy patients with reconstruction by scapula osteocutaneous flap. The 41st annual meeting of Japan Society for Head and Neck Cancer 2017.06.08 Kyoto(Japan)
10. Hoshiai T, Otomaru T, Oki M, Shinozuka O, Taniguchi H. Modal analyses of the maxillary dentition with maxillary cast obturator prostheses comparing different retainer types of metal frameworks. The 126th annual meeting of the Japan Prosthodontic Society 2017.07.01 Kanagawa(Japan)
11. Kamiyanagi A, Sumita YI, Taniguchi H. Evaluation of swallowing function using swallowing sounds for screening use in maxillectomy patients. The 126th annual meeting of the Japan Prosthodontic Society 2017.07.01 Kanagawa(Japan)
12. Suzuki A, Otomaru T, Nakata H, Kon K, Kasugai S, Kuroda S. A modal analysis of two different types of fixed implant supported prosthetic device embedded in edentulous maxilla. 47th Annual Meeting of Japanese Society of Oral Implantology 2017.09.23 Miyagi(Japan)
13. Zhang M, Sumita YI, Liu R, Li N, Hattori M, Taniguchi H. Mandibulectomy and recurrent carcinoma of the left mandible case. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
14. Sumita YI, Namba T, Kamarul HK, Kamiyanagi A, Hattori M, Ino S, Taniguchi H. Obturators to facilitate speech and swallowing in a maxillectomy patient with dementia and cerebral infarction. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
15. Liu R, Sumita YI, Zhang M, Hattori M, Taniguchi H. The long-term follow up maxillectomy patients with o-ring attachment: case report. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
16. Awuti S, Kelimu S, Yoshi S, Hattori M, Sumita YI, Taniguchi H. Position of the artificial tooth on the morphology of denture space in glossectomy. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
17. Hattori M, Patzelt SBM, Kohal RJ, Vach K, Elbashti ME, Sumita YI, Taniguchi H. Use of an intraoral scanner for digitizing an ear model. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
18. Hatano N, Sumita YI, Otomaru T, Yamakoshi N, Taniguchi H. An application of maxillofacial prosthesis in a maxillectomy patient with anterior alveolar bone fracture. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
19. Kelimu S, Hattori M, Awuti S, Elbashti ME, Sumita YI, Taniguchi H. Evaluation of color changes on sand-blasted acrylic surfaces for palatogram. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)

20. Haraguchi M, Shibata M, Ohyama Y, Norime A, Michi Y, Harada H, Tachikawa N, Sumita YI, Taniguchi H. The prospective study of masticatory function and QOL in segmental mandibulectomy patients. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
21. Fujita H, Sumita YI, Namba T, Yanagi A, Ino S, Taniguchi H. Current status of dementia and wearability of maxillofacial prostheses among patients at maxillofacial prosthetics clinic. 4th Joint Meeting of the International Society for Maxillofacial Rehabilitation and the American Academy of Maxillofacial Prosthetics 2017.10.28 San Francisco(USA)
22. Hattori M, Patzelt S, Kohal R, Elbashti ME, Sumita YI, Taniguchi H. Performing digital impressions for simulated trismus condition on maxillectomy model. The 65th Annual Meeting of Japanese Association for Dental Research 2017.11.18 Tokyo (Japan)
23. Sumita YI, Hattori M, Awuti S, Ino S, Kamiyanagi A, Taniguchi H. Maxillofacial prosthetic treatment for a maxillectomy patient with Parkinson's disease. The 65th Annual Meeting of Japanese Association for Dental Research 2017.11.18 Tokyo (Japan)
24. Kelimu S, Hattori M, Elbashti ME, Awuti S, Sumita YI, Taniguchi H. Alternative powder-free method for palatography using sandpaper. The 65th Annual Meeting of Japanese Association for Dental Research 2017.11.18 Tokyo (Japan)
25. Otomaru T. Introduction: Maxillofacial Prosthetics. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)
26. Otomaru T. Prosthetic Treatment in Head & Neck Cancer Patients. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)
27. Kamiyanagi A. Evaluation of Swallowing Ability Using Swallowing Sounds in Maxillectomy Patients. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)
28. Said M. Masticatory Function and OH related-QoL in Partial Maxillectomy Patients. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)
29. Fujita H. Changes of Patient Number in 35 yrs and Maxillofacial Defect Patients with Dementia. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)
30. Yeerken Y. Masticatory Function Evaluation Methods. The Joint Egyptian-Japanese Scientific Cooperation Seminar 2017.11.27 Cairo (Egypt)

Cell Biology

Professor : Takao Nakata
Junior Associate Professor : Tomohiro Ishii
Assistant Professor : Toshifumi Asano
Assistant Professor : Hironori Inaba
Technical Staff : Satoko Nakamura

(1) Outline

We started a new laboratory from April 2009. We are interested in the cellular responses to spatio-temporal activation of signaling molecules. For this purpose, we took synthetic approaches combined with optogenetics. We introduce the photo switches into cells, and analyze signaling systems quantitatively. Research will be conducted by using molecular biology, molecular genetics, cell biology, theoretical biology, and live-imaging techniques.

(2) Research

We are studying cell signaling using optogenetics. We made photo-switch of various signaling proteins and introduced them into cells. Parts of the cells were stimulated by blue lasers. The photo-switches are activated locally within the cells and we observe the cell phenotypes by time-lapse microscope using these techniques. We can understand molecular mechanisms of cell signaling in spatio-temporal fashion and also can manipulate cellular conditions using these switches.

(3) Education

We teach histology and cell biology to 2nd year medical students. The courses are composed of sets of lecture and laboratory study of tissues and organs. Our goal in undergraduate course is to provide students with fundamental knowledge and skill to analyze microscopic samples of normal human body.

In new curriculum, lecture provide students information on fine structure and hints or laboratory work. This helps the students to sketch the tissue in their laboratory work. The aim of our lecture is to provide fundamental knowledge of human tissues and organ to understand clinical lectures. In laboratory work we adopt classical sketch of tissues because we believe it shows the ability of students to search the representative area and extract essential structure. Evaluation depends on paper test, sketch and laboratory test.

In cell biology course we start a little bit advanced lectures such as cell death and cell cycle because we avoid to teach the same contents that they have learned in the past year biology course. We also provide more stimulative lectures in later half of the course such as autophagy, zebrafish genetics and mathematical model.

(4) Publications

[Original Articles]

1. Toshifumi Asano, Toru Ishizuka, Hiromu Yawo. Myogenic Maturation by Optical-Training in Cultured Skeletal Muscle Cells *Methods in Molecular Biology*. 2017.08; 1668; 135-145

2. Hironori Inaba, Koji Yoda, Hiroyuki Adachi. The F-actin-binding RapGEF GflB is required for efficient macropinocytosis in Dictyostelium. *J. Cell. Sci.*. 2017.09; 130(18); 3158-3172

[Misc]

1. Hidemasa Goto, Hironori Inaba, Masaki Inagaki. Mechanisms of ciliogenesis suppression in dividing cells. *Cell. Mol. Life Sci.*. 2017.03; 74(5); 881-890

[Conference Activities & Talks]

1. Tomohiro Ishii. Novel optogenetic tool controlling intracellular calcium signals. Faculty Development 2017 2017.01.07 Tokyo Medical and Dental University
2. Toshifumi Asano, Takao Nakata. Activity-dependent modulation of myogenic differentiation by dynamic optical control. The 16th Congress of the Japanese Society for Regenerative Medicine 2017.03.07 Sendai International Center
3. Takao Nakata. What we can do using Optogenetic tools elucidation of functional difference between CDC42 and RAC1. The 122nd Annual Meeting of The Japanese Association of Anatomists 2017.03.28 Nagasaki University
4. Takao Nakata. Optogenetics of cell signaling-Ca²⁺, cAMP, RhoGTPases, PI3K, what we can say with these tools?. 8th Asia and Oceania Conference of Photobiology (AOCP 2017) 2017.11.15 Seoul, Korea
5. Toshifumi Asano, Takao Nakata. Activity-dependent modulation in myogenic differentiation process. Consortium of Biological Sciences 2017 (ConBio2017) 2017.12.06 Kobe Port Island

[Awards & Honors]

1. TMDU Faculty of Medicine Excellence in Research (Tomohiro Ishii), Tokyo Medical and Dental University, 2017.01

Medical Biochemistry

Professor Yutaka Hata

Assistant Professor Hiroaki Iwasa

Assistant Professor Kyoko Arimoto-Matsuzaki

Assistant Professor Junichi Maruyama

Other two staffs

(1) Research

- 1) The biological and chemical approach to study the Hippo pathway that controls cell proliferation, cell differentiation, and cell death.
- 2) Versatile roles of the tumor suppressor RASSF proteins
- 3) Discovery and development of chemical compounds that suppress cancer stemness and metastasis
- 4) Discovery and development of chemical compounds that facilitate myogenesis and prevent muscle atrophy
- 5) Development of mouse models mimicking human progeria syndromes
- 6) Study of health life span in *Caenorhabditis elegans*

(2) Education

1 : Undergraduate course

We organized the course of Biochemistry for the undergraduate students.

2 : Master course

We organized the course of Biochemistry for the master students.

3 : Others

We gave a lecture about metabolism of cancer cells.

We gave a lecture entitled "How is the life of human maintained?" for the students of Tokyo University of Foreign Studies.

(3) Lectures & Courses

1) Undergraduate

We organize the course, "Medical Biochemistry". The students are requested through these courses to obtain a comprehensive integrated knowledge of human biochemistry, which is important to understand how health is maintained and which molecular and biochemical events cause human diseases and underlie the rational treatments.

2) Graduate and others

We are studying the signaling pathway that regulates cell proliferation, cell differentiation, cell polarity, and cell death. This pathway is well conserved from fly to human. The mutations of the components lead to oncogenesis and organ malformation. Several recent studies suggest that this pathway is implicated in inflammation and cell differentiation such as adipogenesis, osteogenesis, and keratinocyte differentiation. The pathway plays an important role in various human diseases and could be a new therapeutic target. We give lectures about

our current studies to graduate students and others, and provide graduate students with the opportunity to participate in them.

(4) Publications

[Original Articles]

1. Sarkar A, Iwasa H, Hossain S, Xu X, Sawada T, Shimizu T, Maruyama J, Arimoto-Matsuzaki K, Hata Y.. Domain analysis of Ras-association domain family member 6 upon interaction with MDM2. *FEBS Letters*. 2017.01; 591(2); 260-272
2. Shintaro Mandai, Susumu Furukawa, Manami Kodaka, Yutaka Hata, Takayasu Mori, Naohiro Nomura, Fumiaki Ando, Yutaro Mori, Daiei Takahashi, Yuki Yoshizaki, Yuri Kasagi, Yohei Arai, Emi Sasaki, Sayaka Yoshida, Yasuro Furuichi, Nobuharu L Fujii, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Loop diuretics affect skeletal myoblast differentiation and exercise-induced muscle hypertrophy. *Sci Rep*. 2017.04; 7; 46369
3. Manami Kodaka, Xiaoyin Xu, Zeyu Yang, Junichi Maruyama, Yutaka Hata. Application of Split-GFP Reassembly Assay to Study Myogenesis and Myofusion In Vitro. *Methods in Molecular Biology*. 2017.04; 1668; 127-134
4. Xiaoyin Xu, Hiroaki Iwasa, Shakhawoat Hossain, Aradhan Sarkar, Junichi Maruyama, Kyoko Arimoto-Matsuzaki, Yutaka Hata. BCL-XL binds and antagonizes RASSF6 tumor suppressor to suppress p53 expression. *Genes Cells*. 2017.12; 22(12); 993-1003

[Books etc]

1. Kodaka M, Xu X, Yang X, Maruyama J, Hata Y. *Springer Protocol Application of split-GFP reassembly assay to the study of the in vitro myogenesis and myofusion..* Springer,
2. Xu X, Kodaka M, Iwasa H, Hata Y. *Encyclopedia of Signaling Molecules MAGI2/S-SCAM.* Springer,
3. Iwasa H, Shimizu T, Hata Y.. *Encyclopedia of Signaling Molecules RASSF6.* Springer, (ISBN : 978-1-4419-0460-7)

[Misc]

1. Yutaka Hata, Takeru Sawada. Hippo tumor suppressor pathway *Journal of Molecular Targeted Therapy for Cancer*. 14(4); 10-16

Joint Surgery and Sports Medicine

Hideyuki Koga
Masafumi Horie, Kazumasa Miyatake

Department of Joint Reconstruction
Toshifumi Watanabe

Department of Cartilage Regeneration
Kunikazu Tsuji
Hiroki Katagiri

Mari Uomizu, Kim Minde, Etsuko Matsumura
Kei Inomata, Hiroko Ueki, Mai Katakura, Takashi Kondo, Shinji Hagio, Takashi Hoshino
Masaki Amemiya, Naoko Araya, Hiroaki Onuma
Saisei An, Kazumasa Kawata

Miyoko Ojima, Kahaer Abula
Risa Tada, Haruno Kuroda, Yuki Omura

(1) Research

1. Development and establishment of isolation and expansion of mesenchymal stem cells
2. Research of biological characteristics of mesenchymal stem cells
3. Development and improvement of treatment method of articular cartilage defect with mesenchymal stem cells
4. Development of treatment strategy to joint structure injuries with mesenchymal stem cells
5. Development of artificial cartilage and bone
6. Development of novel agents related to bone and cartilage metabolism
7. Genetical approach to bone and cartilage metabolism
8. Clarifying mechanism and control of post-injury and postoperative inflammation with tissue fibrosis
9. Clarifying mechanism of joint pain with novel treatment strategy
10. Genetic approach to secondary hip osteoarthritis
11. Novel treatment strategy for cufftear

(2) Lectures & Courses

We are working with the Orthopaedic and Spinal Surgery as a Department of Orthopaedic Surgery of University Hospital. The doctors start to have education of orthopedic surgery as a member of the department from the staffs of the department of Orthopaedic Surgery according to the orthopaedic education and training program after completing the two-year fundamental education and training program as a junior resident. They experience a lot of traumatic patients and deepen their basic orthopaedic skills for two-year junior orthopaedic training in one of the branch hospitals every year. They expand their skills and obtain orthopaedic specialty educations in the advanced two-year education and training program. After completing a six-year educational program of the orthopaedic surgery, they are recommended to apply to the orthopedic specialist form the Japanese Orthopaedic

Association. They usually apply to enter the graduate school program after 4 or 5 years of clinical experience. We encourage not only orthopedic doctors but doctors of other specialty, veterinarian doctors and physical therapists, etc to work with us.

(3) Clinical Services & Other Works

Treatment for sports injuries

Prevention, conservative treatment and rehabilitation for sports injuries

Anatomic double-bundle anterior cruciate ligament (ACL) reconstruction for ACL injuries

Surgical treatment for knee multiple ligament injuries

Surgical treatment for meniscal injuries to restore meniscal function

Regenerative medicine for unreparable meniscus and cartilage injuries

Treatment for osteoarthritis (OA)

Conservative approaches to early OA

Joint-sparing surgeries such as osteotomies for moderate OA

Total arthroplasties for severe OA

Clinical researches and clinical results for above-mentioned approaches have been presented at both domestic and international congresses, as well as reported in Japanese and English articles.

(4) Clinical Performances

Sports injuries

We have been performing double-bundle ACL reconstruction since 1994 as a pioneer, and reported good clinical outcomes regarding knee stability, ratio of return to sports and patients' satisfaction. As for meniscal surgeries, we have been trying to repair as much as possible to restore meniscal function. In addition, we have developed a novel surgical procedure to restore meniscal function for patients with post-meniscectomy and discoid meniscus. We have also analyzed mechanisms and preventive methods for ACL injuries, and first in the world clarified a detailed ACL injury mechanism. Based on the findings, various approaches to ACL injury prevention and rehabilitation after ACL reconstruction is being conducted.

Arthroplasties

We have developed a new total knee system called Actiyas, named after the combination of active and healed ("iyas" in Japanese), which is specifically designed for Japanese. In order to develop this, we analyzed Japanese bone morphology, and this system is designed for more functional and "active" motion without knee pain, and eventually patients to be "healed". Ceramic is used for the femoral implant, by which we can expect lesser implant wear, resulting in better long-term results. We perform simultaneous bilateral arthroplasties for Bilateral OA patients, helping them earlier return to daily life.

Regenerative medicine for cartilage and meniscus injuries using synovial stem cells

Based on numerous basic researches performed in our laboratory, we started stem cell therapy for cartilage injuries using synovial stem cells since April 2008. In this therapy, we take synovium from patients at day surgery, culture synovial stem cells at the cell processing center in our university, and transplant them arthroscopically. The safety and effectiveness had been already confirmed. In addition, we also started a clinical trial of synovial stem cell transplantation for unreparable meniscal tear since August 2014.

(5) Publications

[Original Articles]

1. Ryusuke Saito, Takeshi Muneta, Nobutake Ozeki, Yusuke Nakagawa, Mio Udo, Katsuaki Yanagisawa, Kunikazu Tsuji, Makoto Tomita, Hideyuki Koga, Ichiro Sekiya. Strenuous running exacerbates knee cartilage erosion induced by low amount of mono-iodoacetate in rats. *BMC Musculoskelet Disord.* 2017.01; 18(1); 36

2. Etsuko Matsumura, Kunikazu Tsuji, Keiichiro Komori, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Pretreatment with IL-1 β enhances proliferation and chondrogenic potential of synovium-derived mesenchymal stem cells. *Cytotherapy*. 2017.02; 19(2); 181-193
3. Wei Ji, J Bolander, YC Chai, H Katagiri, M Marechal, F Luyten. Toward Advanced Therapy Medicinal Products (ATMPs) Combining Bone Morphogenetic Proteins (BMP) and Cells for Bone Regeneration Bone Morphogenetic Proteins: Systems Biology Regulators. 2017.03; 127-169
4. Arata Yuuki, Takeshi Muneta, Toshiyuki Ohara, Ichiro Sekiya, Hideyuki Koga. Associated lateral/medial knee instability and its relevant factors in anterior cruciate ligament-injured knees. *J Orthop Sci*. 2017.03; 22(2); 300-305
5. Jae-Sung An, Takeshi Muneta, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Hideyuki Koga. Osteochondral lesion of lateral tibial plateau with extrusion of lateral meniscus treated with retrograde osteochondral autograft transplantation and arthroscopic centralisation. *AP-SMART*. 2017.04; 8; 18-23
6. Mai Katakura, Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Takeshi Muneta. Effects of different femoral tunnel positions on tension changes in anterolateral ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2017.04; 25(4); 1272-1278
7. Katagiri Kenta, Yu Matsukura, Takeshi Muneta, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Ichiro Sekiya.. Fibrous synovium releases higher numbers of mesenchymal stem cells than adipose synovium in a suspended synovium culture model. *Arthroscopy*. 2017.04; 33(4); 800-810
8. H Katagiri, L F Mendes, F P Luyten. Definition of a Critical Size Osteochondral Knee Defect and its Negative Effect on the Surrounding Articular Cartilage in the Rat. *Osteoarthr. Cartil.*. 2017.05;
9. Mikio Shioda, Takeshi Muneta, Kunikazu Tsuji, Mitsuru Mizuno, Keiichiro Komori, Hideyuki Koga, Ichiro Sekiya. TNF α promotes proliferation of human synovial MSCs while maintaining chondrogenic potential. *PLoS ONE*. 2017.05; 12(5); e0177771
10. Takao Minami, Takeshi Muneta, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Hideyuki Koga. Lateral meniscus posterior root tear contributes to anterolateral rotational instability and meniscus extrusion in anterior cruciate ligament-injured patients. *Knee Surg Sports Traumatol Arthrosc*. 2017.05;
11. Nobutake Ozeki, Takeshi Muneta, Kenichi Kawabata, Hideyuki Koga, Yusuke Nakagawa, Ryusuke Saito, Mio Udo, Katsuaki Yanagisawa, Toshiyuki Ohara, Tomoyuki Mochizuki, Kunikazu Tsuji, Tomoyuki Saito, Ichiro Sekiya. Centralization of extruded medial meniscus delays cartilage degeneration in rats. *J Orthop Sci*. 2017.05; 22(3); 542-548
12. Yuji Kohno, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Keiichiro Komori, Shizuka Fujii, Koji Otabe, Masafumi Horie, Hideyuki Koga, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Takeshi Muneta, Ichiro Sekiya. Yields and chondrogenic potential of primary synovial mesenchymal stem cells are comparable between rheumatoid arthritis and osteoarthritis patients. *Stem Cell Res Ther*. 2017.05; 8(1); 115
13. R Takada, T Jinno, D Koga, K Miyatake, T Muneta, A Okawa. Comparison of wear rate and osteolysis between second-generation annealed and first-generation remelted highly cross-linked polyethylene in total hip arthroplasty. A case control study at a minimum of five years. *Orthop Traumatol Surg Res*. 2017.06; 103(4); 537-541
14. Kunikazu Tsuji, Miyoko Ojima, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Effects of Different Cell-Detaching Methods on the Viability and Cell Surface Antigen Expression of Synovial Mesenchymal Stem Cells. *Cell Transplant*. 2017.06; 26(6); 1089-1102
15. Shimpei Kondo, Takeshi Muneta, Yusuke Nakagawa, Hideyuki Koga, Toshifumi Watanabe, Kunikazu Tsuji, Shinichi Sotome, Atsushi Okawa, Shinji Kiuchi, Hideo Ono, Mitsuru Mizuno, Ichiro Sekiya. Transplantation of autologous synovial mesenchymal stem cells promotes meniscus regeneration in aged primates. *J. Orthop. Res.*. 2017.06; 35(6); 1274-1282

16. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yuji Kohno, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Complete human serum maintains viability and chondrogenic potential of human synovial stem cells: suitable conditions for transplantation. *Stem Cell Res Ther.* 2017.06; 8(1); 144
17. Eriko Grace Suto, Yo Mabuchi, Nobuharu Suzuki, Koji Suzuki, Yusuke Ogata, Miyu Taguchi, Takeshi Muneta, Ichiro Sekiya, Chihiro Akazawa. Prospectively isolated mesenchymal stem/stromal cells are enriched in the CD73(+) population and exhibit efficacy after transplantation. *Sci Rep.* 2017.07; 7(1); 4838
18. Kei Inomata, Ichiro Sekiya, Koji Otabe, Tomomasa Nakamura, Masafumi Horie, Hideyuki Koga, Toshifumi Watanabe, Takeshi Muneta. Acute arterial occlusion after total knee arthroplasty: a case report. *Clin Case Rep.* 2017.08; 5(8); 1376-1380
19. Hideyuki Koga, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Ichiro Sekiya, Takeshi Muneta. Augmentation of the pullout repair of a medialmeniscus posterior root tear by arthroscopic centralization 2017.08; 6(4); 1335-1339
20. Yusuke Nakagawa, Takeshi Muneta, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Mai Katakura, Yusuke Sumi, Ichiro Sekiya, Hideyuki Koga. Arthroscopic centralization achieved good clinical improvements and radiographic outcomes in a rugby player with osteoarthritis after subtotal lateral meniscectomy: A case report. *J Orthop Sci.* 2017.09;
21. Hideyuki Koga, Takeshi Muneta, Roald Bahr, Roald Bahr, Tron Krosshaug . ACL injury mechanisms: Lessons learned from video analysis Rotatory Knee Instability. 2017.11; 27-36
22. Toshifumi Watanabe, Hideyuki Koga, Masafumi Horie, Hiroki Katagiri, Ichiro Sekiya, Takeshi Muneta. Post-Cam Design and Contact Stress on Tibial Posts in Posterior-Stabilized Total Knee Prostheses: Comparison Between a Rounded and a Squared Design. *J Arthroplasty.* 2017.12; 32(12); 3757-3762
23. Hiroki Katagiri, Hideyuki Koga, Takeshi Muneta. Review of Shino et al (1984) on anterior cruciate ligament reconstruction using allograft in the dog *Journal of ISAKOS.* 2017.12; 2(6);
24. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Sekiya I.. Effect of Notchplasty in Anatomic Double-bundle Anterior Cruciate Ligament Reconstruction
25. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Okawa A, Sekiya I.. Effect of posterolateral bundle graft fixation angles on graft tension curves and load sharing in double-bundle anterior cruciate ligament reconstruction using a transtibial drilling technique.
26. Toshifumi Watanabe. In vivo kinematics of a robot-assisted uni- and multi-compartmental knee arthroplasty
27. Toshifumi Watanabe. Intraoperative Joint Gaps Affect Postoperative Range of Motion in TKAs With Posterior-stabilized Prostheses
28. Toshifumi Watanabe. Knee Kinematics in Anterior Cruciate Ligament-Substituting Arthroplasty With or Without the Posterior Cruciate Ligament

[Misc]

1. Hideyuki Koga, Lars Engebretsen, Freddie H Fu, Muneta Takeshi. Revision anterior cruciate ligament surgery: state of the art. *J ISAKOS.* 2017.02; 2(1); 36-46

[Conference Activities & Talks]

1. Hiroko Ueki, Takeshi Tateishi, Hideyuki Koga, Daisuke Hatsushika, Takashi Ogiuchi. Proximal Fifth Metatarsal Stress Fractures; Screening and Treatment for Incomplete Fractures. 5th IOC World Conference on Prevention of Injury & Illness in Sport 2017.03.16
2. Hideyuki Koga. ACL injury mechanisms and its prevention in basketball and handball. 5th IOC World Conference on Prevention of Injury & Illness in Sport 2017.03.16

3. Toshifumi Watanabe, Takeshi Muneta, Hideyuki Koga, Masafumi Horie, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Mai Katakura, Ichiro Sekiya. Post-cam Design and Contact Stress on Tibial Posts in Total Knee Prostheses: Comparison between a Rounded and a Squared Design. Orthopaedic Research Society 2017.03.19 San Diego, CA, USA
4. Mari Uomizu, Tomoyuki Mochizuki, Toshiyuki Ohara, Junpei Matsuda, Nobutake Ozeki, Kunikazu Tsuji, Akimoto Nimura, Takashi Miyamoto, Masafumi Gotoh, Ichiro Sekiya, Takeshi Muneta. Synovium-derived MSCs promote the restoration of tensile strength of the rotator cuff tendon after repair in a rat model. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 San Diego, CA, USA
5. Mai Katakura, Hideyuki Koga, Tomomasa Nakamura, Daisuke Araki, Kanto Nagai, Kyohei Nishida, Ryosuke Kuroda, Takeshi Muneta. Effects of Additional Anterolateral Structure Reconstruction with Different Femoral Tunnel Positions to Anterior Cruciate Ligament Reconstruction on the Pivot Shift Phenomenon. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19
6. Mai Katakura, Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura. Risk Factors for Residual Anterolateral Rotational Instability after Anterior Cruciate Ligament Reconstruction: Evaluation by Quantitative Assessment of the Pivot Shift Phenomenon Using Triaxial Accelerometer. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19
7. Toshifumi Watanabe, Takeshi Muneta, Hideyuki Koga, Masafumi Horie, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Ichiro Sekiya. In-vivo kinematics and range of motion after knee arthroplasty. 2017.04.14 Tokyo, Japan
8. Tetsuya Jinno, Kazumasa Miyatake, Ryohei Takada, Masanobu Hirao. Hip precautions against postoperative dislocation in THA. International Congress for Joint Reconstruction Japan Hip & Knee 2017.04.14 Tokyo, Japan
9. Hideyuki Koga. ACL injury mechanisms and its prevention in basketball and handball. 5th IOC World Conference on Prevention of Injury & Illness in Sport 2017.04.27
10. Miyoko Ojima, Kunikazu Tsuji, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Analyses of biologically active substances in synovial fluid which supports proliferation of synovial mesenchymal stem cells. Osteoarthritis Research Society International 2017 Annual Meeting 2017.04.27 Las Vegas, NV, USA
11. Hiroki Katagiri, Mendes LF, Luyten FP. Definition of a Critical Size Osteochondral Knee Defect and its Negative Effect on the Surrounding Articular Cartilage in the Rat. 5th BSTE 2017.05.04 Belgium
12. Hiroko Ueki, Tomohiko Tateishi, Saisei AN, Daisuke Hatsushika, Hideyuki Koga, Takashi Ogiuchi. PROXIMAL FIFTH METATARSAL STRESS FRACTURES; SCREENING AND TREATMENT FOR INCOMPLETE FRACTURES. XXVI International Conference on Sports Rehabilitation and Traumatology 2017.05.13 Barcelona, Spain
13. Toshifumi Watanabe, Takeshi Muneta, Hideyuki Koga, Masafumi Horie, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Mai Katakura, Atsushi Okawa, Ichiro Sekiya. Post-cam Design and Contact Stress on Tibial Posts in Total Knee Prostheses: Comparison between a Rounded and a Squared Design. Annual Meeting of JOA 2017.05.19 Sendai
14. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Takeshi Muneta, Atsushi Okawa. Comparison Of Wear Rate And Osteolysis Between Second-Generation Annealed And First-Generation Remelted Highly Cross-Linked Polyethylene In Total Hip Arthroplasty. 18th EFORT 2017.05.31 Vienna, Austria
15. Hideyuki Koga, Takao Minami, Ichiro Sekiya, Takeshi Muneta. Impact of posterior root tear on knee instability in anterior cruciate ligament injured patients. 11th ISAKOS Congress 2017.06.04
16. Hideyuki Koga, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Ichiro Sekiya, Takeshi Muneta. Arthroscopic Centralization of an Extruded Meniscus and Its Application to Knee Osteoarthritis to Restore Knee Function. 9th JOSKAS 2017.06.22 Sapporo, Japan
17. Hideyuki Koga. Report of JOSKAS-SIGASCOT Fellowship 2016. 9th JOSKAS 2017.06.22
18. Hideyuki Koga. Quantitative Evaluation of Pivot Shift in Double-bundle Anterior Cruciate Ligament Reconstruction Using Triaxial Accelerometer; Identifying Optimal Conditions to Restore Anterolateral Rotational Stability. 61th Korean Orthopaedic Association Annual Meeting 2017.09.19 Seoul, Korea

19. Mai Katakura, Kenji Hirohata, Kazuyoshi Yagishita, Hideyuki Koga. Discoid lateral meniscus tear in dancers: report of two cases. 27th IADMS (Annual Conference for International Association for Dance Medicine and Science) 2017.10.12 Houston, Texas, USA

Biostructural Science

Associate Professor: Makoto TABATA
Technician: Makoto SUGIURA
Secretary: Tomoko YAMAMOTO
Graduate Student: Takafumi NAKANO
Eri USHIMURA (April-)
Momoko SAKAGUCHI (April-)

(1) Outline

Section of biostructural science is the inheritor of the laboratory of Oral Anatomy II, then we focus understanding of the mechanism of tooth development, tooth cell differentiations, and tooth evolution using methods of histology, cell biology, and molecular biology. We also teach three courses of histology for the second grade of dental student, and attend to the preparation works of gross anatomy.

(2) Research

The study of the mechanisms of dental formation and their evolution is the central focus of our research. Followings are rough description of current research subjects in our laboratory.

- 1)Research of Tooth Germ Developmen
- 2)Research of Ameloblast Differentiation & Function
- 3)Research of Fish Scales & Teeth
- 4)Space Experiments using Fish
- 5)Comparative Morphology of the Tooth

(3) Lectures & Courses

We are inheritor of the laboratory of Oral Anatomy II, then we involved in the education of histology, embryology, and oral histology.

In the first place, anatomy and histology is the study to learn the structure, the name, and the function of "HUMAN BODY". Then the subject histology is not able to separate from subject anatomy, relate to physiology, pathology, and embryology and further become to be the fundamentals of clinical subjects. So we carry out of our subjects, with an awareness of the relationships between histology and other subjects.

On the curriculum of the 2nd grade of dental students, lectures of histology contains practical histology using tissue sections and microscopy. This skills work is a good opportunity to know the variation and the finesse of the human body in histology.

(4) Publications**[Conference Activities & Talks]**

1. Nakano T, Sugiura M, Sakaguchi M, Jinbu Y, Mori Y, Takano Y, Tabata M. Primary cell culture of epithelial sheet of rat incisor: cell reaggregation and identification using cell markers. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17 Matsumoto
2. Shunsuke Fukuba, Tatsuya Akizuki, Shu Hoshi, Takanori Matsuura, Ammar Shujaa Addin, Munehiro Okada, Yasuhiko Tabata, Makoto Tabata, Yuichi Izumi. Comparison between different isoelectric point of biodegradable gelatin/ β -tricalcium phosphate sponge using recombinant human fibroblast growth factor-2 for ridge augmentation. 2017.12.15

Pharmacology

Staffs and Students(April, 2017)

Assistant Professor Yukihiro TAMURA
Technologist Mariko TAKAHASHI

Researchers

Nobuyoshi TOMOMATSU (Maxillofacial Surgery)
Yasuhiro SHIMIZU (Orthodontic Science)
Tomoki UEHARA (Pediatric Dentistry)
Yuki ARAI (Removable Prosthodontics)

Graduate Students

Md. Haque Bhuyan ZAHIRUL
Kenya YONEDA(Regenerative Dental Medicine)
Eri SONE(Maxillofacial Surgery)
Hisami OKAWARA(Removable Prosthodontics)
Michiko OZAWA
Shigeki NAGAHIRO(Pediatric Dentistry)

Lecturers

Etsuko TAKAHASHI
Akira NIFUJI
Nozomi HASEGAWA
Eiichi MURASE
Yoshihiro WAKI
Hiroyuki SETO
Toshimi SATO
Genki KATO
Setsuko MISE
Kiichi NONAKA
KHAN Md Abudulla Al Masud

(1) Research

Research subjects

- 1) Pharmacological analyses of formation and resorption on bones and teeth
- 2) Identification of a new therapeutic target for hard tissue-related diseases
- 3) Translational research for hard tissue regeneration
- 4) Interdisciplinary research toward the application of peptide drug
- 5) Analyses of drug side effects appeared at oral tissues

(2) Lectures & Courses

Purpose of Education

Pharmacology is situated between the basic and clinical sciences and is important for dental students. There is a growing demand on the dental clinicians to know huge knowledge of drugs and how to use them for patients. For these purpose, the first lecture is aimed to teach the scientific aspects of pharmacology and how drugs act on the various organ system. The second lecture deals with drugs of medical and dental fields and the last with drugs of special importance of dentistry. Dental students learn the principle of pharmacology through laboratory practice. Following these learning, they must acquire an adequate background for drug use in general practice.

(3) Publications**[Original Articles]**

1. Md Zahirul Haque Bhuyan, Yukihiko Tamura, Eri Sone, Yuki Yoshinari, Chizuko Maeda, Mariko Takahashi, Yasuhiko Tabata, Ramachandran Murali, Yoshihiro Waki, Kazuhiro Aoki. The intra-articular injection of RANKL-binding peptides inhibits cartilage degeneration in a murine model of osteoarthritis. *J. Pharmacol. Sci.*. 2017.06; 134(2); 124-130
2. Lin DING, Peng ZHANG, Xin WANG, Jia HAO, Kazuhiro AOKI, Shinji KURODA, Shohei KASUGAI. Effect of doxycycline-treated hydroxyapatite surface on bone apposition: A histomophometric study in murine maxillae *Dental Materials Journal*. 2017.11;
3. Mikami R, Mizutani K, Aoki A, Tamura Y, Aoki K, Izumi Y. Low-level ultrahigh-frequency and ultrashort-pulse blue laser irradiation enhances osteoblast extracellular calcification by upregulating proliferation and differentiation via transient receptor potential vanilloid 1. *Lasers Surg Med*. 2017.12; epub;
4. Toru Takemoto, Yuji Kabasawa, Yusuke Higuchi, Yasuhiko Tabata, Kazuhiro Aoki, Yukihiko Tamura, Hiroyuki Harada. Combination of the RANKL-binding peptide W9 and bFGF induces bone regeneration in the rat calvarial defect model. *Dent Oral Craniofac Res*. 2017.12; 4(3); 1-7

[Conference Activities & Talks]

1. Kazuhiro AOKI. Roland gave me a seed of my research. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.16 Matsumoto Dental University
2. Risako Mikami, Akira Aoki, Koji Mizutani, Yukihiko Tamura, Yuichi Izumi. Low-level ultrahigh-frequency and ultrashort-pulse blue laser irradiation enhances osteoblast extracellular calcification by upregulating proliferation and differentiation via TRPV1. The 29th Annual Meeting of Japanese Society for Laser Dentistry 2017.09.23

Connective Tissue Regeneration

Associate Professor Tamayuki SHINOMURA

(1) Outline

Our group is interested in the restoration of damaged connective tissue. In general, connective tissue is characterized by the presence of abundant extracellular matrix, and its function is highly dependent on the properties of extracellular matrix. Therefore, to restore connective tissue normal, it is essential for us to understand the behavior of extracellular matrix molecules. So, we pursue research on the molecular mechanisms underlying the formation and maintenance of extracellular matrix in connective tissues.

(2) Research

Currently, we are engaged in the following research subject.

1. Study on the mechanisms that regulate the expression of type II collagen and aggrecan in chondrocytes.
2. Study on transcription factors necessary for the maintenance of chondrogenic phenotype.
3. Study on the molecular dynamics of extracellular matrix in connective tissues.

(3) Education

We give a lecture on molecular biology in general and laboratory exercise for undergraduate students. Also, in our graduate course, we offer lectures on the synthesis and formation of extracellular matrix focusing on cartilage tissue.

(4) Lectures & Courses

We provide education based on the belief that an integrated and organized connection of various knowledge is important to understand life phenomena.

(5) Publications

[Original Articles]

1. Miyazaki Yumiko, Horie Akihito, Sato Yukiyasu, Tani Hirohiko, Ueda Masashi, Okunomiya Asuka, Matsumura Noriomi, Shinomura Tamayuki. Effects of versican V1 on human embryo attachment in an in vitro implantation model *ACTA OBSTETRICA ET GYNAECOLOGICA JAPONICA*. 2017.02; 69(2); 633
2. Nakayama Y, Kobayashi R, Matsui S, Matsumura H, Iwai Y, Noda K, Yamazaki M, Kurita-Ochiai T, Yoshimura A, Shinomura T, Ganss B, Ogata Y.. Localization and expression pattern of amelotin, odontogenic ameloblast-associated protein and follicular dendritic cell-secreted protein in the junctional epithelium of inflamed gingiva *Odontology*. 2017.07; 105(3); 329-337

3. Miyazaki Yumiko, Horie Akihito, Sato Yukiyasu, Tani Hirohiko, Ueda Masashi, Okunomiya Asuka, Matsumura Noriomi, Shinomura Tamayuki. Effects of versican V1 on human embryo attachment in an in vitro implantation model *The Journal of Obstetrics and Gynaecology Research*. 2017.12; 43(12); 2016

[Conference Activities & Talks]

1. Tamayuki Shinomura. Col2a1 and Agc1 gene expressions regulated by different growth factors are mediated via different enhancer elements. Gordon Research Conference on Cartilage Biology & Pathology 2017.04.02 Renaissance Tuscany II Ciocco, Lucca, Italy

Biochemistry

Professor Testuro Watabe
Associate Professor Miki Yokoyama
Junior Associate Professor Yasuhiro Kumei
Assistant Professor Katarzyna Anna Podyma-Inoue
Technical staff Megumi Naito, Kazue Terasawa
Part-time Lecturer Zeredo, Jorge Luis Lopes, Akira Asari
Graduate student Kazuki Takahashi, Akihiko Inagawa, Takumi Matsuda

(1) Outline

Since cancer is the leading cause of death in Japan, we need to develop novel strategies to cure it. Tumor consists of not only cancer cells but also the non-cancerous cells including fibroblasts, immune cells and cells that comprise the blood and lymphatic vessels. We aim to elucidate the mechanisms how cancer cells become malignant by the various cytokines in cancer microenvironment in order to develop novel therapeutic strategies targeting multiple components of cancer microenvironment.

(2) Research

(1) Understanding the molecular mechanisms underlying endothelial-mesenchymal transition (EndMT)
Endothelial cells undergo differentiation into mesenchymal cells during not only various physiological processes including heart valve formation but also pathological processes including cancer progression, heart failure and diabetes. However, the molecular mechanisms that regulate such endothelial-mesenchymal transition (EndMT) remain to be elucidated. We aim to study the molecular mechanisms underlying EndMT in order to identify novel targets and attempt to develop therapeutic strategies for EndMT-related diseases.

(2) Elucidation of the molecular mechanisms underlying tumor angio- and lymphangiogenesis
Tumor angiogenesis and lymphangiogenesis are key features of tumor progression and metastasis. While multiple signaling pathways have been implicated in the formation of blood and lymphatic vessels, the molecular mechanisms underlying these processes have not yet fully elucidated. Recent findings revealed that members of the transforming growth factor- β (TGF- β) family play pivotal roles on in angiogenesis and lymphangiogenesis, and that abnormalities in TGF- β family signaling lead to development of certain vascular disorders, including hereditary hemorrhagic telangiectasia (HHT), pulmonary arterial hypertension, Marfan syndrome and Loeys-Dietz syndrome. We attempt to elucidate the molecular mechanisms how TGF- β family signals regulate angiogenesis and lymphangiogenesis in tumor microenvironment.

(3) Understanding the molecular mechanisms underlying metastasis of cancer cells
Epithelial-mesenchymal transition (EMT) plays important roles in various physiological and pathological processes, and is regulated by signaling pathways mediated by cytokines including TGF- β . Using various types of in vitro cultured oral carcinoma cells and in vivo systems, we aim to identify the molecules involved in the acquisition of invasive properties of cancer cells, in order to develop novel therapeutic strategies.

(4) Elucidation of the role of LAMP-1/2 proteins in the lysosomal intracellular degradation system
Lysosomes are intracellular organelles, containing various hydrolytic enzymes, essential for maintaining cell

homeostasis such as acquisition of energy and nutrients, biological defense, removal of unnecessary substances. In recent years it has also been found that lysosomes sense the state of energy acquisition of cells and decide whether the cells proliferate or gain nutrition. Lysosomal dysfunction clinically results in progressive and severe effects, especially notable in the nervous system, bone, connective tissue.

Lysosome-associated membrane protein-1/2 is the abundant membrane - spanning glycoprotein present in lysosomal membranes. Most of the proteins of LAMP-1 and LAMP-2 are present on the luminal side of lysosomes, both of which are composed of two homologous domains. However, LAMP-2 deficient mice exhibit a more severe phenotype than LAMP-1 deficient mice and Danone disease develops in humans due to abnormalities of LAMP-2. Accumulation of autophagosome-like vesicles was observed in myocytes of Danone disease, suggesting that LAMP-2 is associated with autophagy. Since LAMP-1 and LAMP-2 are considered to be similar proteins, the reason why they are functionally different remained mystery. We first discovered that the mode of multimerization is different between LAMP-1 and LAMP-2. We reported the crystal structure analysis of the domains of LAMP-1 and LAMP-2 and based on the findings we analyzed the mode of multimerization at the atomic level by site-specific crosslinking reaction utilizing introduction of non-natural amino acid. Then we are generating LAMP-1/2 with mutation in multimerization. We would like to answer the questions "How lysosomes fuse with autophagosomes?", "What is lysosomal identity? (the mechanism by which lysosomes are reformed from autolysosomes after fusion of lysosomes with autophagosomes)?".

(5) Heparan sulfate proteoglycan-dependent cellular logistics

Heparan sulfate proteoglycans (HSPGs) are one of the basic constituents of plasma membranes and have ability to interact with a number of the extracellular ligands. HSPGs have been suggested to mediate the trafficking of various macromolecules from the cell surface. Growth factors, cytokines, lipoproteins, cell penetrating peptides, polycation-nucleic acid complexes, along with exosomes, and pathogens enter cells through HSPG-dependent endocytosis. HSPGs-dependent endocytic events have been involved in tumor progression, stressing the importance of the identification of HSPG species participating in a formation of various endocytic complexes. We have characterized the intracellular trafficking complexes formed in the presence of HSPGs in a rat C6 glioma cell line model. Successful isolation of HSPG-positive transport vesicles followed by detailed proteomic analysis allowed us the identification of over eighty proteins related to vesicular transport; i.e. endocytosis or recycling. Part of HSPGs in glioma cells found to be internalized through clathrin-dependent endocytosis and underwent recycling. Further characterization of HSPG-rich vesicular compartments will help us understand the nature of HSPG-ligand interactions and to design the tools for targeted delivery of ligands into the cells.

(6) Posture, behavior, and motion sickness of common marmosets in low gravities.

In planetary development projects such as manned Mars exploration that will take longer than 3 years, long-term biological adaptation to weightlessness and partial-gravity environments is a critical issue. Since rodents of short lifespan (rats and mice) cannot survive in such a long-term flight, other animals of longer lifespan must be used alternatively so as to conduct appropriate studies on posture and exploration as well as voice communication and social behaviors of animals that have some relevance to long-term manned spaceflight. Common marmoset belonging to the same anthropoid with humans has a lifespan of 15 years is characterized by unique social behavior resembling humans with abundant squealing. In parabolic flight experiment carried out, we first examined the adaptation and social behavior of common marmoset under such conditions as Moon and Mars simulation or weightlessness. We have gained new knowledge on the response and behavior of primates in partial gravities.

(3) Education

For the second-year undergraduate students, we are in charge of the unit, "Molecular aspect of cell biology" and "Laboratory course" under the module of "Molecular basis of biology". The contents of "Molecular aspect of cell biology (lecture)" includes, topics related to the structure and function of membranes, transport across membranes, organization and function of intracellular organelles, intracellular trafficking, cytoskeleton, extracellular matrix, signal transduction, cell cycle and cell death.

For the graduate students, in order to demonstrate various research examples, we lectured on the structure and function of proteoglycans and the structure and role of extracellular matrix.

(4) Lectures & Courses

For the undergraduate students, our aim is to provide the students with the basic knowledge in biochemistry to help them to understand cellular function based on the structure and function of biomolecules. For the graduate students, we encourage them to acquire an ability and research skill to study the cellular responses at molecular levels.

(5) Publications**[Original Articles]**

1. Takashi Ode, Katarzyna A Podyma-Inoue, Kazue Terasawa, Jin-Ichi Inokuchi, Toshihide Kobayashi, Tetsuro Watabe, Yuichi Izumi, Miki Hara-Yokoyama. PDMP, a ceramide analogue, acts as an inhibitor of mTORC1 by inducing its translocation from lysosome to endoplasmic reticulum. *Exp. Cell Res.*. 2017.01; 350(1); 103-114
2. Yuichi Akatsu, Yasuhiro Yoshimatsu, Taishi Tomizawa, Kazuki Takahashi, Akihiro Katsura, Kohei Miyazono, Tetsuro Watabe. Dual targeting of vascular endothelial growth factor and bone morphogenetic protein-9/10 impairs tumor growth through inhibition of angiogenesis. *Cancer Sci.*. 2017.01; 108(1); 151-155
3. Rie Norita, Yasuhiro Suzuki, Yutaka Furutani, Kazuki Takahashi, Yasuhiro Yoshimatsu, Katarzyna A Podyma-Inoue, Tetsuro Watabe, Yasufumi Sato. Vasohibin-2 is required for epithelial-mesenchymal transition of ovarian cancer cells by modulating transforming growth factor- β signaling. *Cancer Sci.*. 2017.03; 108(3); 419-426
4. Doino M, Yokoyama M, Sasaki Y, Kondo K, Yasuda Y, and Arakawa S.. Evaluation of the relationship between salivary concentration of anti-heat shock protein immunoglobulin and clinical manifestations of Behçet's disease *Scandinavian Journal of Rheumatology*. 2017.09; 46(5); 381-387
5. Takeshi Fukuhara, Jia Kim, Shintaro Hokaiwado, Makiko Nawa, Hayato Okamoto, Tomohiko Kogiso, Tetsuro Watabe, Nobutaka Hattori. A novel immunotoxin reveals a new role for CD321 in endothelial cells. *PLoS ONE*. 2017.09; 12(10); e0181502
6. Y Kumei, R Shimokawa, M Kimoto, Y Kawauchi, H Shimokawa, K Makita, K Ohya, K Toda. Gravity stress elevates the nociceptive threshold level with immunohistochemical changes in the rat brain. *Acta Astronaut.* 49(3-10); 381-390

[Conference Activities & Talks]

1. Katarzyna Anna Inoue, Kazuki Takahashi, Takumi Matsuda, Chihiro Takao, Yasuhiro Yoshimatsu and Tetsuro Watabe. Role of TGF- β in the invasiveness of oral carcinoma cells. Joint Symposium of Immunology and Pathological Biochemistry Units 2017.03.08 Tokyo
2. Ren E, Watari I, Hsu J, Mizumachi-Kubono M, Inoue K, Watabe T, Ono T. Unilateral nasal obstruction effects gustatory function in rats. The 39 th Annual Scientific Conference on Dental Research 2017.03.31 Ho Chi Minh city, Vietnam
3. P.S.De Campos, Y.Kumei, K.Hasegawa, L.R.De SouzaMendes Kawamura, J.L.Lopes Zeredo. Evaluation of respiratory movements in a murine model mimicking different stages of Parkinson's disease.. Am Thoracic Soc 2017 Intl Conference 2017.05.17 Washington DC
4. P.S.De Campos, L.R.De SouzaMendes Kawamura, K.Hasegawa, Y.Kumei, J.L.Lopes Zeredo. Cineradiographic analysis of respiratory movements in a murine model for late Parkinson's disease submitted to stress.. Am Thoracic Soc 2017 Intl Conference 2017.05.21 Washington DC
5. Teturo Watabe. Roles of signaling and transcriptional networks in the formation and maintenance of lymphatic vessels. Kitasato Research Forum 2017 on Vascular Biology 2017.05.31 Kitasato University School of Medicine
6. Miki Yokoyama, Takashi Ode, Kazue Terasawa, Katarzyna Anna Inoue, Jin-Ichi Inokuchi and Tetsuro Watabe. PDMP, a ceramide analogue, acts as an inhibitor of mTORC1 by inducing its translocation from lysosome to endoplasmic reticulum. The 59th JCBL Meeting 2017.06.16 Kyoto

7. Tetsuro Watabe. Targeting signaling networks in tumor microenvironment. 1st International Cancer Precision Medical Conference 2017.06.29 Tokyo
8. Katarzyna A. Inoue, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura and Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. FASEB Conference "TGF-B Superfamily: Signaling in Development and Disease" 2017.07.10
9. Miki Yokoyama, Takashi Ode, Kazue Terasawa, Katarzyna Anna Inoue, Jin-Ichi Inokuchi and Tetsuro Watabe. PDMP, a ceramide analogue, acts as an inhibitor of mTORC1 by inducing its translocation from lysosome to endoplasmic reticulum. The 12th Sphingotherapy Conference 2017.07.16
10. Campos PS, Kawamura LRSM, Hasegawa K, Kumei Y, Zeredo JLL. . Analysis of respiratory movements in a murine model for late Parkinson's disease submitted to stress. . 40th Annual Meeting of the Japanese Neuroscience Society 2017.07.18 Makuhari, Japan
11. Tetsuro Watabe. Roles of TGF- β family signals during endothelial-to- mesenchymal transition. the TGFbeta meeting in Uppsala 2017 2017.09.02 Sweden
12. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro, Yoshimatsu, Atsushi Kaida, Masahiko Miura and Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. Platform of Advanced Animal Model Support, FY2017 Technical Training Course for the youth 2017.09.08 Tateshina
13. Tetsuro Watabe. New trends for studying cancer invasion and metastasis. 2017.09.28 Yokohama
14. H. Morisaki, I. Yamanaka, T. Ohata, T. Kosho, K. Wakui, Y. Fukushima, M. Masuno, K. Takahashi, T. Watabe, T. Morisaki. TMEPAI mutation causes MFS/LDS-like phenotypes in 2 Japanese families.. The American Society of Human Genetics 2017 2017.10.17 Orlando
15. Wakasugi E, Watari I, Inoue K, Kubono M, Ono T. GLP-1 related gene analysis in mouse osteoblastic MC3T3-E1 cells using next generation sequencer. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
16. Nin, E, Watari I, Kyo S, Inoue K, Kubono M, Watabe T, Ono T. Unilateral nasal obstruction effects the gustatory receptors in rats. The 76th Annual Meeting of the Japanese Orthodontic Society 2017.10.18 Sapporo
17. Kazuki Takahashi. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. The 2017 Workshop of Intractable Disease Unit (Cancer) of TMDU 2017.11.06 Tokyo
18. Tetsuro Watabe, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura and Katarzyna A. Inoue. Relationship between cell cycle arrest and epithelial to mesenchymal transition (EMT) induced by TGF- β in oral squamous carcinoma cell. ERATO/AMED-CREST/PRESTO Joint International Symposium 2017.12.04 Kyoto
19. Kazuki Takahashi, Katarzyna A. Inoue, Yasuhiro Yoshimatsu, Atsushi Kaida, Masahiko Miura and Tetsuro Watabe. Cell cycle arrest in oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. ConBio 2017 2017.12.06 Kobe
20. Katarzyna A. Inoue, Kazuki Takahashi, Takumi Matsuda, Yasuhiro Yoshimatsu, Miki Yokoyama and Tetsuro Watabe. Exosomes secreted by oral squamous carcinoma cells undergoing TGF- β -induced epithelial to mesenchymal transition. ConBio2017 2017.12.06 Kobe
21. Tetsuro Watabe. Roles of signaling networks during tumor angiogenesis. CardioVascular and Metabolic Week 2017 2017.12.08 Osaka

Cell Signaling

Professor(Principal Investigator)Tomoki NAKASHIMA
Assistant Professor Mikihito HAYASHI
Assistant Professor Takehito ONO

(1) Research

Research Subjects

- 1)Regulation of bone remodeling by bone cells
- 2)Identification of bone-derived systemic regulatory factors (osteokines)
- 3)Mechanism of sensing and adapting to mechanical stress
- 4)Functional analysis of genes by gene manipulations and gene-disrupted mice
- 5)Development of clinical application by experimental animal disease models

(2) Education

Purpose of Education

Organized signal networks in the body are crucial for the higher physiological functions and the tissue organization. To understand the regulation of signal events, we take on cell signaling course including the molecular mechanism of both the “intra” cellular and the “inter” cellular signal transduction. Especially, the course will be focused on the molecular networks of signal transduction in osteoclasts, osteoblasts and osteocytes which is a new integrated field of osteonetwork (systemic network between bone and other systems). Besides, to promote the practical and clinical understanding, the course will deal with the molecular mechanism of osteoporosis and inflammatory bone destructed diseases, such as periodontal disease and rheumatoid arthritis, in parallel with the basic molecular biology.

(3) Publications

[Original Articles]

1. [Cell Signaling : SASAKI Fumiyuki] Sasaki F, Koga T, Saeki K, Okuno T, Kazuno S, Fujimura T, Ohkawa Y, Yokomizo T. Biochemical and immunological characterization of a novel monoclonal antibody against mouse leukotriene B4 receptor 1. PloS one. 2017; 12(9); e0185133
2. [Cell Signaling : SASAKI Fumiyuki] Ikeda K, Koga T, Sasaki F, Ueno A, Saeki K, Okuno T, Yokomizo T. Generation and characterization of a human-mouse chimeric high-affinity antibody that detects the DYKDDDDK FLAG peptide. Biochemical and biophysical research communications. 2017.05; 486(4); 1077-1082
3. [Cell Signaling : NAKASHIMA Tomoki] Kazuki Nagashima, Shinichiro Sawa, Takeshi Nitta, Masanori Tsutsumi, Tadashi Okamura, Josef M Penninger, Tomoki Nakashima, Hiroshi Takayanagi. Identification of subepithelial mesenchymal cells that induce IgA and diversify gut microbiota. Nat. Immunol.. 2017.06; 18(6); 675-682

4. [Cell Signaling : NAKASHIMA Tomoki] Y Fukushima-Nakayama, Takehito Ono, M Hayashi, M Inoue, H Wake, Takashi Ono, T Nakashima. Reduced Mastication Impairs Memory Function. *J. Dent. Res.*. 2017.08; 96(9); 1058-1066
5. [Cell Signaling : NAKASHIMA Tomoki] Ayumi Shoji-Matsunaga, Takehito Ono, Mikihiro Hayashi, Hiroshi Takayanagi, Keiji Moriyama, Tomoki Nakashima. Osteocyte regulation of orthodontic force-mediated tooth movement via RANKL expression. *Sci Rep.* 2017.08; 7(1); 8753
6. [Cell Signaling : NAKASHIMA Tomoki] Kazuki Nagashima, Shinichiro Sawa, Takeshi Nitta, Alejandro Prados, Vasiliki Koliarakis, George Kollias, Tomoki Nakashima, Hiroshi Takayanagi. Targeted deletion of RANKL in M cell inducer cells by the Col6a1-Cre driver. *Biochem. Biophys. Res. Commun.*. 2017.09;

[Misc]

1. [Cell Signaling : ONO TAKEHITO] Takehito Ono. The roles of the immune cells and cytokines in bone fracture healing *Infection, Inflammation and Immunity.* 2017.04; 47(1); 61-64
2. [Cell Signaling : ONO TAKEHITO] Takehito Ono, Hiroshi Takayanagi. Osteoimmunology in Bone Fracture Healing. *Current Osteoporosis Reports.* 2017.08; 15(4); 367-375
3. [Cell Signaling : NAKASHIMA Tomoki] Kazuo Okamoto, Tomoki Nakashima, Masahiro Shinohara, Takako Negishi-Koga, Noriko Komatsu, Asuka Terashima, Shinichiro Sawa, Takeshi Nitta, Hiroshi Takayanagi. Osteoimmunology: The Conceptual Framework Unifying the Immune and Skeletal Systems. *Physiol. Rev.*. 2017.10; 97(4); 1295-1349

[Conference Activities & Talks]

1. [Cell Signaling : NAKASHIMA Tomoki] Tomoki Nakashima. Bone homeostasis and mechano-biology. The 94th Annual Meeting of the Physiological Society of Japan 2017.03.28 Hamamatsu
2. [Cell Signaling : HAYASHI Mikihiro] Mikihiro Hayashi, Tomoki Nakashima, Hiroshi Takayanagi. Autoregulation of osteocyte through estrogen-miRNA-Sema3A-Nrp1 axis. *ASBMR 2017 Annual Meeting* 2017.09.08
3. [Cell Signaling : ONO TAKEHITO] Ayumi Shoji-Matsunaga, Takehito Ono, Keiji Moriyama, Tomoki Nakashima. Osteocyte-derived RANKL is a key regulator of orthodontic tooth movement. *Japanese Association for Dental Research* 2017.11.18
4. [Cell Signaling : ONO TAKEHITO] Takehito Ono, Kazuo Okamoto, Tomoki Nakashima, Takeshi Nitta, Hiroshi Takayanagi. The role of T cells in the process of bone fracture healing. *Japanese Association for Dental Research* 2017.11.19

Periodontology

From April.2017

【Professor】 Yuichi Izumi

【Associate Professor】 Akira aoki

【Junior Associate Professor】 Yasuo Takeuchi, Tatsuya Akizuki

【Assistant Professor】 Koji Mizutani, Sayaka Katagiri, Yuichi Ikeda (May ~)

【Specially appointed researcher】 Yuichi Ikeda (Apr)

【Clinical Fellow】

Yuuka Tsumanuma, Takanori Matsuura, Takahiro Ikawa, Takahiko Shiba

Shogo Maekawa, Hiroki Sato, Mizuki Nagata (~ Sep), Masahiro Noda(Oct ~)

【Graduate Students】

Yasuo Ito, Anri Ohtsu, Tooru Takagi, Ammar Shujaa Addin,

Chantida Pawauputanon Na Mahasarakham, Eri Ikeda, Sayuri Udagawa, Sho Kakizaki,

Daisuke Kido, Rina KOMAZAKI, Risako Tanimoto, Sophannary Kong,

Pawaputanon Na Mahasarakham Chantida, Shinta Suzuki, Nay Aung, Thatawee Khemwong,

Yujin Ohsugi, Naoki Sasaki, Kohei Takeda, Yosuke Tuchiya, Shunsuke Fukuba,

Anongwee Leewananthawet, Prima Buranasin,

Munehiro Okada, Chihiro Kano, Yuji Kato, Rie Kawamura, Keitetsu Kure,

Yutaro Kitanaka, Kohei Nohara, Kazuki Watanabe

【Adult graduate student】

Kaori Fujiwara, Masaki Tsubokawa, Naho Suzuki, Akiko Kobayashi, Miho Ogawa

【Graduate Research Student】

Hideyuki Takamatsu, Yukako Kusunoki, Masahiro Noda(~ Sep), Shogo Takeuchi,

Takeaki Sudo, Kosei Yano, Saori Katayama(~ Jun),

Akihito Nakazato, Takashi Furuichi,

Taiki Mise, Takae Shimoda, Ryo Hirai, Yuto Mukaiyama, Naoaki Yoshida,

Yoshiyuki Iwabuchi, Aya Suzuki, Keiji Komatsu, Shotaro Mori

【Clinical Professor】 Hiroaki Kobayahshi(Jul ~)

【Registered dentist】 : 40

【Assistant Administrative Staff】 Tomomi Anai

(1) Outline

Periodontology is a branch of dental sciences which deals with the research, prevention and treatment of periodontal diseases. Periodontal disease is a general disease name which occurred in the periodontal tissue: gingiva, periodontium, cementum and alveolar bone. At present, it is indicated mainly an acute or chronic inflammatory diseases. The mission of our department was to educate etiology of periodontal diseases, host response, oral bacteria, periodontal medicine, regenerative therapy and so on profoundly, and to find a solution through discussion research outcomes as to periodontal destructive process and to develop a novel periodontal treatment modalities.

(2) Research

- 1) Inflammatory and immunological factors in periodontal diseases
- 2) Periodontopathic bacteria and their pathogenicity

- 3) Influence of periodontal disease on general health
- 4) Analyses of growth factors and bio materials in periodontal regeneration
- 5) Clinical applications of laser in periodontics

(3) Lectures & Courses

Periodontology is a branch of dental science which deals with supporting structures of teeth, diseases and conditions affect them. Main objectives of periodontology in the graduate course is to provide students basic knowledge of etiology of periodontal diseases, its treatment modality and prognosis, and also to study advanced regenerative therapy.

(4) Clinical Performances

Periodontal clinic provides diagnosis, treatment and prevention of periodontal disease. Periodontal surgery and regenerative therapy are also performed in the clinic.

(5) Publications

[Original Articles]

1. Sato H, Suzuki J, Aoyama N, Watanabe R, Kaneko M, Shiheido Y, Yoshida A, Wakayama K, Kumagai H, Ikeda Y, Akazawa H, Komuro I, Isobe M, Izumi Y. A Periodontal pathogen *Porphyromonas gingivalis* deteriorates Isoproterenol-Induced myocardial remodeling in mice. *Hypertens. Res.* 2017; 40(1); 35-40
2. Thanakun S, Pornprasertsuk-Damrongsri S, Izumi Y. C-reactive protein levels and the association of carotid artery calcification with tooth loss. *Oral Dis.* 2017.01; 23(1); 69-77
3. Ode T, Podyma-Inoue KA, Terasawa K, Inokuchi JI, Kobayashi T, Watabe T, Izumi Y, Hara-Yokoyama M. PDMP, a ceramide analogue, acts as an inhibitor of mTORC1 by inducing its translocation from lysosome to endoplasmic reticulum. *Exp. Cell Res.* 2017.01; 350(1); 103-114
4. Kakuta E, Nomura Y, Morozumi T, Nakagawa T, Nakamura T, Noguchi K, Yoshimura A, Hara Y, Fujise O, Nishimura F, Kono T, Umeda M, Fukuda M, Noguchi T, Yoshinari N, Fukaya C, Sekino S, Numabe Y, Sugano N, Ito K, Kobayashi H, Izumi Y, Takai H, Ogata Y, Takano S, Minabe M, Makino-Oi A, Saito A, Abe Y, Sato S, Suzuki F, Takahashi K, Sugaya T, Kawanami M, Hanada N, Takashiba S, Yoshie H. Assessing the progression of chronic periodontitis using subgingival pathogen levels: a 24-month prospective multicenter cohort study. *BMC Oral Health.* 2017.01; 17(1); 46
5. Eick S, Meier I, Spoerlé F, Bender P, Aoki A, Izumi Y, Salvi GE, Sculean A. In Vitro-Activity of Er:YAG Laser in Comparison with other Treatment Modalities on Biofilm Ablation from Implant and Tooth Surfaces. *PLoS ONE.* 2017.01; 12(1); e0171086
6. Kaneko M, Suzuki J, Aoyama N, Watanabe R, Yoshida A, Shiheido Y, Izumi Y, Isobe M. Corrigendum: Toll-like receptor-2 has a critical role in periodontal pathogen-induced myocardial fibrosis in the pressure-overloaded murine hearts. *Hypertens. Res.* 2017.02; 40(2); 212
7. Ogata Y, Nakayama Y, Tatsumi J, Kubota T, Sato S, Nishida T, Takeuchi Y, Onitsuka T, Sakagami R, Nozaki T, Murakami S, Matsubara N, Tanaka M, Yoshino T, Ota J, Nakagawa T, Ishihara Y, Ito T, Saito A, Yamaki K, Matsuzaki E, Hidaka T, Sasaki D, Yaegashi T, Yasuda T, Shibutani T, Noguchi K, Araki H, Ikumi N, Aoyama Y, Kogai H, Nemoto K, Deguchi S, Takiguchi T, Yamamoto M, Inokuchi K, Ito T, Kado T, Furuichi Y, Kanazashi M, Gomi K, Takagi Y, Kubokawa K, Yoshinari N, Hasegawa Y, Hirose T, Sase T, Arita H, Kodama T, Shin K, Izumi Y, Yoshie H. Prevalence and risk factors for peri-implant diseases in Japanese adult patients. A cross-sectional multi-center study by periodontal specialist. *J Oral Sci.* 2017.03; 59(1); 1-11
8. Kachi H, Maruyama N, Maruyama F, Shiba T, Watanabe T, Goda A, Murase K, Michi Y, Takeuchi Y, Izumi Y, Harada K, Nakagawa I. Active microbiota show specific relationships in peri-implantitis and periodontitis. *The Stomatological Society, Japan.* 2017.03; 84(1); 25-36

9. Aoyama N, Suda T, Ikeda Y, Kinebuchi E, Sekiuchi T, Koyanagi T1, Hayakumo S, Mizutani K, Akizuki T, Izumi Y. Systemic Condition of First-visit Patients to the Periodontics Section of Tokyo Medical and Dental University Hospital. *The Journal of the Stomatological Society, Japan.* 2017.03; 84(1); 37-44
10. Maekawa S, Katagiri S, Takeuchi Y, Komazaki R, Ohtsu A, Udagawa S, Izumi Y. Bone metabolic microarray analysis of ligature-induced periodontitis in streptozotocin-induced diabetic mice. *J. Periodont. Res.* 2017.04; 52(2); 233-245
11. Nagata M, Iwasaki K, Akazawa K, Komaki M, Yokoyama N, Izumi Y, Morita I. Conditioned Medium from Periodontal Ligament Stem Cells Enhances Periodontal Regeneration. *Tissue Eng Part A.* 2017.05; 23(9-10); 367-377
12. Aoyama N, Suzuki JI, Sato H, Yoshida A, Shiheido Y, Izumi Y. Japanese workers with long leisure time have deteriorated periodontal condition: A cross-sectional study *Journal of Oral Biosciences.* 2017.05; 59(2); 104-107
13. Watanabe C, Wada J, Mizutani K, Watanabe H, Wakabayashi N. Chronological grey scale changes in supporting alveolar bone by removable partial denture placement on patients with periodontal disease: A 6-month follow-up study using digital subtraction analysis. *J Dent.* 2017.05; 63; 8-13
14. Saito A, Horie M, Ejiri K, Aoki A, Katagiri S, Maekawa S, Suzuki S, Kong S, Yamauchi T, Yamaguchi Y, Izumi Y, Ohshima M. MicroRNA profiling in gingival crevicular fluid of periodontitis—a pilot study *FEBS Openbio.* 2017.07; 7(7); 981-994
15. Pawaputanon N M C, Izu Y, Nishimori K, Izumi Y, Noda M, Ezura Y. Lgr4 Expression in Osteoblastic Cells Is Suppressed by Hydrogen Peroxide Treatment. *J. Cell. Physiol.* 2017.07; 232(7); 1761-1766
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[Books etc]

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2. Noda M, Aoki A, Mizutani K, Lin T, Komaki M, Shibata S, Izumi Y.. Dental Outlook Special Issue 2017 New Paradigm for Dental Medicine Its Future and Our Dreams The 23rd General Meeting of the Japanese Association for Dental Science. Ishiyaku Publishers, Inc., 2017.05
3. Editor Izumi Y, Author Izumi Y, Aoki A, Kobayashi H et al.. Systemic and Periodontal Health Q&A revised edition. Igaku Joho-sha, 2017.08 (ISBN : 978-4-903553-46-7)
4. Tsuda T (Eds)(Chapter: Aoki A). Dental laser applications. Quintessence Publishing Corp., Tokyo, 2017.09 (ISBN : 978-4-7812-0580-9)
5. Coluzzi DJ, Parker S (Chapter: Aoki A). Lasers in Dentistry - Current Concepts. Springer, 2017.09
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[Conference Activities & Talks]

1. Watanabe T, Shiba T, Kachi H, Murase K, Takeuchi Y, Maruyama F, Izumi Y, Nakagawa I.. Disease-specific bacterial networks of peri-implantitis and periodontitis clarified by metatranscriptomics.. The 90th Annual Meeting of Japanese Society of Bacteriology 2017.03.19 Miyagi
2. Takahiro Ikawa, Tatsuya Akizuki, Ammar Shujaa Addin, Takanori Matsuura, Shu Hoshi, Shunsuke Fukuba, Yuichi Izumi. Ridge augmentation using various structures of β -TCP in dogs. 2017 IADR/AADR/CADR General Session & Exhibition 2017.03.22 San Francisco, Calif., USA
3. Daisuke Kido, Koji Mizutani, Kohei Takeda, Takanori Matsuura, Yuichi Izumi. Insulin resistance causes impaired gingival wound healing in diabetic rats. the 95th General Session & Exhibition of the IADR 2017.03.24 San Francisco, Calif., USA
4. Noda M, Aoki A, Mizutani k, Lin T, Komaki M, Shibata S, Izumi,Y. High-Frequency Pulsed Low-Level Diode Laser Therapy Accelerates Wound Healing of Tooth Extraction Socket. The 95th General Session & Exhibition of the IADR 2017.03.25 San Francisco, USA
5. Risako Mikami, Koji Mizutani, Yoshiyuki Sasaki, Takanori Matsuura, Daisuke Kido, Yuto Mukaiyama, Tomonari Suda, Syujirou Ohta, Norihide Takaya, Yuichi Izumi. Screening Factors for Periodontitis During Medical Checkup: A Cross-Sectional Study. 2017 IADR/AADR/CADR General Session & Exhibition 2017.03.25 San Francisco, CA, USA
6. Tsubokawa M, Aoki A, Kakizaki S, Lin Tai-Chen, Mizutani K, Ejiri K, Geena Koshy, Oda S, Sumi Y, Izumi Y. Detection of Subgingival Calculus Using Optical Coherence Tomography :in vitro and clinical evaluation. 24th Annual Conference Academy of Laser Dentistry 2017.04.06 Tuscon, Arizona, USA
7. Tsubokawa M, Aoki A, Kakizaki S, Lin TC ,Mizutani K, Ejiri K, Koshy G, Oda S, Sumi Y, Izumi Y. Detection of Subgingival Calculus Using Optical Coherence Tomography :in vitro and clinical evaluation. The 24th Academy of Laser Dentistry Annual Conference 2017.04.08 Arizona, USA
8. Mizutani K, Noritake K, Tsuruta J, Seki N, Kondo K, Katagiri S, Takeuchi Y, Akizuki T, Arakawa S, Araki K, Izumi Y. The clinical and educational effects of the newly-introduced interprofessional clinical practice. The 60th Spring Meeting Of The Japanese Society Of Periodontology 2017.05.12 Fukuoka
9. Kong S, Aoki A, Iwasaki K, Mizutani K, Suda T, Katagiri S, Ogita M, Ando Y, Izumi Y. Effects of Er:YAG Laser Irradiation on Proliferation of Human Gingival Fibroblasts. The 60th Spring Meeting of Japanese Society of Periodontology 2017.05.12 Fukuoka
10. Udagawa S, Katagiri S, Mekawa S, Komazaki R, Ohtsu A, Sasaki N, Takeuchi Y, Ishihara K, Izumi Y. Evaluation of influence of *Porphyromonas gingivalis* infection on pregnancy and fetuses. The 60th Spring Meeting Of The Japanese Society Of Periodontology 2017.05.13 Fukuoka
11. Chigasaki O, Sasaki Y, Mizutani K, Aoki A, Takeuchi Y, Aoyama N, Ikeda Y, Gokyu M, Umeda M, Izumi Y . Correlation between Red-complex bacterial counts and alveolar bone loss. The 60th Spring Meeting of the Japanese Society of Periodontology 2017.05.13 Fukuoka

12. The clinical and educational effects of the newly-introduced interprofessional clinical practice. 2017.05.13
13. Aoki A. Effective application of Er:YAG laser in periodontics. Morita 2017 laser seminar 2017.05.28
14. Ikeda Y, Abbarin N, Neshatian M, Holcroft J, Ganss B. The Enamel Proteins Amelotin and Odontoblast Induce Hydroxyapatite Mineralization in a Collagen Matrix. the 12th International Conference on the Chemistry and Biology of Mineralized Tissues 2017.05.30 Potsdam, Germany
15. Aoki A. Effect of UV LED on periodontopathic bacteria. Grant meeting for development of new laser/LED devices in dental treatment 2017.06.01 Obu, Aichi prefecture
16. Takahiro Ikawa, Tatsuya Akizuki, Kiichi Maruyama, Wataru Ono, Ammar Shujaa Addin, Yuichi Izumi. Evaluation of three-dimensional morphological changes in teeth extraction sites after ridge augmentation using Bio-Oss and Bio-Gide; a six-month clinical study. National Symposium Osteology Japan 2017.06.03 Tokyo, Japan
17. Maekawa S, Matsuura T, Hoshi S, Mizutani K, Izumi Y. Patient-Reported Outcomes and Clinical Evaluation of Combination Therapy of GTR with Autograft or Xenograft: Interim report of a Randomized Controlled Trial. National Symposium OSTEOLOGY JAPAN 2017.06.03 Tokyo
18. Daisuke Kido, Koji Mizutani, Kohei Takeda, Risako Mikami, Kuniha Konuma, Takanori Matsuura, Yuichi Izumi. Impact of insulin resistance on impaired gingival wound healing in diabetic rats. The 146th Meeting of the Japanese Society of Conservative Dentistry 2017.06.08
19. Aoki A. Recent progress of Er:YAG laser application in periodontal therapy. China-Japan symposium for oral medicine 2017.06.10 Peking, China
20. Shiba T. Prosthetic treatment of patients with advanced chronic periodontitis -Konus-telescope denture : a case report-. 2017.06.24
21. Wada S, Ogawa T, Saito N, Yumoto M, Aoki A, Lin T, Kawamura R, Izumi Y. Tunable MID IR lasers for biological material processing. The 10th MIRAI Conference on Microfabrication and Green Technology 2017.07.01 Hwabaek International Convention Center (HICO), Gyeongju, Korea
22. Watanabe C, Wada J, Mizutani K, Watanabe H, Katsuki A, Wakabayashi N. Chronological effects of removable partial denture placement on periodontally compromised abutment teeth: A digital subtraction analysis. The 126th Scientific Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama
23. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Naoko SEKI, Yuki OHARA, Masayo YASUDA, Hiromi OTSUKA, Shinich ARAKAWA, Kouji ARAKI. . Development of a new IPW program for dental students and dental hygiene students in practical clinical training. Working as a dental team. The 36th General and Scientific Meeting of the Japanese Dental Education Association 2017.07.28
24. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
25. Yoshida Y, Churei H, Wada T, Takeuchi Y, Uo M, Ueno T. Antibacterial performance of mouthguard material incorporated with silver-nanoparticles-embedded EVA masterbatch.. FDI World Dental Congress 2017 2017.08.29 Madrid, Spain
26. Matsuura T, Akizuki T, Hoshi S, Shujaa addin A, Fukuba S, Okada M, Izumi Y.. The efficacy of moldable, in situ hardening β -TCP bone graft to 1-wall intrabony defect in dogs.. the 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
27. Katagiri S, Komazaki R, Takahashi H, Maekawa S, Shiba T, Takeuchi Y, Kitajima Y, Ohtsu A, Udagawa S, Sasaki N, Watanabe K, Sato N, Miyasaka N, Eguchi Y, Anzai K, Izumi Y. *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism.. The 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
28. Takagi T, Aoki A, Izumi Y et.al.. Removal of calcified deposits on microstructure titanium fixture surfaces of dental implants with erbium lasers. The 103rd Annual Meeting of the American Academy of Periodontology 2017.09.10 Boston, USA

29. Kong S, Aoki A, Iwasaki K, Mizutani K, Suda T, Katagiri S, Ogita M, Pavlic V, Izumi Y. Biological Effects of Er:YAG Laser Irradiation on Primary Human Gingival Fibroblasts. The 103rd Annual Meeting of the American Academy of Periodontology 2017.09.10 BOSTON, MA, USA
30. Maekawa S, Onizuka S, Katagiri S, Komazaki R, Ogura K, Takeuchi Y, Akiyama TM, Nitta H, Iwata T, Izumi Y.. Differential gene expression analysis by RNA-seq: Inflamed periodontal tissue of ligature-induced periodontitis in mice.. The 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
31. Maekawa S, Onizuka S, Katagiri S, Ogura K, Ohtsu A, Komazaki R, Udagawa S, Sasaki N, Watanabe K, Takeuchi Y, Miyoshi-Akiyama T, Nitta H, Iwata T, Izumi Y. Differentially expressed genes analysis by RNA-seq : Inflamed periodontal tissue of ligature-induced periodontitis in mice. 103rd Annual meeting American Academy of Periodontology 2017.09.12 Boston, USA
32. Funahashi K, Watanabe T, Shiba T, Muramoto K, Ogawa T, Takeuchi Y, Izumi Y, Moriyama K. Meta-transcriptomic analysis of dental plaque microbiota in cleft lip and palate patients. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.17 Matsumoto
33. Kobayashi T, Matsui M, Suzuki J, Tsutsui TW. Characterization of spontaneously immortalized cells derived from primary dental pulp of rhesus macaque (*Macaca mulatta*). The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.18 Matsumoto
34. Risako Mikami, Akira Aoki, Koji Mizutani, Yukihiko Tamura, Yuichi Izumi. Low-level ultrahigh-frequency and ultrashort-pulse blue laser irradiation enhances osteoblast extracellular calcification by upregulating proliferation and differentiation via TRPV1. The 29th Annual Meeting of Japanese Society for Laser Dentistry 2017.09.23
35. Suzuki N, Kobayashi H, Kano C, Izumi Y . Effect of Lactoferrin on Gingival Fibroblasts. The 147 th Meeting of The Japanese Society of Conservative Dentistry 2017.10.27 MALIOS, Iwate
36. Aoki A. Progress of Er:YAG laser application in periodontal pocket therapy. 20th Anniversary Forum of Er:YAG Laser 2017.11.26 Ochanomizu Solacity Conference Center, Tokyo
37. Aoki A. Periodontal Er:YAG Laser Operation. Continuing Dental Education Course, Dental Alumni Association, Tokyo Medical and Dental University (TMDU) 2017.12.03 Tokyo Medical and Dental University (TMDU), Tokyo
38. Kobayashi T, Matsui M, Suzuki J, Tsutsui TW. Analysis of differentiation for spontaneously immortalized dental pulp cells derived from rhesus macaque. The Fourth Winter Meeting of The Society of The Nippon Dental University 2017.12.09 Tokyo
39. Shunsuke Fukuba, Tatsuya Akizuki, Shu Hoshi, Takanori Matsuura, Ammar Shujaa Addin, Munehiro Okada, Yasuhiko Tabata, Makoto Tabata, Yuichi Izumi. Comparison between different isoelectric point of biodegradable gelatin/ β -tricalcium phosphate sponge using recombinant human fibroblast growth factor-2 for ridge augmentation. 2017.12.15 Kyoto
40. Anri Ohtsu, Yasuo Takeuchi, Shogo Maekawa, Rina Komazaki, Sayuri Udagawa, Naoki Sasaki, Yuichi Izumi. Influence of *Porphyromonas gingivalis* infection on gut microbiome in streptozotocin induced diabetic mice. JSD Diamond Anniversary Meeting in Kyoto 2017.12.16
41. Shinta Suzuki, Akira Aoki, Sayaka Katagiri, Shogo Maekawa, Kenichiro Ejiri, Sophannary Kong, Mizuki Nagata, Yoko Yamaguchi, Mitsuhiro Ohshima, Yuchi Izumi. Detection of hepatocyte growth factor in oral rinse water for possible periodontal diagnosis.. Japanese Society of Periodontology Diamond Anniversary Meeting 2017.12.16 Kyoto International Conference Center, Kyoto,
42. Aung N, Aoki A, Takeuchi Y, Hiratsuka K, Kong S, Shujaa Addin A, Izumi Y. Effects of different UV LED wavelengths on periodontopathic bacteria. JSP Diamond Anniversary Meeting in Kyoto 2017.12.16 Kyoto
43. Aoki A. Lasers and periodontal regeneration. Japanese Society of Periodontology Diamond Anniversary Meeting 2017.12.16 Kyoto International Conference Center, Kyoto

[Awards & Honors]

1. MING CHEN KAO AWARD (Ayano Uekubo), 2017.03
2. Student Scholarship Second Prize (Masaki Tsubokawa), Academy of Laser Dentistry, 2017.04
3. Excellent Poster Award (Takahiro Ikawa), National symposium Osteology Japan, 2017.06
4. Young Investigator Travel Award (Yuichi Ikeda), Twelfth International Conference on the Chemistry and Biology of Mineralized Tissues, 2017.06
5. Best Clinical Research Award, National Symposium OSTEOLOGY JAPAN (Maekawa S), National Symposium OSTEOLOGY JAPAN, 2017.06
6. Advanced Education System Development(Kanako Noritake), Japanese Dental Education Association, 2017.07
7. The First Prize for Best Presentation(Yuichi Ikeda), The Stomatological Society, Japan, 2017.11

Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD (Apr-)

Assistant Professor: Keiko Nakamura, MD, PhD (-Mar)

Junior Associate Professor: Masashi Kizuki, MD, MPH, PhD; Kaoruko Seino, PhD (-Mar)

Assistant Professor: Ayako Morita, PhD

Research Fellow of Japan Society for the Promotion of Science: Yukako Tani, PhD; Satomi Doi, PhD (Apr-Sep)

Project Researcher: Aya Isumi, PhD; Satomi Doi, PhD (Oct-)

(1) Outline

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

(2) Research

The main focus of the department is as follows:

1. Social epidemiology (impact of social inequality, social capital, social network, and social support on health)
2. Life-course epidemiology (impact of child poverty and adverse childhood experiences on health) and international comparison study
3. Prevention on child abuse and neglect
4. Disaster and child and their family's mental health
5. Nutrition during pregnancy or early childhood and health

(3) Education

The faculty of department teach Public Health and Social Medicine for grade 3 medical students, Public Health Practice for grade 4 medical students, and graduate students seminars.

(4) Lectures & Courses

The purpose of this course is to develop the knowledge and skills of the participants to prevent diseases. Participants will: understand broad risk factors from individual factors (e.g., genetic factor) and environmental factors, especially social determinants, their interactions; make causal inference applying a life-course perspective on disease onset (e.g., long-term effect of fetus or childhood exposure); perform advanced statistics; acquire attitudes toward social contribution through writing and publishing scientific papers in international journals. The final goal is that the participants are able to plan and implement health policy or program to prevent diseases in a real life setting.

The participants will be able to: 1. explain the risk of disease.

2. verbalize own research question and develop a hypothesis to test it.

3. develop research field or access secondary data to test the hypothesis.
4. explain an epidemiologic study design.
5. calculate a sample size.
6. analyse basic model (multivariate analysis, logistic analysis, etc) and conduct advanced analysis (multilevel analysis, propensity score matching, multiple imputation, etc)
7. justify the research question logically, in scientific writing in English.
8. develop an intervention (policy or program) and design a study protocol to assess its effectiveness.

(5) Publications

[Original Articles]

1. Rarau P, Vengiau G, Gouda H, Phuanukoonon S, Kevau IH, Bullen C, Scragg R, Riley I, Marks G, Umezaki M, Morita A, Oldenburg B, McPake B, Pulford J. Prevalence of non-communicable disease risk factors in three sites across Papua New Guinea: a cross-sectional study. *BMJ global health*. 2017; 2(2); e000221
2. Minatsu Kobayashi, Seung Chik Jwa, Kohei Ogawa, Naho Morisaki, Takeo Fujiwara. Validity of a food frequency questionnaire to estimate long-chain polyunsaturated fatty acid intake among Japanese women in early and late pregnancy. *Journal of Epidemiology*. 2017.01; 27(1); 30-35
3. Kenichi Yokobayashi, Ichiro Kawachi, Katsunori Kondo, Naoki Kondo, Yuiko Nagamine, Yukako Tani, Kokoro Shirai, Susumu Tazuma, . Association between Social Relationship and Glycemic Control among Older Japanese: JAGES Cross-Sectional Study. *PLoS ONE*. 2017.01; 12(1); e0169904
4. Yukako Tani, Naoki Kondo, Hisashi Noma, Yasuhiro Miyaguni, Masashige Saito, Katsunori Kondo. Eating Alone Yet Living With Others Is Associated With Mortality in Older Men: The JAGES Cohort Survey. *J Gerontol B Psychol Sci Soc Sci*. 2017.01;
5. Rakprasit Jutarat, Nakamura Keiko, Seino Kaoruko, Morita Ayako. Healthcare use for communicable diseases among migrant workers in comparison with Thai workers *Industrial Health*. 2017.01; 55(1); 67-75
6. Kinomoto-Kondo S, Umehara N, Sato S, Ogawa K, Fujiwara T, Arata N, Sago H. The effects of gestational transient thyrotoxicosis on the perinatal outcomes: a case-control study. *Archives of gynecology and obstetrics*. 2017.01; 295(1); 87-93
7. Tabuchi T, Fujiwara T, Shinozaki T. Tobacco price increase and smoking behaviour changes in various subgroups: a nationwide longitudinal 7-year follow-up study among a middle-aged Japanese population. *Tobacco control*. 2017.01; 26(1); 69-77
8. Jutarat Rakprasit, Keiko Nakamura, Kaoruko Seino, Ayako Morita. Healthcare use for communicable diseases among migrant workers in comparison with Thai workers. *Ind Health*. 2017.02; 55(1); 67-75
9. Nawa N, Kogaki S, Ozono K. Listening to public concerns on vaccinations in order to provide information in a timely manner. *Vaccine*. 2017.03; 35(10); 1369
10. Tsuji T, Sasaki Y, Matsuyama Y, Sato Y, Aida J, Kondo K, Kawachi I. Reducing depressive symptoms after the Great East Japan Earthquake in older survivors through group exercise participation and regular walking: a prospective observational study. *BMJ open*. 2017.03; 7(3); e013706
11. Satomi Doi, Asako Sakano, Takashi Muto, Yuji Sakano. Reliability and validity of a Japanese version of the Valuing Questionnaire (VQ) *Japanese Journal of Behavior Therapy*. 2017.04; 43(1); 83-94
12. Ayano Miura, Takeo Fujiwara. Intimate Partner Violence during Pregnancy and Postpartum Depression in Japan: A Cross-sectional Study. *Frontiers in Public Health*. 2017.04; 5; 81
13. Naho Morisaki, Ichiro Kawachi, Emily Oken, Takeo Fujiwara. Social and anthropometric factors explaining racial/ethnic differences in birth weight in the United States. *Scientific Reports*. 2017.04; 7; 46657
14. Fujiwara Takeo, Yagi Junko, Homma Hiroaki, Mashiko Hirofumi, Nagao Keizo, Okuyama Makiko. Symptoms of Post-Traumatic Stress Disorder Among Young Children 2 Years After the Great East Japan Earthquake *Disaster Medicine and Public Health Preparedness*. 2017.04; 11(2); 207-215

15. Omori S, Tanabe H, Banno K, Tsuji A, Nawa N, Hirata K, Kawatani K, Kokubu C, Takeda J, Taniguchi H, Arahori H, Wada K, Kitabatake Y, Ozono K. A Pair of Maternal Chromosomes Derived from Meiotic Nondisjunction in Trisomy 21 Affects Nuclear Architecture and Transcriptional Regulation. *Scientific reports*. 2017.04; 7(1); 764
16. Naho Morisaki, Chie Nagata, Seung Chik Jwa, Haruhiko Sago, Shigeru Saito, Emily Oken, Takeo Fujiwara. Pre-pregnancy BMI-specific optimal gestational weight gain for women in Japan. *Journal of Epidemiology*. 2017.05; 27(9-10); 492-498
17. Kohei Ogawa, Naho Morisaki, Shigeru Saito, Shoji Sato, Takeo Fujiwara, Haruhiko Sago. Association of Shorter Height with Increased Risk of Ischaemic Placental Disease. *Paediatric and Perinatal Epidemiology*. 2017.05; 31(3); 198-205
18. Kohei Ogawa, Seung-Chik Jwa, Minatsu Kobayashi, Naho Morisaki, Haruhiko Sago, Takeo Fujiwara. Validation of a food frequency questionnaire for Japanese pregnant women with and without nausea and vomiting in early pregnancy. *Journal of Epidemiology*. 2017.05; 27(5); 201-208
19. Tatsuo Yamamoto, Jun Aida, Katsunori Kondo, Shinya Fuchida, Yukako Tani, Masashige Saito, Yuri Sasaki. Oral Health and Incident Depressive Symptoms: JAGES Project Longitudinal Study in Older Japanese. *J Am Geriatr Soc*. 2017.05; 65(5); 1079-1084
20. Kato T, Fujiwara T, Kawachi I. Associations between mothers' active engagement with infants at 6months and children's adjustment to school life at ages 5.5 and 11years *CHILD CARE HEALTH AND DEVELOPMENT*. 2017.05; 43(3); 406-414
21. Inoue Y, Stickley A, Yazawa A, Aida J, Kawachi I, Kondo K, Fujiwara T. Adverse childhood experiences, exposure to a natural disaster, and posttraumatic stress disorder among survivors of the 2011 Great East Japan earthquake and tsunami *AMERICAN JOURNAL OF HUMAN BIOLOGY*. 2017.05;
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26. Takeo Fujiwara, Junko Yagi, Hiroaki Homma, Hirobumi Mashiko, Keizo Nagao, Makiko Okuyama, . Suicide risk among young children after the Great East Japan Earthquake: A follow-up study. *Psychiatry Res*. 2017.07; 253; 318-324
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[Books etc]

1. *Social Epidemiology*. 2017.09 (ISBN : 978-4-469-26829-4)
2. *Social Epidemiology*. 2017.09 (ISBN : 978-4-469-26830-0)

[Misc]

1. Inoue Y., Stickley A., Yazawa A., Aida J., Kawachi I., Kondo K., Fujiwara T.. Adverse childhood experiences, exposure to a natural disaster, and posttraumatic stress disorder among survivors of the 2011 Great East Japan earthquake and tsunami *AMERICAN JOURNAL OF HUMAN BIOLOGY*. 2017; 29(2);

[Conference Activities & Talks]

1. Masashi Kizuki, Takeo Fujiwara. Interaction effect between adult attachment pattern and social support on psychological distress. The 27th Annual Scientific Meeting The Japan Epidemiological Association Program and Abstracts 2017.01.27 Kofu city, Yamanashi
2. Tanaka Takakuni, Hong Guang, Izumi Masayuki, Saito Tomoya, Nishi Kentaro, Matsuyama Yusuke, Chiba Mirei, Toda Takashi, Kudou Tadaaki. Association of oral fat sensitivity with mental state in healthy young adults. *The Journal of Physiological Sciences* 2017.03.01
3. Tatsuo Yamamoto, Jun Aida, Katsunori Kondo, Shinya Fuchida, Yukako Tani, Masashige Saito, Yuri Sasaki.. Oral Health and Incident Depressive Symptoms in Older Japanese. *IADR2017* 2017.03.24 San Francisco, USA

4. Morisaki N, Kawachi I, Oken E, Fujiwara T. Social and anthropometric factors explaining racial/ethnic differences in birth weight in the United States.. *Scientific reports* 2017.04.21
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6. Ogawa K, Jwa SC, Kobayashi M, Morisaki N, Sago H, Fujiwara T. Validation of a food frequency questionnaire for Japanese pregnant women with and without nausea and vomiting in early pregnancy.. *Journal of epidemiology* 2017.05.01
7. Takeo Fujiwara. Effectiveness of an Educational Video on Ahaking and Smothering when Used in Maternity Wards at First Week of Age: A Cluster Randomized Controlled Trial . *Sixth Penn State Health International Conference on Pediatric Abusive Head Trauma* 2017.06.30
8. Okuzono S, Fujiwara T, Kato T, Kawachi I. Spanking and subsequent behavioral problems in toddlers: A propensity score-matched, prospective study in Japan.. *Child abuse & neglect* 2017.07.01
9. Ichikawa K, Fujiwara T, Kawachi I. It takes a village: Fixed-effects analysis of neighborhood collective efficacy and children's development.. *Journal of epidemiology* 2017.08.01
10. Takeo Fujiwara. Suicide risk among young children after the Great East Japan Earthquake: A follow-up study. *The 21st International Epidemiological Association (IEA), World Congress of Epidemiology (WCE2017)* 2017.08.21
11. Masashi Kizuki. Diversity of neighborhood retail food stores affects mortality from acute myocardial infarction. *The 21st International Epidemiological Association (IEA) World Congress of Epidemiology (WCE2017)* 2017.08.22 Omiya city, Saitama Prefecture
12. Takeo Fujiwara. Childhood poverty and health: what policy makers should know. *The 21st International Epidemiological Association (IEA), World Congress of Epidemiology (WCE2017)* 2017.08.22
13. Morisaki N, Nagata C, Jwa SC, Sago H, Saito S, Oken E, Fujiwara T. Pre-pregnancy BMI-specific optimal gestational weight gain for women in Japan.. *Journal of epidemiology* 2017.10.01
14. Takeo Fujiwara. Environmental risk factors on autism spectrum disorder: perspective from social epidemiology. *International Symposium on Autism 2017* 2017.10.14 Malaysia
15. Doi, S., Fujiwara, T., & Isumi, A.. Risk factors of intimate partner violence (IPV) during pregnancy. 2017.11.01

Environmental Parasitology

Professor : Shiroh IWANAGA

Lecturer : Takashi KUMAGAI

Assistant Professor : Naoaki SINZAWA, Akina HINO

Project Associate Professor : Mitsuko OHASHI (AMED J-GRID)

PhD Course Students : Emmanuel BLAY (D4),

Kofi KWOFIE (D3),

Michael Amoa-Bosompem (D2),

Sho ARIMOTO (D2)

Master Course Students: Fumiya HIYOSHI (M2),

Takashi SEKINE(M1),

Tsubasa NISHI (M1),

Taishi HIRAYAMA(M1)

(1) Outline

Parasitic infectious diseases including Malaria and some neglected tropical diseases have been still been prevalent over the world and the countermeasures against them are urgent issues in the global public health. The scientific research plays an important role in not only understanding the biology of the parasites, but also in developing the effective vaccines and new drugs.

Our laboratory carries molecular biological studies out on malaria and schistosome parasites. In particular, we are interested in transcriptional and epigenetic regulation of gene expression in malaria parasites, *P. falciparum*, and the communication between schistosome parasites using the extracellular vesicles including small RNAs. We are also interested in the drug resistance of malaria parasites and are thus attempt to identify the drug resistance gene by Plasmodium artificial chromosome, which is developed by us. In addition, we performed the epidemiological studies about Opisthorchis and Schistosomiasis to develop the new diagnostic tools. Furthermore, since 2008, we have carried the research project on infectious diseases out in collaboration with researchers of Noguchi Memorial Institute for Medical Research. In this project, we mainly attempt to identify the new anti-parasitic compounds against African trypanosomiasis and utilize them as lead compound for drug development.

(2) Research

The following studies have been carried out in our laboratory with molecular genetic, cell biological, and biochemical techniques:

- (1) Elucidation of molecular mechanism of transcriptional regulation of Malaria parasite, *P. falciparum*. (the functional analysis of AP2 transcriptional factors)
- (2) Identification of drug resistance genes of Malaria parasite using the artificial chromosome technology.
- (3) Investigation of cell-cell communication of schistosome parasites with extracellular vehicle containing small RNA.
- (4) Host immune response during parasite infection: Th2 response to helminth infection.
- (5) Epidemiological survey of Opisthorchis infection and Schistosomiasis in SE Asian areas using new diagnostic tools based on LAMP method.
- (6) Identification of new anti-parasitic compounds from Ghanaian medical herbs.

(3) Education

Main objective of the parasitology course for undergraduate students is to provide them the basic knowledge of pathogenicity, treatment and diagnosis of parasitic diseases. We also lecture about the global action against parasitic diseases and basic biology of parasites. In the parasitology course for graduate students, they carry out the advanced molecular biology study about the parasites, in particular malaria and *Schistosoma* parasites, using genetic engineering, cellular biological, genome editing technologies. Furthermore, they have to join the weakly seminar, which are “seminar for the selected papers” and “the study session about the advanced molecular biology” .

(4) Lectures & Courses

Lecture and practices of basic and clinical parasitology are given. Further more, Field practice is important for future career. It is important to have field experiences where each student find matters and problems to be clarified. Together with those, final goal is to develop human resources with enough knowledge and experiences.

(5) Clinical Services & Other Works

Clinical services for the diagnosis of parasitic infections are our routine activities. Furthermore, epidemiological surveillance and disease control activities in the endemic fields are intended to enhance health and welfare of residents.

(6) Publications

[Original Articles]

1. Masafumi Yamabe, Takashi Kumagai, Rieko Shimogawara, Emmanuel Awusah Blay, Akina Hino, Koichiro Ichimura, Akira Sato, Hye-Sook Kim, Nobuo Ohta. Novel synthetic compounds with endoperoxide structure damage juvenile stage of *Schistosoma mansoni* by targeting lysosome-like organelles. *Parasitol. Int.* 2017.02; 66(1); 917-924
2. Daisuke Kobayashi, Mitsuko Ohashi, Joseph H N Osei, Esinam Agbosu, Millicent Opoku, Alfred Agbekudzi, Joannitta Joannides, Ryosuke Fujita, Toshinori Sasaki, J H Kofi Bonney, Samuel Dadzie, Haruhiko Isawa, Kyoko Sawabe, Nobuo Ohta. Detection of a novel putative phlebovirus and first isolation of Dugbe virus from ticks in Accra, Ghana. *Ticks Tick Borne Dis.* 2017.06; 8(4); 640-645
3. Eiji Nagayasu, Myo Pa Pa Thet Hnin Htwe Aung, Thanaporn Hortiwakul, Akina Hino, Teruhisa Tanaka, Miwa Higashiarakawa, Alex Olia, Tomoyo Taniguchi, Soe Moe Thu Win, Isao Ohashi, Emmanuel Igwaro Odongo-Aginya, Khin Myo Aye, Mon Mon, Kyu Kyu Win, Kei Ota, Yukari Torisu, Siripen Panthuwong, Eisaku Kimura, Nirianne M Q Palacpac, Taisei Kikuchi, Tetsuo Hirata, Shidow Torisu, Hajime Hisaeda, Toshihiro Horii, Jiro Fujita, Wah Win Htike, Haruhiko Maruyama. A possible origin population of pathogenic intestinal nematodes, *Strongyloides stercoralis*, unveiled by molecular phylogeny. *Sci Rep.* 2017.07; 7(1); 4844
4. Koichiro Suzuki, Naoaki Shinzawa, Keisuke Ishigaki, Keiji Nakamura, Hiroyuki Abe, Aya Fukui-Miyazaki, Kazuyoshi Ikuta, Yasuhiko Horiguchi. Protective effects of in vivo-expressed autotransporters against *Bordetella pertussis* infection. *Microbiol. Immunol.* 2017.09; 61(9); 371-379
5. Itaru Nakamura, Kenji Yagi, Takashi Kumagai, Nobuo Ohta. Positive fecal occult blood test as a diagnostic cue for *Schistosoma mansoni* infection in a developed country. *IDCases.* 2017.10; 10; 108-109
6. Daisuke Kobayashi, Haruhiko Isawa, Ryosuke Fujita, Katsunori Murota, Kentaro Itokawa, Yukiko Higa, Yukie Katayama, Toshinori Sasaki, Tetsuya Mizutani, Shiroh Iwanaga, Nobuo Ohta, Arlene Garcia-Bertuso, Kyoko Sawabe. Isolation and characterization of a new iflavirus from *Armigeres* spp. mosquitoes in the Philippines. *J. Gen. Virol.* 2017.11; 98(11); 2876-2881

7. Fumiji Saito, Kouyuki Hirayasu, Takeshi Satoh, Christian W Wang, John Lusingu, Takao Arimori, Kyoko Shida, Nirianne Marie Q Palacpac, Sawako Itagaki, Shiroh Iwanaga, Eizo Takashima, Takafumi Tsuboi, Masako Kohyama, Tadahiro Suenaga, Marco Colonna, Junichi Takagi, Thomas Lavstsen, Toshihiro Horii, Hisashi Arase. Immune evasion of Plasmodium falciparum by RIFIN via inhibitory receptors. *Nature*. 2017.12; 552(7683); 101-105
8. Takayuki Shiratsuchi, Urvashi Rai, Izumi Kaneko, Min Zhang, Shiroh Iwanaga, Masao Yuda, Moriya Tsuji. A potent malaria vaccine based on adenovirus with dual modifications at Hexon and pVII. *Vaccine*. 2017.12; 35(50); 6990-7000

[Misc]

1. Xiangming Li, Jing Huang, Izumi Kaneko, Min Zhang, Shiroh Iwanaga, Masao Yuda, Moriya Tsuji. A potent adjuvant effect of a CD1d-binding NKT cell ligand in human immune system mice. *Expert Rev Vaccines*. 2017.01; 16(1); 73-80

[Conference Activities & Talks]

1. Takashi Kumagai, et al. The evaluations of the LAMP method and Kato-Katz method for risk mapping of Schistosoma mekongi infections in Champasak province. The 17th Annual Workshop of the Regional Network for Asian Schistosomiasis and Other Helminthic Zoonoses (RNAS+) 2017.10.25 Vientiane, Lao PDR
2. Shiroh Iwanaga. Novel method for identification of drug resistance genes from P. falciparum using the artificial chromosome technology.. SYMPOSIUM TO COMMEMORATE THE 90TH ANNIVERSARY OF DR. HIDEYO NOGUCHI' S ARRIVAL IN GHANA 2017.11.16 Ghana, Accra

Forensic Medicine

Professor
Koichi UEMURA

Associate Professor
Toshihiko AKI

Junior Associate Professor
Kana UNUMA

Assistant Professor
Takeshi FUNAKOSHI

Specially Appointed Assistant Professor
Kanao NORITAKE

Graduate Student
Naho HIRAYAMA
Ryo WATANABE
Midori NAGAI
Rina KASEDA
Tomomi SANO
Renho TAKAHASHI
Mako FURUKAWA

(1) Research

Research Subjects

- 1) Toxicology
- 2) Alcohol medicine
- 3) Forensic pathology

(2) Education

Purpose of education

Forensic medicine provides fundamental human rights, public safety and nation's welfare to make a fair judgment on the items on the law which requires the medical knowledge. Education of forensic medicine is included forensic medicine in a narrow sense and medical law. Purpose of education in forensic medicine is to provide students opportunity to study the essential knowledge of the relationship between medical and society (include law, ethics, suit and administration). Students are also taught a blood type and an alcohol medicine in a practical training.

(3) Clinical Services & Other Works

Practical services

Forensic Medicine provides the expert opinion on a living body and a corpse to clarify causes of wound and death, mainly entrusted by a public prosecutor or the police, thereby, contributing fair trial in a court.

(4) Publications**[Original Articles]**

1. [Forensic Medicine : UNUMA Kana] Kana Unuma, Toshihiko Aki, Kanako Noritake, Takeshi Funakoshi, Koichi Uemura. A CO-releasing molecule prevents annexin A2 down-regulation and associated disorders in LPS-administered rat lung. *Biochem. Biophys. Res. Commun.*. 2017.06; 487(3); 748-754
2. [Forensic Medicine : UEMURA Koichi] Ryo Watanabe, Kana Unuma, Kanako Noritake, Takeshi Funakoshi, Toshihiko Aki, Koichi Uemura.. Ataxia telangiectasia and rad3 related (ATR)-promyelocytic leukemia protein (PML) pathway of the DNA damage response in the brain of rats administered arsenic trioxide. *J. Toxicologic Pathology*. 2017.07; 30; 333-337
3. [Forensic Medicine : UEMURA Koichi] Kanako Noritake, Toshihiko Aki, Moe Kimura, Takeshi Funakoshi, Kana Unuma, Koichi Uemura. Restoration of YAP activation rescues HL-1 cardiomyocytes from apoptotic death by ethanol. *J Toxicol Sci*. 2017.10; 42(5); 545-551

[Misc]

1. [Forensic Medicine : UEMURA Koichi] Toshihiko Aki, Kana Unuma, and Koichi Uemura. Emerging roles of mitochondria and autophagy in liver injury during sepsis. *Cell Stress*. 2017.11; 1(2); 79-89
2. [Forensic Medicine : UEMURA Koichi] Toshihiko Aki, Kanako Noritake, Takeshi Funakoshi, Koichi Uemura.. Modes of Chemically Induced Cell Death. *Comprehensive Toxicology 3rd ed Volume 1 (General subjects)*. 2017.12;

Health Care Management and Planning

Professor Kazuo KAWAHARA
Assistant Professor Makiko SUGAWA
Graduate Student Jian CHEN

Woonkwan HYUN
Masakazu KIKUCHI
Yoko KOMURA
Daisuke KUMAZAWA
Masao MURATA
Hisashi OMOTE
Masataka YANO
Hayato TAKAYAMA
Ritsuki NEGISHI
Katsunori OHOYAMA

(1) Outline

By analyzing the Japanese healthcare policies and system and by reviewing their interaction with society, the structural characteristics and issues can be clarified. To resolve or find better ways to handle these issues, we conduct research into public health and welfare, and its related disciplinary areas. With the cooperation of active policy makers and personnel from the healthcare departments, the research results can be applied to the present healthcare policies and system. Through this education on collecting data, clarifying issues, analyzing the situation, and evaluating options, students taking this course are expected to grow in their ability to make healthcare policies.

(2) Research

In the academic areas mentioned above, we conduct research under the following topic areas:

- 1) The significance of public healthcare planning, its challenges, and influences on the healthcare system
We conduct research on issues related to new healthcare policies including planning, analysis, issue resolution, and making positive changes to the healthcare plan. This research area includes the Japanese emergency medical service and the impartial evaluation of the travel distance of aid agents and the time required for them to reach their destination.
- 2) Structural choices concerning national blood services
In Japan, we experienced HIV infection from tainted blood products. There were various causes for this event, and improvements are required in all processes: collecting blood, screening blood, manufacturing blood products, and following-up on the usage of these products. By analyzing background information related to the adverse events and their causes, we can propose the most appropriate policies related to blood services, thus ensuring safety, and securing a stable supply. To achieve a stable supply of blood products, we also conduct epidemiological studies to review guidelines on collecting blood.
- 3) The government role in preventing medical errors

Issues related to medical errors and adverse events have recently attracted a great deal of attention in Japan. We study the role that the government should play regarding various medical errors and their prevention as well as review and address the financial loss caused by blood-related adverse events and policies on prevention.

4) Structural analyses of healthcare system in the community

By reviewing and analyzing activities related to disease prevention and health promotion conducted by local healthcare centers, we research the role of the local healthcare system and its effectiveness and efficiency.

5) Systemizing and evaluating public health policies

We review the processes of creating public health policies and systems, address the association with the creating processes and stakeholders such as political parties and lobby groups, evaluate their policies, and then suggest improvements to these policies and systems.

6) The role of healthcare communication to fill in gaps between medical providers and patients, and to share the uncertainties related to medicine and healthcare

7) The influence of healthcare communication on patient and medial safety

8) Reviewing communication tools and skills, and their systematic introduction into the healthcare system in order to realize patient participation and proactive involvement in treatment processes

(3) Publications

[Original Articles]

1. Takamichi Kogure, Masahiko Sumitani, Hiroaki Abe, Jun Hozumi, Reo Inoue, Kazuhito Mietani, Kazuo Kawahara, and Yoshitsugu Yamada. . Ischemic Ulcer Pain Is Both Nociceptive and Neuropathic Pain Based on a Discriminant Function Analysis Using the McGill Pain Questionnaire *Journal of Pain& Palliative Care Pharmacotherapy*. 2017.04; 0(0); 1-7

Molecular Epidemiology

Professor: Masaaki MURAMATSU

Associate Professor : Noriko SATO

Assistant Professor : Chihiro Imai

Adjunct Instructor : Katsuko SUDO, Jun-ichi TAGUCHI

Graduate Student: Kaung Si Thu,

Khin Thet Thet Zaw, Yuko Maeda, Fujitani,

Tay Zar Kyaw, Tadaaki Katsuta, Jyun-ya Hagiwara, Shilpa Pavethynath

Norihiko Satake, Maidina Abudushataer, Ake Ko Ko Minn, Zong Yuan, Kenji Suzuki, Hirokazu Sakamoto,

Yui Tsubota

Research Student: Tong Daike

(1) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

(2) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
4. The role of epigenetic regulation and fetal programming in common diseases.
5. Application of personal genome to preemptive & preventive medicine.

(3) Education

Masaaki Muramatsu: Holistic Study of Disease Prevention I

Masaaki Muramatsu: Environmental/Social Health

Masaaki Muramatsu: Negotiation and Debate in English

Noriko Sato, Masaaki Muramatsu: Bioscience I

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

(4) Lectures & Courses

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as their interactions by applying the technology and information of human genome to epidemiology. Our goal is not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences.

(5) Publications**[Original Articles]**

1. Sariya Dechamethakun, Noriko Sato, Shinobu Ikeda, Motoji Sawabe, Seiji Mori, Yoshiji Yamada, Masashi Tanaka Masaaki Muramatsu and Tomio Arai. Association of Macrophage Capping Protein (CAPG) Arg335His Polymorphism and Cancer Susceptibility in the Elderly Japanese Journal of Gerontology and Geriatric Research. 2017.04; 6(2); 417
2. Noriko Sato, Katsuko Sudo, Masayo Mori, Chihiro Imai, Masaaki Muramatsu, Masahiro Sugimoto. Early gestational maternal low-protein diet diminishes hepatic response to fasting in young adult male mice. Sci Rep. 2017.08; 7(1); 9812
3. Kumpei Tanisawa, Nobuyoshi Hirose, Yasumichi Arai, Hiroshi Shimokata, Yoshiji Yamada, Hisashi Kawai, Motonaga Kojima, Shuichi Obuchi, Hirohiko Hirano, Hiroyuki Suzuki, Yoshinori Fujiwara, Yu Taniguchi, Shoji Shinkai, Kazushige Ihara, Maki Sugaya, Mitsuru Higuchi, Tomio Arai, Seiji Mori, Motoji Sawabe, Noriko Sato, Masaaki Muramatsu, Masashi Tanaka. Inverse association between height-increasing alleles and extreme longevity in Japanese women. J. Gerontol. A Biol. Sci. Med. Sci.. 2017.08;
4. Khin Thet Thet Zaw , Sato Noriko, Ikeda Shinobu, Kaung Si Thu , Naka Mieno Makiko, Arai Tomio, Mori Seiji, Furukawa Tetsushi, Sasano Tetsuo, Sawabe Motoji, Tanaka Masashi, Muramatsu Masaaki. Association of ZFH3 gene variation with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study Journal of Cardiology. 2017.08; 70(1-2); 180-184
5. Rina Komazaki, Sayaka Katagiri, Hirokazu Takahashi, Shogo Maekawa, Takahiko Shiba, Yasuo Takeuchi, Yoichiro Kitajima, Anri Ohtsu, Sayuri Udagawa, Naoki Sasaki, Kazuki Watanabe, Noriko Sato, Naoyuki Miyasaka, Yuichiro Eguchi, Keizo Anzai, Yuichi Izumi. Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. Sci Rep. 2017.10; 7(1); 13950

[Misc]

1. Sariya Dechamethakun, Masaaki Muramatsu. Long noncoding RNA variations in cardiometabolic diseases. J. Hum. Genet.. 2017.01; 62(1); 97-104
2. Kazuki Mochizuki*, Chihiro Imai, Noriko Sato, Takeo Kubota. The roles of epigenetics in developmental programming/Developmental Origins of Health and Disease theory journal OBM Genetics. 2017.09;
3. Kazuki Mochizuki, Chihiro Imai, Noriko Sato, Takeo Kubota. The roles of epigenetics in developmental programming/Developmental Origins of Health and Disease theory. OBM Genetics. 2017.10; 1(4);

[Conference Activities & Talks]

1. Hidemi Takimoto , Motoko Okamitsu , Noriko Sato , Tay Zar Kyaw , Nay Chi Htun , Chihiro Imai , Yuiri Tsubota , Reiko Tajirika-Shirai , Satoshi Yago , Tomoko Aoyama , Naoyuki Miyasaka. Dietary intakes from 3-day weighed dietary records among pregnant participants in the Birth Cohort - Gene and Environment Interaction Study of TMDU (BC-GENIST). The 21st World Congress of Epidemiology (WCE2017) 2017.08.21

2. Noriko Sato, Hidemi Takimoto, Motoko Okamitsu, Tay Zar Kyaw, Chihiro Imai, Nay Chi Htun, Satoshi Yago, Tomoko Aoyama, Seiji Yamaguchi and Naoyuki Miyasaka. Study design: the evaluation of interindividual differences in neonatal epigenome - the BC-GENIST project. the 21st World Congress of Epidemiology, International Epidemiological Association 2017.08.21 Saitama, Japan
3. Hidemi Takimoto, Motoko Okamitsu, Noriko Sato, Tay Zar Kyaw, Nay Chi Htun, Chihiro Imai, Yuri Tsubota, Reiko Tajirika-Shirai, Satoshi Yago, Tomoko Aoyama, Naoyuki Miyasaka. Dietary intakes from 3-day weighed dietary records among pregnant participants in the Birth Cohort - Gene and ENvironment Interaction Study of TMDU (BC-GENIST). the 21st World Congress of Epidemiology, International Epidemiological Association 2017.08.21 Saitama, Japan

Research Development

Faculty Staff
Professor
Kozo TAKASE

Graduate Students
Doctor course
Akemi HIRABAYASHI
Tomoko IZUGAMI
Akira MIURA
Yasumasa OOSHIRO
Hideki TERUYA
Masakazu HARAMO
Rinshuu SHIMABUKURO
Kazushige ENDOH

Master course (Master of Medical Administration)
Hirotaka IMAYUKI
Michio UEMATSU
Miwako KADOTA
Mizue NAGASAWA
Hiroko HAYAO
Junichi FURUTA
Kengo WAKABAYASHI

(1) Research

- 1) Introduction of Clinical Pathway in hospital
- 2) Medical law suit and professional information
- 3) Quality management of medical law suit
- 4) Organizational logic for hospital
- 5) Health care policy and rational
- 6) Management of medical information and privacy
- 7) Hospitality in medicine
- 8) Clinical guideline and medical quality
- 9) Patient satisfaction and patient experience
- 10) Development of medical engineering apparatus

(2) Education

- 1) Hospital Information Management
- 2) Medical Informatics, statistics
- 3) TQM in medicine
- 4) Biological bias and data management

5) Medical Law and Ethics

6) Medical induction course for Judges and Prosecutors (collaborated with the Supreme Court and Department of Justice)

7) Health Promotion Policy program (General Medicine, Risk Management in Medicine) with Hitotsubashi University

(3) Lectures & Courses

Study on development of medical system and hospital management

Goals/outline:

The goals supposed in the lecture are mastering the technique of implementation of research development and acquiring the ability of management of projects.

(4) Clinical Services & Other Works

Kozo TAKASE

Committee member of Legal Training for Judicial Apprentice, Japanese Supreme Court

Committee member of Tokyo District Court

Chief Editorial Board of Japanese Society for Clinical Pathway

(5) Publications

[Original Articles]

1. Rinshu Shimabukuro, Kozo Takase, Sachiko Ohde, Isao Kusakawa. Handheld fetal Doppler device for assessing heart rate in neonatal resuscitation *Pediatrics International*. 2017.10; 59; 1069-1073

Health Policy and Informatics

Professor:Kiyohide FUSHIMI

Graduate Student:Asako TUKASAKI, kyoko SHINODA,
Ayako MATSUO, Motoko TAIMA(SANO), Toshihiro TAMAKI,
Yuya MIZUNO, Tetu OHNUMA, Akira HOMMA, Eishi UECHI,
Nobuo SAKATA, Tomomitu ICHIKAWA, Mariko KODAN,
Norihiro INOUE, Kyoko HIRANO, Mihoko OTA, Ken KAWASAKI,
Natsuko KANAZAWA, Shunsuke EDAKUBO, Yoshiteru YANO,
Yoko NUKAYA, Senri WATANABE, Risa SUZUKI, Akihito UDA,
Yuka SATO

Graduate Research Student:Masahiro INOUE

(1) Research

- 1) Functional differentiation and coordination of healthcare facilities
- 2) Development and application of patient case mix system for Japanese healthcare settings
- 3) Application of information technology to standardization of health care and sharing of health care information.

(2) Education

Health policy informatics is a branch of health policy science which deals with the application of information technology to health policy research. Main objective of health policy informatics in the graduate course is to acquire ability to independently design, manage and accomplish researches in health policy and health informatics fields.

(3) Publications

[Original Articles]

1. Toshiaki Isogai, Hideo Yasunaga, Hiroki Matsui, Hiroyuki Tanaka, Motoyuki Hisagi, Kiyohide Fushimi. Factors affecting in-hospital mortality and likelihood of undergoing surgical resection in patients with primary cardiac tumors. *J Cardiol.* 2017.01; 69(1); 287-292
2. Takahiro Inoue, Hiroyo Kuwabara, Kiyohide Fushimi. Regional Variation in the Use of Percutaneous Coronary Intervention in Japan. *Circ. J.* 2017.01; 81(2); 195-198
3. Yukiyo Sakamoto, Yasuhiro Yamauchi, Hideo Yasunaga, Hideyuki Takeshima, Wakae Hasegawa, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Guidelines-concordant empiric antimicrobial therapy and mortality in patients with severe community-acquired pneumonia requiring mechanical ventilation. *Respir Investig.* 2017.01; 55(1); 39-44

4. Miho Ishimaru, Sachiko Ono, Sayaka Suzuki, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Artificial nutrition dependence after cetuximab versus cisplatin combined with radiotherapy for advanced head and neck cancer: A propensity score-matched analysis. *Head Neck*. 2017.02; 39(2); 320-325
5. Takashi Tagami, Hiroki Matsui, Yuuta Moroe, Reo Fukuda, Ami Shibata, Chie Tanaka, Kyoko Unemoto, Kiyohide Fushimi, Hideo Yasunaga. Antithrombin use and 28-day in-hospital mortality among severe-burn patients: an observational nationwide study. *Ann Intensive Care*. 2017.02; 7(1); 18
6. Yosuke Ono, Sachiko Ono, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yuji Tanaka. Clinical features and practice patterns of treatment for adrenal crisis: a nationwide cross-sectional study in Japan. *Eur. J. Endocrinol.* 2017.03; 176(3); 329-337
7. Yosuke Ono, Sachiko Ono, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yuji Tanaka. Clinical characteristics and outcomes of myxedema coma: Analysis of a national inpatient database in Japan. *J Epidemiol*. 2017.03; 27(3); 117-122
8. Yusuke Sasabuchi, Hiroki Matsui, Hideo Yasunaga, Kiyohide Fushimi. Increase in avoidable hospital admissions after the Great East Japan Earthquake. *J Epidemiol Community Health*. 2017.03; 71(3); 248-252
9. Maiko Yagi, Hideo Yasunaga, Hiroki Matsui, Kojiro Morita, Kiyohide Fushimi, Masashi Fujimoto, Teruyuki Koyama, Junko Fujitani. Impact of Rehabilitation on Outcomes in Patients With Ischemic Stroke: A Nationwide Retrospective Cohort Study in Japan. *Stroke*. 2017.03; 48(3); 740-746
10. Masaya Sato, Ryosuke Tateishi, Hideo Yasunaga, Hiromasa Horiguchi, Hiroki Matsui, Haruhiko Yoshida, Kiyohide Fushimi, Kazuhiko Koike. The ADOPT-LC score: a novel predictive index of in-hospital mortality of cirrhotic patients following surgical procedures, based on a national survey. *Hepatology Res.* 2017.03; 47(3); E35-E43
11. Hiroyuki Odagiri, Hideo Yasunaga, Hiroki Matsui, Shigeru Matsui, Kiyohide Fushimi, Mitsuru Kaise. Hospital volume and adverse events following esophageal endoscopic submucosal dissection in Japan. *Endoscopy*. 2017.04; 49(4); 321-326
12. Hiroki Matsui, Taisuke Jo, Kiyohide Fushimi, Hideo Yasunaga. Outcomes after early and delayed rehabilitation for exacerbation of chronic obstructive pulmonary disease: a nationwide retrospective cohort study in Japan. *Respir. Res.* 2017.04; 18(1); 68
13. Takeshi Oichi, Hirotaka Chikuda, Junichi Ohya, Ryo Ohtomo, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Sakae Tanaka, Hideo Yasunaga. Mortality and morbidity after spinal surgery in patients with Parkinson's disease: a retrospective matched-pair cohort study. *Spine J*. 2017.04; 17(4); 531-537
14. Masato Takeuchi, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi. Pediatric urolithiasis associated with acute gastroenteritis: an inpatient database study in Japan. *Eur. J. Pediatr.* 2017.04; 176(4); 501-507
15. Yoshifumi Mizobuchi, Keiji Muramatsu, Makoto Ohtani, Junichiro Satomi, Kiyohide Fushimi, Shinya Matsuda, Shinji Nagahiro. The Current Status of Microvascular Decompression for the Treatment of Hemifacial Spasm in Japan: An Analysis of 2907 Patients Using the Japanese Diagnosis Procedure Combination Database. *Neurol. Med. Chir. (Tokyo)*. 2017.04; 57(4); 184-190
16. Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Resuscitative endovascular balloon occlusion of the aorta or resuscitative thoracotomy with aortic clamping for noncompressible torso hemorrhage: A retrospective nationwide study. *J Trauma Acute Care Surg*. 2017.05; 82(5); 910-914
17. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Naoto Yokogawa, Kiyohide Fushimi, Hideo Yasunaga. Treatments and in-hospital mortality in acute myocardial infarction patients with rheumatoid arthritis: a nationwide retrospective cohort study in Japan. *Clin. Rheumatol.* 2017.05; 36(5); 995-1004
18. Yukiyo Sakamoto, Yasuhiro Yamauchi, Hideo Yasunaga, Hideyuki Takeshima, Wakae Hasegawa, Taisuke Jo, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Development of a nomogram for predicting in-hospital mortality of patients with exacerbation of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2017.05; 12; 1605-1611

19. Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Association between Nurse Staffing and In-Hospital Bone Fractures: A Retrospective Cohort Study. *Health Serv Res.* 2017.06; 52(3); 1005-1023
20. Akahito Sako, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Hidetaka Hamasaki, Hisayuki Katsuyama, Tetsuro Tsujimoto, Atsushi Goto, Hidekatsu Yanai. Hospitalization with hypoglycemia in patients without diabetes mellitus: A retrospective study using a national inpatient database in Japan, 2008-2012. *Medicine (Baltimore).* 2017.06; 96(25); e7271
21. Hironori Uematsu, Kazuto Yamashita, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Estimating the disease burden of methicillin-resistant *Staphylococcus aureus* in Japan: Retrospective database study of Japanese hospitals. *PLoS ONE.* 2017.06; 12(6); e0179767
22. Y Sasabuchi, H Yasunaga, H Matsui, A K Lefor, K Fushimi, M Sanui. Epidural analgesia is infrequently used in patients with acute pancreatitis : a retrospective cohort study. *Acta Gastroenterol. Belg.* 2017.06; 80(3); 381-384
23. Shinichiro Kobori, Tatsuhiko Kubo, Makoto Otani, Keiji Muramatsu, Yoshihisa Fujino, Hiroaki Adachi, Hiromasa Horiguchi, Kiyohide Fushimi, Shinya Matsuda. Coexisting infectious diseases on admission as a risk factor for mechanical ventilation in patients with Guillain-Barré syndrome. *J Epidemiol.* 2017.07; 27(7); 311-316
24. Tomoki Wada, Hideo Yasunaga, Kent Doi, Hiroki Matsui, Kiyohide Fushimi, Yoichi Kitsuta, Susumu Nakajima. Relationship between hospital volume and outcomes in patients with traumatic brain injury: A retrospective observational study using a national inpatient database in Japan. *Injury.* 2017.07; 48(7); 1423-1431
25. Toru Sugihara, Hideo Yasunaga, Hiroki Matsui, Go Nagao, Akira Ishikawa, Tetsuya Fujimura, Hiroshi Fukuhara, Kiyohide Fushimi, Makoto Otori, Yukio Homma. Accessibility to surgical robot technology and prostate-cancer patient behavior for prostatectomy. *Jpn. J. Clin. Oncol.* 2017.07; 47(7); 647-651
26. Tomoki Wada, Hideo Yasunaga, Hayato Yamana, Hiroki Matsui, Takehiro Matsubara, Kiyohide Fushimi, Susumu Nakajima. Development and validation of a new ICD-10-based trauma mortality prediction scoring system using a Japanese national inpatient database. *Inj. Prev.* 2017.08; 23(4); 263-267
27. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. In-hospital management and outcomes in patients with peripartum cardiomyopathy: a descriptive study using a national inpatient database in Japan. *Heart Vessels.* 2017.08; 32(8); 944-951
28. Motoko Sano, Kiyohide Fushimi. Association of Palliative Care Consultation With Reducing Inpatient Chemotherapy Use in Elderly Patients With Cancer in Japan: Analysis Using a Nationwide Administrative Database. *Am J Hosp Palliat Care.* 2017.08; 34(7); 685-691
29. Masao Iwagami, Hideo Yasunaga, Hiroki Matsui, Hiromasa Horiguchi, Kiyohide Fushimi, Eisei Noiri, Masaomi Nangaku, Kent Doi. Impact of end-stage renal disease on hospital outcomes among patients admitted to intensive care units: A retrospective matched-pair cohort study. *Nephrology (Carlton).* 2017.08; 22(8); 617-623
30. Wakae Hasegawa, Yasuhiro Yamauchi, Hideo Yasunaga, Hideyuki Takeshima, Yukiyo Sakamoto, Taisuke Jo, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Prognostic nomogram for inpatients with asthma exacerbation. *BMC Pulm Med.* 2017.08; 17(1); 108
31. Daisuke Shinjo, Hisateru Tachimori, Keiko Sakurai, Tetsu Ohnuma, Kenji Fujimori, Kiyohide Fushimi. Factors affecting prolonged length of stay in psychiatric patients in Japan: A retrospective observational study. *Psychiatry Clin. Neurosci.* 2017.08; 71(8); 542-553
32. Hirokazu Urushiyama, Taisuke Jo, Hideo Yasunaga, Yasuhiro Yamauchi, Hiroki Matsui, Wakae Hasegawa, Hideyuki Takeshima, Yoshihisa Hiraishi, Akihisa Mitani, Kiyohide Fushimi, Takahide Nagase. Adjuvant chemotherapy versus chemoradiotherapy for small cell lung cancer with lymph node metastasis: a retrospective observational study with use of a national database in Japan. *BMC Cancer.* 2017.09; 17(1); 613
33. Hayato Yamana, Mutsuko Moriwaki, Hiromasa Horiguchi, Mariko Kodan, Kiyohide Fushimi, Hideo Yasunaga. Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. *J Epidemiol.* 2017.10; 27(10); 476-482

34. Manabu Kawata, Yusuke Sasabuchi, Hiroshi Inui, Shuji Taketomi, Hiroki Matsui, Kiyohide Fushimi, Hiro-taka Chikuda, Hideo Yasunaga, Sakae Tanaka. Annual trends in knee arthroplasty and tibial osteotomy: Analysis of a national database in Japan. *Knee*. 2017.10; 24(5); 1198-1205
35. Daisuke Shinjo, Kiyohide Fushimi. The degree of severity and trends in hospital standardized mortality ratios in Japan between 2008 and 2012: a retrospective observational study. *Int J Qual Health Care*. 2017.10; 29(5); 705-712
36. Kojiro Morita, Hiroki Matsui, Hayato Yamana, Kiyohide Fushimi, Tomoaki Imamura, Hideo Yasunaga. Association between advanced practice nursing and 30-day mortality in mechanically ventilated critically ill patients: A retrospective cohort study. *J Crit Care*. 2017.10; 41; 209-215
37. Taisuke Jo, Hideo Yasunaga, Yusuke Sasabuchi, Nobuaki Michihata, Kojiro Morita, Yasuhiro Yamauchi, Wakae Hasegawa, Hideyuki Takeshima, Yukiyo Sakamoto, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Association between dementia and discharge status in patients hospitalized with pneumonia. *BMC Pulm Med*. 2017.10; 17(1); 128
38. Toshiaki Isogai, Hiroki Matsui, Hiroyuki Tanaka, Kiyohide Fushimi, Hideo Yasunaga. Seasonal variation in patient characteristics and in-hospital outcomes of Takotsubo syndrome: a nationwide retrospective cohort study in Japan. *Heart Vessels*. 2017.10; 32(10); 1271-1276
39. Sandeep Shakya, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. In-hospital complications after implantation of cardiac implantable electronic devices: Analysis of a national inpatient database in Japan. *J Cardiol*. 2017.11; 70(5); 405-410
40. Masaya Sato, Ryosuke Tateishi, Hideo Yasunaga, Hiroki Matsui, Hiromasa Horiguchi, Kiyohide Fushimi, Kazuhiko Koike. Mortality and hemorrhagic complications associated with radiofrequency ablation for treatment of hepatocellular carcinoma in patients on hemodialysis for end-stage renal disease: A nationwide survey. *J. Gastroenterol. Hepatol.*. 2017.11; 32(11); 1873-1878
41. Yusuke Okubo, Nobuaki Michihata, Koichi Yoshida, Naho Morisaki, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Impact of pediatric obesity on acute asthma exacerbation in Japan. *Pediatr Allergy Immunol*. 2017.12; 28(8); 763-767

[Conference Activities & Talks]

1. Shinjo, D., Sato, D., Wada, H., Ishikawa, K.B., Fushimi, K.. Prediction model of 30-day unplanned readmission in patients with acute myocardial infarction in Japan. 33rd PCSI (Patient Classification Systems International) Conference 2017.10.09 Sydney, Australia

Life Sciences and Bioethics

Masayuki Yoshida
 Yusuke Ebana
 Hiroko Kohbata
 Mizuko Osaka
 Eiichiro Kanda

(1) Outline

Department of Life Sciences and Bioethics (Bioethics Research Center) offers classes and seminars regarding bioethics, research ethics, and clinical ethics in Graduate School of Medical and Dental Sciences, Graduate School of Health Care Sciences, and School of Medicine. Our lecture includes fundamental bioethics and research ethics so that students can absorb the current concept of the bioethics and research ethics. We try to include clinical materials such as cases of genetic counseling, where ethics-based approach is critically important.

Apart from class for juniors, we give bioethics seminars for hospital staff and faculties based on the research ethics guideline revised 2008, in which attendance of bioethics lecture is mandatory for any person who conducts medical research.

We dynamically participated in extra-campus activities; such as the ethical committee members of the National Institute of Health etc.

(2) Publications

[Original Articles]

1. Nakazawa Harumasa, Chang Kyungho, Shinozaki Shohei, Yasukawa Takashi, Ishimaru Kazuhiro, Yasuhara Shingo, Yu Yong-Ming, Martyn J A Jeevendra, Tompkins Ronald G, Shimokado Kentaro, Kaneki Masao. iNOS as a Driver of Inflammation and Apoptosis in Mouse Skeletal Muscle after Burn Injury: Possible Involvement of Sirt1 S-Nitrosylation-Mediated Acetylation of p65 NF-kappaB and p53. PLoS One. 2017; 12(1); e0170391
2. Islam Md Monirul, Sato Shinobu, Shinozaki Shingo, Takenaka Shigeori. Cyclic ferrocenylnaphthalene diimide derivative as a new class of G-quadruplex DNA binding ligand. Bioorg Med Chem Lett. 2017.01; 27(2); 329-335
3. Ebana Yusuke. Impact of Clinical and Genetic Factors on Superior Vena Cava Arrhythmogenicity in Atrial Fibrillation Japanese Circulation Society Scientific Meeting Abstracts. 2017.03; 81; OJ-114
4. Furukawa Tetsushi, Liu Lian, Ebana Yusuke, Nitta Jun-ichi, Takahashi Yoshihida, Miyazaki Shinsuke, Komura Masatoshi, Tanaka Toshihiro, Isobe Mitsuaki. Genetic Background of Atrial Fibrillation Japanese Circulation Society Scientific Meeting Abstracts. 2017.03; 81; TP2-1
5. Ebana Yusuke. Precision Medicine Based on Genetic Information Combined Analysis Using GWAS and Array Data Detecting Associated Pathway and Shared Genomic Structure Japanese Circulation Society Scientific Meeting Abstracts. 2017.03; 81; SY14-3
6. Shintaro Akiyama, Toshimitsu Fujii, Katsuyoshi Matsuoka, Ebana Yusuke, Mariko Negi, Kento Takenaka, Masakazu Nagahori, Kazuo Ohtsuka, Mitsuaki Isobe, Mamoru Watanabe. Endoscopic features and

- genetic background of inflammatory bowel disease complicated with Takayasu arteritis. *J. Gastroenterol. Hepatol.* 2017.05; 32(5); 1011-1017
7. Miyachi Y, Tsuchiya K, Komiya C, Shiba K, Shimazu N, Yamaguchi S, Deushi M, Osaka M, Inoue K, Sato Y, Matsumoto S, Kikuta J, Wake K, Yoshida M, Ishii M, Ogawa Y.. Roles for Cell-Cell Adhesion and Contact in Obesity-Induced Hepatic Myeloid Cell Accumulation and Glucose Intolerance. *Cell Reports.* 2017.05; 18(11); 2766-2779
 8. Siew-Kee Low, Atsushi Takahashi, Yusuke Ebana, Kouichi Ozaki, Ingrid E Christophersen, Patrick T Ellinor, , Soichi Ogishima, Masayuki Yamamoto, Mamoru Satoh, Makoto Sasaki, Taiki Yamaji, Motoki Iwasaki, Shoichiro Tsugane, Keitaro Tanaka, Mariko Naito, Kenji Wakai, Hideo Tanaka, Tetsushi Furukawa, Michiaki Kubo, Kaoru Ito, Yoichiro Kamatani, Toshihiro Tanaka. Identification of six new genetic loci associated with atrial fibrillation in the Japanese population. *Nat. Genet.* 2017.06; 49(6); 953-958
 9. Ohigashi Hirokazu, Tamura Natsuko, Ebana Yusuke, Harigai Masayoshi, Maejima Yasuhiro, Ashikaga Takashi, Isobe Mitsuaki. Effects of immunosuppressive and biological agents on refractory Takayasu arteritis patients unresponsive to glucocorticoid treatment *Journal of Cardiology.* 2017.06; 69(5-6); 774-778
 10. Hiroko Terui-Kohbata, Masayuki Yoshida. Current condition of genetic medicine for hereditary breast cancer. *Molecular and Clinical Oncology.* 2017.07; 7(1); 98-102
 11. Yusuke Ebana, Kouichi Ozaki, Lian Liu, Hitoshi Hachiya, Kenzo Hirao, Mitsuaki Isobe, Michiaki Kubo, Toshihiro Tanaka, Tetsushi Furukawa. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25. *J Cardiol.* 2017.10; 70(4); 366-373
 12. Shinsuke Miyazaki, Yusuke Ebana, Lian Liu, Hiroaki Nakamura, Hitoshi Hachiya, Hiroshi Taniguchi, Takamitsu Takagi, Takatsugu Kajiyama, Tomonori Watanabe, Miyako Igarashi, Shigeki Kusa, Takashi Nida, Yoshito Iesaka, Tetsushi Furukawa. Chromosome 4q25 variants and recurrence after second-generation cryoballoon ablation in patients with paroxysmal atrial fibrillation. *Int. J. Cardiol.* 2017.10; 244; 151-157
 13. Ebana Yusuke, Ozaki Kouichi, Liu Lian, Hachiya Hitoshi, Hirao Kenzo, Isobe Mitsuaki, Kubo Michiaki, Tanaka Toshihiro, Furukawa Tetsushi. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25 *Journal of Cardiology.* 2017.10; 70(3-4); 366-373
 14. Yusuke Ebana, Junichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Masahito Suzuki, Lian Liu, Kenzo Hirao, Eiichiro Kanda, Mitsuaki Isobe, Tetsushi Furukawa. Association of the Clinical and Genetic Factors With Superior Vena Cava Arrhythmogenicity in Atrial Fibrillation. *Circ. J.* 2017.12; 82(1); 71-77
 15. Takahashi Sayako, Terui-Kohbata Hiroko, Ebana Yusuke, Yoshida Masayuki. Analysis of the Present Recognition Toward a Central IRB (cIRB) System in Japanese Medical Schools *JOURNAL OF EMPIRICAL RESEARCH ON HUMAN RESEARCH ETHICS.* 2017.12; 12(5); 394-395
 16. Ebana Yusuke, Nitta Junichi, Takahashi Yoshihide, Miyazaki Shinsuke, Suzuki Masahito, Liu Lian, Hirao Kenzo, Kanda Eiichiro, Isobe Mitsuaki, Furukawa Tetsushi. Association of the Clinical and Genetic Factors With Superior Vena Cava Arrhythmogenicity in Atrial Fibrillation *Circulation Journal.* 2017.12; 82(1); 71-77

[Misc]

1. Yusuke Ebana. Ethics required for clinical research *Endocrinology, Diabetology & Metabolism.* 2017.08; 45(2); 86-90

[Conference Activities & Talks]

1. Yusuke Ebana. Combined Analysis Using GWAS and Array Data Detecting Associated Pathway and Shared Genomic Structure. The 81st Annual Scientific Meeting of the Japanese Circulation Society 2017.03.17
2. Mizuko Osaka, Masayuki Yoshida.. Neutrophil-depletion prevents development of atherosclerosis in LDLR null mice. The 81st Annual Scientific Meeting of the Japanese Circulation Society 2017.03.17 Kanazawa, Japan

3. Mizuko Osaka, Michiyo Deushi, Hiromi Tsuru, Masayuki Yoshida. Neutrophil plays an important role on the formation of atherosclerotic lesion.. 2017.06.17 Tokyo, Japan
4. Mizuko Osaka, Michiyo Deushi, Hiromi Tsuru, Masayuki Yoshida. Neutrophil plays an important role on the development of atherosclerosis.. 49th Annual Scientific Meeting of the Japan Atherosclerosis Society 2017.07.06 Hiroshima, Japan

[Others]

1. Grant-in-Aid for Young Scientists (B) JSPS KAKENHI (16K19048)
S-nitrosylation, a novel posttranslational protein modification, mediated glycolipid metabolism disorder and chronic inflammation. 2016-2017
2. Takeda Science Foundation for Medical Research
The missing link between the metabolic syndrome pathogenesis and chronic inflammation. 2016-2018
3. Grant-in-Aid for Exploratory Research JSPS KAKENHI (16K15120)
Elucidation of a role of de-nitrosylation in septic myocardial injury and development for therapeutic drugs.
PI: Toshihiro Tanioka. Role on Project: Co- Investigator 2016-2017

Forensic Dentistry

Professor Koichi SAKURADA
Assistant Professor Hajime UTSUNO
Assistant Professor Namiko ISHII
Graduate Student Saki MINEGISHI

(1) Outline

Forensic dentistry plays an important role in society through the use identification of victims after major accidents or disasters using dental findings, as well as the identification of cadavers or persons from biological samples in relation to crime. In particular, the establishment of two laws related to cause of death investigation in June 2012 further promoted research, identification, and education related to individual identification. The primary function of our laboratory is the identification of individuals from hard tissues such as teeth and bones, soft tissues, body fluids, or facial images, using the latest molecular biological and imaging techniques.

(2) Research

1. Individual identification
 - Identification based on dental findings
 - Identification using hard tissues such as teeth and bones, soft tissues, and body fluids
 - Identification based on facial reconstruction and image analysis
2. Child abuse and neglect
3. Dental accidents and lawsuits
4. Problems associated with the dental care system
5. Forensic toxicology

(3) Education

We teach dental students a relation between death investigation systems and dentists and make them understand that society expects them as dentists to perform individual identification based on dental findings. Also, students are likely to have opportunities to assist the regional administrative and police activities in the future. To protect the rights of the deceased individuals and improve public health, dental students need to acquire basic knowledge about forensic medical sciences including postmortem changes and cause of death identification. To foster independent researchers, we teach graduate students the latest research directions in forensic dentistry and how to plan their own research project. In addition, students learn practical individual identification methods and their importance through forensic autopsy.

(4) Lectures & Courses

We believe that students learn more effectively in an environment where they can simultaneously conduct practical work and research.

(5) Clinical Services & Other Works

Forensic autopsy for the identification of cadavers and other related activities. Individual identification following accidents or disasters. Participation in disaster prevention and individual identification training programs held by various communities.

(6) Publications**[Original Articles]**

1. Tomoko Akutsu, Hisako Saito, Hirotarō Iwase, Ken Watanabe, Ayari Takamura, Koichi Sakurada, Sachio Miyasaka. The applicability of ELISA detection of gastric mucosa-expressing proteins for the identification of vomit. *Int. J. Legal Med.*. 2017.03; 131(2); 359-364
2. Suguru Torimitsu, Yohsuke Makino, Hisako Saitoh, Ayaka Sakuma, Namiko Ishii, Daisuke Yajima, Go Inokuchi, Ayumi Motomura, Fumiko Chiba, Rutsuko Yamaguchi, Mari Hashimoto, Yumi Hoshioka, Hirotarō Iwase. Stature estimation in a contemporary Japanese population based on clavicular measurements using multidetector computed tomography. *Forensic Sci. Int.*. 2017.06; 275; 316.e1-316.e6
3. Ken Watanabe, Tomoko Akutsu, Ayari Takamura, Koichi Sakurada. Practical evaluation of an RNA-based saliva identification method. *Sci. Justice*. 2017.11; 57(6); 404-408

[Books etc]

1. Koichi Sakurada. Teeth speak louder than words age estimation from teeth and bones . DENTAL DIAMOND, 2017.01
2. Koichi Sakurada. Teeth speak louder than words age estimation using the racemization and the radioisotope . DENTAL DIAMOND, 2017.02
3. Koichi Sakurada. Teeth speak louder than words sex estimation from teeth and bones . DENTAL DIAMOND, 2017.03
4. Koichi Sakurada. Teeth speak louder than words bitemark and abuse . DENTAL DIAMOND, 2017.04
5. Koichi Sakurada. Teeth speak louder than words blood typing and DNA typing from a tooth . DENTAL DIAMOND, 2017.05
6. Koichi Sakurada. Synthesis of antidote candidates which are effective against sarin poisoning. CHEMISTRY, 2017.06
7. Koichi Sakurada. Teeth speak louder than words The powerful information that one tooth has and the future of forensic dentistry . DENTAL DIAMOND, 2017.06
8. Masanori Takahashi, Tamiyuki Tsuzuki, Yoshihiro Yamada, Koichi Sakurada et al.. Forensic Dental Science. 2017.11 (ISBN : 978-4-8160-1333-1)

[Misc]

1. Koichi Sakurada. Individual identification from saliva stains *The Journal of Tokyo Dental Association*. 2017.07; 65(7); 3-10
2. Koichi Sakurada. Current examination of objects related to biological samples:focusing on saliva identification *Acta Crim. Japon*. 2017.12; 83(6); 150-157

[Conference Activities & Talks]

1. Koichi Sakurada. What is the mission of forensic medicine and dentistry? private identification . The 6th Round-Table Conference with Reporters 2016 2017.02.16 Tokyo Medical and Dental University
2. Koichi Sakurada. What is the mission of forensic dentistry?. The 2nd Kyoto Forensic Dentistry Seminar 2017.03.04 Kyoto Prefectural University of Medicine

3. Susumu Ohtani, Ran Iguchi, Hidenori Nene, Noboru Adachi, Saki Minegishi, Koichi Sakurada, Kanako Noritake, Joji Funakoshi, Koichi Uemura. Comparison of D-asparatic acid in the hard tissue. The 101st Congress of the Japanese Society of Legal Medicine 2017.06.08 Nagaragawa Convention Center
4. Hajime Utsuno, Namiko Ishii, Saki Minegishi, Koichi Sakurada. Study on the subnasal point estimation from Japanese male skulls. The 101st Congress of the Japanese Society of Legal Medicine 2017.06.08 Nagaragawa Convention Center
5. Saki Minegishi, Namiko Ishii, Hajime Utsuno, Kanako Noritake, Jyoji Funakoshi, Koichi Uemura, Ayaka Sakuma, Hisako Saitoh, Susumu Ohtani, Koichi Sakurada . Basic study on standard sample manufacture for age estimation by the amino acid racemization. The 101st Congress of the Japanese Society of Legal Medicine 2017.06.09 Nagaragawa Convention Center
6. Hajime Utsuo, Toru Kageyama, Keiichi Uchida, Kazuhiko Kibayashi, Koichi Sakurada . Establishment of prediction Method for Mid-Facial Region of Unknown Human Mongoloid Skeletal Remains . 17th Meeting of the International Association for Craniofacial Identification 2017.07.17 Australia
7. Koichi Sakurada. Crime investigation Significance of clarifying the origine of a person . Open campus in Tokyo Medical and Dental University 2017.07.28 Tokyo Medical and Dental University
8. Hisako Saitoh, Ayaka Sakuma, Namiko Ishii, Hajime Utsuno, Saki Minegishi, Disuke Yajima, Go Inokuchi, Ayumi Motomura, Yousuke Makino, Fumiko Chiba, Suguru Torimitsu, Koichi Sakurada, Hirotaro Iwase . Three cases that postmortem Ct reconstruction images were effective for collecting dental findings. The 86 Kanto District Meeting of the Japanese Society of Legal Medicine 2017.10.28 Kyorin University
9. Tomoko Akutsu, Ken Watanabe, Sairi Takamura, Koichi Sakurada. Evaluation of skin or sweat-enriched mRNA markers by a real-time RT-PCR assay. The 86 Kanto District Meeting of the Japanese Society of Legal Medicine 2017.10.28 Kyorin University
10. Hisako Saitoh, Ayaka Sakuma, Namiko Ishii, Hajime Utsuno, Saki Minegishi, Daisuke Yajima, Go Inokuchi, Ayumi Motomura, Hiroyuki Inoue, Akika Nagasawa, Yousuke Makino, Fumiko Chiba, Koichi Sakurada, Hirotarou Iwase.. Usefulness of the CT reconstitution images for taking dental findings.. 11th Meeting of Japanese Society of Forensic Dental Science 2017.11.18 Meikai University
11. Namiko Ishii, Hisako Saitoh, Hajime Utsuno, Saki Minegishi, Koichi Sakurada.. Improvement of the age estimation method using the racemization reaction of aspartic acid in dentin.. 11th Meeting of Japanese Society of Forensic Dental Science 2017.11.18 Meikai University
12. Hiroaki Ichioka, Koichi Sakurada, Hisako Saitoh, Maki Ohtani, Wataru Kumagaya, Hiroshi Ikegaya.. Education effect of the dental chart making training for dentistry clinicians. 11th Meeting of Japanese Society of Forensic Dental Science 2017.11.18 Meikai University
13. Torimitsu S, Makino Y, Saitoh H, Sakuma A, Ishii N, Yajima D, Inokuchi G, Motomura A, Chiba F, Yamaguchi R, Hoshioka Y, Iwase H. Sex estimation based on pelvis analysis in a Japanese population using multidetector computed tomography.. The 11th Congress Of The Japanese Society Of Forensic Dental Science 2017.11.18
14. Koichi Sakurada. Project for Promoting Leading-edge Research in Oral Science, Symposium, Society and Education. The 82nd Annual Meeting of the Stomatological Society of Japan 2017.11.19 Tokyo Medical and Dental University

[Social Contribution]

1. Individual identification using dental findings and others (79cases), 2017.01.01 - 2017.12.31
2. Individual identification training program for dentist (Second, Tokyo metropolitan) (Koichi Sakurada) , Tokyo Dental Association, Tokyo Dental Association, 2017.02.09
3. Lecture of Hachinan Dental assoxiation (Koichi Sakurada), Hachinan Dental Assiciation, 2017.11.13
4. 2th Individual identification training program (Namiko Ishii, Hjime Utsuno, Koichi Sakurada), Chiba University, Chiba Dental Association, Inohana Kaikann of Chiba University, 2017.11.26
5. 2017 Individual Identification training program (First, Tokyo metropolitan) (Koichi Sakurada), Tokyo Dental Association, Japan Dental Association Bulding, 2017.11.28

Health Care Economics

Koichi Kawabuchi
Isao Igarashi

(1) Outline

The role of health care extends to improving such aspects of life as dietary habit and relationship with others, and is deeply connected to quality of life. Looking back, however, discussion on healthcare has too often originated from political dynamics and interests of parties involved, and not from the voices of general public. This is due partially to the lack of quality data available among the people. The reality of healthcare and what it brings to the society are not necessarily always clear to the general public. In terms of dental care especially, it is hard to say that enough evidences have been established and widely recognized among people to the extent that matches to its importance in providing quality life. Thus, we apply economics in conducting interdisciplinary review of healthcare along with other related fields, and pursue how the healthcare system should be for the people.

(2) Research

Research activities involve conducting analysis on phenomena and observations in health care from the viewpoint of macro as well as micro economics.

Main focuses are:

- 1) Cross-sectional research on healthcare, dental care, nursing care, long-term care, and pharmaceuticals from the viewpoint of economics
- 2) Proposals on policy making in efficient delivery of healthcare, nursing care, and long-term care
- 3) Borderless and mutual development of various specialties such as dental care, healthcare, economics, management and accounting.

(3) Education

Understanding the methods of research on phenomena and observations in health care field through economics point of view. As we have many part-time students with jobs as well as foreign students, the lecture will be centered around such topics as the approach to a research theme in economics and other social sciences (especially empirical studies) , how to proceed with the research, and paper writing. Specifically, we will provide outline of healthcare economics by a weekly lecture for Ph. D. candidates as well as once a year lecture for the master course. Some of them adapt more interactive style of problem solving with input from visiting lecturers. Emphasis is placed on methods of quantitative analysis, learning both theoretical and empirical approaches to phenomena and observations in health care field through economics point of view. Lectures for undergraduate education will be focused on the outline of healthcare economics in dental care, with specific themes as 1) Economical analysis of dental healthcare, 2) Expenditure on dental care, 3) Reimbursement, and 4) Quality assessment of dental care.

(4) Lectures & Courses

Faced with recent changes in healthcare and long-term care, core hospitals and other healthcare related institutions in communities with responsibility of supporting front-line healthcare long for personnel competent in healthcare management. Call for such personnel is strong among research organizations and public offices as well, looking for those who are proficient in qualitative and quantitative analysis. Therefore, we aim to train students to be capable in making immediate contribution to the healthcare and welfare field, and to educate future "academic doctors" who can voice their messages in policy making.

(5) Clinical Services & Other Works

Igarashi, Assistant Professor in our department, practices three times a week in the clinic for Oral Diagnosis and General Dentistry of the Dental Hospital. Findings from our research activities are shared to the public through papers, reports, lectures and symposiums in both academic and less academic settings. Comments on healthcare reform, for instance, have been televised on and printed in various media.

(6) Publications

[Misc]

1. Koichi kawabuchi. Impact of fiscal Year 2016 Medical Fee Revision on Medical Institution Management Japan Hospitals. 2017.07; (36); 29-37

[Conference Activities & Talks]

1. G.M. Rabiul Islam, Koichi Kawabuchi. The economic and sociodemographic factors associated with infant and young child feeding practices in Bangladesh. The 12th Annual Conference of JHEA 2017.09.02

Dental Education Development

Professor: Ikuko MORIO
 Assistant: Professor Naoko SEKI
 Graduate Student: Chinatsu MATSUKAWA
 Graduate Student: Akira TAKINAGA
 Graduate Student: NGUYEN THI THANH TAM
 Graduate Student: Mio NAITO
 Graduate Student: Ai OSATO

(1) Research

- 1) Research on curriculum for health care professional education
- 2) Comparative study of domestic and international dental education
- 3) Research and development of educational methods in health care professional education
- 4) Research and development of English education programs in health care professional education

(2) Education

Main educational goal of this section as part of graduate school is to help students in health care sciences learn the basics of medical/dental curriculum: educational objectives, strategies and evaluation. This section is currently involved in the undergraduate dental education as the coordinators of multiple modules: the students' research project, courses for global communication, and the electives including various English courses and courses for international exchange for dental students.

(3) Clinical Services & Other Works

[Coordination for Seminar, Symposium, Workshop or other events]

1. Essential Expertise for Clinical Dentistry 2 (Seminar/Hands-on), Tokyo, Japan (TMDU). January 19, February 9, March 7 and 27.
2. Essential Expertise for Clinical Dentistry 3 (Seminar/Hands-on), Tokyo, Japan (TMDU). August 22-25, 29, 30.
3. International Faculty Development Course 2017 : Essential Expertise for Clinical Dentistry for Dental Professionals (Seminar/Hands-on), Tokyo, Japan. November 14-17.
4. International Dental Program 2017, Tokyo, Japan. November 13-20.

(4) Publications

[Original Articles]

1. Kano Y, Nakajima M, Aida A, Seki N, Foxton RM, Tagami J. Influence of enamel prism orientations on color shifting at the border of resin composite restorations. *Dent Mater J*. 2017.12; doi: 10.4012/dmj.2017-094.

[Misc]

1. Moross J, Seki N, Morio I. English education for healthcare professionals in Japan. *Japanese Dental Science Review*. 2017.03; 53(4); 111-116

[Conference Activities & Talks]

1. Naito M, Shinada K, Kunitsuka K, Onishi T, Yamamoto R, Seki N, Morio I, Taniyama K. Intervention survey on oral health at newspaper printing factories . 90th Annual Meeting of the Japan Society for Occupational Health 2017.05.13 Tokyo
2. The clinical and educational effects of the newly-introduced interprofessional clinical practice. 2017.05.13
3. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Naoko SEKI, Yuki OHARA, Masayo YASUDA, Hiromi OTSUKA, Shinich ARAKAWA, Kouji ARAKI. . Development of a new IPW program for dental students and dental hygiene students in practical clinical training. Working as a dental team. The 36th General and Scientific Meeting of the Japanese Dental Education Association 2017.07.28
4. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
5. Nguyen TTT, Seki N, Morio I. Perceived stress and lifestyle habits of first-year Japanese and Vietnamese dental students. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
6. KAWAGUCHI Y, TAKEHARA S, SEKI N, MORIO I, TAGAMI J. International short-term dental education program at Tokyo Medical and Dental University 1. Outbound program. 36th Annual Meeting of the Japanese Dental Education Association 2017.07.28 Matsumoto City
7. TAKEHARA S, KAWAGUCHI Y, MORIO I, SEKI N, TAGAMI J. International short-term dental education program at Tokyo Medical and Dental University 3. Effect of inbound and outbound programs. 36th Annual Meeting of the Japanese Dental Education Association 2017.07.28 Matsumoto City
8. MORIO I, SEKI N, KAWAGUCHI Y, TAKEHARA S, TAGAMI J. International short-term dental education program at Tokyo Medical and Dental University 2. Inbound program. 36th Annual Meeting of the Japanese Dental Education Association 2017.07.28 Matsumoto City
9. Nguyen TTT, Seki N, Moross J, Hosaka K, Sunaga M, Morio I, Kinoshita A. The effectiveness of newly developed computer-assisted simulation materials on overseas learners. The 28th SEAADE (South East Asia Association for Dental Education) Annual Scientific Meeting 2017.08.11 Taipei, Taiwan

[Awards & Honors]

1. Best Poster Award, Japan Society for Occupational Health, 2017.05
2. Advanced Education System Development(Kanako Noritake), Japanese Dental Education Association, 2017.07

Oral Health Promotion

Professor Yoko Kawaguchi
 Associate Professor Masayuki Ueno
 Assistant Professor Takashi Zaito
 Assistant Professor Akiko Ohshiro
 Office administrator Kyoko Kanetomi (from April)
 Registered Resident Hiromi Nishiyama
 Graduate Student
 Nguyen Thi Hoang Yen (till September)
 Yuka Shizuma
 Kaung Myat Thwin
 Toshiya Kanazawa
 Takashi Tanemura
 Jin Aoki
 Mitsue Kamisawa
 Zar Chi Kyaw Myint
 Nguyen Thi Nhat Vy (from October)
 Research Student
 Tomoya Saito (from April)

(1) Research

Research Subjects

Research topics are innovative, academic and international research in the field of dental public health and preventive dentistry to proceed with oral health promotion that contributes to human health. The current main research themes are:

1. Epidemiology and prevention of dental disease
2. Oral health care system
3. Relationship between oral health and general health
4. Oral health promotion
5. Diagnosis and treatment system construction of oral malodor
6. International oral health

(2) Lectures & Courses

1) Graduate School Education, Oral Health Promotion

The educational purpose is to foster professionals in dental public health and preventive dentistry who can think oral health problems as related issues with living environment, life style, health policy and social condition, and can conduct innovative, academic and international research on oral health for maintaining and improving oral health.

2) Undergraduate School Education

The department is in charge of module units of “Introduction to dentistry”, “Environment and society II”

and “Comprehensive problem exercise” for the third year dental students, and module units of “Basis for dentistry”, “Prevention and health management I”, “Prevention and health management II” and “Dentistry and nutrition” for the fourth year dental students. The department is also in charge of “Experiential research exercise” for the fourth year dental students, and “Comprehensive clinical practice phase I & II” for the fifth and sixth year dental students, in cooperation with other departments.

(3) Clinical Services & Other Works

Clinical Services

“Fresh breath clinic” in Dental hospital, Tokyo Medical and Dental University is a special clinic for diagnosis, treatment and prevention of oral malodor. About half of oral malodor patients are referred from other departments in the dental hospital or outside dental clinics. Other patients visit the clinic by finding the information of the clinic from mass media such as the internet, newspapers and television.

For oral malodor examination, gas chromatography and gas sensor instrument are used to measure the concentration of volatile sulfur compounds (VSCs) along with the organoleptic test. Oral malodor is treated based on diagnosis by precise measurement and oral examination, besides psychological aspects of the patient are paid attention. Treatment of oral malodor needs continuous periodontal disease management and oral care in cooperation with oral care department in the dental hospital and patient’s family dentist.

(4) Publications

[Original Articles]

1. Yuka Shizuma, Takashi Zaitso, Masayuki Ueno, Mari Ohnuki, Yoko Kawaguchi. Relationship between self-assessment and clinical evaluation of dental plaque and gingival condition in Japanese adolescents. *International Journal of Dental Hygiene*. 2017.04; 16(1); 144-150
2. Anastasiya Blizniuk, Masayuki Ueno, Takashi Zaitso, Yoko Kawaguchi. Association between self-reported and clinical oral health status in Belarusian adults. *Journal of Investigative and Clinical Dentistry* . 2017.05; 1-6
3. Takashi Zaitso, Toshiya Kanazawa, Yuka Shizuma, Akiko Oshiro, Sachiko Takehara, Masayuki Ueno, Yoko Kawaguchi. Relationships between occupational and behavioral parameters and oral health status. *Industrial Health*. 2017.05; 55; 1-10
4. Ei Ei Aung, Masayuki Ueno, Takashi Zaitso, Sayaka Furukawa, Yoko Kawaguchi. Effects of tooth brushing, mouth washing and tongue cleaning on three volatile sulfur compounds - A randomized clinical trial - *International Journal of Oral Health*. 2017.07; 13; 25-31
5. Yen Hoang Thi Nguyen, Masayuki Ueno, Takashi Zaitso, Toai Nguyen, Yoko Kawaguchi. Caries arresting effect of silver diamine fluoride in Vietnamese preschool children *International Journal of Clinical Preventive Dentistry*. 2017.10; 13(3); 147-154
6. Kaung Myat Thwin, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Effectiveness of silver damine fluoride in arresting early childhood caries in Myanmar preschool children *Global Journal of Oral Science*. 2017.11; 3; 18-26

[Books etc]

1. *Oral Health and Preventive Dentistry*. 2017.02 (ISBN : 978-4-263-45802-0)
2. *Volatile Biomarker Analysis and Advanced Gas-sensing Instruments*. 2017.08 (ISBN : 978-4-7813-1250-7)

[Misc]

1. Takashi Zaitso, Yoko Kawaguchi. Perspectives for Tele-dental system in Space and Antarctic Environments. *The International Journal of Oral Health*. 2017.06; 13; 13-16
2. Masayuki Ueno, Sachiko Takehara, Takashi Zaitso, Akiko Ohiro, Yoko Kawaguchi. Dental license renewal and continuing dental education system in other countries Japan *Journal of Dental Practice Administration*. 2017.11; 52(3); 147-153

[Conference Activities & Talks]

1. Takashi Zaitso, Yen Nguyen, Yoko Kawaguchi. The Relationship of Dental Diseases with Life style Related Diseases of Workers. The 95th General Session & Exhibition of the IADR 2017.03.22 the Moscone West, San Francisco, Calif., USA
2. Yen Nguyen, Masayuki Ueno, Takashi Zaitso, Toai Nguyen, and Yoko Kawaguchi. Effectiveness of Silver Diamine Fluoride on Arresting Dental Caries. The 95th General Session & Exhibition of the IADR 2017.03.22 the Moscone West, San Francisco, Calif., USA
3. Masayuki Ueno, Yoko Kawaguchi. Association between height and dentition status. The 66th General Meeting of Japanese Society for Oral Health 2017.05.31
4. Kaung Myat Thwin, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Relationship between dental caries and oral health behaviors in Myanmar children. 2017.05.31
5. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
6. Ei Ei Aung, Masayuki Ueno, Takashi Zaitso, Sayaka Furukawa, Yoko Kawaguchi. Effects of Tooth Brushing, Mouth Washing and Tongue Cleaning on Three Volatile Sulfur Compounds - A Randomized Clinical Trail -. The 12th JUNTHai Conference 2017.09.04
7. Kaung Myat Thwin, Takashi Zaitso, Masayuki Ueno, Yoko Kawaguchi. Effectiveness of silver diamine fluoride in arresting early childhood caries among Myanmar preschool children. The 9th Asian Conference of Oral Health Promotion for School Children 2017.09.22
8. Present situation and future perspectives of Asian Academy of Preventive Dentistry. 2017.10.27
9. Yoko Kawaguchi. Better oral health for older persons. 2017.11.03 Sydney, Australia
10. Takashi Zaitso. Space Dentistry -Oral Health Promotion in Space and Antarctic Environments-. the 65th Annual Meeting of the Japanese Association for Dental Research 2017.11.19 Showa University, Tokyo, Japan

Sports Medicine and Dentistry

[Associate Professor] Toshiaki Ueno
[Assistant Professor] Hiroshi Churei
[Clinical fellow] Kairi Hayashi
[Graduate Student] Yuriko Yoshida, Nana Shiota, Gen Tanabe, Chiho Shibata, Phyu Sin Tun, Rio Kinjo, Nanami Ito, Thet Khaing Aung
[Research Student] Aki Kanasaki, Yuumi Takahashi
[Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino
[Part-time Resident] Keisuke Abe, Kenji Takeuchi, Takaaki Fukuda, Takahiro Sirako, Hiromi Miura, Kayoko Kurihara, Chie Ichihara

(1) Outline

Sport medicine/dentistry is a branch of clinical medical and dental sciences which deals with the clinical management of oral health of athletes and sports-active people, the safety measures of sports-related traumatic injuries and disorders, and medical and dental supports to improve athletic performance.

(2) Research

- 1) Oral health promotion of athletes and sports-active people
 - (1) Field survey of oral health conditions in athletes and sports-active people
 - (2) Changes of oral environment associated with physical and sporting activities
 - (3) Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
 - (1) Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
 - (2) Development and innovation of sports mouthguard
 - (3) Development and innovation of sports faceguard
 - (4) Development and innovation of scuba diving mouthpiece
- 3) Correlations between occlusion and general motor functions
 - (1) Biomechanical assessment of motor performance associated with occlusion
 - (2) Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
 - (1)Effect of occlusion on static posture
 - (2)Influence of occlusion on dynamic posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

(3) Education

academic classes for sports medicine/dentistry in undergraduate and graduate courses in undergraduate and graduate courses are listed as follows;

- 1)D1:Shigaku-Gaisetū
- 2)D3:Sogo-Kadai-Ensyū
- 3)D3:Rinsyo-Taiken-Jissyu

- 4)D4:Kenkyu-Taiken-Jissyu
- 5)D5:Hatten-Shika-Rinsyo/Sports Dentistry
- 6)D5-D6:Hokatsu Rinsyo-Jissyu Phase I to II
- 7)OH2:Kiso-Kagaku-Jissyu
- 8)OH3:Seijin-Koukuhoken-Eiseigaku
- 9)OH3-OH4:Koukuhoken-Eisei-Jissyu
- 10)OE4:Sports dental engineering
- 11)Master course:Kankyo-Syakai-Ishigaku
- 12)PhD course: Tokuron, Ensyu and Kenkyu-Jissyu of Sports Medicine and Dentistry
- 13)Clinical training course:Sports Dentistry

(4) Lectures & Courses

Main objectives of academic education programs of sports medicine/dentistry in from undergraduate to graduate courses is to provide the students to study the oral health conditions in athletes and sports-active people, the changes of oral environment associated with physical and sporting activities, the possible correlations between occlusion and general motor functions and body posture, the novel techniques of sports mouthguard and faceguard, the relations between mastication and occlusion and brain functions, and so on. Students are also taught to advanced knowledge on sports medicine/dentistry and up-to-date techniques to fabricate custom mouthguard and faceguard.

(5) Clinical Services & Other Works

Sports dentistry clinic in Dental Hospital of Tokyo Medical and Dental University offers comprehensive care and clinical management for athletes and sports-active people suffered dental diseases and traumatic injuries. Custom-fitted protective gears such as mouthguard and faceguard against sports-related dental and maxillofacial trauma are also handled for participants in contact sports such as a boxing, American football, rugby football, hockey, lacrosse, and martial art. Sports dentistry clinic is positioned as a dental branch of Clinical Center for Sports Medicine and Dentistry under TMDU Sports Science Organization. In addition, Our clinic maintains close cooperation with Japan Institute of Sports Science/National Training Center under Japan Sport Council.

(6) Clinical Performances

< Certified specialists >

Toshiaki Ueno (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by Japanese Academy of Sports Dentistry, 3.Mouthguard technical instructor certified by JASD, 4.Dental specialist certified by Japanese Academy of Maxillofacial Prosthetics, 5.Dental Material Senior Advisor certified by Japanese Society of Dentl Materials and Devices)

Hiroshi Churei (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3. MG technical instructor certified by JASD)

Kairi Hayashi (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Sachiko Fujino (1.JASA Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3.MG technical instructor certified by JASD)

Yuriko Yoshida (1.MG technical instructor certified by JASD)

Aki Kanasaki(1. Sports dental hygienist certified by JASD)

(7) Publications

[Original Articles]

1. Mitsuyama A, Takahashi T, Ueno T. Effects of teeth clenching on soleus H reflex during lower limb muscle fatigue J Prosthodontic Res. 2017.04; 61(2); 202-209
2. Mitsuyama Akihiro, Takahashi Toshiyuki, Ueno Toshiaki. Effects of teeth clenching on the soleus H reflex during lower limb muscle fatigue JOURNAL OF PROSTHODONTIC RESEARCH. 2017.04; 61(2); 202-209

3. Nakamura T, Yoshida Y, Churei H, Aizawa J, Hirohata K, Ohmi T, Ohji S, Takahashi T, Enomoto M, Ueno T, Yagishita K. The effect of teeth clenching on dynamic balance at jump-landing: a pilot study *J Appl Biomech.* 2017.06; 33(3); 211-215
4. Shirako T, Churei H, Iwasaki N, Takahashi H, Ueno T. Evaluation of the flexural properties of a new temporary splint material for use in dental trauma splints *J Dent Sci.* 2017.09; 12(3); 308-311
5. Shirako T, Churei H, Wada T, Uo M, Ueno T. Establishment of experimental models to evaluate the effectiveness of dental trauma splints *Dent Mater J.* 2017.11; 36(6); 731-739
6. Lloyd JD, Nakamura WS, Maeda Y, Takeda T, Leesungbok R, Lazarchik D, Dorney B, Gonda T, Nakajima K, Yasui T, Iwata Y, Suzuki H, Tsukimura N, Churei H, Kwon KR, Choy MMH, Rock JB. Mouthguards and their use in sports: Report of the 1st International Sports Dentistry Workshop, 2016 *Dent Traumatol.* 2017.12; 33(6); 421-426
7. Lloyd Jeffrey D., Nakamura Wayne S., Maeda Yoshinobu, Takeda Tomotaka, Leesungbok Richard, Lazarchik David, Dorney Brett, Gonda Tomoya, Nakajima Kazunori, Yasui Toshikazu, Iwata Yoshihiro, Suzuki Hiroshi, Tsukimura Naoki, Churei Hiroshi, Kwon Kung-Rock, Choy Melvin M. H., Rock James B.. Mouthguards and their use in sports: Report of the 1st International Sports Dentistry Workshop, 2016 *DENTAL TRAUMATOLOGY.* 2017.12; 33(6); 421-426

[Misc]

1. Yasui T, Gonda T, Maeda Y, Ishigami K, Ueno T, Matsumoto M, Takamata T, Koide K, Kawara M. Do mouthguards prevent or reduce dental injuries and concussions during sports events? A literature review *Int J Sports Dent.* 2017.10; 10(1); 7-11

[Conference Activities & Talks]

1. Siota N, Sunaga M, Tanabe G, Churei H, Takahashi T, Kinoshita A, Ueno T. Development and effectiveness of an interactive computer-assisted learning (CAL) material in undergraduate dental traumatology. 39th Asia Pacific Dental Congress 2017.05.22 Macau, China
2. Yoshida Y, Churei H, Wada T, Takeuchi H, Uo M, Ueno T. Antibacterial performance of mouthguard material incorporated with silver-nanoparticles-embedded EVA masterbatch. 105th FDI Annual World Dental Congress 2017.08.29 Madrid, Spain
3. Tanabe G, Hata T, Tun PS, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards.. The 2017 ADM Annual Meeting 2017.10.07 Nuremberg

Educational System in Dentistry

Professor Kouji ARAKI
 Associate Professor Jun TSURUTA
 Junior Associate Professor(non-full time) Kouji IIDA
 Hiroki KATAOKA
 Graduate Student Moriyuki KATOH
 Kazuki TAKAHASHI Akitaka HATTORI Kanako TODA
 Graduate research Student Shunsuke OZAWA (~ 2017.3)
 Secretary Satomi ITOH

(1) Outline

Main object of educational system in dentistry in the graduate course is to provide opportunity to study evaluation method for dental education curriculum, inspection method of the validity and reliability of the evaluation system for dental education, evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods, and dental clinical skills improvement by the virtual reality simulation system.

(2) Research

- 1) The development of evaluation method for dental education curriculum
- 2) The development of inspection method of the validity and reliability of the evaluation system for dental education
- 3) The development of evaluation system compared between international and Japanese education level in undergraduate or after the graduation periods
- 4) The development of the program for dental clinical skills improvement by the virtual reality simulation system

(3) Education

The education to the postgraduate students performs a lecture, practice, and Lab.

The education to the undergraduate students performs of a lecture and practice of all human general oral diagnoses.

(4) Lectures & Courses

The aim of the lecture is to understand the purpose and method about the evaluation of dental education system. In addition, it is to understand the level and inspection method of international dental education. The aim of the practice is to understand a method of data analysis provided by the evaluation system for the dental education, In addition, it is to understand the comparison with the international education level.

The aim of the Lab is to manage the teaching materials developed for simulation education and is to understand

the inspection method of the evaluation for new education system.

(5) Clinical Services & Other Works

In the Clinic of Oral Diagnosis and General Dentistry, University Hospital, we performs manner and oral diagnosis education, for a student during clinical training.

(6) Publications

[Original Articles]

1. Ken-ichi Tonami, Sachi Umemori, Hiroshi Nitta, Kouji Araki, Shiro Mataka . Changes in Student Evaluations of a Medical Ethics Class 3 Years Later. *European Journal of General Dentistry*. 2017.09; 6(3); 123-126
2. Yasuyuki Kimura, Ken-ichi Tonami, Shiro Mataka, Kouji Araki. Analysis of new outpatients' responses to a survey of their reasons for visiting a dental clinic. *European Journal of General Dentistry*. 2017.10; 6(3); 111-114
3. Kanako NORITAKE, Jun TSURUTA, Ken-ichi TONAMI, Sachi Umemori, Shigeru ODA, Shiro MATAKI, and Kouji ARAKI. Development of Undergraduate Dental Student Interview and Diagnostic Skills during Clinical Practice of Medical Interviews *The Journal of the Stomatological Society, Japan..* 2017.11; 84(3); 103-110
4. Chien PJ, Suzuki T, Tsujii M, Ye M, Minami I, Toda K, Otsuka H, Toma K, Arakawa T, Araki K, Iwasaki Y, Shinada K, Ogawa Y, Mitsubayashi K. Biochemical Gas Sensors (Biosniffers) Using Forward and Reverse Reactions of Secondary Alcohol Dehydrogenase for Breath Isopropanol and Acetone as Potential Volatile Biomarkers of Diabetes Mellitus. *Anal Chem*. 2017.11; 89(22); 12261-12268
5. Kazuki Takahashi, Jun Tsuruta, Ken-ichi Tonami, Kouji Araki. Relation between Manual Dexterity and the Accuracy of Cavity Preparation. *Anal of Oral Health and Dental Research*. 2017.12;

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. Tthe association between secondhand smoking and number of remaining teeth among older Japanese. *The 27th Annual Scientific Meeting of the Japan Epidemiological Association* 2017.01.27 Koufu
2. Ken-ichi Tonami, Shizuko Ichinose, Kazunobu Sano, Naohiko Iwasaki, Hidekazu Takahashi, Shiro Mataka, Kouji Araki. Analysis of the dentin surface after Xe excimer lamp irradiation. *The 95th General Session & Exhibition of the IADR* 2017.03.22 San Francisco
3. Koji Mizutani, Kanako Noritake, Jun Tsuruta, Naoko Seki, Keiko Kondoh, Satyaka Katagiri, Yasuo Takeuchi, Tatsuya Akizuki, Hidehiro Shioyama, Shinichi Arakawa, Kouji Araki, Yuichi Izumi. The clinical and educational effects of the newly-introduced interprofessional clinical practice. *The 60th Spring Meeting of The Japanese Society of Periodontology* 2017.05.13 Fukuoka
4. Ohwatari T, Takahashi K, Kyosaka Y, Inokoshi M, Inoue M, Minakuchi S, Fukayama H, Shimoyama K. Medications in 5,699 medically compromised elderly dental patients. 2017.06.16 Nagoya
5. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka. Factor analysis of students' perception of inter-personal relations during "Introduction to the behavioral science" class. *31th IADR-SEA 28th SEAADE* 2017.08.10 Taipei
6. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka . Effects of the Great East Japan Earthquake on students' perception of inter-personal relations. *ADEE Annual Conference* 2017.08.23 Vilnius, Lithuania
7. Jun Tsuruta, Kanako Toda. Study for the qualifying system of member societies of Japanese Association for Dental Science. 2017.09.10 Tokyo

8. K. Tonami, S. Umemori, K. Araki, S. Mataka. Change in students' perception of inter-personal relationship during experiential learning at welfare facilities. Japanese Association of Health Communication 2017.09.16 Kyoto

[Social Contribution]

1. The Journal of Dental Education,peer reviewer, 2015.08.01 - Now
2. European Journal of Dental Education,peer reviewer, 2017.09.01 - Now

Educational Media Development

Professor KINOSHITA Atsuhiro
Assistant Professor SUNAGA Masayo
Graduate Student MIYOSHI Tomoe
Graduate Student HOBO Koki
Graduate Student CAO Ridan
Graduate Student AKIYAMA Kyoko
Graduate Student HARADA Yusuke(April ~)
Graduate Student TAKENOUCHI Akane(April ~)
Graduate Student TAKATSUNA Yukiko

(1) Research

1) Development of computer-assisted clinical simulation system for medical and dental practice training.

In our university, we executed the Establishment of Computer-Assisted Education System on Clinical Simulation for Medical and Dental Practice Training project, which was adopted as part of the Support Program for Distinctive University Education in 2005, and developed the computer simulation materials on clinical education by utilizing digital clinical data from our Medical and Dental hospitals. We have expanded our study into a new project, 'Progress of Computer-Assisted Simulation for Medical and Dental Practice Training. Computer-Assisted Simulation Promoting Clinical Inference, Decision-making, Problem Solving and Cooperation Abilities of Health Professionals', which was subsequently selected to be part of the Program for Promoting the University Education Reform in 2009 by the Ministry of Education, Culture, Sports, Science and Technology. After utilizing the simulation materials for our students, we will evaluate and analyze their educational efficacy. Furthermore, we will develop a computer-assisted clinical simulation system for the entire university.

2) Development of new education system using information and communication technologies for medical and dental students.

At our university, we executed the Integration of Information and Communication Technologies into Clinical Training project, which was adopted as part of the Support Program for the Contemporary Educational Needs in 2007. The aim of this program is to integrate traditional educational methods with advanced information and communication technologies in order to allow clinical training, practical training and lectures to be effectively interlinked. By expanding digital content and employing an automatic visual recording system, we are planning to establish a digital archive of treatments and surgeries, demonstrations of dental techniques, lectures and student training. We will then launch an on-demand distribution system in order to incorporate this content into clinical education, which the students will be able to use for their self-evaluation and learning.

3) Development and utilization of an educational media for medical and dental students.

- Development and Study of Dental Model and Kit for Practical Training:

Dental and dental hygiene students must acquire skills for measuring periodontal pockets and must learn to identify the base of the pocket. However, few dental models are commercially available, and students cannot measure deep periodontal pockets by practicing on one another. Thus, we developed a new dental model with which the students can practice the probing of deep periodontal pockets, and plan to evaluate its effectiveness in training and evaluation of examiners.

- Development of Composing and Screening System for Original 3D Movies from Operator's Viewpoint:

If students can experience and recognize three-dimensional space from the operator's (instructor's) viewpoint during their practice sessions and lectures, it would have educational benefits. Thus, we plan to develop a

Composing and Screening System for Original 3D Movies from an Operator's Viewpoint. Furthermore, we will improve the quality of distance learning and remotely operated instruction using the superimposing method.

- Development of Dental Handpiece System with CCD camera:

We plan to develop a system equipped with a CCD camera, mirror and reverse image units in order to allow students in the lecture room to observe dental treatment sites in real-time, thereby giving them a sense of being at a clinic.

(2) Education

We will assist graduate students in understanding new educational systems and media utilizing information-communication technologies, such as the computer-assisted education system, the e-learning system and the live broadcasting lecture system. We will also assist these students in mastering how to create related educational media and apply it to medical, dental, nursing and dental hygiene education, as well as interprofessional cooperation.

First-year students at the School of Dentistry, and first and second-year students at the School of Oral Health Care Sciences will learn to process media information and create media content, as well as how to search the Internet for information that is necessary for their study and research activities. They will also learn how to make use of various databases.

Fourth-year students at the School of Dentistry will acquire the practical knowledge, communication skills and attitude to build good relationships with patients by gaining clinical experience at an early stage. This practice consists of two units; clinical experience in the teaching clinic and the computer-assisted simulation practice. This experience will enhance the students' abilities, enabling them to be effective clinicians.

(3) Publications

[Original Articles]

1. Tomoe Miyoshi, Koki Hobo, Masayo Sunaga, Atsuhiro Kinoshita. Effects of an interactive simulation material for clinical dentistry on knowledge acquisition. *J. Med. Dent. Sci.* 2017.09; 64(3); 35-42
2. Koki Hobo, Kanako Noritake, Masayo Sunaga, Tomoe Miyoshi, Ridan Cao, Hiroshi Nitta, Yuji Kabasawa, Atsuhiro Kinoshita. Effectiveness of an interactive simulation material for clinical dentistry on knowledge acquisition and memory retention in dental residents *J. Med. Dent. Sci.* 2017.12; 64(4); 43-52

[Conference Activities & Talks]

1. Nana Shiota, Masayo Sunaga, Toshiyuki Takahashi, Atsuhiro Kinoshita, Toshiaki Ueno. Effectiveness of interactive computer-assisted learning (CAL) material on sports-related dental trauma for knowledge acquisition. The 39th Asia Pacific Dental Congress (APDC), Final Program and Abstract Book, p229, 22-25 May 2017.05.22 Macau
2. Masayo Sunaga, Hiromi Otsuka, Junichi Furuya, Yumi Hoshino, Atsuhiro Kinoshita. Development and evaluation of computer-assisted learning material regarding oral health care methods for elderly persons requiring long-term care as interprofessional education material for dental hygiene students. The 39th Asia Pacific Dental Congress (APDC), Final Program and Abstract Book, p181, 22-25 May 2017.05.22 Macau
3. Tam Nguyen Thi Thanh, Naoko Seki, Janelle Moross, Keiichi Hosaka, Masayo Sunaga, Ikuko Morio, Atsuhiro Kinoshita. The effectiveness of newly developed computer-assisted simulation materials on overseas learners. The 28th Annual Scientific Meeting South East Asia Association For Dental Education (SEAADE), 10-11 August 2017.08.11 Taipei

Insured Medical Care Management

Professor Masumi AI
J Associate Professor Junichiro ISHIOKA
Graduate Student Hiroshi KAWAMURA

(1) Outline

Our department supports an appropriate practice on insured medical care and billing for medical service fees at the TMDU medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

(2) Research

1) Development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

2) Studies on management and supports for billing for medical service fees at insurance medical institutions.

3) Studies on affairs of medical insurance system and provision of medical services.

In addition, the staff has been engaged in clinical studies and epidemiological studies on lipid metabolism, diabetes mellitus, atherosclerosis, laboratory medicine, and urology.

(3) Education

The staff has been in charge for education of social health insurance system and rules for insured medical treatment at the TMDU medical hospital (May 2016 and February 2017).

A doctor course student is in his second year.

(4) Lectures & Courses

*Providing practical supports for an appropriate insured medical care in the clinical fields.

Providing individual support for an appropriate billing for medical service fees at the medical hospital.

We also focus on development of methodology and materials for education on medical insurance system and rules for insured medical treatment.

(5) Clinical Services & Other Works

The staff has been in charge for assisting appropriate medical fee claims, and also providing clinical service on diabetes, dyslipidemia, atherosclerosis, geriatrics, and Urology.

(6) Clinical Performances

As a managing section of the medical hospital, we collaborate all kinds of hospital workers practically and efficiently to provide an appropriate insured medical care.

(7) Publications**[Original Articles]**

1. Hiroaki Ikezaki, Masumi Ai, Ernst J Schaefer, Seiko Otokozawa, Bela F Asztalos, Katsuyuki Nakajima, Yanhua Zhou, Ching-Ti Liu, Paul F Jacques, L Adrienne Cupples, Norihiro Furusyo. Cardiovascular disease prevalence and insulin resistance in the Kyushu-Okinawa Population Study and the Framingham Offspring Study. *J Clin Lipidol.* 2017.02; 11(2); 348-356
2. Anne P Beigneux, Kazuya Miyashita, Michael Ploug, Dirk J Blom, Masumi Ai, MacRae F Linton, Weerapan Khovidhunkit, Robert Dufour, Abhimanyu Garg, Maureen A McMahon, Clive R Pullinger, Norma P Sandoval, Xuchen Hu, Christopher M Allan, Mikael Larsson, Tetsuo Machida, Masami Murakami, Karen Reue, Peter Tontonoz, Ira J Goldberg, Philippe Moulin, Sybil Charrière, Loren G Fong, Katsuyuki Nakajima, Stephen G Young. Autoantibodies against GPIHBP1 as a Cause of Hypertriglyceridemia. *N. Engl. J. Med.*. 2017.04; 376(17); 1647-1658
3. Hajime Tanaka, Yasuhisa Fujii, Hiroshi Tanaka, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Sho Uehara, Noboru Numao, Takeshi Yuasa, Shinya Yamamoto, Hitoshi Masuda, Junji Yonese, Kazunori Kihara. Stepwise algorithm using computed tomography and magnetic resonance imaging for diagnosis of fat-poor angiomyolipoma in small renal masses: Development and external validation. *Int. J. Urol.*. 2017.07; 24(7); 511-517

[Misc]

1. Masumi Ai. Triglyceride and HDL cholesterol as risk factors and the treatment targets for atherosclerosis 2017.04; 106(4); 725-734

[Others]

1. IRB Member, Sony Corporation 2012-

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD

Junior Associate Professor: Kaoruko Seino, PhD

JSPS Research Fellow: Md. Mosiur Rahman, PhD

International Researcher: Layla McCay, MBChB;

Research Fellow: AL-SOBAlHI Saber, RN, MPH; PhD

Graduate Student: Aya Anzai, RN; Omar Mohammad Mashal, MD;

Shiro Ochi, MSc, PhD; Tomoko Terada, MD;

Dasavanh Manivong, MD, MSc; Delgermaa Doshzeveg, MPH;

Iskander Isaac Maro, MD, MPH; Hoang Thuy Linh Nguyen, MD, MPH; Ahmad Shekib Arab, MD;

Yuri Tashiro, MPharm, MPH; Deogratius Bintabara MD, MSc; TJ Robionson Moncatar, RN, MPH;

Kathryn Lizbeth Lucena Siongo, RN, RM; Tran Dai Tri Han, MD, MPH; Hue Man Vo, MD;

HASAN S M Mahmudul Hasan, DMD; Shayo Festo Kasmir, MD

(1) **Outline**

The department of Global Health Entrepreneurship seeks to elucidate physical, social, economic and cultural factors determining inequity in health. The department works closely with WHO and other international agencies to help develop guidelines of scientific evaluation and recommended practices.

(2) **Research**

Major Research Topics:

- 1) Transfiguration of the ecosystem and its interaction with human health
- 2) Socio-cultural factors determining health
- 3) Social entrepreneurship development through applying the Healthy Settings approach
- 4) Use of information technology to improve public health
- 5) International health workforce and trade in health services
- 6) Universal health coverage in ageing society

(3) **Education**

PhD programs

Our doctoral program provides a flexible curriculum that allows students to customize their research goals, methods, and activities based upon their own interests and preferences. Students on the Public Health Medicine (PHM) track of the Disease Prevention Global Leader Program (DP-GLP) attain the skills required for public health professionals with an international perspective. The program prepares them for leadership roles in public institutions. Advanced students from many countries around the world are now enrolled. All the classes are conducted in English, thus facilitating the acquisition of international communication skills.

A rich variety of educational activities have been arranged in the program. These include: individual discussion sessions with professors and other faculty members; field investigations; and seminars on various topics such as community health care, community medicine, public health policy, biostatistics, academic presentation, development of foreign language skills, and communication skills. Students work closely with faculty members

on an individual basis in setting the right direction for their research and confirmation of their progress.

Master Programs

Master degree students receive systematic intensive training that leads to the acquisition of broad expertise in the field of global public health. This program is open to students who have majored in any field.

(4) Lectures & Courses

The objective of our postgraduate education is to provide professional qualifications to high-caliber people who exhibit leadership in the advancement of public health and promotion of health on an international scale. The department helps students attain the knowledge, skills, attitude, and experiences that are necessary for competent health specialists and social entrepreneurs in healthcare.

By completion of the doctoral course, the participants are expected to be able to:

- Assess health and well being the populations in local, national, and international settings,
- Assess evidence to show effectiveness of health interventions, programs and strategies,
- Think strategically to develop local, national, and international policies,
- Manage projects to successful completion
- Demonstrate leadership in local, national, or international public health programs
- Communicate properly when listening, presenting, writing, and negotiating
- Pursue a full-cycle of an academic, public health research project
- Facilitate learning of staff, students, and colleagues, and
- Practice and respect professional ethics in a socio-culturally diverse environment.

(5) Publications

[Original Articles]

1. Rakprasit J, Nakamura K, Seino K, Morita A.. Healthcare use for communicable diseases among migrant workers in comparison with Thai workers. *Industrial Health*. 2017.01; 55; 67-75
2. Md Jahirul Islam, Mosiur Rahman, Lisa Broidy, Syed Emdadul Haque, Yu Mon Saw, Nguyen Huu Chau Duc, Md Nurruzzaman Haque, Md Mostafizur Rahman, Md Rafiqul Islam, Md Golam Mostofa. Assessing the link between witnessing inter-parental violence and the perpetration of intimate partner violence in Bangladesh. *BMC Public Health*. 2017.02; 17(1); 183
3. Mosiur Rahman, Md Jahirul Islam, Syed Emdadul Haque, Yu Mon Saw, Md Nurruzzaman Haque, Nguyen Huu Chau Duc, Saber Al-Sobaihi, Thu Nandar Saw, Md Golam Mostofa, Md Rafiqul Islam. Association between high-risk fertility behaviours and the likelihood of chronic undernutrition and anaemia among married Bangladeshi women of reproductive age. *Public Health Nutr*. 2017.02; 20(2); 305-314
4. Jutarat Rakprasit, Keiko Nakamura, Kaoruko Seino, Ayako Morita. Healthcare use for communicable diseases among migrant workers in comparison with Thai workers. *Ind Health*. 2017.02; 55(1); 67-75
5. Shagdarsuren T, Nakamura K, McCay L. . Association between perceived neighborhood environment and health of middle-aged women living in rapidly changing urban Mongolia. *Environmental Health and Preventive Medicine*. 2017.05; 22; 50
6. Rafal S Sobota, Catherine M Stein, Nuri Kodaman, Isaac Maro, Wendy Wieland-Alter, Robert P Igo, Albert Magohe, LaShaunda L Malone, Keith Chervenak, Noemi B Hall, Mecky Matee, Harriet Mayanja-Kizza, Moses Joloba, Jason H Moore, William K Scott, Timothy Lahey, W Henry Boom, C Fordham von Reyn, Scott M Williams, Giorgio Sirugo. A chromosome 5q31.1 locus associates with tuberculin skin test reactivity in HIV-positive individuals from tuberculosis hyper-endemic regions in east Africa. *PLoS Genet*.. 2017.06; 13(6); e1006710
7. Isaac I Maro, Abigail M Fellows, Odile H Clavier, Jiang Gui, Catherine C Rieke, Jed C Wilbur, Robert D Chambers, Benjamin G Jastrzembki, John E Mascari, Muhammad Bakari, Mecky Matee, Frank E

- Musiek, Richard D Waddell, C Fordham von Reyn, Paul E Palumbo, Ndeserua Moshi, Jay C Buckey. Auditory Impairments in HIV-Infected Children. *Ear Hear.* 2017.07; 37(4); 443-451
8. Nakamura K, Chiba M, Seino K. Factors influencing reduction of risk of lifestyle related disease among children. *Annual Report 2016.* 2017.08; 32; 452-456
 9. Deogratius Bintabara, Rose N M Mpembeni, Ahmed Abade Mohamed. Knowledge of obstetric danger signs among recently-delivered women in Chamwino district, Tanzania: a cross-sectional study. *BMC Pregnancy Childbirth.* 2017.08; 17(1); 276
 10. Ahmed Zohirul Islam, Mosiur Rahman, Md Golam Mostofa. Association between contraceptive use and socio-demographic factors of young fecund women in Bangladesh. *Sex Reprod Healthc.* 2017.10; 13; 1-7
 11. Nguyen HTL, Nakamura K, Seino K, Vo VT. Association between a wider availability of health information and health care utilization in Vietnam: Cross-sectional study *J Med Internet Res.* 2017.12; 19(12); e405
 12. Bintabara D, Nakamura K, Seino K. Determinants of facility readiness for integration of family planning with HIV testing and counseling services: evidence from the Tanzania service provision assessment survey, 2014–2015 *BMC Health Services Research.* 2017.12; 17; 844
 13. Deogratius Bintabara, Keiko Nakamura, Kaoruko Seino. Determinants of facility readiness for integration of family planning with HIV testing and counseling services: evidence from the Tanzania service provision assessment survey, 2014-2015. *BMC Health Serv Res.* 2017.12; 17(1); 844

[Books etc]

1. Nakamura K, Ai CJA. *Healthy Cities – The Theory, Policy, and Practice of Value - Based Urban Health Planning.* Springer, 2017.01

[Conference Activities & Talks]

1. Seino K, Nakamura K, Oneil M.. Heat-coping practices and social interactions among elderly urban dwellers.. AASSA-SCJ Workshop 2017.03.02 Tokyo
2. Nakamura K.. Healthy Cities and Sustainable Development Goals.. Workshop on Healthy Cities and SDGs 2017.08.17 Phnom Penh, Cambodia
3. Nguyen HTL, Nakamura K, Seino K. . The association between social media sources for health information and healthcare utilization in Vietnam. . World Epidemiological Association 2017 Conference. 2017.08.20 Ohmiya, Japan
4. Bintabara D, Nakamura K, Seino K. . The role of antenatal care in predicting birth preparedness among rural women in Tanzania. . World Epidemiological Association 2017 Conference. 2017.08.20 Ohmiya, Japan
5. Nakamura K.. Health Promotion and Health Promoting School: WHO recommendations.. HCSO-AFHC Symposium: Healthy School 2017.10.16
6. Nakamura K. Training Opportunity at WHO Collaborating Centre for Healthy Cities and Urban Policy Research. 2017.11.25

Geriatrics and Vascular Medicine

Professor : Under selection

Associate Professor : Eiji KANEKO

Junior Associate Professor : Masashi BEPPU

Assistant Professor : Yasuko ABE

Graduate Student : Kenji TOYOSHIMA, Marie NAKAMURA, Risa SUZUKI

(1) Research

- 1) Cell biological mechanisms of atherogenesis
- 2) Mechanisms involved in dyslipidemia
- 3) Mechanisms of aging and age-related diseases
- 4) Undergraduate and postgraduate education in geriatrics

(2) Education

- 1) Undergraduate education of medical students with a particular emphasis on geriatrics
- 2) Development of research on aging and age-related diseases with a particular emphasis on atherosclerosis

(3) Clinical Services & Other Works

As a division of the Department of Internal Medicine, we are taking care of elderly patients who are better treated by us rather than by highly specialized experts both at the outpatient clinics and the ward of our university hospital. We also provide subspecialty service such as oriental herbal medicine, mononuclear cell transplantation for PAD, and dyslipidemia clinic.

(4) Publications

[Original Articles]

1. Nakazawa Harumasa, Chang Kyungho, Shinozaki Shohei, Yasukawa Takashi, Ishimaru Kazuhiro, Yasuhara Shingo, Yu Yong-Ming, Martyn J A Jeevendra, Tompkins Ronald G, Shimokado Kentaro, Kaneki Masao. iNOS as a Driver of Inflammation and Apoptosis in Mouse Skeletal Muscle after Burn Injury: Possible Involvement of Sirt1 S-Nitrosylation-Mediated Acetylation of p65 NF-kappaB and p53. *PLoS One*. 2017; 12(1); e0170391
2. Suguru Mabuchi, Risa Suzuki, Mari Sasaki, Marie Nakamura, Norihiko Izumimoto, Tomomi Hakamada, Kenji Toyoshima, Yasuko Abe, Eiji Kaneko, Kentaro Shimokado. Case report of severe iron deficiency anemia caused by proton pump inhibitor in an elderly patient. *Geriatr Gerontol Int*. 2017.04; 17(4); 662-663

[Conference Activities & Talks]

1. Sasaki M, Shinozaki S, Shimokado K.. Sulforaphane promotes murine hair growth by accelerating the degradation of dihydrotestosterone.. The 8th IAGG Master Class on Ageing in Asia 2017.03.26

Rehabilitation Medicine

Associate Professor Tetsuya JINNO
Graduate Student
Chisato HOSHINO
Kazuko KATSUKI

(1) Research

Research Subjects

- 1) Rehabilitation for total joint arthroplasty
- 2) Three dimensional motion analysis of upper/lower extremities and gait analysis
- 3) Patient safety in rehabilitation medicine
- 4) Biomechanical research for prevention of sports injury

(2) Lectures & Courses

Purpose of Education:

Rehabilitation medicine consists of physical, occupational and speech therapy. Main theme of rehabilitation medicine in graduate course is to study 3-dimensional motion analysis in activities of daily living and molecular biological analysis of disuse atrophy.

(3) Publications

[Original Articles]

1. Tetsuya Jinno, Daisuke Koga, Yoshinori Asou, Sadao Morita, Atsushi Okawa, Takeshi Muneta. Intraoperative evaluation of the effects of femoral component offset and head size on joint stability in total hip arthroplasty *Journal of Orthopaedic Surgery*. 2017.01; 25(1); 1-5
2. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Takeshi Muneta, Atsushi Okawa. Comparison of bone remodeling between an anatomical short stem and a straight stem in one-stage bilateral total hip arthroplasty *The Journal of Arthroplasty*. 2017.02; 32(2); 594-600
3. Naofumi Taniguchi, Tetsuya Jinno, Daisuke Koga, Tetsuo Hagino, Atsushi Okawa, Hirotaka Haro. Cementless Hip Stem Anteversion in the Dysplastic Hip: A Comparison of Tapered Wedge vs Metaphyseal Filling *The Journal of Arthroplasty*. 2017.05; 32(5); 1547-1552
4. Kashitaro Hyodo, Tadashi Masuda, Junya Aizawa, Tetsuya Jinno, Sadao Morita. Hip, knee, and ankle kinematics during activities of daily living: a cross-sectional study. *Brazilian Journal of Physical Therapy* . 2017.05; 21(3); 159-166
5. Ryohei Takada, Tetsuya Jinno, Daisuke Koga, Atsushi Okawa. Comparison of wear rate and osteolysis between second-generation annealed and first-generation remelted highly cross-linked polyethylene in total hip arthroplasty. A case control study at a minimum of five years. *Orthopaedics & Traumatology: Surgery & Research*. 2017.06; 103(4); 537-541

[Conference Activities & Talks]

1. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Takeshi Muneta, Atsishi Okawa. Comparison Of Wear Rate And Osteolysis Between Second-Generation Annealed And First-Generation Remelted Highly Cross-Linked Polyethylene In Total Hip Arthroplasty. 18th EFORT Congress 2017.06.01 Viena(Austria)

[Others]

1. Train-the-Trainer Program for OrthAlign Plus, 2017.06
Hip Training Course @ OrthAlign

Gerodontology and Oral Rehabilitation

Professor

MINAKUCHI Shunsuke

Associate Professor

TOHARA Haruka

Junior Associate Professor

SEKITA Toshiaki, KOBAYASHI Ken-ichi, KUBOTA Kazumasa

Assistant Professor

AKIBA Norihisa, INOKOSHI Masanao, KANAZAWA Manabu, KOMAGAMINE Yuriko, MOTOMURA Kazuo, NAKANE Ayako, SATO Yusuke, WAKASUGI Yoko, OKUBO Mai

Project Assistant Professor

HAMA Yohei

Dental Resident

YOSHIZAKI Taro, NAKMURA Toshinarim, HIRAYAMA Daisuke, INOUE Minoru, YOSHIKAZUMI Yuu, SATO Marie, KAMOCHI Go, OOWADA Gaku, SOEDA Hitomi, SUZUKI Hiroyuki, Hara Takeshi

Graduate Student

AMAGAI Noriko, ANNDOU Mariko, ARAKIDA Toshio, ASAMI Mari, BABA Yuuya, CHANTARAMANEE Ariya, DOUKE Midori, KAGIFUKU Yuko, KAIKILYIA Yalikulun, Sato Eriko, KHAING Myat Thu, KUROSAWA Yukiko, KYOSAKA Yuka, MATSUBARA Mariko, MATSUDA Yuhei, MIURA Akemi, MIYAYASU Anna, SHIMIZU Haruki, SHIMIZUBATA Makoto, SHINOZAKI Hiromichi, SHIMADA Ryo, TAGASHIRA Itoe, TUN Min Bo, VO Lam Thuy, YAMAGUCHI Kouhei, YAMAZAKI Yasuhiro, YOSHIMI Kanako, YOSHINAKA Shin, HIROKO Namai, Awutsadaporn Katheng, Thaw Di Cho Too, KAKU Jakuenn, Negoro Masatoshi, SOEDA Yumika, HASEGAWA Syouhei, HADA Tamaki, HATANNO Keita, HARA Yoshiko, YOSHIDA Saori,

Student

HIGASHINAKAGAWA Anri, JOKO Natsuka, KANEKO Seiko, KAWASHIMA Mina, NAMIKI Chizuru, NISHIKI Gen, NISHIMIYA Yui, OKANO Sakiko, TAKADA Shintaro, TAMURA Atsuko, UEDA Kaori, UENO Taro, Tsugawa Eriko, YAGUCHI Shiho, SAI TUN NAING, KONISHI Emi, KAWAI Yosuke, KAWAKATSU Miri, OBARA Mana, IMADA Ryoko, HAYASHI, Ayano, YOSHII Eiji

Staff

YAJIMA Yuriko, YOSHIZAKI Ayaka, TERADA Mito, FUKUSHIMA Rie

(1) Research

- 1) Medical management of Elderly Patients During Dental Treatment
- 2) New Examination Method for Dry Mouth
- 3) Oral Stereognosis Ability in the Elderly
- 4) Threshold of Mucous Membrane under Denture Base in Elderly Oral Mucosa Patients
- 5) State of the art Lasers in Zirconia Prosthetic Processing and Pain-free Treatment

- 6) Denture Mobility
- 7) Deglutition in Elderly Patients Requiring Nursing Care
- 8) Eating and Swallowing Rehabilitation in Post-Oral Tumor Surgery Patients
- 9) Dysphagia of Medullary Infarction Patients
- 10) Dental Approaches to Dysphagia
- 11) Screening Methods of Silent Aspiration
- 12) Swallowing Dynamics and Brain Activity
- 13) Stress analyses of implant overdenture
- 14) Factorial analysis of complete denture prosthesis
- 15) Resilient denture lining material
- 16) CAD/CAM system for fabricating complete dentures
- 17) Evaluations of masticatory performance using color-changeable chewing gum
- 18) Development of novel restorative materials for root caries
- 19) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 20) Ultrastructural analysis of zirconia-veneering ceramic interface

(2) Education

Given the increased health needs of an aging society, we aim to integrate diverse clinical specialties related to geriatric dental practice and to educate individuals of fundamental studies in each field. We emphasize a comprehensive approach to patient interactions by examining daily life functionality rather than focusing only on their diseases.

With regard to dysphagia, which can lead to aspiration pneumonia, we provide comprehensive education on causes, diagnostic methods, and rehabilitation options from a dentistry point of view. Since we regard rehabilitation as the medicine of daily living, we emphasize that dysphagia rehabilitation should be considered a method to ameliorate disability rather than diseases by introducing practical approaches in addition to factual knowledge.

(3) Clinical Performances

We manage the prosthodontic, special care and dysphagia rehabilitation departments.

(4) Publications

[Original Articles]

1. Shinozaki H, Tohara H, Matsubara M, Inokuchi N, Yamazaki Y, Nakane A, Wakasugi Y, Minakuchi S. Relationship between jaw opening force and hyoid bone dynamics in healthy elderly subjects *Clinical Interventions in Aging*. 2017; 12; 629-634
2. Shoko Oba, Haruka Tohara, Ayako Nakane, Makoto Tomita, Shunsuke Minakuchi, Hiroshi Uematsu. Screening tests for predicting the prognosis of oral intake in elderly patients with acute pneumonia. *Odontology*. 2017.01; 105(1); 96-102
3. Khaing Myat Thu, Vo Lam Thuy, Manabu Kanazawa, Shunsuke Minakuchi. Evidences of Applicability of Implant Supported Overdentures during Present Decade; A Review. *Myanmar Dental Journal*. 2017.01; 24(1); 32-41
4. Chieko Kubota, Manabu Kanazawa, Yohei Hama, Yuriko Komagamine, Shunsuke Minakuchi. Association between chewing-stimulated salivary flow under the effects of atropine and mixing ability assessed using a color-changeable chewing gum. *J Prosthodont Res*. 2017.01; 61(4); 387-392
5. NAKAMURA Toshinari, AKIBA Norihisa, TANIMOTO Hiroyuki,HIRAYAMA Daisuke and MINAKUCHI Shunsuke. Influence of a home reliner on denture displacement and patient reported outcome. 2017.03; 84(1); 8-18

6. Inokoshi M, Zhang F, Vanmeensel K, De Munck J, Minakuchi S, Naert I, Vleugels J, Van Meerbeek B. Residual compressive surface stress increases the bending strength of dental zirconia. *Dent Mater.* 2017.04; 33(4); e147-e154
7. Tsunataka Abo, Tomoyuki Miyamoto, Takutoshi Inoue, Kazumasa Kubota, Keiko Abe, Kanji Doushita, Haruhisa Fukuyama. Anesthetic Management of a Patient with Human Immunodeficiency Virus (HIV) Undergoing a Sagittal Split Ramus Osteotomy (SSRO). *Journal of Japan Dental Society Anesthesiology.* 2017.04; 45(2); 214-216
8. Kotomi Ota, Tomoyuki Miyamoto, Kazumasa Kubota, Haruhisa Fukayama. Management during Tooth Extraction of a Patient with Glanzmann's Thrombasthenia. *Journal of Japan Dental Society Anesthesiology.* 2017.04; 45(2); 178-180
9. Taro Yoshizaki, Norihisa Akiba, Masanao Inokoshi, Masayuki Shimada, Shunsuke Minakuchi. Hydrophilic nano-silica coating agents with platinum and diamond nanoparticles for denture base materials. *Dental Material Journal.* 2017.05; 36(3); 333-339
10. Hiroyuki Tanimoto, Norihisa Akiba, Toshinari Nakamura, Huizi Zhao, Hirona Suzuki, Akira Uno, Motohiro Uo, Shunsuke Minakuchi. An objective estimation of the removability of three home reliners. *Dent Mater J.* 2017.05; 36(3); 309-318
11. Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Shunsuke Minakuchi. Fabrication of the complete denture applying CAD/CAM system. *Annals of Japan Prosthodontic Society.* 2017.07; 9(3); 236-241
12. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Noriko Amagai, Shunsuke Minakuchi. The effect of new complete denture fabrication and simplified dietary advice on nutrient intake and masticatory function of edentulous elderly: A randomized-controlled trial. *Clin Nutr.* 2017.08;
13. Yoko Wakasugi, Haruka Tohara, Nami Machida, Ayako Nakane, Shunsuke Minakuchi. Can grip strength and/or walking speed be simple indicators of the deterioration in tongue pressure and jaw opening force in older individuals? *Gerodontology.* 2017.08; 1-5
14. Yuhei Matsuda, Manabu Kanazawa, Yuriko Komagamine, Masashi Yamashiro, Sumio Akifusa, Shunsuke Minakuchi. Reliability and Validity of the MD Anderson Dysphagia Inventory Among Japanese Patients. *Dysphagia.* 2017.08;
15. Toshiaki Sekita, Syuhei Takeuchi, Syunsuke Minakuchi. Measuring system for an attitude angle of a denture using an Inertial Measurement Unit. *J Prosthodont Res.* 2017.09;
16. Noriko Amagai, Yuriko Komagamine, Manabu Kanazawa, Maiko Iwaki, Ayami Jo, Hiroyuki Suzuki, Shunsuke Minakuchi. The effect of prosthetic rehabilitation and simple dietary counseling on food intake and oral health related quality of life among the edentulous individuals: A randomized controlled trial. *J Dent.* 2017.10; 65; 89-94
17. Hitomi Soeda, Yusuke Sato, Eijiro Yamaga, Shunsuke Minakuchi. A structural equation model to assess the influence of neuroticism on oral health-related quality of life in complete denture wearers. *Gerodontology.* 2017.12; 34(4); 446-454
18. Mai Okubo, Yusuke Sato, Yuki Hiraajima, Shunsuke Minakuchi. Learning effects of different training models for border molding from the perspective of dental students. *BMC Oral Health.* 2017.12; 17(1); 152
19. Yamazaki Y, Toraha H, Nakane A, Wakasugi Y, Yamaguchi K, Minakuchi S. Excessive anterior cervical muscle tone affects hyoid bone kinetics during swallowing in healthy individuals. *Clinical Interventions in Aging.* 2017.12; 12; 1-8
20. Y Hama, A Hosoda, Y Komagamine, S Gotoh, C Kubota, M Kanazawa, S Minakuchi. Masticatory performance-related factors in preschool children: establishing a method to assess masticatory performance in preschool children using colour-changeable chewing gum. *J Oral Rehabil.* 2017.12; 44(12); 948-956
21. Kazumasa Kubota, Tomoyuki Miyamoto, Takutoshi Inoue and Haruhisa Fukayama. Anesthetic management of a patient with benign tracheal tumor identified at induction of general anesthesia. *Journal of Clinical Anesthesia.* 2017.12; (43); 66-67

22. Nami Ogawa, Takashi Mori, Ichiro Fujishima, Hidetaka Wakabayashi, Masataka Itoda, Kenjiro Kunieda, Takashi Shigematsu, Shinta Nishioka, Haruka Tohara, Minoru Yamada, Sumito Ogawa. Ultrasonography to Measure Swallowing Muscle Mass and Quality in Older Patients With Sarcopenic Dysphagia. *J Am Med Dir Assoc.* 2017.12;
23. Kamiyanagi A, Sumita Y, Ino S, Chikai M, Nakane A, Tohara H, Minakuchi S, Seki Y, Endo H, Taniguchi H. Evaluation of swallowing ability using swallowing sounds in maxillectomy patients. *J Oral Rehabil.* 2017.12; 45(2); 126-131

[Conference Activities & Talks]

1. KM. Thu, D. Sato, M. Kanazawa, M. Tanoue, K. Oda, Y. Kadiliya, A. Miyayasu, M. Asami, VL. Thuy, S. Minakuchi. Single Implant Retained Mandibular Overdenture [1-IOD] in Edentulous Patient with Massive Osteotomy; A Case Report. 37th Myanmar Dental Conference 2017.01.19 Yangon, Myanmar
2. Minakuchi S. Mastication will contribute to healthy longevity. 37th Myanmar Dental Conference 2017.01.20 Yangon
3. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Uo M, Minakuchi S. Crystallographic analysis of alumina sandblasted highly translucent dental zirconia. 95th General Session and Exhibition of the IADR 2017.03 San Francisco
4. Maiko Iwaki, Manabu Kanazawa, Toshio Arakida, Tetzuya Suzuki, Shunsuke Minakuchi. Digital impression and jaw relation record for the fabrication of complete dentures. 2017.04.22
5. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Shunsuke Minakuchi. Effect of simple dietary advice combined with denture fabrication by dentist on nutrient intake of edentulous elderly. The 71th Annual Meeting of Japan Society of Nutrition and Food Science 2017.05.20 Okinawa
6. Kazumasa Kubota, Shunsuke Minakuchi, Haruhisa Fukuyama. Anesthetic Management for a Patient Diagnosed with Chronic Kidney Disease Scheduled for Transplanted of Scapular Osteocutaneous Flap Harvest. The 28th Annual Meeting of Japanese Society of Gerodontology 2017.06.15 Nagoya
7. Seiko Kaneko, Minoru Inoue, Marie Sato, Akiko Takahashi, Anri Higashinakagawa, Eriko Tsugawa, Shiho Yaguchi, Toshiaki Sekita. A Case of Odontorrhagia after a Tooth Extraction due to Poor Control of Warfarin. The 28th Annual Meeting of Japan Society of Gerodontology 2017.06.15 Nagoya
8. Yoshiko Hara, Haruka Tohara, Ayako Nakane, Yu Yoshizumi, Kohei Yamaguchi, Ryoko Imada, Masao Kinukawa, Takehiko Takemae, Mariko Matsubara, Eriko Kajisa, Itoe Tagashira, Syunsuke Minakuchi. Effort for Oral Intake of a Gastrostomy Patient with Intractable Hiccups. The 28th Annual Meeting of Japanese Society of Gerontology 2017.06.16 Nagoya
9. Ohwatari T, Takahashi K, Kyosaka Y, Inokoshi M, Inoue M, Minakuchi S, Fukayama H, Shimoyama K. Medications in 5,699 medically compromised elderly dental patients. 2017.06.16 Nagoya
10. Inokoshi M. Basic knowledge of contemporary CAD/CAM and ceramics materials. TMDU Exciting Room 2017.06.17 Tokyo
11. Iwaki Maiko, Kanazawa manabu, Miyayasu Anna, Sato Daisuke, Kasugai Shohei, Minakuchi Shunsuke. Prospective study of immediate Loaded two-implants mandibular overdentures: 5-years follow up. 2017.06.30 Yokohama
12. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Shunsuke Minakuchi. The effect of new complete denture fabrication and simplified dietary advice on nutrient intake and masticatory function of edentulous elderly. The 126th Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama
13. Gou Kamochi, Norihisa Akiba, Tarou Yoshizaki, Masayuki Morisawa, Taturou Uchida, Shunsuke Minakuchi, Masayuki Shimada. Photocatalytic effect of tungsten oxide coated denture base resin. The 126rd Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama

14. Sekita T, Takeuti S, Kobayashi K, Higashinakagawa A, Takahashi A, Irie S . Measuring system for denture using by an Inertial Measurement Unit . The 126rd Annual Meeting of Japan Prothodontic Society 2017.07.01 Yokohama
15. Sekita T, Takeuti S, Kobayashi K, Higashinakagawa A, Takahashi A, Irie S. Measuring system for denture using by an Inertial Measurement Unit. The 126th Annual Meeting of the Japan Prosthodontic Society 2017.07.02 Yokohama
16. Kobayashi K, Takahashi M, Abe A, Takeuchi S, Hoshino T, Kobayashi K, Sekita T. Prosthetic treatment for severe class II case with aesthetic problem. The 126th Annual Meeting of the Japan Prosthodontic Society 2017.07.02 Yokohama
17. Kosei Kobayashi, Kenichi Kobayashi. Restoring Esthetics and Anterior Guidance by Twin-stage Procedure. The 126th Annual Meeting of the Japan Prosthodontic Society 2017.07.02 Yokohama
18. Seki N, Kanazawa M, Komagamine Y, Moross J, Mizutani K, Hosaka K, Komada W, Sunaga M, Kawaguchi Y, Morio I, Kinoshita A. Introduction of the international course to teach clinical dental expertise at Tokyo Medical and Dental University, graduate school -the first report-. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.28 Nagano
19. Hama Y, Minakuchi S, Sasaki K, Maeda T, Hamura A, Ichinohe T, Okiji T. The Dental Education Consortium to promote healthy longevity -Second report- Agendas after the second year. Annual Meeting of the 36th Japanese Dental Education Association 2017.07.29 Matsumoto
20. Yuriko Komagamine, Manabu Kanazawa, Anna Miyayasu, Vo Lam. Thuy, Yuri Omura, Daisuke Sato, Shohei Kasugai, Shunsuke Minakuchi. Masticatory Performance with Magnet Retained Mandibular Two Implant Overdentures. 31st ISDR-SEA 2017.08.12 Taipei International Convention Center, Chinese Taipei
21. Minakuchi S. Long-term care insurance system on oral health in Japan : the system and new challenges. 31st IADR-SEA 2017.08.13 Taipei International Convention Center, Chinese Taipei
22. Y. Komagamine, M. Kanazawa, D. Sato, A. Miyayasu, M. Asami, R Shimada, KM Thu, VL Thuy, S. Kasugai, S. Minakuchi. Comparison of patient-reported outcomes between immediately and conventionally loaded mandibular two-implant overdentures: A preliminary study. 17th biennial meeting of the International College of Prosthodontists 2017.09.08 Santiago, Chile
23. M. Kanazawa, M. Iwaki, D. Sato, A. Miyayasu, M. Asami, R Shimada, KM Thu, VL Thuy, S. Kasugai, S. Minakuchi. Immediate Loading of two-implant mandibular overdentures: 5-year prospective study. 17th biennial meeting of the International College of Prosthodontists 2017.09.08 Santiago, Chile
24. Koji Hara. The deterioration of two swallowing muscles strength in aging . Japanese Society of Dysphagia Rehabilitation English Session 2017.09.15 Chiba, Japan
25. K Yamaguchi, H Tohara, A Nakane, K Hara, S Minakuchi. EFFECT OF AGING, TOOTH LOSS, PERIORAL MUSCLE MASS AND SKELETAL MUSCLE MASS ON OCCLUSAL FORCE IN HEALTHY ELDERLY. 7th ESSD Congress and World Dysphagia Summit 2017.09.21 Barcelona
26. Inokoshi M, Nozaki K, Takagaki T, Van Meerbeek B, Minakuchi S. Initial curing characteristics of composite cements under ceramic restorations. CED-IADR/NOF Oral Health Research Congress 2017 2017.09.22 Vienna
27. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. The effect of new complete denture fabrication combined with simplified dietary advice on protein intake of edentulous elderly. The 28th general meeting of Japanese Society for Mastication Science and Health Promotion 2017.09.23 Tokyo
28. G. Tanabe, T. Hada, PS. Tun, H. Churei, T. Wada, M. Uo, H. Takahashi, T. Ueno. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards. The 2017 Academy of Dental Materials Annual Meeting 2017.10.07 Nuremberg
29. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Mechanical property and microstructural analysis of an ion-releasing S-PRG filler contained cement. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.15 Niigata

30. Shimizu H, Inokoshi M, Takagaki T, Uo M, Minakuchi S. Bonding effectiveness of 4META/MMA-TBB resin to surface-treated highly translucent dental zirconia. The 36th Annual Meeting of Japan Society for Adhesive Dentistry 2017.11.26 Tokyo

[Awards & Honors]

1. Best Paper Award in Junior Scientist Session(Khaing Myat Thu) , 37th Myanmar Dental Conference, 2017.01

[Others]

1. Kobayashi K, Principle of tooth preparation, 2017.02
Hands-on course
2. Kobayashi K, Principle of tooth preparation, 2017.05
Hands-on course

Laboratory Medicine

Professor Shuji TOHDA
Assistant Professor Mai ITOH
Graduate Students Mika OHTAKA, Erika SHIRATORI, Yuki KODA

(1) Outline

Laboratory medicine is a field of research to develop analytical methods of pathophysiology of various diseases, new diagnostic tests, and diagnosis-supporting system using laboratory tests.

(2) Research

Our research subjects are as follows:

- 1) Cellular and molecular mechanism of abnormal growth of acute leukemia cells and drug-sensitivity tests for molecularly targeted therapy
- 2) Molecular diagnostic tests for cancer and detection of minimal residual cancer cells
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Molecular diagnostic tests for infectious diseases

(3) Education

To graduate students, we provide opportunity to study and develop novel diagnostic tests using cellular and molecular biological techniques in our laboratories.

To undergraduate students, we give a lecture and practical training on laboratory medicine.

(4) Lectures & Courses

Main objective of Laboratory Medicine in the graduate course is to provide students opportunity to study analysis of pathophysiology, development of new diagnostic tests, and establishment of diagnosis-supporting system using laboratory tests. We focus on the analysis of pathophysiology of hematological malignancies and the development of molecular diagnostic tests for cancer and infectious diseases.

(5) Clinical Services & Other Works

We are performing laboratory tests for hematology, clinical chemistry, immunology, and microbiology in cooperation with doctors and technologists of clinical laboratory in University hospital. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(6) Clinical Performances

We are developing new diagnostic methods collaborating with various clinical departments. We are also supporting them in their diagnostic procedure.

(7) Publications

[Original Articles]

1. S Nogami, N Kawaguchi-Ihara, E Shiratori, M Ohtaka, M Itoh, S Tohda. Detection of the MYD88 mutation by the combination of the allele-specific PCR and quenching probe methods. *Int J Lab Hematol.* 2017.04; 39(2); 163-168
2. Yuki Okuhashi, Mai Itoh, Shuji Tohda. Hedgehog Stimulation Suppresses Clonogenicity and Activates NOTCH Signalling in T-lymphoblastic Leukaemia Jurkat Cells. *Anticancer Res.* 2017.05; 37(9); 5005-5009
3. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. *J. Med. Virol.* 2017.07; 89(7); 1241-1247
4. Miyako Murakawa, Yasuhiro Asahina, Hiroko Nagata, Mina Nakagawa, Sei Kakinuma, Sayuri Nitta, Fukiko Kawai-Kitahata, Satoshi Otani, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Ayako Sato, Yasuhiro Itsui, Seishin Azuma, Toshihiko Nouchi, Yohei Furumoto, Tooru Asano, Yoshimichi Chuganji, Shuji Tohda, Mamoru Watanabe. ITPA gene variation and ribavirin-induced anemia in patients with genotype 2 chronic hepatitis C treated with sofosbuvir plus ribavirin. *Hepatol. Res.* 2017.07; 29(5); 584-593
5. Erika Shiratori, Mai Itoh, Shuji Tohda. MYD88 Inhibitor ST2825 Suppresses the Growth of Lymphoma and Leukaemia Cells. *Anticancer Res.* 2017.11; 37(11); 6203-6209
6. Mika Ohtaka, Mai Itoh, Shuji Tohda. BMI1 Inhibitors Down-regulate NOTCH Signaling and Suppress Proliferation of Acute Leukemia Cells. *Anticancer Res.* 2017.11; 37(11); 6047-6053

[Conference Activities & Talks]

1. Mika Ohtaka, Mai Itoh, and Shuji Tohda. BMI1 inhibitors suppress cell growth and NOTCH signalling of acute leukemia cells. 46th Annual Scientific Meeting of the International Society for Experimental Hematology 2017.08.26 Frankfurt, Germany

Intensive Care Medicine

Professor and Chairman
Hidenobu Shigemitsu (2016.9.1 -)

Professor
Hideo Takahashi(2017.4.1 -)

Junior Associate Professor
Michio Nagashima (2017.4.1 -)

Assistant Professor
Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)
Kenji Wakabayashi (2015.4.1 -)
Fumi Maruyama (Intensive Care Unit) (2017.2.1 -)
Mai Katahira (Intensive Care Unit) (2017.4.1 - 2018.3.31)
Shin Inukai (Intensive Care Unit) (2017.4.1 -)
Akihiro Haramo (Intensive Care Unit) (2015.4.1 - 2017.3.31)
Arisa Fukagawa (Intensive Care Unit) (2016.4.1 - 2017.3.31)
Kanae Ochiai (Intensive Care Unit) (2016.7.1 - 2017.1.31)

Fellow:
Nobuhiro Shiota (Intensive Care Unit) (2017.4.1 -)
Yuka Mishima (Intensive Care Unit) (2017.4.1 -)
Sachiyo Sato (Intensive Care Unit) (2017.4.1 -)
Jun Fujinaga (Intensive Care Unit) (2017.4.1 -)

Postgraduate students:
Mariko Senda (2014.4.1 -)
Yusuke Mitsui (2016.4.1 -)
Shotaro Matsumoto (2016.4.1 -)
Nobuhiro Shiota (2017.4.1 -)

(1) Outline

Critical care medicine provides intensive care and treatment for critically ill patients. To treat critically ill patients, intensivists have to catch the changes of the patients' condition by monitoring and evaluation, and practice appropriate therapy. It is important that intensivists practice minute-to-minute titration therapy in cooperation with other multidisciplinary professionals.

Practice of critical care medicine includes intensive care for various types of shock, acute respiratory distress syndrome/acute lung injury, sepsis, multiple organ dysfunction syndrome, abnormal acid-base balance, electrolyte disturbance, acute kidney injury, central nervous system dysfunction, and hospital-acquired infection, mechanical ventilation, pharmacological support, cardiopulmonary support system, blood purification, and nutrition support.

(2) Research

Our themes of research are derived from clinical questions in critically ill patients.

Clinical research:

1) Effective Medical Creation (EMC) project, in liaison with Yamaha Co. and world-renowned designer Hiroko Koshino.

Basic research:

1) Role of microvesicles in patients on ECMO (Shiota, funded by Grant-in-Aid for Young Scientists B)

2) Role of microvesicles in bronchopulmonary dysplasia (Wakabayashi, funded by Grant-in-Aid for Young Scientists B)

3) Role of urinary microvesicles in acute liver failure (Wakabayashi, funded by National Center of Child Health and Development)

(3) Education

Undergraduate education

Lectures: Fourth-year medical students

1) Mechanical ventilation (Wakabayashi)

Clinical clerkship: Fifth-year and Sixth-year medical students

Critical care medicine is a branch of faculty of medicine which deals with monitoring and care of critically ill patients. Main objective of critical care medicine is to provide students opportunity to study diagnosis and treatment of critically ill patients in the intensive care unit (ICU). Students are taught on clinical practice in the ICU. Students take charge of 1-2 patients with attending physician and intensivist. Students do an oral presentation at ICU educational rounds.

Conference: Students are assigned to read recent articles of critical care medicine and make presentations by power point at the conference.

Residents: Residents in training rotate the ICU for 2-3 months. They study respiratory, circulatory, and metabolic management of critically ill patients. They learn how to use ultrasound and bronchoscope.

(4) Lectures & Courses

US-based training system has been in place at the Department of Intensive Care Medicine under the Prof Shigemitsu who was a program director of ACGME-accredited fellowship program at the University of Nevada. We regularly hold educational conferences on every Tuesday called 'academic day'.

(5) Clinical Services & Other Works

Intensivists are staying in the ICU, and take charge treatment of critically ill patients in the ICU.

Every morning, intensivists, nurses, pharmacist, nutritionist, rehabilitation staffs, infection control staffs, medical engineers, and attending physicians get together, go round, and talk about the best treatment of the patients. From March 2017, we also started a novel Rapid Response System (we named as RAS: Risk Assessment System), in collaboration with the Department of Acute Critical Care and Disaster Medicine.

(6) Clinical Performances

Our early rehabilitation program based on the multidisciplinary round was awarded a 'best team prize' in 2017, and presented at an invited seminar at the national conference of Japanese Society of Respiratory Care Medicine.

(7) Publications

[Original Articles]

1. Michael Wilson, Kenji Wakabayashi, Szabolcs Bertok, Charlotte Oakley, Brijesh Patel, Kieran O'Dea, Joanna Cordy, Peter Morley, Andrew Bayliffe and Masao Takata. Inhibition Of TNF Receptor p55 By

A Domain Antibody Attenuates The Initial Phase Of Acid-Induced Lung Injury In Mice *Frontiers in Immunology*. 2017.02;

2. Tatham KC, O'Dea KP, Romano R, Donaldson HE, Wakabayashi K, Patel BV, Thakuria L, Simon AR, Sarathchandra P, Harefield POPSTAR investigators, Marczin N, Takata M. Intravascular donor monocytes play a central role in lung transplant ischaemia-reperfusion injury *Thorax*. 2017.04;
3. Chieko Mitaka, Tetsu Ohnuma, Takanori Murayama, Fumio Kunimoto, Michio Nagashima, Tetsuhiro Takei, Naoya Iguchi, Makoto Tomita, . Effects of low-dose atrial natriuretic peptide infusion on cardiac surgery-associated acute kidney injury: A multicenter randomized controlled trial. *J Crit Care*. 2017.04; 38; 253-258
4. Tsuboi N, Abe M, Matsumoto S, Nishimura N, Nakagawa S. The Effect of Clinical Experience on the Learning Curve of Pediatric Intensive Care Unit Residents for the Central Venous Catheter Placement Procedure *J Pediatr Intensive Care*. 2017.06; 00; 1-4

[Books etc]

1. Shigemitsu H, Orjioke, Luraschi C. Idiopathic Interstitial Pneumonias. Jaycee Brothers Medical Publishers, 2017.06

[Misc]

1. Kenji Wakabayashi. Management of shock - Mechanisms of interaction between shock and organ injury *Emergency and Intensive Care Medicine*. 2017.05; 29(5- 6); 385-390

[Conference Activities & Talks]

1. Kenji Wakabayashi. Role of inflammation in ventilator-induced lung injury. Education seminar for specialist in neonatology 2017.05.13 Sendai

[Awards & Honors]

1. Top Doctors, Vegas Seven Magazine, 2017.02
2. Best ICU doctor, University Medical Center, Las Vegas, Nevada, 2017.03
3. Las Vegas Sun Health Care Quarterly: Top Doctors, Vegas Inc, 2017.05

Liaison Psychiatry and Palliative Medicine

Associate Professor Eisuke MATSUSHIMA
Assistant Professor Miho MIYAJIMA
Project Assistant professor Kanako Ichikura,
Visiting Lecture Tetsuya Matsuda, Katsuya Ota,
Takashi Hosaka, Kouichi Fujiwara,
Toshitaka Yamakawa,
Clinical Psychologist Nao Nakayama, Tomoko Sugano,
Graduate Student Noriko Ishiduka, Toshi Kuriyama,
Hiroshi Koubou, Toshimi Takano, Rie Tani,
Takamasa Noda, Noriko Yoshida,
Hiroko Arioka, Nami Kondou,
Hiroki Sakurai, Mariko Takaki,
Sumie Nemoto, Reiko Matsuda,
Kisaragi Suzuki, Yoko Suzuki,
Jun Nakagawa, Mayo Fujiwara,
Kanako Amano, Sayaka Ozaka,
Saori Koshimoto, Shiho Matsuoka,
Kazuhiro Kosugi, Takafumi Watanabe,
Mayuko Iijima, Yu Okura, Jun Kakou,
Kensuke Komatsu,
Research Student Okihiko Aihara, Ryuho Ibaraki.
Technical Assistant Wakana Takeshita,
Yoshimi Morita, Tomoaki Watanabe,
Office Assistant Yoriko Mizukane, Satoko Ogi,

(1) Outline

The purpose of the section is to help understanding characteristics of psychosocial distress in patients with physical and mental disorders from a comprehensive viewpoint. Objects are mainly physical patients accompanied with pain, anxiety, depressive mood and so on. Students study these patients' symptoms, how to diagnose, practice of treatment and methods of preventive measures.

(2) Research

- 1) Assessment of mental state in cancer and other physical patients using written questionnaire
- 2) Research on quality of life (QOL) in cancer patients and their families
- 3) Investigation cognitive function of patients with organic disorders (SLE, diabetics, and so on) undergoing a battery of psychometry tests and neuroimaging examinations
- 4) Explanation for the relationship between physical symptoms and mental states in patients with psychoso-

matic diseases including chronic pain and irritable bowel syndrome (IBS)

5) Examination for physiological phenomenon of psychiatric patients using eye mark recorder, electroencephalogram (EEG) and functional MRI (fMRI)

(3) Clinical Services & Other Works

Psychosomatic clinic provides consultation-liaison psychiatry services at the request of the treating medical or surgical staffs. Patients accompanied with insomnia, anxiety, depressive mood and delirium are treated with psychotherapy and prescription medicines.

(4) Publications

[Original Articles]

1. Ichikura Kanako, Kobayashi Sayaka, Matsuoka Shiho, Suzuki Tsuyoshi, Nishimura Katsuji, Shiga Tsuyoshi, Hagiwara Nobuhisa, Ishigooka Jun, Suzuki Shin-ichi,. Avoidance behavior associated with depression in patients with implantable cardioverter defibrillators *International Journal of Clinical and Health Psychology*. 2017.01; 17; 1-8
2. Naoki Matsuo, Tatsuya Morita, Yoshinobu Matsuda, Kenichiro Okamoto, Yoshihisa Matsumoto, Keisuke Kaneishi, Takuya Odagiri, Hiroki Sakurai, Hideki Katayama, Ichiro Mori, Hirohide Yamada, Hiroaki Watanabe, Taro Yokoyama, Takashi Yamaguchi, Tomohiro Nishi, Akemi Shirado, Shuji Hiramoto, Toshio Watanabe, Hiroyuki Kohara, Satofumi Shimoyama, Etsuko Aruga, Mika Baba, Koki Sumita, Satoru Iwase. Predictors of responses to corticosteroids for anorexia in advanced cancer patients: a multicenter prospective observational study. *Support Care Cancer*. 2017.01; 25(1); 41-50
3. Koji Amano, Isseki Maeda, Tatsuya Morita, Mika Baba, Tomofumi Miura, Takashi Hama, Ichiro Mori, Nobuhisa Nakajima, Tomohiro Nishi, Hiroki Sakurai, Satofumi Shimoyama, Takuya Shinjo, Hiroto Shirayama, Takeshi Yamada, Shigeki Ono, Taketoshi Ozawa, Ryo Yamamoto, Naoki Yamamoto, Hideki Shishido, Hiroya Kinoshita. C-reactive protein, symptoms and activity of daily living in patients with advanced cancer receiving palliative care. *J Cachexia Sarcopenia Muscle*. 2017.03;
4. Masanori Mori, Akemi Naito Shirado, Tatsuya Morita, Kenichiro Okamoto, Yoshinobu Matsuda, Yoshihisa Matsumoto, Hirohide Yamada, Hiroki Sakurai, Etsuko Aruga, Keisuke Kaneishi, Hiroaki Watanabe, Takashi Yamaguchi, Takuya Odagiri, Shuji Hiramoto, Hiroyuki Kohara, Naoki Matsuo, Hideki Katayama, Tomohiro Nishi, Takashi Matsui, Satoru Iwase. Predictors of response to corticosteroids for dyspnea in advanced cancer patients: a preliminary multicenter prospective observational study. *Support Care Cancer*. 2017.04; 25(4); 1169-1181
5. Ohkura Yu, Haruta Shusuke, Shindoh Junichi, Tanaka Tsuyoshi, Ueno Masaki, Udagawa Harushi. Efficacy of prophylactic splenectomy for proximal advanced gastric cancer invading greater curvature *World J. Surg. Oncol.*. 2017.05; 15; 106
6. Shinsuke Hidese, Kotaro Hattori, Daimei Sasayama, Tomoko Miyakawa, Ryo Matsumura, Yuuki Yokota, Ikki Ishida, Junko Matsuo, Takamasa Noda, Sumiko Yoshida, Toshiya Teraishi, Hiroaki Hori, Miho Ota, Hiroshi Kunugi. Cerebrospinal fluid neural cell adhesion molecule levels and their correlation with clinical variables in patients with schizophrenia, bipolar disorder, and major depressive disorder. *Prog. Neuropsychopharmacol. Biol. Psychiatry*. 2017.06; 76; 12-18
7. Yoko Suzuki, Miho Miyajima, Katsuya Ohta, Noriko Yoshida, Mayo Fujiwara, Masaki Okumura, Mitsuru Nakamura, Tetsuo Sasano, Tokuhiro Kawara, Masato Matsuura, Eisuke Matsushima. Changes in corrected QT interval during electroconvulsive therapy *Clinical Neurophysiology*. 2017.06; 128(6); e166
8. Kanako Ichikura, Aya Yamashita, Taro Sugimoto, Seiji Kishimoto, Eisuke Matsushima. Patterns of stress coping and depression among patients with head and neck cancer: A Japanese cross-sectional study. *Psychooncology*. 2017.08;
9. Jun Kako, Masamitsu Kobayashi, Yusuke Kanno, Keita Tagami. Intranasal Vinegar as an Effective Treatment for Persistent Hiccups in a Patient With Advanced Cancer Undergoing Palliative Care. *J Pain Symptom Manage*. 2017.08; 54(2); e2-e4

10. Noriko Ishizuka, Toshimi Takano, Yuji Miura, Koichi Suyama, Akihiko Shimomura, Eisuke Matsushima. Psychological Distress and Resilience among Partners of Cancer Patients Receiving Outpatient Chemotherapy International Journal of Clinical Medicine. 2017.08; 8(8); 481-495
11. Nao Nakayama, Naoko Mori, Sae Ishimaru, Wataru Ohyama, Yuki Yuza, Takashi Kaneko, Eiichiro Kanda, Eisuke Matsushima. Factors associated with posttraumatic growth among parents of children with cancer. Psychooncology. 2017.09; 26(9); 1369-1375
12. Pu Shenghong, Setoyama Shiori, Noda Takamasa. Association between cognitive deficits and suicidal ideation in patients with major depressive disorder Sci Rep. 2017.09; 7; 11637
13. Yoshiya Moriguchi, Takamasa Noda, Kosei Nakayashiki, Yohei Takata, Shiori Setoyama, Shingo Kawasaki, Yoshihiko Kunisato, Kazuo Mishima, Kazuyuki Nakagome, Takashi Hanakawa. Validation of brain-derived signals in near-infrared spectroscopy through multivoxel analysis of concurrent functional magnetic resonance imaging. Hum Brain Mapp. 2017.10; 38(10); 5274-5291
14. Mariko Kobayashi, Sue P Heiney, Kaori Osawa, Miwa Ozawa, Eisuke Matsushima. Effect of a group intervention for children and their parents who have cancer. Palliat Support Care. 2017.10; 15(5); 575-586
15. Yoko Suzuki, Miho Miyajima, Katsuya Ohta, Noriko Yoshida, Rie Omoya, Mayo Fujiwara, Takafumi Watanabe, Masaki Okumura, Hiroaki Yamazaki, Masayuki Shintaku, Issei Murata, Shigeru Ozaki, Takeshi Sasaki, Mitsuru Nakamura, Hiroshi Suwa, Tetsuo Sasano, Tokuhiro Kawara, Masato Matsuura, Eisuke Matsushima. Is prolongation of corrected QT interval associated with seizures induced by electroconvulsive therapy reduced by atropine sulfate? Pacing Clin Electrophysiol. 2017.11; 40(11); 1246-1253
16. Ei Kinai, Kensuke Komatsu, Maiko Sakamoto, Toshibumi Taniguchi, Aya Nakao, Hidetoshi Igari, Kiyonori Takada, Aki Watanabe, Ai Takahashi-Nakazato, Misao Takano, Yoshimi Kikuchi, Shinichi Oka, . Association of age and time of disease with HIV-associated neurocognitive disorders: a Japanese nationwide multicenter study. J. Neurovirol.. 2017.12; 23(6); 864-874
17. Shinsuke Kito, Yuki Matsuda, Yurie Sewaki, Junpei Sekiya, Takeshi Fujii, Takamasa Noda, Satoru Ikezawa, Harumasa Takano, Kanako Nakazawa, Mami Nomura, Shiori Setoyama, Kazuyuki Nakagome. A 6-Month Follow-up Case Study of Low-Frequency Right Prefrontal Repetitive Transcranial Magnetic Stimulation in Treatment-Resistant Bipolar Depression. J ECT. 2017.12; 33(4); e43-e44
18. Noda Takamasa, Nakagome Kazuyuki, Setoyama Shiori, Matsushima Eisuke. Working memory and prefrontal/temporal hemodynamic responses during post-task period in patients with schizophrenia: A multi-channel near-infrared spectroscopy study J. Psychiatr. Res.. 2017.12; 95; 288-298
19. Yu Ohkura, Junichi Shindoh, Masaki Ueno, Toshiro Iizuka, Shusuke Haruta, Harushi Udagawa. A new postoperative pain management (intravenous acetaminophen: Acelio®) leads to enhanced recovery after esophagectomy: a propensity score-matched analysis. Surg. Today. 2017.12;
20. Ayako Matsuda, Yosuke Yamada, Noriko Ishizuka, Eisuke Matsushima, Kunihiko Kobayashi, Takayoshi Ohkubo, Kazue Yamaoka.. Effects of a Self-Monitoring Quality of Life Intervention for Patients with Cancer Receiving Palliative Care in Japan: Study Protocol for a Randomized Controlled Trial. Asian Pacific Journal of Cancer Prevention. 2017.12;
21. Go Taniguchi, Miho Miyajima, Masako Watanabe, Yoshiko Murata, Daichi Sone, Yutaka Watanabe, Mitsutoshi Okazaki, Motonori Kobayashi-Kimura, Masaaki Kato, Teiichi Onuma. . Nonconvulsive status epilepticus in the elderly associated with newer antidepressants used at therapeutic doses: A report of three cases. Epilepsy Behav. (accepted).

[Conference Activities & Talks]

1. Kako J, Morita T, Yamaguchi T, Sekimoto A, Kobayashi M, Kinoshita H, Ogawa A, Zenda S, Uchitomi Y, Inoguchi H, Matsushima E. Evaluation of duration of washout period following fan therapy for breathlessness: a methodological pilot study. . EAPC 2017 15th World Congress of the European Association for Palliative Care 2017.05.18

2. Fumiya Sakane, Koichi Fujiwara, Miho Miyajima, Yoko Suzuki, Toshitaka Yamakawa, Manabu Kano, and Taketoshi Maehara. Seizure Prediction and Mechanism Analysis of Generalized Epilepsy Based on Heart Rate Variability. 39th International Conference of the IEEE Engineering in Medicine and Biology Society 2017.07.11
3. Saori Koshimoto, Masako Arimoto, Keiko Saitou, Mayumi Uchibori, Akiko Hashizume, Yasuaki Nakajima, Eisuke Matsushima. Need for nutritional counselling by patients receiving outpatient chemotherapy. 19th World Congress of International Psycho-Oncology and Psycho-Social Academy 2017.08.17
4. Umezawa S, Fujimori M, Matsushima E, Kinoshita H, Uchitomi Y. Preferences of advanced cancer patients for communication on anticancer treatment cessation and the transition to palliative care. 19th World Congress of Psycho-oncology and Psychosocial Academy 2017.08.17
5. Ichikura Kanako, Yamashita Aya, Matsuoka Shiho, Nakayama Nao, Ariizumi Yousuke, Sumi Takuro, Sugimoto Taro, Asakage Takahiro, Matsushima Eisuke. Stress coping skill training for patients with head and neck cancer: Interim report of a randomized controlled trial. 19th World Congress of Psycho-Oncology and Psychosocial Academy 2017.08.18 Berlin, Germany
6. Miho Miyajima, Koichi Fujiwara, Toshitaka Yamakawa, Yoko Suzuki, T. Sasai-Sakuma, Manabu Kano, Taketoshi Maehara, Yutaka Watanabe, Satsuki Watanabe, Yoshiko Murata, Tetsuo Sasano, Eisuke Matsushima. Seizure Prediction in Localization-related Epilepsy by Heart Rate Variability Monitoring. XXIII World Congress of Neurology 2017.09.16

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata
Research student Xue Bingyang

(1) Research

- 1) Kinetics of drug action in disease states
- 2) Therapeutic drug monitoring and clinical pharmacokinetics

(2) Education

Department of Pharmacokinetics and Pharmacodynamics is in charge of the education of pharmacokinetics and pharmacodynamics for the establishment of safe and effective drug therapy. In the graduate course, the lecture on the recent progress of the pharmacokinetic analysis will be given. Students will have the practice of pharmacokinetic analysis and animal experiments.

(3) Publications

[Original Articles]

1. Yasuyoshi Ishiwata, Masashi Nagata, Kohta Tsuge, Hiromitsu Takahashi, Sayo Suzuki, Kohsuke Imai, Masatoshi Takagi, Hirokazu Kanegane, Tomohiro Morio, Masato Yasuhara. Population Pharmacokinetics of Intravenous Busulfan in Japanese Pediatric Patients With Primary Immunodeficiency Diseases. *J Clin Pharmacol.* 2017.10;

[Conference Activities & Talks]

1. M. Odaka, M. Nagata, T. Mizuno, T. Uchida, N. Kurashima, H. Takahashi, et al. Effect of cardiopulmonary bypass surgery on unbound fraction of cefazolin in plasma. *ASCPT2017* 2017.03.17 Washington DC
2. Nagata M., Kimura Y., Ishiwata Y., Takahashi H., Yasuhara M.. Epinephrine is involved in clozapine-induced acute hyperglycemia. *2017 AAPS Annual Meeting and Exposition* 2017.11.12 San Diego
3. Kawano Y., Nagata M., Arimori K., Kohno T., Ichimiya A., Uehara K., Aoyama T.. Caffeine increases cisplatin-induced apoptosis via inhibition of Akt pathway and ATM-mediated cell cycle checkpoint pathway in HCC cell lines. *2017 AAPS Annual Meeting and Exposition* 2017.11.12 San Diego

Medical Education Research and Development

Professor Yujiro TANAKA
 Junior Associate Professor Makoto TAKAHASHI
 Junior Associate Professor Eriko OKADA
 Junior Associate Professor Yasuhiro ITSUI
 Junior Associate Professor Toshifumi KUDO
 Senior Resident Fukiko KITAHATA

(1) Outline

Department of General Medicine was established in 2000, when Prof. Yujiro Tanaka assumed the role of chairman of the department. Since then, our aim has been to coordinate and support a wide range of new innovations for the department of medicine and its affiliated hospitals. Accordingly, we launched the following projects to carry out our mission; 1) Designing a new postgraduate clinical training program for TMDU affiliated hospitals, 2) Forming a patient support system including social casework, 3) Establishing the Center for Cell Therapy, and 4) Reforming undergraduate medical education.

In response to the expansion of our activities, we have had some reforms in our organizations. 1) We founded the Center for Postgraduate Medical Education in 2002. (Director: Prof. Tanaka. Associate Director: Dr. Masanaga Yamawaki/former, Dr. Yoshihito Momohara/former, and Dr. Makoto Takahashi/previous) 2) In 2002, we also established the Center for Health and Welfare. And two years later in 2004, it was developed into an independent center as the Department of Medicine when Dr. Masayoshi Shichiri was appointed as the Director. 3) The Center for Cell Therapy, which was first established as a part of the Blood Transfusion Department in March, 2001, became an independent organization in 2003. Then Dr. Tomohiro Morio became the director. 4) Prof. Tanaka became a member of the Board of Education and worked at the committee for curriculum renovations in the Department of Medicine. Then he became the chair of the Education Committee in 2004.

In addition to the curriculum reforms, the Department of General Medicine has been in charge of early clinical training, PBL implementation, supervising patient-doctor communication education, OSCE (objective structured clinical examination) preparation, and BSL (bedside learning). We have also promoted educational alliances with Harvard University since 2002 and with Imperial College, London since 2003.

As mentioned above, a couple of years after their launch, the Center for Health and Welfare and the Center for Cell Therapy became independent from the Department of General Medicine. Meanwhile, new working groups were formed within the department in 2004; the Working Group for Ward Management and the Safety Management Committee. The Department of General Medicine also devised an evaluation system for the residency training program (EPOC), which was later adopted as a national online evaluation system for postgraduate clinical training. We are working in close cooperation with Center for Interprofessional Education which we took in part of its establishment to materialize the interprofessional education introduced due to a revision of new curriculum in 2011.

(2) Research

Research on continuing education in clinical EBM (Tanaka)

Although the theory of EBM (Evidence-Based Medicine) has become common knowledge, there are many practical problems yet to be solved. Research on teaching and assessment techniques for under-and post-

graduate clinical training are ongoing.

Medical risk education using the HAZOP method-through analyzing basic surgical procedure (Takahashi)
Structured risk analysis methods, HAZOP, are applied for medical risk management. We have also developed computer software for risk analysis with HAZOP. As a method of medical education for medical risk as well, HAZOP is a comprehensive method that is effective in reducing medical errors.

Review of clinical training in postgraduate clinical education (Takahashi)
The performance evaluation system using EPOC, which is used in 60% of educational hospitals in Japan, was primarily developed at Tokyo Medical and Dental University. We applied this system to a clerkship program to compare its educational effect with that of a residency program.

General research on medical education (Tanaka, Takahashi, Itsui, Kudou, Okada)
We are developing a comprehensive research project regarding postgraduate medical education, primary care in rural regions, development of clinical competence, and a new PBL system.

(3) Education

Undergraduate Education

As a division, which is responsible for the education of students and residents, our primary goal is to foster doctors who have both a 'patient-centered perspective as a specialist' and 'up-to-date knowledge as a generalist'. To achieve our goal, we are designing and offering a continuing medical educational (CME) program for clerkship students, emphasizing on educational systems spreading among multiple departments. Since we think it is crucial to foster medical prospective with a patient-centered perspective, we introduced an early exposure course (MIC: Medical Introductory Course) for the 1st and 2nd year medical students, as well as some medicine oriented English courses, including a special course titled "Language and Philosophy of Western Medicine" regarding some of the needs of this globalized era of medicine. In addition, we are managing a training course for simulated patients who can contribute to medical education cooperating with the International Center for Medical Education at the University of Tokyo. To improve the quality of clinical training, we are currently developing an evaluation system for tutors and trainers.

Postgraduate Education (Clinical Training)

Our department has offered the postgraduate clinical training since 2004 according to the new national residency system in Japan. We have also played an important role in developing the online evaluation system for postgraduate clinical training (EPOC), which is used in 60% of education hospitals in Japan. Results of the questionnaire in March, 2013 showed one of the highest satisfaction rate among all national universities.

Postgraduate Education (Master' s degree courses)

We have been offering master' s degree courses in Medical Administration since this MMA program started in 2004, and were in charge of two courses this year, "Human resources management" and "Leadership in the medical care."

(4) Clinical Services & Other Works

Second Opinion (Itsui)

Our hospital is open to the public who ask for second opinions about their recommended treatments so that we can continue to contribute to the provision of safe and high-quality advanced medical technology. Over 300 consultation cases have been performed for patients coming from other hospitals nationwide. The purpose of this section is to assist the patients to exercise their right of self-determination and to be informed of new treatments and diagnostic tests. To provide a qualified second opinion, we have organized the network of specialists in TMDU.

Patient Safety (Kudou)

Dr.Ooka is the General Risk Manager of our university hospital, and our department regularly organizes seminars and training courses. In collaboration with other departments (e.g., Skills Laboratory Center, Infectious Control Committee, etc.), we are working for greater safety and quality of healthcare.

(5) Publications**[Original Articles]**

1. Yamamoto Y, Ichinose T, Nakamura M, Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y.. Successful complete surgical resection of a large venous malformation of the lower extremity: A case report. *Ann Vasu Dis.* 2017.01; 10(1); 59-62
2. Igari K, Kudo T, Toyofuku T, Inoue Y. Open Surgical Repair for Inflammatory Abdominal Aortic and Iliac Artery Aneurysms. *Ann Vasc Surg.* 2017.02; 39; 105-110
3. Yamamoto Y, Ichinose T, Nakamura M, Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y. Successful Complete Surgical Resection of a Large Venous Malformation of the Lower Extremity: A Case Report. *Ann Vasc Dis.* 2017.03; 10(1); 59-62
4. Igari K, Kudo T, Toyofuku T, Inoue Y. The use of dielectric blood coagulometry in the evaluation of coagulability in patients with peripheral arterial disease. *BMC Clin Pathol.* 2017.08; 17; 14
5. Igari K, Kudo T, Toyofuku T, Inoue Y. Endothelial dysfunction in patients with Buerger disease. *Vasc Health Risk Manag.* 2017.08; 13; 317-323
6. Igari K, Kudo T, Toyofuku T, Inoue Y. Endovascular Reintervention for Failing Infrainguinal Bypass Grafts. *Ann Vasc Surg.* 2017.08; 43; 218-225

[Conference Activities & Talks]

1. Kudo T. Chair: Presentation Award 8. Japan Endovascular Treatment Conference (JET) 2017. 2017.02.18 Tokyo
2. Igari K, Kudo T, Toyofuku T, Inoue Y. The chimney graft placement in the inferior mesenteric artery in endovascular aneurysm repair . 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.25 Seoul (Korea)
3. Kudo T, Yamamoto Y, Ichinose T, Nishizawa M, Igari K, Toyohuku T, Inoue Y.. Multiple recurrent pseudoaneurysms after EVAR in a patient with Behçet' s disease.. The 10th Korea-Japan Joint Meeting for Vascular Surgery 2017.04.14 Busan (Korea)
4. Kudo T, Ichinose T, Yamamoto Y, Nishizawa M, Igari K, Toyohuku T, Inoue Y.. Emergency endovascular repair for ruptured abdominal aortic and iliac aneurysms.. The 10th Korea-Japan Joint Meeting for Vascular Surgery 2017.04.15 Busan (Korea)
5. Igari K, Kudo T, Toyofuku T, Inoue Y. The relationship between inflammatory biomarkers and ischemic severity of patients with peripheral arterial disease. 85th EAS Congress 2017.04.24 Prague (Czech Republic)
6. Igari K, Kudo T, Toyofuku T, Inoue Y. The endovascular procedures of abdominal aortic aneurysms with challenging neck anatomy. 66th ESCVS 2017.05.14 Thessaloniki (Greece)
7. YOHEI FURUMOTO, AKIHIRO ARAKI, SAYURI NITTA, HIROKO NAGATA, KENTO TAKENAKA, KOUHEI SUZUKI, ERIKO OKADA, TAKAO HORIUCHI, MAMORU WATANABE. Report of successful rescue of disrupted capsafter rule endoscopy retention. Asian Pacific Digestive Week 2017.09.26 Hongkong
8. Nakagawa M, Asahina Y, Nagata H, Kaneko S, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tanaka Y, Watanabe M. Evaluation of an early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C patients treated with All-Oral DAAs - propensity score-matched analysis of a prospective database -. AASLD, The Liver Meeting 2017 2017.10.22 Washington D.C (USA)

Acute Critical Care and Disaster Medicine

Professor Yasuhiro Otomo

(1) Outline

1. Purpose of Education

We, the department of acute critical care and disaster medicine, investigate following wide range of fields, such as the search for mechanisms of biological response to severe stresses, the development of strategy for multiple organ dysfunction from the view of intensive care medicine, basic and clinical research about trauma, trauma preventive medicine and disaster medicine. Our targets of research are practical and cutting edge to work not only as a medical scientist but as a researcher for government projects.

2. Research Subjects

Basic research of the mechanism of multiple organ dysfunction following hemorrhagic/septic shock
Development of strategy for multiple organ dysfunction
Basic and clinical research of multiple trauma
Trauma epidemiology and trauma preventive medicine
Disaster medicine
Clinical research of cerebrovascular disease on acute phase

3. Clinical Services

Our emergency center was authorized to hold the 21st level I center in Tokyo on April 1, 2007. We give treatments over 8000 patients annual who are under critical condition like multiple organ dysfunction, severe sepsis and septic shock, life-threatening trauma as well. We also contribute to medical services, rushing to the emergency scene by a Doctor-Car/Helicopter at times.

(2) Publications

[Original Articles]

1. Akira Endo, Atsushi Shiraishi, Hiroki Matsui, Kenichi Hondo, Yasuhiro Otomo. Assessment of Progress in Early Trauma Care in Japan over the Past Decade: Achievements and Areas for Future Improvement. *J. Am. Coll. Surg.* 2017.02; 224(2); 191-198.e5
2. Akira Endo, Atsushi Shiraishi, Kiyohide Fushimi, Kiyoshi Murata, Yasuhiro Otomo. Increased Severe Trauma Patient Volume is Associated With Survival Benefit and Reduced Total Health Care Costs: A Retrospective Observational Study Using a Japanese Nationwide Administrative Database. *Ann. Surg.* 2017.06;
3. Akira Endo, Atsushi Shiraishi, Yasuhiro Otomo, Makoto Tomita, Hiroki Matsui, Kiyoshi Murata. Open-chest versus closed-chest cardiopulmonary resuscitation in blunt trauma: analysis of a nationwide trauma registry. *Crit Care.* 2017.07; 21(1); 169
4. Akira Endo, Miko Okamura, Shunsuke Yoshikawa, Yasuhiro Otomo, Tomohiro Morio. Multilateral Functional Alterations of Human Neutrophils in Sepsis: From the Point of Diagnosis to the Seventh Day. *Shock.* 2017.10;

5. Akira Endo, Atsushi Shiraishi, Shigeki Kushimoto, Yasuhiro Otomo. Verification of conventional criteria of the lethal triad and development of novel criteria as an indicator of decision making

Clinical Oncology

Professor MIYAKE Satoshi
Project Associate Professor
OOOKA Shinya
Project Assistant Professor

SAKASHITA Hiroyuki
Graduate Student
KAWASAKI Machiko
Graduate Student
SATO Noriyuki

(1) Outline

Department of Clinical Oncology was established in May 2012 to promote the field of palliative medicine and cancer chemotherapy according to “Training Program for Next Generation Specialists to Promote Cancer Therapy”. As for the education in medical school, we are involved in the course of Hematology-Oncology block and have a class of palliative medicine in the third year grade. In addition, we have a class of clinical ethics mainly focusing on the end-of-life care. As for the post-graduate education, we organized the “Training Program for Next Generation Specialists to Promote Cancer Therapy”.

(2) Research

- 1)Application of palliative care when the patient is diagnosed as cancer.
- 2)Improvement of QOL in the end-of -life care of cancer patients.
- 3)Communication skills in the team health care.
- 4)Multi-institutional research in pancreatic cancer treatment.
- 5)The role of biomarkers for newly developed anti-cancer drugs in lung cancer.

(3) Education

- 1)Hematology/Oncology
- 2)GI tract cancer
- 3)Lung cancer
- 4)Ethics
- 5)Communication

(4) Clinical Services & Other Works

Department of Clinical Oncology manages Cancer Center of the medical school hospital.
There are five divisions below.

- 1)Division of palliative medicine

- 2) Division of cancer chemotherapy
- 3) Division of cancer registry
- 4) Division of coordination of cancer treatment
- 5) Division of cancer consultation and support

Dentistry for Persons with Disabilities

Associate Professor
Osamu SHINOZUKA

Junior Associate Professor (Part-time)
Minoru INADA
Goro SEKIGUCHI
Naoki HAYASHI
Yohei TAKEUCHI
Syohei TAMURA
Moriyuki NAKAMURA

Assistant Professor
Yasuka KUSUMOTO

Graduate Student
Aiko HOSHIAI

Hospital Staff
Taiji HOSHIAI
Ayana NATORI
Anna KUMAKURAI
Hirotohi Yamawaki

Clinical Junior Associate Professor (Part-time)
Seiji SAKURAI
Tomo SUZUKI
Yosuke KINOSHITA

(1) Research

- 1) Formation of oral biofilm
- 2) Elimination of oral biofilm of persons with disabilities
- 3) Oral health status of the medically compromised patients
- 4) Oral management of genetic syndrome

(2) Lectures & Courses

Our department was started as a graduate course of the special dentistry section on April, 1999. The sections are the dentistry for persons with disabilities and medically compromised individuals .

The main objective of this course is to provide the opportunity for students to understand the outline of the reconstruction of functional and esthetic disorders of oral and/or maxillofacial areas by means of the high-advanced dental cares for patients with special needs.

(3) Clinical Performances

The clinical purpose of our department is to treat oral problems of special patients who are unable to receive normal dental care by reason of a disability which may be physical, mental, medical, or emotional, or combination of any of these under using behavior management and systemic support.

For example,

- 1) The patients requiring behavior management are physically disabled, intellectual disability, autistic spectrum disorder, etc.
- 2) The patients requiring systemic support are internal impediment, dental phobia, etc.

(4) Publications**[Original Articles]**

1. A modal analysis of fixed implant supported prosthetic device of the six abutments placed in edentulous maxilla Japanese Journal of Maxillo Facial Implants. 2017.12; 16(4); 275-283

[Books etc]

1. Periodontics for Special needs Patients . 2017.01 (ISBN : 978-885103643)
2. Special Needs Dentistry. 2017.02 (ISBN : 978-4-263-45801-3)

[Conference Activities & Talks]

1. A case report of the systemic management by clear sight system ® and transthoracic echocardiogram during dental treatment in a patient with dilated cardiomyopathy. 2017.03.03
2. Modal analyses of the maxillary dentition with maxillary cast obturator prostheses comparing different retainer types of metal frameworks . 2017.07.01
3. The survey on dental-treatments under intravenous sedation in the clinic for patients with disabilities at the dental association. 2017.10.28
4. Dental treatment in a patient with hypertrophic obstructive cardiomyopathy. 2017.10.28

General Dentistry

Associate Professor Shigeru ODA
Junior Associate Professor Masayuki HIDEISHIMA
Junior Associate Professor Ken-ichi TONAMI
Assistant Professor Sachi UMEMORI
Assistant Professor Kanako NORITAKE
Hospital Staff Shuuhei NAKAMURA
Hospital Staff Yuko MITSUMA
Hospital Staff Maiko IWAKI
Hospital Staff Yasuyuki KIMURA
Hospital Staff Shota HAYASHI
Hospital Staff Naoki ISHIHARA
Hospital Staff Kiichi MARUYAMA
Hospital Staff Shogo MAEKAWA

(1) Outline

Recent dentistry is sectionalized into various specialized fields of research and education. On the other hand, as a general practitioner, a dentist must possess not only integrated knowledge and skills of all the fields but also should be competent to apply such generalized knowledge and skills to individual patients. The department of General Dentistry performs researches and education for practicing such general and holistic dentistry. General dentistry related to clinical and affective education for dental students and residents. Therefore, the research theme includes dental education as well as oral diagnosis and general dentistry, cooperating with the department of Educational System in Dentistry, Behavioral Dentistry and Educational Media Development. Researches for sleep apnea syndrome have been also conducted in association with Dental Clinic for Sleep Disorders. The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry which missions in the Dental Hospital are initial diagnosis for new outpatients and general dental practice. Clinics of General Dentistry 1 and 2, where dental students and residents are trained, also relate to the department of General Dentistry.

(2) Research

Recent research themes are listed below.

1. Study for structure of health problems and treatment planning for dental patients.
2. Study for verification and improvement of oral diagnosis.
3. Study for dental education for dental students and residents.

(3) Education

The educational objective of General Dentistry is that the students/residents acquire transversal academic framework of dental knowledge and skills and competency to provide patients with personalized treatment.

(4) Lectures & Courses

1. Introduction to the Behavioral Science. (For the 2nd-year dental students)
2. Holistic Oral Diagnosis. (For the 5th-year dental students)
3. Comprehensive Clinical Training Phase I Phase II. (For the 5th and 6th-year dental students)
4. Clinical training (For the dental residents)

(5) Clinical Services & Other Works

The clinic of department of General Dentistry is Oral Diagnosis and General Dentistry. In the clinic, dental examination and health assessment for new outpatients are conducted to decide initial treatment plan and a clinic in charge for the patients. The patients who need comprehensive dental care and who cannot cooperate students' practice also attend this clinic to receive general dental practice.

(6) Clinical Performances

In the Dental Hospital, the clinic of Oral Diagnosis and General Dentistry is the first clinic for new outpatients. That is, the clinic is responsible for constructing good relationship between patients and the hospital. Therefore, the doctors pay attention actively to psychosocial aspects of patients during examination. In diagnosing and deciding clinic for patients, initial-treatment plans are introduced to patients. In this process, doctors think treatment plans together with patients thoroughly to obtain sound informed consent. Many patients who visits the dental hospital demands high medical level of the university hospital while not a few patients needs primary care. Oral Diagnosis and General Dentistry provides such patients with general dental practice to meet various kinds of patients' needs, makes effort to improve patients' satisfaction.

(7) Publications**[Original Articles]**

1. Uezato A, Enomoto M, Tamaoka M, Hobo M, Inukai S, Hideshima M, Miyazaki Y, Nishikawa T, Yagishita K. Shorter sleep onset latency in patients undergoing hyperbaric oxygen treatment. *Psychiatry Clin Neurosci.* 2017.01; 71(1); 73-74
2. Maekawa S, Katagiri S, Takeuchi Y, Komazaki R, Ohtsu A, Udagawa S, Izumi Y. Bone metabolic microarray analysis of ligature-induced periodontitis in streptozotocin-induced diabetic mice. *J. Periodont. Res.* 2017.04; 52(2); 233-245
3. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Meiyo Tamaoka, Yasunari Miyazaki, Kenji Fueki, Noriyuki Wakabayashi. Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial *J Prosthodont Res.* 2017.07; 61(3); 259-267
4. Maiko Iwaki, DDS, PhD. A case report of oral rehailitation using an over denture with magnetic attachments *Annals of Japan Prosthodontic Society.* 2017.07; 9(7); 255-258
5. Saito A, Horie M, Ejiri K, Aoki A, Katagiri S, Maekawa S, Suzuki S, Kong S, Yamauchi T, Yamaguchi Y, Izumi Y, Ohshima M. MicroRNA profiling in gingival crevicular fluid of periodontitis—a pilot study *FEBS Openbio.* 2017.07; 7(7); 981-994
6. Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Shunsuke Minakuchi. Fabrication of the complete denture applying CAD/CAM system. *Annals of Japan Prosthodontic Society.* 2017.07; 9(3); 236-241
7. Hiroyuki Suzuki, Manabu Kanazawa, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Noriko Amagai, Shunsuke Minakuchi. The effect of new complete denture fabrication and simplified dietary advice on nutrient intake and masticatory function of edentulous elderly: A randomized-controlled trial. *Clin Nutr.* 2017.08;

8. Ken-ichi Tonami, Sachi Umemori, Hiroshi Nitta, Kouji Araki, Shiro Mataka . Changes in Student Evaluations of a Medical Ethics Class 3 Years Later *European Journal of General Dentistry*. 2017.09; 6(3); 123-126
9. Yasuyuki Kimura, Ken-ichi Tonami, Shiro Mataka, Kouji Araki. Analysis of new outpatients' responses to a survey of their reasons for visiting a dental clinic *European Journal of General Dentistry*. 2017.10; 6(3); 111-114
10. Komazaki R, Katagiri S, Takahashi H, Maekawa S, Shiba T, Takeuchi Y, Kitajima Y, Ohtsu A, Udagawa S, Sasaki N, Watanabe K, Sato N, Miyasaka N, Eguchi Y, Anzai K, Izumi Y. Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. *Sci Rep*. 2017.10; 7(1); 13950
11. Noriko Amagai, Yuriko Komagamine, Manabu Kanazawa, Maiko Iwaki, Ayami Jo, Hiroyuki Suzuki, Shunsuke Minakuchi. The effect of prosthetic rehabilitation and simple dietary counseling on food intake and oral health related quality of life among the edentulous individuals: A randomized controlled trial. *J Dent*. 2017.10; 65; 89-94
12. Kanako NORITAKE, Jun TSURUTA, Ken-ichi TONAMI, Sachi Umemori, Shigeru ODA, Shiro MATAKI, and Kouji ARAKI. Development of Undergraduate Dental Student Interview and Diagnostic Skills during Clinical Practice of Medical Interviews *The Journal of the Stomatological Society, Japan*.. 2017.11; 84(3); 103-110
13. Koki Hobo, Kanako Noritake, Masayo Sunaga, Tomoe Miyoshi, Riden Cao, Hiroshi Nitta, Yuji Kabasawa and Atsuhiko Kinoshita. Effects of an interactive simulation material for clinical dentistry on knowledge acquisition and memory retention in dental residents *Journal of Medical and Dental Sciences*. 2017.12; 64(4); 43-52
14. Kazuki Takahashi, Jun Tsuruta, Ken-ichi Tonami, Kouji Araki. Relation between Manual Dexterity and the Accuracy of Cavity Preparation *Annals of Oral Health and Dental Research*. 2017.12; 1(1); A12-A17

[Books etc]

1. Editor Izumi Y, Author Izumi Y, Aoki A, Kobayashi H et al.. *Systemic and Periodontal Health Q&A* revised edition. Igaku Joho-sha, 2017.08 (ISBN : 978-4-903553-46-7)
2. Izumi Y, Oda S, Kikuchi S, Akizuki T et al.. *The basic techniques of periodontal surgery*. Ishiyaku Pub,Inc., 2017.12

[Misc]

1. HIDEISHIMA M. Author's Answers of Questions from Readers (DE No.196) "Oral Appliances for Sleep Apnea Syndrome" *The Journal of the Japanese Society for Dental Materials and Devices, The Journal of Dental Engineering*. 2017.09; 36(4); 260

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. The association between secondhand smoking and number of remaining teeth among older Japanese. *The 27th Annual Scientific Meeting of the Japan Epidemiological Association* 2017.01.27 Koufu
2. Ken-ichi Tonami, Shizuko Ichinose, Kazunobu Sano, Naohiko Iwasaki, Hidekazu Takahashi, Shiro Mataka, Kouji Araki. Analysis of the dentin surface after Xe excimer lamp irradiation. *The 95th General Session & Exhibition of the IADR* 2017.03.22 San Francisco
3. Tsubokawa M, Aoki A, Kakizaki S, Lin TC, Mizutani K, Ejiri K, Koshy G, Oda S, Sumi Y, Izumi Y. Detection of Subgingival Calculus Using Optical Coherence Tomography :in vitro and clinical evaluation. *The 24th Academy of Laser Dentistry Annual Conference* 2017.04.08 Arizona, USA
4. Maiko Iwaki, Manabu Kanazawa, Toshio Arakida, Tetzuya Suzuki, Shunsuke Minakuchi. Digital impression and jaw relation record for the fabrication of complete dentures. 2017.04.22
5. The clinical and educational effects of the newly-introduced interprofessional clinical practice. 2017.05.13

6. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Shunsuke Minakuchi. Effect of simple dietary advice combined with denture fabrication by dentist on nutrient intake of edentulous elderly. The 71th Annual Meeting of Japan Society of Nutrition and Food Science 2017.05.20 Okinawa
7. Maekawa S, Matsuura T, Hoshi S, Mizutani K, Izumi Y. Patient-Reported Outcomes and Clinical Evaluation of Combination Therapy of GTR with Autograft or Xenograft: Interim report of a Randomized Controlled Trial. National Symposium OSTEOLOGY JAPAN 2017.06.03 Tokyo
8. Iwaki Maiko, Kanazawa manabu, Miyayasu Anna, Sato Daisuke, Kasugai Shohei, Minakuchi Shunsuke. Prospective study of immediate Loaded two-implants mandibular overdentures: 5-years follow up. 2017.06.30 Yokohama
9. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Ayami Jo, Shunsuke Minakuchi. The effect of new complete denture fabrication and simplified dietary advice on nutrient intake and masticatory function of edentulous elderly. The 126th Annual Meeting of Japan Prosthodontic Society 2017.07.01 Yokohama
10. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Naoko SEKI, Yuki OHARA, Masayo YASUDA, Hiromi OTSUKA, Shinich ARAKAWA, Kouji ARAKI. . Development of a new IPW program for dental students and dental hygiene students in practical clinical training. Working as a dental team. The 36th General and Scientific Meeting of the Japanese Dental Education Association 2017.07.28
11. UMEMORI Sachi, Tonami K, Noritake K, Mataka S, Araki K, . The usefulness of the small test to assess the level of knowledge of dental students during clinical training. The 36th General Scientific Meeting of the Japanese Dental Education Association 2017.07.28
12. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka. Factor analysis of students' perception of inter-personal relations during "Introduction to the behavioral science" class. 31th IADR-SEA 28th SEAADE 2017.08.10 Taipei
13. SH Le, K Tonami, , S Umemori, LT Nguyen, LT Ngo, S Mataka. Effect of preoperative anxiety on healing recovery after oral surgery. 31th IADR-SEA 28th SEAADE 2017.08.10 Taipei
14. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka . Effects of the Great East Japan Earthquake on students' perception of inter-personal relations. ADEE Annual Conference 2017.08.23 Vilnius, Lithuania
15. M. Kanazawa, M. Iwaki, D. Sato, A. Miyayasu, M. Asami, R Shimada, KM Thu, VL Thuy, S. Kasugai, S. Minakuchi. Immediate Loading of two-implant mandibular overdentures: 5-year prospective study. 17th biennial meeting of the International College of Prosthodontists 2017.09.08 Santiago, Chile
16. Katagiri S, Komazaki R, Takahashi H, Maekawa S, Shiba T, Takeuchi Y, Kitajima Y, Ohtsu A, Udagawa S, Sasaki N, Watanabe K, Sato N, Miyasaka N, Eguchi Y, Anzai K, Izumi Y. *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. The 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
17. Maekawa S, Onizuka S, Katagiri S, Komazaki R, Ogura K, Takeuchi Y, Akiyama TM, Nitta H, Iwata T, Izumi Y.. Differential gene expression analysis by RNA-seq: Inflamed periodontal tissue of ligature-induced periodontitis in mice. The 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
18. Maekawa S, Onizuka S, Katagiri S, Ogura K, Ohtsu A, Komazaki R, Udagawa S, Sasaki N, Watanabe K, Takeuchi Y, Miyoshi-Akiyama T, Nitta H, Iwata T, Izumi Y. Differentially expressed genes analysis by RNA-seq : Inflamed periodontal tissue of ligature-induced periodontitis in mice. 103rd Annual meeting American Academy of Periodontology 2017.09.12 Boston, USA
19. K. Tonami, S. Umemori, K. Araki, S. Mataka. Change in students' perception of inter-personal relationship during experiential learning at welfare facilities. Japanese Association of Health Communication 2017.09.16 Kyoto
20. Hiroyuki Suzuki, Manabu Kanazawa, Noriko Amagai, Yuriko Komagamine, Maiko Iwaki, Shunsuke Minakuchi. The effect of new complete denture fabrication combined with simplified dietary advice on protein intake of edentulous elderly. The 28th general meeting of Japanese Society for Mastication Science and Health Promotion 2017.09.23 Tokyo

21. Shota Hayashi, Masayuki Hideshima, Naoki Ishihara, Tomohiro Kurashima, Shusuke Inukai, Yuuko Mitsuma, Shuhei Nakamura, Toshihide Fujie, Yasunari Miyazaki, Meiyo Tamaoka. Conversion from continuous positive airway pressure therapy to oral appliance therapy for obstructive sleep apnea in Tokyo Medical and Dental University Hospitals. 16th the Japanese Academy of Dental Sleep Medicine 2017.11.04 Yamaguchi, Japan
22. Anri Ohtsu, Yasuo Takeuchi, Shogo Maekawa, Rina Komazaki, Sayuri Udagawa, Naoki Sasaki, Yuichi Izumi. Influence of *Porphyromonas gingivalis* infection on gut microbiome in streptozotocin induced diabetic mice. JSD Diamond Anniversary Meeting in Kyoto 2017.12.16
23. Shinta Suzuki, Akira Aoki, Sayaka Katagiri, Shogo Maekawa, Kenichiro Ejiri, Sophannary Kong, Mizuki Nagata, Yoko Yamaguchi, Mitsuhiko Ohshima, Yuchi Izumi. Detection of hepatocyte growth factor in oral rinse water for possible periodontal diagnosis. Japanese Society of Periodontology Diamond Anniversary Meeting 2017.12.16 Kyoto International Conference Center, Kyoto,

[Awards & Honors]

1. Eugene Seidner Student Scholarship 2nd prize (Shigeru Oda), The 24th Academy of Laser Dentistry Annual Conference, Arizona, USA, April 6-8, 2017, 2017.04
2. Student Scholarship Second Prize (Masaki Tsubokawa), Academy of Laser Dentistry, 2017.04
3. Best Clinical Research Award, National Symposium OSTEOLOGY JAPAN (Maekawa S), National Symposium OSTEOLOGY JAPAN, 2017.06
4. Advanced Education System Development (Kanakano Noritake), Japanese Dental Education Association, 2017.07

Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
Hospital Staff	Anna Suzuki-Miura, Kaoru Kawasaki, Takeshi Watanabe
Graduate Student	Yukiko Shinohara, Anna Suzuki-Miura, Rou Mikuzuki Kaoru Kawasaki, Shiori Sugawara, TU Thi Huyen Trang Takayuki Suga, Kazuya Watanabe
Lecturer (part-time)	Haruhiko Motomura, Ayano Katagiri, Tatsuya Yoshikawa

(1) Outline

Psychosomatic dentistry is the only one department in Japan, which research and develop new diagnosis and treatment methods for MUOS such as BMS, AO, PBS etc.

(2) Research

- 1) Study on pathophysiological mechanisms of oral psychosomatic disorders
- 2) Psychosomatic study on oro-facial medically and psychiatrically unexplained symptoms
- 3) Brain imaging of oral psychosomatic disorders
- 4) Psychopharmacological study on oral psychosomatic disorders

(3) Education

It is not uncommon to see the patients diagnosed with “Oral Psychosomatic Disorders”, so there is a growing need for proper treatment of the disorders from both sides of doctors and patients. It is, therefore, extremely important for dental students to instruct in psychosomatic dentistry. However, few Dental Universities in Japan are following this. At the same time, there’s a great deal of misunderstanding about psychosomatic dentistry, in spite of we have many years of consistent education. For example, “Your work is only hearing to complaints from patients”, “Patients with not otherwise specified mental illness is eventually referred to your clinic”, or “The mission of your clinic is to calm down your patients with unidentified dental and oral complaints”.

So, regarding undergraduate medical education, we focus on not only lessons from lectures and books but also practical experience through clinical training. We have comprehensive medical teaching for fifth and sixth-year students. Students can listen to patient’s complaints directly and deepen their understanding. Actually they can see patients with dental psychosomatic disorders, and they know that these disorders are treatable. Moreover, they can learn negative effects of wrong ideas as a psychogenic disorder, and they can understand serious distress in patients and family members.

This practice is arduous effort, but in the future, it is hoped that efforts will be made to facilitate uniformed services for patients with dental psychosomatic disorders, enhance coping skills for refractory cases, and reduce

trouble with patients by the graduates of our department who mastered psychosomatic dentistry. It is important to have identity as a dentist on practice of psychosomatic dentistry. Therefore we have advanced strengthening of human resource development. In particular, we focus on cultivation of dentists who can be readily applied their knowledge of psychosomatic medicine to clinical practice. And we are working towards establishment of ‘psychosomatic dentistry’ introduced psychotherapy. Also regarding education for graduate student, we focus on clinical practice for development of dentists who have great skill in psychosomatic dentistry.

(4) Clinical Services & Other Works

We take charge of “Psychosomatic Dentistry clinic” in dental hospital of Tokyo Medical and Dental University. This special clinic is for patients with oral psychosomatic disorders, such as glossodynia (burning mouth syndrome), atypical facial pain, atypical odontalgia, oral dysesthesia, occlusal discomfort (dysesthesia).

Main psychosomatic treatment is psychopharmacological one with SSRIs (Selective Serotonin Reuptake Inhibitors), SNRI (Serotonin-Noradrenaline Reuptake Inhibitor), SDAs (Serotonin-Dopamine antagonists) etc. And supportive psychotherapies are applied.

Intractable cases are increasing year by year, we take care of every patient and have good clinical courses about 70% of them.

We believe there are exactly “oral psychosomatic disorders”, and dentists should be in charge of treatment. Psychosis, as a matter of course, should be taken care by psychiatrists, so we discriminate them from oral psychosomatic disorders, and properly refer to psychiatry.

On the other hand, on “functional somatic symptoms secondary to psychiatry disorders”, which are refer to us from psychiatrists, we do our best in cooperation with psychiatrists.

We have about 600 new outpatients per year, and almost of them were referred from other specialists not only in dentistry but also internal medicine, otorhinolaryngology, dermatology, psychosomatic medicine, and psychiatry. They come from the Metropolitan area, of course, Osaka, Kyushu, Hokkaido and so on. We take fine-grained care and follow up, total number of patients is up to 10,000 per year.

We have a mission to meet the demand of these patients and their families, so better treatment outcome and increasing efficiency are required, and cooperation with other medical specialists is needed.

(5) Clinical Performances

Psychosomatic dentistry clinic is very unique, specialized for patients with MUOS. We have treated a large number of patients with various oral psychosomatic problems. With our unrivalled clinical experiences for MUOS, we offer our best clinical setting for the treatments of every MUOS.

(6) Publications

[Original Articles]

1. Yojiro Umezaki, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Two Cases of Oral Somatic Delusions Ameliorated With Brain Perfusion Asymmetry: A Case Report. *Clin Neuropharmacol.* 2017.02;
2. Miho Takenoshita, Anna Miura, Yukiko Shinohara, Rou Mikuzuki, Shiori Sugawara, Trang Thi Huyen Tu, Kaoru Kawasaki, Takeru Kyuragi, Yojiro Umezaki and Akira Toyofuku. Clinical features of atypical odontalgia; three cases and literature reviews *BioPsychoSocial Med.* 2017.08; 11; 21
3. Lou Mikuzuki, Hiroto Saito, Ayano Katagiri, Shinji Okada, Shiori Sugawara, Asako Kubo, Kinuyo Ohara, Jun Lee, Akira Toyofuku, Koichi Iwata. Phenotypic change in trigeminal ganglion neurons associated with satellite cell activation via extracellular signal-regulated kinase phosphorylation is involved in lingual neuropathic pain. *Eur. J. Neurosci.* 2017.09; 46(6); 2190-2202
4. Trang T H Tu, Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Takayuki Suga, Takeshi Watanabe, Motoko Watanabe, Yojiro Umezaki, Tatsuya Yoshikawa, Haruhiko Motomura, Miho Takenoshita, Akira Toyofuku. Evaluating Burning Mouth Syndrome as a comorbidity of Atypical Odontalgia: the impact on pain experiences. *Pain Pract.* 2017.10;

5. Shiori Sugawara, Shinji Okada, Ayano Katagiri, Hiroto Saito, Tatsuro Suzuki, Hiroki Komiya, Kohei Kanno, Kinuyo Ohara, Toshimitsu Iinuma, Akira Toyofuku, Koichi Iwata. Interaction between calcitonin gene-related peptide-immunoreactive neurons and satellite cells via P2Y₁₂ R in the trigeminal ganglion is involved in neuropathic tongue pain in rats. *Eur. J. Oral Sci.* 2017.12; 125(6); 444-452

[Misc]

1. Hirofumi Matsuoka, Itsuo Chiba, Yuji Sakano, Akira Toyofuku, Yoshihiro Abiko. Cognitive behavioral therapy for psychosomatic problems in dental settings. *Biopsychosoc Med.* 2017.06; 11; 18

[Conference Activities & Talks]

1. Takayuki Suga, Takeshi Watanabe, Tu Trang T.H, Kaoru Kawasaki, Shiori Sugawara, Lou Mikuzuki, Yukiko Shinohara, Anna Miura, Miho Takenoshita, Akira Toyofuku. A high discrepancy of neurovascular compression on symptomatic and asymptomatic side in atypical odontalgia patients. 24th World congress on psychosomatic medicine 2017.09.14 China National Convention Center, Beijing, China
2. Miho Takenoshita, Anna Miura, Yukiko Shinohara, Rou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Trang Tu Thi Huyen, Takayuki Suga, Takeshi Watanabe, Hirofumi Matsuoka, Yoshihiro Abiko, Akira Toyofuku. 1. Clinical study on pain catastrophizing of patients with burning mouth syndrome and atypical odontalgia. 2017.09.14
3. Yukiko Shinohara, K Kawasaki, Trang Tu Thi Huyen, T Watanabe, A Toyofuku. Regional cerebral blood flow pattern in "Phantom bite syndrome" is different from that of "Delusional disorder somatic type". 24th World congress on psychosomatic medicine 2017.09.14 China National Convention Center, Beijing, China
4. THI HUYEN TRANG TU, Kawasaki K, Sugawara S, Watanabe T, Suga T, Mikuzuki L, Shinohara Y, Miura A, Takenoshita M, Toyofuku A. Atypical odontalgia with comorbid burning mouth syndrome: a 4-year retrospective study. 24th World congress on psychosomatic medicine 2017.09.15 China National Convention Center, Beijing, China
5. Kaoru Kawasaki, Trang Tu Thi Huyen, Shiori Sugawara, Akira Toyofuku. Is salivary volume reduction related to drug reactivity of burning mouth syndrome?. 24th World congress on psychosomatic medicine 2017.09.15 China National Convention Center, Beijing, China
6. Takeshi Watanabe, Takayuki Suga, TRANG T.H. TU, Kaoru Kawasaki, Shiori Sugawara, Lou Mikuzuki, Yukiko Shinohara, Anna Miura, Miho Takenoshita, Akira Toyofuku. Amitriptyline doesn't induce QTc prolongation in the treatment of oral chronic pain. 24th World congress on psychosomatic medicine 2017.09.15 China National Convention Center, Beijing, China
7. Anna Miura, Yukiko Shinohara, Lou Mikuzuki, Kaoru Kawasaki, Shiori Sugawara, Tu Thi Huyen Trang, Takayuki Suga, Takeshi Watanabe, Miho Takenoshita, Akira Toyofuku. Psychiatric Comorbidities in Atypical Odontalgia.. 24th World congress on psychosomatic medicine 2017.09.15 China National Convention Center, Beijing, China

Behavioral Dentistry

Professor	Shiro Mataki
Associate Professor	Hiroshi Nitta
Research Associate	Sachi Umemori
Graduate Student	Ayako Kubota
Graduate Student	Le Son Hoang (Vietnam)

(1) Research

- 1) Construction of educational system of behavioral dentistry for dental students
- 2) Application of behavioral science to development of dental educational curriculum
- 3) Patients' evaluation of the dental hospital and the dental educational system
- 4) Application of behavioral science to dental clinic

(2) Lectures & Courses

Topic of Behavioral Dentistry included characteristics of human behavior, especially of relationship between patients and dental staff based on the informed consent. Main objective of behavioral dentistry in the graduate course is to provide students opportunity to study application of behavioral science to deal with dental patients showing various perception and behavior in clinic.

(3) Clinical Services & Other Works

Behavioral Dentistry provides medical interview for preliminary diagnosis and general dental practice at the clinic of oral diagnosis and general dentist cooperating with General Dentistry.

(4) Publications

[Original Articles]

1. Ken-ichi Tonami, Sachi Umemori, Hiroshi Nitta, Kouji Araki, Shiro Mataki . Changes in Student Evaluations of a Medical Ethics Class 3 Years Later *European Journal of General Dentistry*. 2017.09; 6(3); 123-126
2. Nitta H, Katagiri S, Nagasawa T, Izumi Y, Ishikawa I, Izumiyama H et al.. The number of microvascular complications is associated with an increased risk for severity of periodontitis in type 2 diabetes patients: Results of a multicenter hospital-based cross-sectional study. *J Diabetes Investig*. 2017.09;
3. Yasuyuki Kimura, Ken-ichi Tonami, Shiro Mataki, Kouji Araki. Analysis of new outpatients' responses to a survey of their reasons for visiting a dental clinic *European Journal of General Dentistry*. 2017.10; 6(3); 111-114
4. Yuki Ohara, Naomi Yoshida, Hisashi Kawai, Shuichi Obuchi, Hideyo Yoshida, Shiro Mataki, Hirohiko Hirano, Yutaka Watanabe. Development of an oral health-related self-efficacy scale for use with older adults. *Geriatr Gerontol Int*. 2017.10; 17(10); 1406-1411

5. Ayako Kubota, Meiko Oki, Yasuko Kawakami, Kiyoko Kanamori, Hiroji Shimomura, Shiro Mataka, Kumiko Sugimoto. Effectiveness of Individual Oral Health Education for Japanese University Students International Journal of Dentistry and Oral Health. 2017.10; 3(5);
6. Kanako NORITAKE, Jun TSURUTA, Ken-ichi TONAMI, Sachi Umemori, Shigeru ODA, Shiro MATAKI, and Kouji ARAKI. Development of Undergraduate Dental Student Interview and Diagnostic Skills during Clinical Practice of Medical Interviews The Journal of the Stomatological Society, Japan.. 2017.11; 84(3); 103-110

[Conference Activities & Talks]

1. UMEMORI Sachi, Aida J, Tonami K, Tabuchi T, Araki K, Mataka S, Kondo K. The association between secondhand smoking and number of remaining teeth among older Japanese. The 27th Annual Scientific Meeting of the Japan Epidemiological Association 2017.01.27 Koufu
2. UMEMORI Sachi, Tonami K, Noritake K, Mataka S, Araki K, . The usefulness of the small test to assess the level of knowledge of dental students during clinical training. The 36th General Scientific Meeting of the Japanese Dental Education Association 2017.07.28
3. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka. Factor analysis of students' perception of inter-personal relations during "Introduction to the behavioral science" class. 31th IADR-SEA 28th SEAADE 2017.08.10 Taipei
4. SH Le, K Tonami, , S Umemori, LT Nguyen, LT Ngo, S Mataka. Effect of preoperative anxiety on healing recovery after oral surgery. 31th IADR-SEA 28th SEAADE 2017.08.10 Taipei
5. Ken-ichi Tonami, Sachi Umemori, Son Hoang Le, Kouji Araki, Hiroshi Nitta, Shiro Mataka . Effects of the Great East Japan Earthquake on students' perception of inter-personal relations. ADEE Annual Conference 2017.08.23 Vilnius, Lithuania
6. Maekawa S, Onizuka S, Katagiri S, Komazaki R, Ogura K, Takeuchi Y, Akiyama TM, Nitta H, Iwata T, Izumi Y.. Differential gene expression analysis by RNA-seq: Inflamed periodontal tissue of ligature-induced periodontitis in mice.. The 103rd Annual Meeting of American Academy of Periodontology 2017.09.10 Boston, USA
7. K. Tonami, S. Umemori, K. Araki, S. Mataka. Change in students' perception of inter-personal relationship during experiential learning at welfare facilities. Japanese Association of Health Communication 2017.09.16 Kyoto

Professional Development in Health Sciences

Professor Kazuki Takada
Associate Professor Jun Tsuruta
Associate Professor Mina Nakagawa
Junior Associate Professor Kumiko Yamaguchi

(1) Outline

Worldwide, accelerated aging and the shift in disease burdens have created a demand for innovations in health sciences, healthcare, and the healthcare delivery system. Innovation requires not only a vast amount of knowledge and superior skills, but also critical and creative thinking skills. Innovation concerning new drugs and medical devices further requires understanding of the entire flow and process of research and development. In our department, we provides educational opportunities for learners to acquire high-level and practical knowledge of the followings: history of medical and dental education in Japan, professional education/development/certification in Japan and North American/European countries, key pedagogical theories and learning methods, process-based approach and logic models in curriculum development, and competencies and their assessment/evaluation.

(2) Research

- Needs assessment in health care and in professional development in health science fields · Curriculum development for professionals of the future needs in health sciences
- Interprofessional education curriculum development

(3) Clinical Services & Other Works

Medical Hospital
Kazuki TAKADA : Rheumatology
Mina NAKAGAWA : Gastroenterology and Hepatology

Dental Hospital
Jun TSURUTA : Oral Diagnosis and General Dentistry

(4) Publications

[Original Articles]

1. Keiko Okumura, Kumiko Yamaguchi, Tatsuya Tamaki, Kazuhiro Oinuma, Hikaru Tomoe, Keiichi Akita. Prospective analyses of female urinary incontinence symptoms following total hip arthroplasty. *Int Urogynecol J.* 2017.04; 28(4); 561-568
2. Kentaro Matsuura, Hiromi Sawai, Kazuho Ikeo, Shintaro Ogawa, Etsuko Iio, Masanori Isogawa, Noritomo Shimada, Atsumasa Komori, Hidenori Toyoda, Takashi Kumada, Tadashi Namisaki, Hitoshi Yoshiji, Naoya Sakamoto, Mina Nakagawa, Yasuhiro Asahina, Masayuki Kurosaki, Namiki Izumi, Nobuyuki Enomoto, Atsunori Kusakabe, Eiji Kajiwara, Yoshito Itoh, Tatsuya Ide, Akihiro Tamori, Misako Matsubara, Norifumi Kawada, Ken Shirabe, Eiichi Tomita, Masao Honda, Shuichi Kaneko, Sohji Nishina, Atsushi

- Suetsugu, Yoichi Hiasa, Hisayoshi Watanabe, Takuya Genda, Isao Sakaida, Shuhei Nishiguchi, Koichi Takaguchi, Eiji Tanaka, Junichi Sugihara, Mitsuo Shimada, Yasuteru Kondo, Yosuke Kawai, Kaname Kojima, Masao Nagasaki, Katsushi Tokunaga, Yasuhito Tanaka, . Genome-Wide Association Study Identifies TLL1 Variant Associated With Development of Hepatocellular Carcinoma After Eradication of Hepatitis C Virus Infection. *Gastroenterology*. 2017.05; 152(6); 1383-1394
3. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. *J. Med. Virol.* 2017.07; 89(7); 1241-1247
 4. Miyako Murakawa, Yasuhiro Asahina, Hiroko Nagata, Mina Nakagawa, Sei Kakinuma, Sayuri Nitta, Fukiko Kawai-Kitahata, Satoshi Otani, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Ayako Sato, Yasuhiro Itsui, Seishin Azuma, Toshihiko Nouchi, Yohei Furumoto, Tooru Asano, Yoshimichi Chuganji, Shuji Tohda, Mamoru Watanabe. ITPA gene variation and ribavirin-induced anemia in patients with genotype 2 chronic hepatitis C treated with sofosbuvir plus ribavirin. *Hepatol. Res.* 2017.07; 29(5); 584-593
 5. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatol. Res.* 2017.08; 47(9); 941-952
 6. Goto Fumio, Kakinuma Sei, Miyoshi Masato, Tsunoda Tomoyuki, Kaneko Shun, Sato Ayako, Asano Yu, Otani Satoshi, Azuma Seishin, Nagata Hiroko, Kawai-Kitahata Fukiko, Murakawa Miyako, Nitta Sayuri, Itsui Yasuhiro, Nakagawa Mina, Asahina Yasuhiro, Watanabe Mamoru. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells *Hepatology Research*. 2017.08; 47(9); 941-952
 7. Yasuo Nakajima, Satoru Muro, Hisayo Nasu, Masayo Harada, Kumiko Yamaguchi, Keiichi Akita. Morphology of the region anterior to the anal canal in males: visualization of the anterior bundle of the longitudinal muscle by transanal ultrasonography. *Surg Radiol Anat.* 2017.09; 39(9); 967-973
 8. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina. Reply to: "Imaging Basis of AFP and WFA+M2BP as Indicators of the risk of HCC after SVR". *J. Hepatol.* 2017.10;
 9. Murakawa Miyako, Asahina Yasuhiro, Nagata Hiroko, Nakagawa Mina, Kakinuma Sei, Nitta Sayuri, Kawai-Kitahata Fukiko, Otani Satoshi, Kaneko Shun, Miyoshi Masato, Tsunoda Tomoyuki, Asano Yu, Sato Ayako, Itsui Yasuhiro, Azuma Seishin, Nouchi Toshihiko, Furumoto Yohei, Asano Tooru, Chuganji Yoshimichi, Tohda Shuji, Watanabe Mamoru. ITPA gene variation and ribavirin-induced anemia in patients with genotype 2 chronic hepatitis C treated with sofosbuvir plus ribavirin. *Hepatology Research*. 2017.10; 47(11); 1212-1218
 10. Kaneko Shun, Kakinuma Sei, Asahina Yasuhiro, Kamiya Akihito, Miyoshi Masato, Tsunoda Tomoyuki, Inoue-Shinomiya Emi, Nitta Sayuri, Sato Ayako, Asano Yu, Nagata Hiroko, Kawai-Kitahata Fukiko, Murakawa Miyako, Itsui Yasuhiro, Nakagawa Mina, Azuma Seishin, Watanabe Mamoru. A novel culture model for coinfection of hepatitis B and hepatitis C viruses using human induced pluripotent stem cell-derived hepatic cells for analyses of changes in host-innate immune responses *HEPATOLOGY*. 2017.10; 66; 69A
 11. Nitta Sayuri, Murakawa Miyako, Kato Takanobu, Sato Ayako, Tsunoda Tomoyuki, Miyoshi Masato, Asano Yu, Kaneko Shun, Nagata Hiroko, Kawai-Kitahata Fukiko, Itsui Yasuhiro, Nakagawa Mina, Azuma Seishin, Kakinuma Sei, Asahina Yasuhiro. The analysis of NS5A Resistance-Associated Substitutions (RAS): In vitro study of NS5A recombinant hepatitis C in infectious cell culture system for various RAS detected after treatment failure in chronic hepatitis C patients *HEPATOLOGY*. 2017.10; 66; 480A
 12. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina, Ayako Sato, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro

Itsui, Seishin Azuma, Sei Kakinuma, Toshihiko Nouchi, Hideki Sakai, Makoto Tomita, Mamoru Watanabe. Effect of interferon-based and -free therapy on early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C. *J. Hepatol.* 2017.11; 67(5); 933-939

13. Shinya Maekawa, Mitsuaki Sato, Natsuhiko Kuratomi, Taisuke Inoue, Yuichiro Suzuki, Akihisa Tatsumi, Mika Miura, Shuya Matsuda, Masaru Muraoka, Natsuko Nakakuki, Fumitake Amemiya, Shinichi Takano, Mitsuharu Fukasawa, Yasuhiro Nakayama, Tatsuya Yamaguchi, Tadashi Sato, Minoru Sakamoto, Miyako Murakawa, Mina Nakagawa, Yasuhiro Asahina, Nobuyuki Enomoto. Association between alanine aminotransferase elevation and UGT1A1*6 polymorphisms in daclatasvir and asunaprevir combination therapy for chronic hepatitis C. *J. Gastroenterol.* 2017.11;

[Conference Activities & Talks]

1. Jun Tsuruta, Kumiko Yamaguchi, Ayako Ichikawa, Yoko Yoshihashi, Mina Nakagawa, Kazuki Takada, . Behavior changes of dental students after final-year IP program . ADEA/ADEE Joint meeting, London 2017.05.08
2. Satoru Muro, Yasuo Nakajima, Hisayo Nasu, Kumiko Yamaguchi, Keiichi Akita.. Anterior Region of the Anal Canal: Transanal Ultrasonography and Histological Study.. 34th Annual Meeting - American Association of Clinical Anatomists 2017.07.21 Minneapolis, USA
3. Mina Nakagawa, Kumiko Yamaguchi, Janelle Moross, Ayako Ichikawa, Yoko Yoshihashi, Chiharu Kawakami, Jun Tsuruta, Kazuki Takada, Yujiro Tanaka and Junji Tagami. Introduction of interprofessional education (IPE) for medical and dental students. AMEE 2017 2017.08.29 Helsinki
4. Kumiko Yamaguchi, Mina Nakagawa, Chiharu Kawakami, Yoko Yoshihashi, Ayako Ichikawa, Kazuki Takada. Improvement of the patient-centered medicine portion of IPE program by adding patients' lectures . ANNUAL CONFERENCE 2017, AN INTERNATIONAL ASSOCIATION FOR MEDICAL EDUCATION 2017.08.30
5. Mina Nakagawa, Kumiko Yamaguchi, Janelle Moross, Kazuki Takada, Yujiro Tanaka, Junji Tagami. Introduction of interprofessional education (IPE) for medical and dental students. ANNUAL CONFERENCE 2017, AN INTERNATIONAL ASSOCIATION FOR MEDICAL EDUCATION 2017.08.30
6. Murakawa M, Asahina Y, Nakagawa M, Nitta S, Kawai-Kitahata F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Sato A, Itsui Y, Kakinuma S, Azuma S, Watanabe M. On-treatment higher levels of alpha-fetoprotein and M2BPGi are associated with development of hepatocellular carcinoma during nucleos(t)ide analog therapy in patients with HBV chronic infection. AASLD, The Liver Meeting 2017 2017.10.21 Washington DC (USA)
7. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Nitta S, Sato A, Asano Y, Nagata H, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A novel culture model for coinfection of hepatitis B and hepatitis C viruses using human induced pluripotent stem cell-derived hepatic cells for analyses of changes in host-innate immune responses . AASLD The Liver Meeting 2017 2017.10.22 Washington DC
8. Nakagawa M, Asahina Y, Nagata H, Kaneko S, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tanaka Y, Watanabe M. Evaluation of an early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C patients treated with All-Oral DAAs - propensity score-matched analysis of a prospective database -. AASLD, The Liver Meeting 2017 2017.10.22 Washington D.C (USA)

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio

Assistant Professor: KAWAGISHI Masahiko

Assistant Professor: SAITO Kenta

Assistant Professor: SATO Keisuke

Lab Manager, Administrative Assistant: TAGUCHI Mie

(1) Research

Our lab has focused in two major directions:

(1) How are cytoplasmic proteins transported in cells, and what other intracellular elements are necessary for their quality control during transport? How are the dynamics of cytoskeletal proteins in neurons regulated and coordinated?

Neuronal cells such as neurons and glial cells are atypical and asymmetric in their morphology; both of them having long processes. They have to endure the burden of energy-consuming long-distance intracellular transport, and develop specialized cytoskeletal structures. Both intracellular transport and cytoskeletal dynamics are inseparably interrelated, and essential for the cellular homeostasis and function. One of the main interests of our laboratory is to understand how their dynamics are regulated and how these dynamics define neuronal morphologies and functions.

(2) How do inhalation anesthetics exert their effects on synaptic transmissions?

Our interests are in deciphering the long-lasting mystery of inhalation anesthetic effects on synaptic transmissions, major mechanism in mammals that insures secure and painless surgical operations. We use electrophysiological preparations as well as newly developed spectroscopic techniques to identify their principles.

(2) Education

Department of neuroanatomy and cellular neurobiology takes charge of basic neuroscience education for medical undergraduate student (Lectures and Wet labs), especially from the morphological point of view.

For graduate school students, our group offers introductory courses on both optical and electron microscopy (Lectures and Wet labs), with close relation to molecular and cellular neurobiology.

(3) Publications

[Conference Activities & Talks]

1. Masahiko KAWAGISHI, Yuki OBARA, Takayuki SUZUKI, Masumi HAYASHI, Kazuhiko MISAWA, Sumio TERADA. Direct label-free measurement of the distribution of small molecular weight compound using coherent Raman microspectroscopy. The 122nd Annual Meeting of the Japanese Association of Anatomists 2017.03.29 Nagasaki, Nagasaki, JAPAN

Systems Neurophysiology

Professor Izumi Sugihara
Associate Professor Yuriko Sugiuchi
Lecturer Yoshiko Izawa
Assistant Professor Mayu Takahashi
JSPS Postdoctoral Research Fellow Hermina Nedeltescu
Students (dorc) 6
Part-time lecturer Hirofumi Fujita

(1) Outline

Department of Systems Neurophysiology, formerly Department of Physiology #1 of the medical school, is one of the basic medicine departments and take charge of research and education in the field of neurophysiology and related neurosciences.

(2) Research

Our main interest lies in clarifying the structures that underlies function of the central nervous system and then understanding their function. We are focused on the part of the central nervous system that is involved in control of eye movements. The eye movement control system is located in the cerebrum, brainstem and cerebellum, has been studied in great detail and is important clinically. The cerebellum itself is another site of focus. Dysfunction of the cerebellum causes ataxia, a movement disorder associated with impaired control of movement. We use electrophysiological, morphological and cell-biological approaches.

1) Cerebellar function

Distinct regions in the cerebellum make specific connections with different areas of the brain and are involved in the control of various movements including eye movements. For example, the neuronal circuitry that connects the lateral cerebrum, pontine nuclei, cerebellar cortex (hemisphere), cerebellar nucleus (dentate nucl.), thalamus and cerebrum is important for initiation, execution and control of movements. To understand cerebellar function, it is important to understand the organization of the cerebellum into distinct anatomical regions, to characterize the specific neuronal circuitry of these regions, and to identify how the cerebellum is organized into regions and functions by way of the input and output systems. Our systematic approach to this question includes (developmental) anatomy, molecular biology, and electrophysiology. We have expertise in neuronal labeling with marker molecules and tracers, single-axonal reconstruction, three-dimensional mapping of neuronal projection patterns.

(3) Education

We participate in Introductory Neurophysiology, Neuroscience and Physiology Lab courses for medical students (2nd year) as well as in courses for graduate students. We mainly teach the neurophysiology sections in these courses. Our goal is for students to understand normal function of nerve cells and the nervous system and,

on this ground, to understand pathological states of the nervous system in disease. For this purpose, we give clinically-oriented lectures and laboratory courses linked with morphology and pharmacology.

(4) Lectures & Courses

Our lectures cover transport and electric potential of the cell membrane, excitation and synaptic transmission (Introductory Neurophysiology), sensory systems, motor systems, autonomic nervous systems, and higher brain function (Neuroscience), i.e. neurophysiology in general from the molecular, cellular through the organismic levels. To promote students' self-learning attitude, we sometimes employ an "active-learning" style. In the laboratory course, we promote student-teacher discussion in small groups. We have had three "elective research course" students.

(5) Publications

[Original Articles]

1. Luo Y, Fujita H, Nedelescu H, Biswas MS, Sato C, Ying S, Takahashi M, Akita K, Higashi T, Aoki I, Sugihara I. Lobular homology in cerebellar hemispheres of humans, non-human primates and rodents: a structural, axonal tracing and molecular expression analysis. *Brain Structure and Function*. 2017.05; 222(6); 2449-2472
2. Vibulyaseck S, Fujita H, Luo Y, Tran AK, Oh-Nishi A, Ono Y, Hirano S, Sugihara I. Spatial rearrangement of Purkinje cell subsets forms the transverse and longitudinal compartmentalization in the mouse embryonic cerebellum. *Journal of Comparative Neurology*. 2017.05; 525(14); 2971-2990
3. Tang T, Xiao J, Suh CY, Burroughs A, Cerminara NL, Jia L, Marshall SP, Wise AK, Apps R, Sugihara I, Lang EJ. Heterogeneity of Purkinje cell simple spike - complex spike interactions: zebrin- and non-zebrin-related variations. *Journal of Physiology*. 2017.08; 595(15); 5341-5357
4. Luo Y, Patel RP, Sarpong GA, Sasamura K, Sugihara I. Single axonal morphology and termination to cerebellar aldolase C stripes characterize distinct spinocerebellar projection systems originating from the thoracic spinal cord in the mouse. *Journal of Comparative Neurology*. 2017.11; 526(4); 681-706

[Misc]

1. Lang EJ, Apps R, Bengtsson F, Cerminara NL, De Zeeuw CI, Ebner TJ, Heck DH, Jaeger D, Jörntell H, Kawato M, Otis TS, Ozyildirim O, Popa LS, Reeves AM, Schweighofer N, Sugihara I, Xiao J. . The roles of the olivocerebellar pathway in motor learning and motor control. *Cerebellum*. 2017.02; 16(1); 230-252
2. Luo Y, Fujita H, Nedelescu H, Biswas MS, Sato C, Ying S, Takahashi M, Akita K, Higashi T, Aoki I, Sugihara I. Lobular homology in cerebellar hemispheres of humans, non-human primates and rodents: a structural, axon tracing and molecular expression analysis. *Brain Structure and Function*. 2017.05; (222); 2449-2472

[Conference Activities & Talks]

1. Vibulyaseck S, Fujita H, Luo Y, Ono Y, Hirano S, Sugihara I.. Differentiation and migration of Purkinje cell subsets in the cerebellar primordium. 9th CBIR/ONSA Symposium for Inspiring Young Scientists 2017.02.11 Tokyo
2. Izumi Sugihara. The ansiform lobule (crus I in the rodent cerebellum) is unique in its conformation, axonal connection, striped pattern, evolution and development in the mammalian cerebellum. The 8th International Symposium of the Society for Research on the Cerebellum and Ataxias (SRCA): from Development to Disease 2017.05.25 Winnipeg, Manitoba, Canada
3. Mayu Takahashi. Functional roles of commissural connections between the superior colliculi. Seminars on neural basis of motor control (Satellite symposium in honor of David Robinson) 2017.05.25
4. Mayu Takahashi, Yoshikazu Shinoda. Roles of commissural connections between the bilateral superior colliculi on eye and head movements. Gordon Research Conference on "Eye Movements" 2017.07.10

5. Sugihara I, Luo Y.. Historical inconsistency in definitions of cerebellar hemispheric lobules (crus I and crus II of the ansiform lobule) of non-human primates.. Neuroscience 2017, November 11-16 in Washington DC. 2017.11.11 Washington DC
6. Sugihara I, Luo Y.. Single axon morphology of the spinocerebellar projection in the mouse. 2017, November 11-16 in Washington DC. 2017.11.12 Washington DC

Pharmacology and Neurobiology

Professor: Tsutomu TANABE
 Assistant professor: Hironao SAEGUSA
 Assistant professor: Makoto FUJIKAWA
 Assistant professor: Daisuke TANAKA

(1) Outline

Many intriguing mysteries left in the issue of brain function like (1) learning and memory, (2) cognition and behavior, (3) generation of consciousness, (4) personality and mentality. On the other hand, in the modern-day world with a complicated human relations and prolonged life span, necessity of deeper understanding and development of the means to cure the numerous neurological disorders and pain is enormously increased.

(2) Research

1. Regulation of Microglial function in Neuroinflammation/Neurodegenerative diseases
2. Regulation of Macrophage function in Inflammatory bowel disease and Rheumatoid arthritis
3. Energy metabolic imaging at single cell level of cancer stem cell/cancer cell using Bioluminescence and FRET and Imaging
4. Energy metabolic imaging at single cell level of neuron, microglia and astrocyte in the degenerative area of the mouse model of various neurodegenerative diseases
5. Neural mechanisms of pleasure and motivation in feeding
6. Molecular basis of Calcium channelopathy
7. Alteration of Neuron-Glia interaction in Neurological disorders

(3) Education

Undergraduate course: Pharmacology course provides the principle of pharmacological basis of therapeutics. Several representative therapeutic drugs in each disease will be picked up and systematic lectures -from basic pharmacology to mechanism of action, drug metabolism, clinical application and side effects- will be provided. Students are projected to acquire self-learning skills during the course and expected to be ready for handling clinical cases by pharmacological means.

We consider education through the pharmacology lab work is important. Students are given opportunity to dissect out several tissues (heart, skeletal muscle, ileum and vas deferens) from living animals by themselves and test the effect of a number of drugs including specific agonist, antagonist and non-selective drugs. Lab work course is divided into two parts. In the first part, students were given several known drugs for testing the known effect on these tissues. In the second part, students are given two unknown drugs and requested to identify the name and concentration of each drug using the tissues they prepare by themselves.

Graduate course: During the first couple of months, students are requested to acquire basic techniques of biochemistry, molecular biology, pharmacology and electrophysiology that are routinely used in our laboratory. Then students will be given a small project to do using the techniques they have learned during the initial

training. Students are also required to read relevant scientific papers and conduct seminar style lectures to other lab members monthly. After completion of the initial phase, students start their own project under the supervision of the faculties in the lab.

(4) Publications

[Conference Activities & Talks]

1. Daisuke H. Tanaka, Shusheng Li, Tsutomu Tanabe. Expression of gustatory "disgust" reactions recruit specific amygdaloid nuclei in mice. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.21 Chiba, Japan

Molecular Neuroscience

Professor Kohichi Tanaka
 Associate Professor Tomomi Aida
 Assistant Professor Saeko Ishida
 Assistant Professor Yuichi Hiraoka (2015/5/1)

Graduate Student (doctor course)
 Zhao Zhuoyang
 Kaori Sugiyama
 Takehisa Handa

Graduate Student (master course)
 Mina Kusunose
 Moeko Tanaka
 Haruka Takigawa
 Hiroshi Ogawa

Technical Staff
 Harumi Ishikubo

Secretary
 Satomi Ohno

(1) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

(2) Research

1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice. Clinical phenotypes of spinocerebellar ataxia type-5 (SCA5) and spectrin-associated autosomal recessive cerebellar ataxia type-1 (SPARCA1) are mirrored in mice lacking β -III spectrin (β -III^{-/-}). One function of β -III spectrin is the stabilization of the Purkinje cell-specific glutamate transporter EAAT4 at the plasma membrane. In β -III^{-/-} mice EAAT4 levels are reduced from an early age. In contrast levels of the glutamate transporter GLAST, expressed in Bergmann glia, only fall progressively from 3 months onwards. Here we elucidated the roles of these two glutamate transporters in cerebellar pathogenesis mediated through loss of β -III spectrin function by studying EAAT4 and GLAST knockout mice as well as crosses of both with β -III^{-/-} mice. Our

data demonstrate that EAAT4 loss, but not abnormal AMPA receptor composition, in young β -III^{-/-} mice underlies early Purkinje cell hyper-excitability and that subsequent loss of GLAST, superimposed on the earlier deficiency of EAAT4, is responsible for Purkinje cell loss and progression of motor deficits. Yet the loss of GLAST appears to be independent of EAAT4 loss, highlighting that other aspects of Purkinje cell dysfunction underpin the pathogenic loss of GLAST. Finally, our results demonstrate that Purkinje cells in the posterior cerebellum of β -III^{-/-} mice are most susceptible to the combined loss of EAAT4 and GLAST, with degeneration of proximal dendrites, the site of climbing fibre innervation, most pronounced. This highlights the necessity for efficient glutamate clearance from these regions and identifies dysregulation of glutamatergic neurotransmission particularly within the posterior cerebellum as a key mechanism in SCA5 and SPARCA1 pathogenesis.

We investigated the cytoprotective effect of geranylgeranylacetone (GGA) on RGCs degeneration using a normal tension glaucoma (NTG) mouse model, which lacks GLAST. Three-week-old GLAST^{+/-} mice were given oral administration of GGA at 100, 300, or 600 mg/kg/day or vehicle alone, and littermate control mice were given vehicle alone for 14 days, respectively. The number of RGCs of GLAST^{+/-} mice significantly decreased, as compared to that of control mice. RGC loss was significantly suppressed by administration of GGA at 600 mg/kg/day, compared with vehicle alone. Following GGA administration, HSP70 was significantly upregulated together with reduction in the activities of caspase-9 and -3. Our studies highlight HSP70 induction in the retina is available to suppress RGC degeneration, and thus GGA may be applicable for NTG as a promising therapy.

2. Development of genome editing technologies

Although CRISPR/Cas enables one-step gene cassette knock-in, assembling targeting vectors containing long homology arms is a laborious process for high-throughput knock-in. We recently developed the CRISPR/Cas-based precise integration into the target chromosome (PITCh) system for a gene cassette knock-in without long homology arms mediated by microhomology-mediated end-joining.

Here, we identified exonuclease 1 (Exo1) as an enhancer for PITCh in human cells. By combining the Exo1 and PITCh-directed donor vectors, we achieved convenient one-step knock-in of gene cassettes and floxed allele both in human cells and mouse zygotes. Our results provide a technical platform for high-throughput knock-in.

(3) Education

Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

(4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate the pathology of these diseases, leading to unveil the mechanism of cognition.

(5) Publications**[Original Articles]**

1. Tomoharu Nakamori, Tomomi Kato, Hiroyuki Sakagami, Kohichi Tanaka, Hiroko Ohki-Hamazaki. Regulation of visual Wulst cell responsiveness by imprinting causes stimulus-specific activation of rostral cells. *Sci Rep.* 2017.02; 7; 42927
2. Ken-Ichiro Kubo, Kimiko Deguchi, Taku Nagai, Yukiko Ito, Keitaro Yoshida, Toshihiro Endo, Seico Benner, Wei Shan, Ayako Kitazawa, Michihiko Aramaki, Kazuhiro Ishii, Minkyung Shin, Yuki Matsunaga, Kanehiro Hayashi, Masaki Takeyama, Chiharu Tohyama, Kenji F Tanaka, Kohichi Tanaka, Sachio Takashima, Masahiro Nakayama, Masayuki Itoh, Yukio Hirata, Barbara Antalffy, Dawna D Armstrong, Kiyofumi Yamada, Ken Inoue, Kazunori Nakajima. Association of impaired neuronal migration with cognitive deficits in extremely preterm infants. *JCI Insight.* 2017.05; 2(10);
3. Taisuke Miyazaki, Miwako Yamasaki, Kouichi Hashimoto, Kazuhisa Kohda, Michisuke Yuzaki, Keiko Shimamoto, Kohichi Tanaka, Masanobu Kano, Masahiko Watanabe. Glutamate transporter GLAST controls synaptic wrapping by Bergmann glia and ensures proper wiring of Purkinje cells. *Proc. Natl. Acad. Sci. U.S.A.* 2017.07; 114(28); 7438-7443
4. Kaori Sugiyama, Tomomi Aida, Masatoshi Nomura, Ryoichi Takayanagi, Hanns U Zeilhofer, Kohichi Tanaka. Calpain-Dependent Degradation of Nucleoporins Contributes to Motor Neuron Death in a Mouse Model of Chronic Excitotoxicity. *J. Neurosci.* 2017.09; 37(36); 8830-8844

[Misc]

1. Saeko ISHIDA. DEPDC5, causative gene of focal epilepsy ___ Understanding the pathogenesis using Depdc5 KO rats 2017.12; (39); 43

[Conference Activities & Talks]

1. Uchida Mizuki, Hida Hirotake, Mori Kentaro, Kitagaki Shinji, Ozaki Norio, Tanaka Kohichi, Yoshimi Akira, Noda Yukihiro. Functional roles of glial glutamate transporter in psychobehavioral abnormalities of mice administered phencyclidine repeatedly. *Journal of Pharmacological Sciences* 2017.03.01
2. Saeko ISHIDA. Focal epilepsy gene, DEPDC5. *The Japanese Pharmacological Society* 2017.03.17

Neuropathology

Professor: Hitoshi Okazawa

Practical professor: Kazuhiko Tagawa

Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone, Toshiki Uchihara

Assistant professor: Kyota Fujita

Project Assistant professor: Xigui Chen, Hidenori Homma, Emiko Yamanishi

Graduate Student : Kanoh Kondo, Hikari Tanaka, Maiko Inotsume, Yuki Yoshioka

(1) Outline

The goals of our research are to elucidate molecular mechanisms of neurodegenerative disorders as well as of mental retardation, and to develop novel therapeutics for those intractable diseases. In neurodegeneration, we are now focusing on polyglutamine diseases including hereditary spinocerebellar degenerations and Huntington's disease. Knowledge from transcriptome and proteome analyses of the pathologies will lead to new types of molecular therapeutics. In reference to mental retardation, we are developing animal models and analyzing molecular pathologies of our original molecule PQBP1 whose mutations cause mental retardation with microcephaly. This line of research is also for developing new therapeutics of the common but intractable diseases.

(2) Research

Research Contents

Following studies have been intensively carried out in our laboratory.

- 1) Investigation of molecular pathologies of neurodegenerative diseases.
- 2) Studies on impairment of DNA-repair in polyglutamine diseases.
- 3) Development of new seed drugs for neurodegeneration.
- 4) Development of new seed drug for mental retardation.
- 5) Investigation of molecular functions of Oct-3/4

Below is the brief report of this year's progress.

1. Preclinical pathology during development affects the post-onset adulthood symptoms in spinocerebellar ataxia type 1 (Fujita K, et al, Nat Commun. 2017)

Spinocerebellar ataxia type1 (SCA1) is one of the major models of neurodegenerative disease. At the same as other neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS), disease modifying therapy for SCA1 has not developed. Although a lot of knowledge for pathology caused by mutation has also been accumulated, it has not been clear neither when it occurs, what it is, nor how to treat it. For instance, in context of therapeutic strategies of AD, there were many clinical investigations to remove amyloid-beta, however, clinical symptoms did not improve or stop the progression despite elimination of amyloid-beta. This fact tells us that it is quite important to uncover that when irreversible pathology of neurodegenerative diseases occurs and what the pathology is.

In our previous study, we studied about the effect of stage-specific expression of YAPdeltaC to symptoms of SCA1 model mice (Ataxin-1 knock-in mice) and their survival time using our newly developed Tet-ON YAPdeltaC system in Atxn1-KI mice. As a result, expression of YAPdeltaC from embryo stage to 8 weeks after

birth made significant improvement of symptoms and survival duration, however, almost no effect found with expression of YAPdeltaC after 8 weeks.

Moreover, we revealed that YAPdeltaC works collaboratively with normal Ataxin1 as transcriptional coactivator enhancing RORalpha, that plays a role of regulation of gene expression in cerebellar neurons at developmental stage. Because mutant Ataxin1 deprives YAPdeltaC from RORalpha, it inhibits expressions of genes necessary for maturation of cerebellar neurons. We also found that forcible expression of YAPdeltaC increases its binding of RORalpha and that makes a recovery of gene expressions required to mature cerebellar neurons.

Clinical studies to examine candidate drugs by starting the clinical trial before onset are now undergoing in USA, and are also planned in Japan. Our study showed that recovery of gene expressions required for maturation of cerebellar neurons in developmental stage improves clinical symptoms of SCA1 model mice in adulthood. Because genetic diagnosis can be available for SCA1 patients, it could be possible to develop prophylactic or disease modifying therapy in the future by increasing amount of YAPdeltaC at preclinical stage. This study presented a great example that preclinical therapy was needed for neurodegenerative diseases commonly, not only for AD. At the same time, it has great significance that revealed its therapeutic target molecule.

2. Insights into familial middle-age dementia suggest new avenues for treatment (Fujita K, et al, Nat Commun. 2018)

Frontotemporal lobar degeneration (FTLD) is one of the most common causes of early-onset dementia, and can lead to personality changes, impaired speaking, and motor dysfunction. While most cases occur sporadically, several inherited forms of FTLD have been linked to genetic mutations, which can offer clues to the cause of the disease and potential approaches to treatment. In a study published in Nature Communications, researchers have now uncovered several key events that occur in a common form of familial FTLD linked to mutations in the PGRN gene.

FTLD is a neurodegenerative disease caused in part by the build-up of protein aggregates in neurons. Different forms of FTLD—including the two major hereditary forms of the disease, FTLD-tau and FTLD-TDP—are associated with the build-up of different proteins. The hallmark of FTLD-tau is accumulated tau protein, a well-known player in neurological disorders such as Alzheimer's disease. The hallmark of FTLD-TDP (the form linked to defective PGRN) is the accumulation of TDP43, whose role in the disease is poorly understood. One of the reasons less is known about FTLD-TDP is that the current disease models in mice look don't precisely mimic the way PGRN is mutated in patients. We developed a new model by introducing a mutation in PGRN gene associated with FTLD-TDP. In contrast to the earlier models, the mice in our study exhibit behavioral and cognitive symptoms that very closely mirror the disease pathology seen in humans.

Using this model, the researchers set out to understand what differentiates PGRN-mutant mice from their healthy counterparts. They focused their search on phosphorylation, a process that is normally involved in cell signaling but is often implicated in neurodegenerative diseases. Phosphorylated proteins have an additional chemical charge that can alter their behavior. In patients with FTLD-tau, as well as in Alzheimer's disease, phosphorylation of tau is thought drive its accumulation in neurons.

The research team performed a comprehensive search for proteins that are phosphorylated when PGRN is mutated. Notably, they discovered that tau is phosphorylated and specifically localized to synapse in the mutant mice. This was a surprising find, given that tau does not accumulate and have not been implicated in the TDP form of the disease (FTLD-TDP). Nevertheless, they found that phosphorylated tau causes synapse loss, and may disrupt communication between neurons. The toxic tau was seen as early as 4 weeks in mice, while TDP43 did not appear until 24 weeks—suggesting that tau may play a more important role early in the disease.

Our study shows that tau phosphorylation (but not tau aggregation) is central to the pathology of both forms of FTLD as well as of Alzheimer's disease. In the case of FTLD-TDP, phosphorylated tau appears to drive early synapse changes long before TDP43 protein aggregates appear. The therapeutic implications of the study are clear, as the findings suggest that targeting tau phosphorylation may be an effective way to treat the disease at its earliest stages.

Over the course of the study, the team uncovered a number of molecular events that cause mutated PGRN to lead to tau phosphorylation. With many of the key signaling players now identified, the team is hopeful that future efforts can focus on possible treatment strategies for this form of the disease.

Tau pathway looks to be a very promising treatment target for familial FTLD associated with PGRN mutations. We're very excited to see how our findings will eventually translate into clinical improvement for these patients.

(3) Education

As educational tasks, we have lecture and experiment classes of neuropathology for medical/dental graduate school program and medical school program. We also have general pathology and neuropathology classes for graduate school for health sciences, and clinical anatomical and therapeutic pathology classes for research students.

(4) Lectures & Courses

We provide students with opportunities to learn practical research techniques on neuropathology, especially neurodegenerative diseases.

(5) Publications

[Original Articles]

1. Yamanishi, E., Hasegawa, K., Fujita, K., Ichinose, S., Yagishita, S., Murata, M., Tagawa, K., Akashi, T., Eishi, Y., Okazawa, H.. A novel form of necrosis, TRIAD, occurs in human Huntington's disease. *Acta Neuropathologica Communications*.. 2017.03; 5(19);
2. Sato K, Kerever A, Kamagata K, Tsuruta K, Irie R, Tagawa K, Okazawa H, Arikawa-Hirasawa E, Nitta N, Aoki I, Aoki S.. Understanding microstructure of the brain by comparison of neurite orientation dispersion and density imaging (NODDI) with transparent mouse brain. *Acta Radiol Open*. 2017.04; 6(4); 2058460117703816
3. Fujita K., Motoki K., Tagawa K., Chen X., Hama H., Nakajima K., Homma H., Tamura T., Miyawaki A., Okazawa H.. HMGB1 triggers neurite degeneration via TLR4-MARCKS, and is a potential therapeutic target for alzheimer's disease *JOURNAL OF THE NEUROLOGICAL SCIENCES*. 2017.10; 381; 64-65
4. Chen X., Mao Y., Xu M., Fujita K., Motoki K., Sasabe T., Homma H., Tagawa K., Tamura T., Okazawa H.. Targeting tead/yap-transcription-dependent necrosis, triad, ameliorates Huntington's disease pathology *JOURNAL OF THE NEUROLOGICAL SCIENCES*. 2017.10; 381; 219
5. Kyota Fujita, Ying Mao, Shigenori Uchida, Xigui Chen, Hiroki Shiwaku, Takuya Tamura, Hikaru Ito, Kei Watase, Hidenori Homma, Kazuhiko Tagawa, Marius Sudol, Hitoshi Okazawa. Developmental YAPdeltaC determines adult pathology in a model of spinocerebellar ataxia type 1. *Nat Commun*. 2017.11; 8(1); 1864
6. Ryusuke Irie, Koji Kamagata, Aurelien Kerever, Ryo Ueda, Suguru Yokosawa, Yosuke Otake, Hisaaki Ochi, Hidekazu Yoshizawa, Ayato Hayashi, Kazuhiko Tagawa, Hitoshi Okazawa, Kolske Takahashi, Kanako Sato, Masaaki Hori, Eri Arikawa-Hirasawa, Shigeki Aoki. The Relationship between Neurite Density Measured with Confocal Microscopy in a Cleared Mouse Brain and Metrics Obtained from Diffusion Tensor and Diffusion Kurtosis Imaging. *Magn Reson Med Sci*. 2017.12;

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1. Hitoshi Okazawa. Ultra-Early Phase pathologies of Alzheimer's disease and other neurodegenerative diseases. *Proc Jpn Acad Ser B Phys Biol Sci*.. 2017.06; 93(6); 361-377
2. Hitoshi Okazawa. PQBP1, an intrinsically disordered/denatured protein at the crossroad of intellectual disability and neurodegenerative diseases. *Neurochem Int*.. 2017.06;

[Conference Activities & Talks]

1. Hitoshi Okazawa. Impaired DNA Damage Repair in SCA1 and Other CAG Repeat Diseases. Gordon Research Conference - CAG Triplet Repeat Disorders 2017.06.06 Mount Snow Grand Summit Hotel (Vermont, America)

2. Kyota Fujita, Kazumi Motoki, Kazuhiko Tagawa, Xigui Chen, Hiroshi Hama, Kazuyuki Nakajima, Hidenori Homma, Takuya Tamura, Masahisa Katsuno, Takashi Saito, Takaomi Saido, Gen Sobue, Atsushi Miyawaki, Hitoshi Okazawa. . HMGB1, a pathogenic molecule that induces neurite degeneration via TLR4-MARCKS, is a potential therapeutic target for Alzheimer's disease. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.20 Makuhari Messe
3. Juliana Bosso Taniguchi, Kanoh Kondo, Kyota Fujita, Chen Xigui, Hidenori Homma, Takeaki Sudo, Ying Mao, Kei Watase, Toshihiro Tanaka, Kazuhiko Tagawa, Takuya Tamura, Shin-Ichi Muramatsu, Hitoshi Okazawa.. RpA1 ameliorates symptoms of mutant ataxin-1 knock-in mice and enhances DNA damage repair. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.20 Makuhari Messe
4. Masaki Sone, Koto Furotani, Taka-aki Yajima, Takuya Tamura, Hitoshi Okazawa.. Effect of specific inhibition of synaptic delivery of APP by loss-of-function of yata on the Drosophila Alzheimer's disease model. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.21 Makuhari Messe
5. Xigui Chen, Mao Ying, Xu Min, Kyota Fujita, Kazumi Motoki, Toshikazu Sasabe, Hidenori Homma, Miho Murata, Kazuhiko Tagawa, Takuya Tamura, Kaye Julia, Steven Finkbeiner, Giovanni Blandino, Marius Sudol, Kanoh Kondo, Hitoshi Okazawa.. Targeting TEAD/YAP-transcription-dependent necrosis, TRIAD, ameliorates Huntington's disease pathology. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.22 Kyoto International Conference Center (Kyoto,Japan)
6. Hitoshi Okazawa. Common pathologies across multiple neurodegenerative diseases revealed from unbiased approaches. MyNEURO 2017 2017.08.13 Hotel Istana (Kuala Lumpur,Malaysia)
7. Juliana Bosso Taniguchi, Kanoh Kondo, Kyota Fujita, Xigui Chen, Hidenori Homma , Ying Mao , Kazuhiko Tagawa , Hitoshi Okazawa.. RPA1 AMELIORATES SYMPTOMS OF MUTANT ATAXIN-1 KNOCK-IN MICE AND ENHANCE DNA DAMAGE REPAIR. XXIII World Congress of Neurology (WCN 2017) 2017.09.17 Kyoto International Conference Center (Kyoto,Japan)
8. Kyota Fujita, Kazumi Motoki, Kazuhiko Tagawa, Xigui Chen, Hiroshi Hama, Kazuyuki Nakajima, Hidenori Homma, Takuya Tamura, Atsushi Miyawaki, Hitoshi Okazawa.. HMGB1 TRIGGERS NEURITE DEGENERATION VIA TLR4-MARCKS, AND IS A POTENTIAL THERAPEUTIC TARGET FOR ALZHEIMER' S DISEASE. XXIII World Congress of Neurology (WCN 2017) 2017.09.17 Kyoto International Conference Center (Kyoto,Japan)
9. Hitoshi Okazawa. Gene Therapy Against Spinocerebellar Ataxia. XXIII World Congress of Neurology (WCN2017) 2017.09.19 Kyoto International Conference Center (Kyoto,Japan)
10. Hitoshi Okazawa. Conceptual merge between aging and neurodegeneration. 16th Surugadai International Symposium & Joint Usage/Research Program of Medical Research Institute International Symposium 2017.10.11 Tokyo Medical and Dental University
11. Hitoshi Okazawa. HMGB1 and Neurodegeneration. 8th International DAMPs and Alarmins Symposium (iDEAs) 2017.11.06 Cold Spring Harbor Laboratory (New York,America)
12. Hitoshi Okazawa. Common pathologies across multiple neurodegenerative diseases revealed from unbiased approaches. 12th International Symposium of the Institute Network 2017.11.28 The Institute of Medical Science, The University Of Tokyo

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui
Specially-appointed professor;Makoto Aihara
Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Takeshi Yoshida
Assistant Professor;Shintaro Horie, Tae Yokoi, Tomoka Ishida, Kousei Shinohara
Graduate student;Natsuko Nagaoka, Minami Uchida, keijia Cao, Yuxin Fang

(1) Outline

Our department was established in 1944. Prof. Jin Ohtsuka initiated research on myopia in 1946, and Emeritus Prof. Takashi Tokoro established high myopia clinic in 1974 as the world only clinic specific to pathologic myopia. To date, clinical practice as well as basic research on myopia have continuously been performed in our department. Uveitis clinic was established by Emeritus Prof. Manabu Mochizuki in 1988. Since Prof. Kyoko Ohno-Matsui was appointed to a professorship in our department, clinical practice and basic research on wide variety of fields such as glaucoma, cataract, diabetic retinopathy, vitreoretinal disorder, and macular diseases in addition to myopia and uveitis have been actively performed.

(2) Research

1. High myopia

- 1) Analysis of retinochoroidal complications in high myopia (choroidal neovascularization, myopic tractional retinopathy)
- 2) Evaluation of the molecular mechanism of choroidal angiogenesis using the cultured cells as well as experimental animals (collaboratory project with Department of Cellular Physiological Chemistry)
- 3) Gene analysis of highly myopic patients (collaborator project with Kyoto University)
- 4) Establishment of a novel therapy to prevent an axial elongation or the formation of posterior staphyloma

2. Ocular immunology and inflammation

- 1) Evaluation of the molecular mechanism of immunoregulation in intraocular inflammation
- 2) Pathogenic mechanism of intraocular inflammatory diseases
- 3) Development of novel treatments of intraocular inflammation
- 4) Molecular diagnosis of virus-infected uveitis and intraocular lymphomas.

3. Neuro-ophthalmology

- 1) Evaluation of the change of the circulation as well as the glucose metabolism in the visual cortex using positron emission tomography (PET) in various ocular disorders
- 2) Mechanism of visual pathway in normal conditions as well as in the patients with amblyopia.

4. Vitreoretinal disorder

- 1) Development of a novel treatment for vitreoretinal disorders like retinal detachment, diabetic retinopathy, and macular holes.

5. Strabismus and amblyopia clinic

- 1) Effect of the visual background on binocular vision as well as the influence of strabismus on dynamic visual acuity.

(3) Education

Undergraduate education of ophthalmology is composed of 1) classes on histology and physiology of the eye, and on diagnosis and treatment of ocular disorders, 2) combination block in which clinical examination is trained, and the diagnostic process is actively learned through group discussion using case series, 3) pre-clerkship and clerkship in which the medical students practically learn the major ocular disorders by seeing the patients and discussing in the conference.

After the initial residency of the first two years, the residency in ophthalmology is programmed for four years according to the educational program on diploma of ophthalmology by Japanese ophthalmological society.

The graduate students are expected to be academic doctors who develop and perform highly-qualified ophthalmologists, as well as become scientists who can perform basic research focusing on their clinical interest.

(4) Lectures & Courses

Main objective of ophthalmology and visual science in the graduate course is to obtain the highly-advanced knowledge in the diagnosis and the treatment of various ocular disorders and to perform the basic research based on clinical experience.

(5) Clinical Services & Other Works

Clinical practice is organized by the general ophthalmology clinic as well as the several subspecialty clinics. When the patients visited our department, they are screened in the general clinic, and then the final decision of the diagnosis and treatment is made in cooperation with each subspecialty clinic. Subspecialty clinics include high myopia clinic, uveitis clinic, glaucoma clinic, vitreoretinal disorder clinic, diabetic retinopathy clinic, neuro-ophthalmology clinic, and medical retina clinic. Approximately, 1,300 surgeries are performed per year (e.g., cataract surgery, vitreoretinal surgery, glaucoma surgery, strabismus surgery).

(6) Publications**[Original Articles]**

1. Ishida T, Jonas JB, Ishii M, Shinohara K, Ikegaya Y, Ohno-Matsui K. PERIPAPILLARY ARTERIAL RING OF ZINN-HALLER IN HIGHLY MYOPIC EYES AS DETECTED BY OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY. *Retina (Philadelphia, Pa.)*. 2017.02; 37(2); 299-304
2. Yokoi T, Zhu D, Bi HS, Jonas JB, Jonas RA, Nagaoka N, Moriyama M, Yoshida T, Ohno-Matsui K. Parapapillary Diffuse Choroidal Atrophy in Children Is Associated With Extreme Thinning of Parapapillary Choroid. *Invest. Ophthalmol. Vis. Sci.*. 2017.02; 58(2); 901-906
3. Jonas JB, Ohno-Matsui K, Holbach L, Panda-Jonas S. Retinal pigment epithelium cell density in relationship to axial length in human eyes. *Acta Ophthalmol.* 2017.02; 95(1); e22-e28
4. Jonas JB, Ohno-Matsui K, Panda-Jonas S. Optic Nerve Head Histopathology in High Axial Myopia. *J. Glaucoma.* 2017.02; 26(2); 187-193
5. Jonas JB, Ohno-Matsui K, Holbach L, Panda-Jonas S. Association between axial length and horizontal and vertical globe diameters. *Graefes Arch. Clin. Exp. Ophthalmol.*. 2017.02; 255(2); 237-242
6. Terada Y, Kamoi K, Ohno-Matsui K, Miyata K, Yamano C, Coler-Reilly A, Yamano Y. Treatment of rheumatoid arthritis with biologics may exacerbate HTLV-1-associated conditions: A case report. *Medicine (Baltimore)*. 2017.02; 96(6); e6021
7. Satoko Nakano, Sunao Sugita, Yasuhiro Tomaru, Ayumi Hono, Takako Nakamuro, Toshiaki Kubota, Hiroshi Takase, Manabu Mochizuki, Masayo Takahashi, Norio Shimizu. Establishment of Multiplex Solid-Phase Strip PCR Test for Detection of 24 Ocular Infectious Disease Pathogens. *Invest. Ophthalmol. Vis. Sci.*. 2017.03; 58(3); 1553-1559
8. Ohno-Matsui K, Alkabes M, Salinas C, Mateo C, Moriyama M, Cao K, Yoshida T. FEATURES OF POSTERIOR STAPHYLOMAS ANALYZED IN WIDE-FIELD FUNDUS IMAGES IN PATIENTS WITH UNILATERAL AND BILATERAL PATHOLOGIC MYOPIA. *Retina (Philadelphia, Pa.)*. 2017.03; 37(3); 477-486

9. Jonas JB, Weber P, Nagaoka N, Ohno-Matsui K. Glaucoma in high myopia and parapapillary delta zone. *PLoS ONE*. 2017.04; 12(4); e0175120
10. Suga M, Shinohara K, Ohno-Matsui K. Lacquer cracks observed in peripheral fundus of eyes with high myopia. *Int Med Case Rep J*. 2017.04; 10; 127-130
11. Ayano Imai, Hiroshi Takase, Ken-Ichi Imadome, Go Matsuda, Ichihiro Ohnishi, Kouhei Yamamoto, Takumi Kudo, Yoji Tanaka, Taketoshi Maehara, Osamu Miura, Ayako Arai. Development of Extranodal NK/T-cell Lymphoma Nasal Type in Cerebrum Following Epstein-Barr Virus-positive Uveitis. *Intern. Med.*. 2017.05; 56(11); 1409-1414
12. Yukiko Terada, Koju Kamoi, Takashi Komizo, Kazunori Miyata, Manabu Mochizuki. Human T Cell Leukemia Virus Type 1 and Eye Diseases. *J Ocul Pharmacol Ther*. 2017.05; 33(4); 216-223
13. Kaori Kasahara, Muka Moriyama, Kei Morohoshi, Takeshi Yoshida, Noriaki Simada, Natsuko Nagaoka, Tae Yokoi, Kosei Shinohara, Yuichiro Kaneko, Mitsuki Suga, Kyoko Ohno-Matsui. SIX-YEAR OUTCOMES OF INTRAVITREAL BEVACIZUMAB FOR CHOROIDAL NEOVASCULARIZATION IN PATIENTS WITH PATHOLOGIC MYOPIA. *Retina* . 2017.06; 37(6); 1055-1064
14. Yuxin Fang, Jost B Jonas, Tae Yokoi, Kejia Cao, Kosei Shinohara, Ohno-Matsui K. Macular Bruch's membrane defect and dome-shaped macula in high myopia. *PLoS ONE*. 2017.06; 12(6); e0178998
15. Ohno-Matsui K. WHAT IS THE FUNDAMENTAL NATURE OF PATHOLOGIC MYOPIA? *Retina (Philadelphia, Pa.)*. 2017.06; 37(6); 1043-1048
16. Mitsuhito Hirano, Nobuhiro Ohno, Ryuji Tanosaki, Manabu Mochizuki, Kyoko Ohno-Matsui, Kaoru Uchimar, Arinobu Tojo, Koju Kamoi. Adult T-cell leukemia cell-induced uveitis: rapid increase in adult T-cell leukemia cells disrupts the blood-ocular barrier. *Int. J. Hematol.*. 2017.07;
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19. Jost B Jonas, Ohno-Matsui K, Wen Jun Jiang, Songhomitra Panda-Jonas. BRUCH MEMBRANE AND THE MECHANISM OF MYOPIZATION: A New Theory. *Retina (Philadelphia, Pa.)*. 2017.08; 37(8); 1428-1440
20. Ishida T, Yoshida T, Shinohara K1, Cao K, Nakahama K, Morita I, Ohno-Matsui K. Potential role of sirtuin 1 in Müller glial cells in mice choroidal neovascularization *PLoS One*. 2017.09; 12(9);
21. Muka Moriyama, Kejia Cao, Satoko Ogata, Ohno-Matsui K. Detection of posterior vortex veins in eyes with pathologic myopia by ultra-widefield indocyanine green angiography. *Br J Ophthalmol*. 2017.09; 101(9); 1179-1184
22. Danny S C Ng, Timothy Y Y Lai, Chui Ming Gemmy Cheung, Ohno-Matsui K. Anti-Vascular Endothelial Growth Factor Therapy for Myopic Choroidal Neovascularization. *Asia Pac J Ophthalmol (Phila)*. 2017.10; 6(6); 554-560
23. Ohno-Matsui K, Yuxin Fang, Kengo Uramoto, Kosei Shinohara, Tae Yokoi, Tomoka Ishida, Jost B Jonas. Peri-dome Choroidal Deepening in Highly Myopic Eyes With Dome-Shaped Maculas. *Am. J. Ophthalmol.*. 2017.11; 183; 134-140
24. Chui Ming Gemmy Cheung, Jennifer J Arnold, Frank G Holz, Kyu Hyung Park, Timothy Y Y Lai, Michael Larsen, Paul Mitchell, Ohno-Matsui K, Shih-Jen Chen, Sebastian Wolf, Tien Yin Wong. Myopic Choroidal Neovascularization: Review, Guidance, and Consensus Statement on Management. *Ophthalmology*. 2017.11; 124(11); 1690-1711
25. Jost B Jonas, Natsuko Nagaoka, Yu Xin Fang, Pascal Weber, Ohno-Matsui K. Intraocular Pressure and Glaucomatous Optic Neuropathy in High Myopia. *Invest. Ophthalmol. Vis. Sci.*. 2017.11; 58(13); 5897-5906

26. Kaori Kasahara, Naoyuki Maeda, Takashi Fujikado, Makoto Tomita, Muka Moriyama, Mutsumi Fuchihata, Ohno-Matsui K. Characteristics of higher-order aberrations and anterior segment tomography in patients with pathologic myopia. *Int Ophthalmol.* 2017.12; 37(6); 1279-1288
27. Tomoka Ishida, Kei Morohoshi, Yayoi Takeuchi, Ryoko Soma, Minami Uchida, Ohno-Matsui K. Swept-source optical coherence tomographic findings in eyes with metastatic choroidal tumor. *Am J Ophthalmol Case Rep.* 2017.12; 8; 44-47

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1. Manabu Mochizuki, Sunao Sugita, Koju Kamoi, Hiroshi Takase. A new era of uveitis: impact of polymerase chain reaction in intraocular inflammatory diseases. *Jpn. J. Ophthalmol.* 2017.01; 61(1); 1-20
2. Manabu Mochizuki, Koju Kamoi. F1000Prime Recommendation of [Gül A et al., *Ann Rheum Dis* 2012, 71(4):563-6] . F1000 Prime.

[Conference Activities & Talks]

1. Ohno-Matsui K. RETINA JEOPARDY English session . 1st TOKYO RETINA JEOPARDY 2017.02.21 Tokyo
2. Ohno-Matsui K. Influence of Myopic Macular Degeneration Severity on Treatment Outcomes of Myopic Choroidal Neovascularization in the MYRROR Study. 2017APAO 2017.03.03
3. Ohno-Matsui K. Myopic CNV. 2017APAO 2017.03.04
4. Ohno-Matsui K. Imaging in Myopic Maculopathy. 2017APAO 2017.03.04
5. Ohno-Matsui K. The impact of pathologic myopia on visual impairment in asia and beyond. 2017APAO 2017.03.04 Singapore(Suntec Singapore)
6. Ohno-Matsui K. Randomized trials on treatment of myopic CNV: MYRROR and RADIANCE. 2017APAO 2017.03.04 Singapore(Suntec Singapore)
7. Kamoi K, Ide M, Mochizuki M, Uchimaru K, Tojo A, Ohno-Matsui K. Human T-cell leukemia virus type 1 uveitis in the non-endemic metropolitan region. HTLV2017 2017.03.07 Tokyo
8. Wei C, Kamoi K, Ando N, Ohno-Matsui K. HTLV-1 virus infection to intraocular tissues contribute to the development of HTLV-1 uveitis. HTLV2017 2017.03.07 Tokyo
9. Hiroshi Takase. Proposal of Revised IWOS Diagnostic criteria. 6th International Workshop on Ocular Sarcoidosis 2017.04.28 Bali, Indonesia
10. Jonas JB, Ohno-Matsui K, Nagaoka N, Weber P. Parapapillary delta zone as risk factor of glaucoma in high myopia. ARVO 2017.05.11 Baltimore,USA
11. Ohno-Matsui K. Being too thin is not always a bad thing for choroid. 40th Annual Macula Society Meeting 2017.06.07 Singapore
12. Ohno-Matsui K, Shinohara K. Novel Ultra-Wide-Field OCT Method to Advance the Visualization of Posterior Staphyloma in Pathologic Mopia. 40th Annual Macula Society Meeting 2017.06.09 Singapore
13. Ohno-Matsui K. New insights into myopic maculopathy in pathologic myopia. Macula Symposium Singapore 2017.06.11 Singapore
14. Ohno-Matsui K. What swept-source OCT tells us about dome-shaped macula. Macula Symposium Singapore 2017.06.11 Singapore
15. Ohno-Matsui K. Massive subretinal deposits in recurrent VKH. MaculART 2017 2017.07.02 Paris, France
16. Ohno-Matsui K. Mysteries of dome-shaped macula. MaculART 2017 2017.07.03 Paris, France
17. Ohno-Matsui K. Ultra wide-field OCT of posterior staphyloma. MaculART 2017 2017.07.03 Paris, France
18. Ohno-Matsui K. What is the origin of myopic CNV?. MaculART 2017 2017.07.05 Paris, France

19. Ohno-Matsui K. Pathological myopia (New classification and natural course). 17th Euretina congress 2017.09.07 Barcelona, Spain
20. Ohno-Matsui K, Cheung G, Wong T, Li T, Leal S. The impact of myopic macular degeneration on treatment outcomes of myopic choroidal neovascularisation with intravitreal aflibercept: Insights from the MYRROR study. 17th Euretina congress 2017.09.08 Barcelona, Spain
21. Ohno-Matsui K. Staphyloma and dome-shaped maculopathy. 17th Euretina congress 2017.09.09 Barcelona, Spain
22. Fang Y, Yokoi T, Nagaoka N, Shinohara K, Onishi Y, Ishida T, Yoshida T, XU X, Cao K, Jonas JB, Ohno-Matsui K. Progression of maculopathy due to pathologic myopic: long-term study of more than 10 years. International myopia conference 2017 2017.09.14 Birmingham, England
23. Ohno-Matsui K. Strange pattern of choroidal thickening; It was not just VKH... The retina society meeting 2017 2017.10.05 Boston, USA
24. Ohno-Matsui K, Shinohara K. Ultra-widefield OCT method to advance the visualization of posterior staphylomas and accompanying vitreoretinal changes in pathologic myopia. The retina society meeting 2017 2017.10.07 Boston, USA
25. Sergio Schwartzman, Irene Van der Horst-Bruinsma, Alfredo Adan, Hiroshi Goto, Koju Kamoi, Martina Kron, Alexandra P. Song, Kevin Douglas, Sophia Pathai and C. Stephen Foster. Impact of Adalimumab on Immunosuppressant Use in Patients with Active and Inactive Non-Infectious Intermediate, Posterior, or Pan-Uveitis in the Ongoing Open Label Study: Visual-III. The American College of Rheumatology's Annual Meeting 2017. 2017.11.03 San Diego
26. Ohno-Matsui K. New imaging findings in pathologic myopia. AAO(American Academy of Ophthalmology) 2017 2017.11.11 Neworleans, USA
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28. Ohno-Matsui K, Stanga P, Moussa M, Sadda S. Spectral domain and swept source OCT in the diagnosis and management of vitreoretinal and uveitic disorders. AAO(American Academy of Ophthalmology) 2017 2017.11.12 Neworleans, USA
29. Ohno-Matsui K, Cheung G, Lai T, Hirakata A. The cutting edge of pathologic myopia. AAO(American Academy of Ophthalmology) 2017 2017.11.13 Neworleans, USA
30. Hiroshi Takase. Standards and Challenges in the management of vitreoretinal lymphoma. Annual Meeting of Korean Uveitis Society 2017.11.18 Seoul, Korea
31. Ohno-Matsui K. State-of-the art imaging of pathologic myopia. The 2nd Taiwan - Japan Vitreoretinal Joint Meeting 2017.12.03 Tokyo

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Yasuhiro Suzuki

Assistant Professor: Taku Itou, Tarou Fujikawa, Yuichiro Inaba

Hospital Staff: Takamori Takeda, Natsuko Kurata, Yumiko Tateishi,

Kohei Kajino, Tomoki O-oka

Graduate Student: Keiko Ohno, Ayane Makabe, Takamori Takeda, Ayako Maruyama, Yusuke Kiyokawa, Motomu Honjo

(1) Research

- 1) Deafness gene analysis
- 2) Neurophysiological study of hearing
- 3) Histoanatomical study of ear, nose, throat, head, and neck
- 4) Eye movement analysis in patients with dizziness
- 5) Clinical study of treatment and prognosis in patients with allergic rhinitis, acute and chronic sinusitis, and benign tumors
- 6) Treatment of tinnitus
- 7) Treatment using endoscope
- 8) Development of a new mapping procedure for cochlear implant
- 9) Bio-Marker of external ear canal carcinoma

(2) Lectures & Courses

Pre-graduate clinical education

Clinical systematic lecture covers anatomy, a general idea of diseases, their pathological conditions and treatments in the field of otorhinolaryngology. Clinical clerkship I (general diagnostic training) provides instruction in the diagnosis and testing techniques of the otorhinolaryngological field; clinical clerkship II (clinical training) provides detailed explanations of disease mechanisms, training in the performance of examinations, and clinical responsibilities involving both inpatient and outpatient care. Clinical clerkship III provides advanced training beyond the scope of clinical clerkship II. In particular, students develop an advanced understanding of otorhinolaryngological diseases by conducting outpatient procedures (including taking histories, visual inspection, and palpation), and gaining practical experience in assessment and diagnosis of patients' conditions. Furthermore, in the clinical clerkship III, students also attend a "micro-conference" on teaching. Finally, students are assigned to patients throughout their treatment, consistently dealing with the same individuals before, during, and after surgery; this allows the students to become familiar with the course of clinical care.

(3) Clinical Performances

Otorhinolaryngology clinic provides full examinations and treatment for diseases in ear, nose, throat, head, and neck, including dizziness, sudden deafness, facial palsy, infectious disease and benign as well as malignant disease in the otorhinolaryngeal area. We have performed the first implementation of bone anchored hearing aid implant in Japan and since then we have experienced many patients for this surgery. We also have performed

surgery for patients with malignant disease as well as skull base lesions in collaboration with the Department of the Head and Neck Surgery. Our outpatient clinic includes general ear, nose and throat clinic as well as allergy, sinusitis, dizziness, otitis media, tumor, deafness, and tinnitus clinic.

(4) Publications

[Original Articles]

1. Hirai Chiaki, Yamamoto Yukiko, Takeda Takamori, Tasaki Akihisa, Inaba Yuichiro, Kiyokawa Yusuke, Suzuki Yasuhiro, Tsutsumi Takeshi. Nystagmus at the Onset of Vertiginous Attack in Ménière's Disease. *Otology & Neurotology*. 2017.01; 38(1); 110-113
2. Yurie Mori, Yoshiyuki Kawashima, Masatoki Takahashi, Ayako Maruyama, Taro Fujikawa & Takeshi Tsutsumi. Bilateral cochlear ossification in a patient with Takayasu arteritis *Acta Oto-Laryngologica Case Reports*. 2017.01; 2(1); 150-154
3. Ohno K, Kimura Y, Matsuda Y, Takahashi M, Honjyou M, Arai T, Tsutsumi T.. Increased number of IgG4-positive plasma cells in chronic rhinosinusitis. *Acta Otolaryngol*. 2017.04; 137(2); 186-190
4. kawada k, Kawano T, Sugimoto T, Yamaguchi K, Kawamura Y, Matsui T, Okuda M, Ogo T, Kume Y, Nakajima Y, Andres Mora, Okada T, Hoshino A, Tokairin Y, Nakajima Y, Okada R, Kiyokawa Y, Nomura F, Asakage T, Shimoda R, Ito T. Case of superficial cancer located at the pharyngoesophageal junction which was dissected by endoscopic laryngopharyngeal surgery combined with endoscopic submucosal dissection *Case Rep Otolaryngol*. 2017.08;
5. kawada k, Kawano T, Okada T, Yamaguchi K, Kawamura Y, Matsui T, Okuda M, Ogo T, Kume Y, Nakajima Y, Andres Mora, Hoshino A, Tokairin Y, Nakajima Y, Okada R, Kiyokawa Y, Nomura F, Ariizumi Y, Sugimoto T, Asakage T, Ito T. The usefulness of intra-oropharyngeal U-turm method using trans-nasal endoscopy for detecting superficial squamous cell carcinoma of the base of the tongue *J Otolaryngol ENT Res*. 2017.08; 8; 240
6. Hiroshi Nakanishi, Yoshiyuki Kawashima, Kiyoto Kurima, Jae Jin Chae, Astin M Ross, Gineth Pinto-Patarroyo, Seema K Patel, Julie A Muskett, Jessica S Ratay, Parna Chattaraj, Yong Hwan Park, Sriharsha Grevich, Carmen C Brewer, Michael Hoa, H Jeffrey Kim, John A Butman, Lori Broderick, Hal M Hoffman, Ivona Aksentijevich, Daniel L Kastner, Raphaela Goldbach-Mansky, Andrew J Griffith. mutation and cochlear autoinflammation cause syndromic and nonsyndromic hearing loss DFNA34 responsive to anakinra therapy. *Proc. Natl. Acad. Sci. U.S.A.*. 2017.09; 114(37); E7766-E7775
7. Ayako Maruyama, Atsunobu Tsunoda, Masatoki Takahashi, Seiji Kishimoto, Masami Suzuki. Nasopharyngeal pleomorphic adenoma presenting as otitis media with effusion: case report and literature review. *Am J Otolaryngol*. 35(1); 73-76

[Conference Activities & Talks]

1. Tsutsumi T, Makabe A, Hirai C, Yamamoto Y, Takeda T, Kawashima Y.. Time course of caloric nystagmus in cases with spinocerebellar degeneration.. ARO 40th Annual MidWinter Meeting 2017.02.11 Baltimore
2. Taro Fujikawa, et al.. Malnutrition and Delirium Interrupt Postoperative Swallowing Improvement in Elderly Patients with Head and Neck Cancer. The 14th Taiwan-Japan Conference on Otolaryngology-Head and Neck Surgery 2017.12.01

Neurology and Neurological Science

Professor YOKOTA Takanori
 Junior Associate Professor ISHIBASHI Satoru
 Junior Associate Professor NISHIDA Yoichiro
 Assistant Professor OHKUBO Takuya
 Assistant Professor SATO Nozomu
 Assistant Professor OZAKI Kokoro
 Assistant Professor HATTORI Takaaki
 Assistant Professor NUMASAWA Yoshiyuki
 Project Professor SANJO Nobuo
 Project Junior Associate Professor NAGATA Tetsuya
 Project Assistant Professor KUWAHARA Hiroya
 Project Assistant Professor YOSHIOKA Kotaro
 Project Assistant Professor YUI Daishi
 Project Assistant Professor SAKAUE Fumika
 Project Researcher ASADA Ken
 Graduate Student ITO Yoko
 Graduate Student HIGASHI Miwa
 Graduate Student Yagi Yohsuke
 Graduate Student ZENIYA Satoshi
 Graduate Student IWASAWA Eri
 Graduate Student OHYAGI Masaki
 Graduate Student HASEGAWA Jyuri
 Graduate Student SHINTAKU Hiroshi
 Graduate Student FURUKAWA Fumiko
 Graduate Student MIYASHITA Akiko
 Graduate Student FUJITA Kyohe
 Graduate Student MAJIMA Takamasa
 Graduate Student ONO Daisuke
 Graduate Student HIRATA Kose
 Graduate Student ISHIZU Nobutaka
 Graduate Student LI Fu Ying
 Graduate Student SONG Jin Dong
 Graduate Student GUO Huijia
 Graduate Student HU Yajun
 Graduate Student ZHANG Yong Quan
 Graduate Student SU SU Lei Mon
 Graduate Student REYILA Mamuti
 Graduate Student MAMUTI HASIYATI
 Graduate Student DAIZO Kaiichi
 Graduate Student YASUDA Eiji
 Graduate Student MITSUHASHI Yuta
 Graduate Student TAMURA Keigo
 Graduate Student KUNIEDA Taiki
 Research Student SANO Tatsuhiko
 Research Student TAMAKI Toshihiro

(1) Research

- 1) Development of base technology on nucleic acid medicine and its application to neurological disorders
- 2) Discovery of biomarker in body fluid for neurological diseases
- 3) Pathogenesis of Alzheimer disease
- 4) Pathogenesis and therapies of amyotrophic lateral sclerosis (ALS)
- 5) Pathogenesis and therapies of cerebrovascular diseases
- 6) Genetical and pathomechanical studies of spinocerebellar ataxias
- 7) Regulation of blood-brain barrier
- 8) Electrophysiological studies
- 9) Leading-edge neuroradiological studies
- 10) Neuropathological studies of biopsied and autopsied samples

(2) Lectures & Courses

Neurology is a medical specialty concerned with the diagnosis and treatment of disorders of the nervous system including the brain, spinal cord, peripheral nerves, autonomic nerves and skeletal muscles. Since the nervous system extends to the whole body and regulate all the organs, neurologists have to examine and understand many symptoms of the whole brain and body.

The Department of Neurology and Neurological Science at Tokyo Medical and Dental University offers a unique “clinical neurological training for specialist” in a three-year residency program. This program is designed to provide the highest quality clinical training in the clinical practice of neurology, either in an academic or a practice career. To accomplish this, the program integrates extensive practical exposure to all aspects of current clinical neurology with a firm grounding in underlying scientific principles and methods of clinical investigations such as electrophysiology, neuromuscular pathology, stroke, dementia, neuroimaging, and neurogenetics. The faculty and staff are committed to facilitate resident education and training.

After completion of their training for three years, senior residents are equipped with a lot of clinical experience as attending doctors or teaching assistants in the university hospital and affiliated hospitals. They are eligible for the board certification by the Japanese Society of Neurology.

(3) Clinical Services & Other Works

We daily see about 100 out-patients and 36 in-patients, and offer in- and out-patient consultation services through the weekday and on weekends. We diagnose and treat patients with stroke, multiple sclerosis, Parkinson's disease, spinocerebellar ataxia, ALS, myopathies, neuropathies, meningitis/encephalitis, and hundreds of other neurological issues. We also have the “out-patients clinic specialized to patients with amnesia.” Our patients will be reliably evaluated and diagnosed with some skillful techniques, such as the electrophysiological, neuroradiological, and neuropsychological tests and pathological diagnosis of biopsied nerves and muscles.

(4) Publications

[Original Articles]

1. Yohsuke Yagi, Takuya Ohkubo, Hideya Kawaji, Akira Machida, Haruka Miyata, Saori Goda, Sugata Roy, Yoshihide Hayashizaki, Harukazu Suzuki, Takanori Yokota. Next-generation sequencing-based small RNA profiling of cerebrospinal fluid exosomes. *Neurosci. Lett.* 2017.01; 636; 48-57
2. Keisuke Abe, Takuya Ohkubo, Takanori Yokota.. TDP-43 in the skin of amyotrophic lateral sclerosis patients. *Journal of Medical and Dental Sciences.* 2017.01; 64(1); 9-17
3. Kazumasa Soga, Kinya Ishikawa, Tokuro Furuya, Tadatsune Iida, Tetsuo Yamada, Noboru Ando, Kiyobumi Ota, Hiromi Kanno-Okada, Shinya Tanaka, Masayuki Shintaku, Yoshinobu Eishi, Hidehiro Mizusawa, Takanori Yokota. Gene dosage effect in spinocerebellar ataxia type 6 homozygotes: A clinical and neuropathological study. *J. Neurol. Sci.* 2017.02; 373; 321-328

4. Sakiko Chikazawa, Takaaki Hanafusa, Kokoro Ozaki, Takeshi Namiki, Maki Amano, Makiko Ueno, Shown Tokoro, Ken Igawa, Takefumi Sato, Kinya Ishikawa, Takanori Yokota, Hiroo Yokozeki. Incomplete Behçet's disease with calf muscle pain and MRI hyperintensity due to possible thrombophlebitis. *Eur J Dermatol.* 2017.02; 27(1); 76-77
5. Taro Ishiguro, Nozomu Sato, Morio Ueyama, Nobuhiro Fujikake, Chantal Sellier, Akemi Kanegami, Eiichi Tokuda, Bitu Zamiri, Terence Gall-Duncan, Mila Mirceta, Yoshiaki Furukawa, Takanori Yokota, Keiji Wada, J Paul Taylor, Christopher E Pearson, Nicolas Charlet-Berguerand, Hidehiro Mizusawa, Yoshitaka Nagai, Kinya Ishikawa. Regulatory Role of RNA Chaperone TDP-43 for RNA Misfolding and Repeat-Associated Translation in SCA31. *Neuron.* 2017.04; 94(1); 108-124.e7
6. Yoshiyuki Numasawa, Takaaki Hattori, Sumio Ishiai, Zen Kobayashi, Tomoyuki Kamata, Minoru Kotera, Satoru Ishibashi, Nobuo Sanjo, Hidehiro Mizusawa, Takanori Yokota. Depressive disorder may be associated with raphe nuclei lesions in patients with brainstem infarction. *Journal of Affective Disorder.* 2017.04; 213; 191-198
7. Zen Kobayashi, Emi Fukatsu, Sakiko Itaya, Miho Akaza, Kiyobumi Ota, Yoshiyuki Numasawa, Satoru Ishibashi, Hiroyuki Tomimitsu, Shuzo Shintani. Fist sign in inclusion body myositis. *Neuromuscul. Disord.* 2017.04; 27(4); 385-386
8. Ohyagi M, Ishibashi S, Ohkubo T, Kobayashi Z, Mizusawa H, Yokota T, Emoto H, Kiyosawa M. . Subacute Supranuclear Palsy in anti-Hu Paraneoplastic Encephalitis. *Canadian Journal of Neurological Sciences.* 2017.06; 44(4); 444-446
9. Masaki Ohyagi, Satoru Ishibashi, Takuya Ohkubo, Zen Kobayashi, Hidehiro Mizusawa, Takanori Yokota, Hirofumi Emoto, Motohiro Kiyosawa. Subacute Supranuclear Palsy in anti-Hu Paraneoplastic Encephalitis. *Can J Neurol Sci.* 2017.07; 44(4); 444-446
10. Hiroaki Yokota, Tomoyuki Kamata, Nobuo Sanjo, Takanori Yokota. Serum retinol levels are associated with brain volume loss in patients with multiple sclerosis. *Multiple Sclerosis Journal* 2017. 2017.07; 3(3);
11. Maya Higuma, Nobuo Sanjo, Hiroshi Mitoma, Mitsuru Yoneyama, Takanori Yokota. Whole-day gait monitoring in patients with Alzheimer's disease: a relationship between attention and gait cycle. *Journal of Alzheimer's Disease Reports* 2017 . 2017.07; 1(1); 1-8
12. Nozomu Sato, Nozomi Toide, Mami Kizawa, Takuya Ohkubo, Satoru Ishibashi, Nobuo Sanjo, Takanori Yokota. Methotrexate-associated lymphoproliferative disorder in a patient with neuromyelitis optica spectrum disorder: An implication for pathogenesis mediated by Epstein-Barr virus. *J. Neurol. Sci.* 2017.08; 379; 219-221
13. Yuki Kishimoto, Akane Fujii, Osamu Nakagawa, Tetsuya Nagata, Takanori Yokota, Yoshiyuki Hari, Satoshi Obika. Synthesis and thermal stabilities of oligonucleotides containing 2'-O,4'-C-methylene bridged nucleic acid with a phenoxazine base. *Org. Biomol. Chem.* 2017.10; 15(38); 8145-8152
14. Shuta Toru, Tadashi Kanouchi, Takanori Yokota, Yosuke Yagi, Akira Machida, Takayoshi Kobayashi. Utility of Autonomic Function Tests to Differentiate Dementia with Lewy Bodies and Parkinson Disease with Dementia from Alzheimer Disease. *Eur. Neurol.* 2017.11; 79(1-2); 27-32
15. Tetsuya Kanai, Akiyuki Uzawa, Yasunori Sato, Shigeaki Suzuki, Naoki Kawaguchi, Keiichi Himuro, Fumiko Oda, Yukiko Ozawa, Jin Nakahara, Norihiro Suzuki, Yuko K Takahashi, Satoru Ishibashi, Takanori Yokota, Takashi Ogawa, Kazumasa Yokoyama, Nobutaka Hattori, Shoko Izaki, Satoru Oji, Kyoichi Nomura, Juntaro Kaneko, Kazutoshi Nishiyama, Ichiro Yoshino, Satoshi Kuwabara. A clinical predictive score for postoperative myasthenic crisis. *Ann. Neurol.* 2017.11; 82(5); 841-849
16. Yajun Hu, Yuji Hashimoto, Takashi Ishii, Mamut Rayle, Kazumasa Soga, Nozomu Sato, Michi Okita, Miwa Higashi, Kokoro Ozaki, Hidehiro Mizusawa, Kinya Ishikawa, Takanori Yokota. Sequence configuration of spinocerebellar ataxia type 8 repeat expansions in a Japanese cohort of 797 ataxia subjects. *J. Neurol. Sci.* 2017.11; 382; 87-90
17. Yuko Yamagishi, Hidekazu Suzuki, Masahiro Sonoo, Satoshi Kuwabara, Takanori Yokota, Kyoichi Nomura, Atsuro Chiba, Ryuji Kaji, Takashi Kanda, Kenichi Kaida, Shu-Ichi Ikeda, Tatsuro Mutoh, Ryo Yamasaki, Hiroshi Takashima, Makoto Matsui, Kazutoshi Nishiyama, Gen Sobue, Susumu Kusunoki. Markers for Guillain-Barré syndrome with poor prognosis: a multi-center study. *J. Peripher. Nerv. Syst.* 2017.12; 22(4); 433-439

[Conference Activities & Talks]

1. Masahito Yamada, Tsuyoshi Hamaguchi, Kenji Sakai, Moeko Noguchi-Shinohara, Ichiro Nozaki, Yu Taniguchi, Atsushi Kobayashi, Atsuko Takeuchi, Tetsuyuki Kitamoto, Yoshikazu Nakamura, Nobuo Sanjo, Tadashi Tsukamoto, Masaki Takao, Shigeo Murayama, Yasushi Iwasaki, Mari Yoshida, Hiroshi Shimizu, Akiyoshi Kakita, Hitoshi Takahashi, Hiroyoshi Suzuki, Hironobu Naiki, Hidehiro Mizusawa. Iatrogenic Creutzfeldt-Jakob disease related to dura mater grafts.. Prion2017 2017.05.23 Edinburgh, UK
2. Tsuyoshi Hamaguchi, Kenji Sakai, Atsushi Kobayashi, Tetsuyuki Kitamoto, Ryusuke Ae, Yoshikazu Nakamura, Nobuo Sanjo, Tadashi Tsukamoto, Hidehiro Mizusawa, Masahito Yamada. Clinical and pathological characterization of "sporadic Creutzfeldt-Jakob disease" with histories of neurosurgery to identify iatrogenic cases. . Prion2017 2017.05.23 Edinburgh, UK
3. Fumiko Furukawa, Tetsuya Kitamoto, Hidehiro Yosikazu Nakamura, Masahito Yamada, Tadashi Tsukamoto, Hidehiro Mizusawa, Takanori Yokota, Nobuo Sanjo. Clinicopathological features of Gerstmann-Sträussler-Scheinker syndrome with P105L mutation.. Prion2017 2017.05.23 Edinburgh, UK
4. Ken Asada, Emanuele Canestrari, Zain Paroo. A druggable target for rescuing miRNA defects. The 43rd Naito Conference, "Noncoding RNA : Biology, Chemistry, & Diseases" 2017.06.29 Hokkaido
5. Haruka Miyata, Kotaro Yoshioka, Huijia Guo, Taiki Kunieda, Yutaro Asami, Kie Tanaka, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata, Takanori Yokota. Efficient inhibition of microRNA by Hetero Duplex Oligonucleotide, HDO-antimiR.. 2017.07.12
6. Fumiko furukawa, Nobuo Sanjo, Yoichiro Nishida, Etsuro Matsubara, Hiroki Akiba, Tsumoto Kohei, Takashi Saito, Takaomi Saido, Takanori Yokota. Analysis of Anti-amyloid β Oligomer Antibody Immunoreactivity in APP Knock-in Mice.. Alzheimer's Association International Conference 2017 2017.07.16 London, UK
7. Masahito Yamada, Tsuyoshi Hamaguchi, Yu Taniguchi, Kenji Sakai, Tetsuyuki Kitamoto, Masaki Takao, Shigeo Murayama, Yasushi Iwasaki, Mari Yoshida, Hiroshi Shimizu, Akiyoshi Kakita, Hitoshi Takahashi, Hiroyoshi Suzuki, Hironobu Naiki, Nobuo Sanjo, Hidehiro Mizusawa. Possible human-to-human transmission of cerebral β -amyloidosis via cadaveric dura mater grafting.. Alzheimer's Association International Conference 2017 2017.07.16 London, UK
8. Hiroya Kuwahara, Jindong Song, Takahiro Shimoura, Kie Yoshida-Tanaka, Tadahaya Mizuno, Tatsuki Mochizuki, Kazutaka Nishina, Tetsuya Nagata, Hiroyuki Kusuhara, Takanori Yokota.. Modulation of blood-brain barrier function by heteroduplex oligonucleotide in vivo.. The 40th Annual Meeting of the Japan Neuroscience Society 2017.07.22 Chiba
9. Ichinose K, Ishibashi S, Miyashita A, Sanjo N, Uchida K, Suzuki Y, Sekine M, Kobayashi D, Eishi Y, Yokota T. Clinicopathological features of neuromuscular sarcoidosis and its immunoreactivity profiles of P.acnes.. XX III World Congress of Neurology 2017.09.16
10. Akane Yamada, Yoshiyuki Numasawa, Takaaki Hattori, Kokoro Ozaki, Yoichiro Nishida, Satoru Ishibashi, Tadashi Kanouchi, Nobuo Sanjo, Takanori Yokota. Signal changes of skeletal muscle MRI in peripheral nerve disorders.. XX III World Congress of Neurology 2017.09.16
11. Hiroaki Yokote, Tomoyuki Kamata, Shuta Toru, Nobuo Sanjo, Takanori Yokota. Brain volume loss is present in Japanese patients with multiple sclerosis with no evidence of disease activity.. XX III World Congress of Neurology 2017.09.16 Kyo
12. Tsuyoshi Hamaguchi, Kenji Sakai, Atsushi Kobayashi, Tetsuyuki Kitamoto, Ryusuke Ae, Yoshikazu Nakamura, Nobuo Sanjo, Kimihito Arai, Mizuho Koide, Fumiaki Katada, Tadashi Tsukamoto, Hidehiro Mizusawa. Investigation of clinical and pathological features of "sporadic Creutzfeldt-Jakob disease" with history of neurosurgery identify iatrogenic cases.. XX III World Congress of Neurology 2017.09.16 Kyoto, JPN
13. Kenji Sakai, Tsuyoshi Hamaguchi, Nobuo Sanjo, Hiroyuki Murai, Yasushi Iwasaki, Tadanori Hamano, Mari Honma, Moeko Noguchi-Shinohara, Ichiro Nozaki, Yoshikazu Nakamura, Tetsuyuki Kitamoto, Hidehiro Mizusawa, Masahito Yamada. Diffusion-weighted MR images in dura mater graft-associated Creutzfeldt-Jakob disease.. XX III World Congress of Neurology 2017.09.16 Kyoto, JPN
14. Yoshiyuki Numasawa, Takaaki Hattori, Sumio Ishiai, Zen Kobayashi, Tomoyuki Kamata, Minoru Kotera, Satoru Ishibashi, Nobuo Sanjo, Hidehiro Mizusawa, Takanori Yokota. Components of depressive disorder due to Raphenuclei damage: subclass analysis of patients with brainstem infarction.. XX III World Congress of Neurology 2017.09.16

15. Miwa Higashi, Kokoro Ozaki, Takaaki Hattori, Takashi Ishii, Kazumasa Soga, Nozomu Sato, Makoto Tomita, Hidehiro Mizusawa, Kinya Ishikawa, and Takanori Yokota.. Pontine magnetic resonance imaging findings differentiate the spinocerebellar degeneration subgroups.. XX III World Congress of Neurology 2017.09.16
16. Daisuke Ono, Satoru Ishibashi, Takanori Yokota. Paraspinal Muscle Density on Computed Tomography decreases in Amyotrophic Lateral Sclerosis. XX III World Congress of Neurology 2017.09.19 Kyoto
17. Kotaro Yoshioka, Taiki Kunieda, Yutaro Asami, Yumiko Sujino, Kie Tanaka, Wenying Piao, Hiroya Kuwahara, Kazutaka Nishina, Tetsuya Nagata and Takanori Yokota. Dual overhanging-duplex oligonucleotide improved efficacy and safety in gene therapy for FAP. XX III World Congress of Neurology 2017.09.20 Kyoto, JPN
18. Tadashi Tsukamoto, Nobuo Sanjo, Tsuyoshi Hamaguchi, Yoshikazu Nakamura, Tetsuyuki Kitamoto, Masahito Yamada, Hidehiro Mizusawa, and Prion Disease Surveillance Committee, Japan. Analysis of cases in which prion disease was denied by the Prion disease Surveillance Committee in Japan in 2016.. Asia Pacific Prion Symposium 2017.10.20 Melbourne, Australia
19. Fumiko Furukawa, Ryusuke Ae, Yoshikazu Nakamura, Tsuyoshi Hamaguchi, Masahito Yamada, Tadashi Tsukamoto, Hidehiro Mizusawa, Takanori Yokota, Nobuo Sanjo. Analysis of clinical features of patients with lower limb muscle weakness in GSS with P102L mutation.. Asia Pacific Prion Symposium 2017.10.20 Melbourne, Australia

[Patents]

1. CHIMERIC DOUBLE-STRANDED NUCLEIC ACID, Patent Number : 9816089

Psychiatry and Behavioral Sciences

Professor

Toru NISHIKAWA, Takayuki OKADA

Associate Professor

Akeo KURUMAJI

Junior Associate Professor

Takashi TAKEUCHI

Assistant Professor

Daisuke JITOKU, Akihito UEZATO, Yuichiro ABE (~ 2017.1),

Hitoshi MUTO, Takehiro TAMURA, Takako NAKANOTANI

Kazuo TAKIGUCHI (2017.2 ~)

Medical Staff

Hiroki SHIWAKU, Kohei MISE, Satoshi TAKAHASHI,

Tomonori TOMISHIGE (~ 2017.3), Masashi NAGASE ((~ 2017.3),

Mariko SUNAHARA ((~ 2017.3), Koutarou KAWAMATA (2017.4 ~),

Ryouta SHIOE (2017.4 ~)

Research assistant

Masakazu UMINO (2017.4 ~)

Technical Assistant

Asami UMINO, Masakazu UMINO (~ 2017.3)

Clinical Psychologist

Kazunori MURAKAMI, Yukari WAKAYAMA, Yasuhiro OKA,

Hisashi YAMADA, Toshikazu SHINOTAKE (2017.5 ~)

Psychiatric Social Worker

Yoshifumi KANEKO, Noriko NUMAGUCHI,

Sayaka KOJIMA (~ 2017.2), Norikazu MONTA (2017.3 ~),

Sumiko NOGUCHI (2017.4 ~)

Graduate Students

Masakazu UMINO, Kazuo TAKIGUCHI, Momoko KOBAYASHI,

Megumi GOTO, Ko FURUTA, Shigehiro OGATA, Hidetoshi KINOSHITA,

Ryotaro SAITO, Koji TAKEDA, Takehiro TAMURA ,

Yosuke SEKIGUCHI (2017.4 ~), Yoshiko NOMURA (2017.4 ~),

Asami ISHIZUYA (2017.4 ~)

(1) **Outline**

Our laboratory is committed to comprehensive research on endogenous psychosis, neurosis, and epilepsy through biological, psychological and social approaches. In collaboration with external research facilities, we are also involved in social psychiatry, child and adolescent psychiatry, and brain imaging studies.

(2) **Research**

1) Studies in neurochemistry

(i) Molecular genetic studies to clarify the causes and conditions of neuropsychiatric diseases:

Using animal models with psychotic symptom-causing agents, we are involved in a study to isolate new candi-

date gene clusters associated with the pathogenesis and pathophysiology of neuropsychiatric disorders from the viewpoint of developmental pharmacology. We are examining the effects of candidate gene clusters in patients with neuropsychiatric disorders.

(ii) Studies in biochemical pharmacology to develop new therapeutic methods for neuropsychiatric disorders.

2) Neurophysiological and psychophysiological studies

(i) Studies of neurotransmitter receptor binding in neuropsychiatric disorders with PET:

We are working together with the National Institute of Radiological Sciences to investigate the binding activities of dopamine receptors in various brain areas of the patients with schizophrenia and mood disorders.

(ii) A study of sleep stages and behavior in neuropsychiatric diseases:

A study is being carried out to examine sleep stages and behavior using an originally developed automatic analysis device (polysomnography) in patients with various psychiatric disorders.

A study on brain functioning in psychiatric disorders by using the near-infrared spectroscopy (NIRS): To obtain an insight into biological markers of psychiatric disorders, changes in regional brain functions during psychological tasks are examined by measuring the relative concentrations of oxyhemoglobin using NIRS in combination with MRI in the brain areas of the patients with schizophrenia and mood disorders.

3) Psychopathological studies

We are conducting psychological studies of neuropsychiatric diseases from the aspects of phenomenology, anthropology, and linguistics, while employing a psychotherapeutic approach. Other research activities include a review of basic psychiatric concepts and a basic study for the classification and diagnosis of psychiatric disorders, which are important recent issues. In addition to endogenous psychosis including schizophrenia and manic depressive disorder, we are also involved in psychoanalytic studies of neurosis and borderline personality disorder, which are attracting increasing attention, and psychotherapies for them, as well as pathological research on pathography and art therapy in terms of creativity.

(3) Education

Following the two-year period of mandatory clinical training, basic professional training in psychiatry will be provided for 6-9 months mainly in the university. In the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists, and undergo practical training at affiliated medical facilities to become qualified psychiatrists. Undergraduate education, which places emphasis on clinical clerkship training after a systematic series of lecture course and seminar-based classes, is designed to develop students' problem-solving skills, and increase their motivation to learn neuropsychiatry, with support from external facilities.

(4) Lectures & Courses

In the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment and laws and regulations related to clinical practice, and acquire other general knowledge, all being essential for biologic, la psychological, social, and ethical approaches to neuropsychiatric diseases.

(5) Clinical Services & Other Works

Clinical practice

Approximately eighty new outpatients visit our department every month, about 30% of which are classified as having "mood disorders" (F3) by ICD-10, followed by "neurotic, stress-related, and somatoform disorders" (F4) and "schizophrenia, schizophrenic and paranoid disorders" (F2). We are also actively involved in consultation and liaison psychiatry for inpatients in other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance dependence, and neurosis requiring intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. Since this facility, the psychiatric department of a general hospital, is used for university education and training, most inpatients are classified as F2, followed by F4 and F3 (ICD-10). We also provide care and treatment for patients with sleep rhythm disorders and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided mECT (modified electroconvulsive therapy) for inpatients, and individual and group psychotherapy for the patients in our psychiatric ward and clinic and day care center in close collaboration with rehabilitation facilities in the community. The day care team consists of a doctor, two nurses. And a psycho-social-worker or a clinical psychologist. Day care (partial hospitalization) is the transitional element between inpatient and outpatient care and its indications have a wide range of psychiatric disorders as follows: schizophrenia,

depression, bipolar disorder, adjustment disorder and personality disorders. Each member has the own aim and the team gives care with different types of framework. Our day care team regards the potentiality of group very important and the group process could contribute to therapeutic effect. With this kind of experience, patients could develop their ability to communicate with other people and readapt to social situations.

(i) A study of biological indicators in schizophrenia with eye cameras:

We are not only involved in studies of monozygotic twins, early-onset patients, and children at a high risk in Japan, but also in an international joint research project of the WHO as a center in charge of operations.

(6) Clinical Performances

Since the 2011 fiscal year, we have been conducting the clinical trial of D-cycloserine for negative symptoms such as avolition, flattening of affect, and poverty of thought and cognitive dysfunction of schizophrenia. We also have been treating patients with schizophrenia with clozapine, which has been approved for refractory schizophrenia. We have started getting systematically involved in the treatment of patients complaining of pain or dysesthesia in oral regions in liaison with the Dental Hospital, which is the unique characteristics of our university. In the 2014 fiscal year, we started the psychoeducational program for patients with bipolar disorder, which focuses on the prevention of relapse. In addition, there is an increasing number of liaison activities for the prevention of delirium especially in the surgical wards, the intervention to patients with suicide attempts in the emergency room, and the mental support for peripartum patients in cooperation with the staffs.

(7) Publications

[Original Articles]

1. Uezato A, Enomoto M, Tamaoka M, Hobo M, Inukai S, Hideshima M, Miyazaki Y, Nishikawa T, Yagishita K. Shorter sleep onset latency in patients undergoing hyperbaric oxygen treatment. *Psychiatry Clin Neurosci.* 2017.01; 71(1); 73-74
2. Yojiro Umezaki, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Two Cases of Oral Somatic Delusions Ameliorated With Brain Perfusion Asymmetry: A Case Report. *Clin Neuropharmacol.* 2017.02;
3. An adolescent case of steroid psychosis with ulcerative colitis 2017.02; 32(2); 259-264
4. Ishiwata S, Hattori K, Sasayama D, Teraishi T, Miyakawa T, Yokota Y, Matsumura R, Yoshida F, Nishikawa T, Kunugi H. . Plasma and cerebrospinal fluid G72 protein levels in schizophrenia and major depressive disorder. *Psychiatry Res.* 2017.04; (254); 244-250
5. Shiwaku H, Kimura Y, Narushima K, Matsuda H, Nishikawa T. . Unilateral atonia and asymmetric cholinergic dysfunction in the ROSS syndrome. *Biol Psychiat.* 2017.05; 83(2); e31-e32
6. Akeo Kurumaji, Michio Itasaka, Akihito Uezato, Kazuo Takiguchi, Daisuke Jitoku, Mizue Hobo, Toru Nishikawa. A distinctive abnormality of diffusion tensor imaging parameters in the fornix of patients with bipolar II disorder. *Psychiatry Res.* 2017.06; 266; 66-72
7. Conell J, Bauer R, Glenn T, Alda M, Arda R, Baune BT, Berk M, Bersudsky Y, Bilderbeck A, Bocchetta A, Bossini L, Paredes Castro AM, Cheung EY, Chillotti C, Choppin S, Del Zompo M, Dias R, Dodd S, Duffy A, Etain B, Fagiolini A, Garnham J, Geddes J, Gildebro J, Gonzalez-Pinto A, Goodwin GM, Grof P, Harima H, Hassel S, Henry C, Hidalgo-Mazzei D, Kapur V, Kunigiri G, Lafer B, Lam C, Larsen ER, Lewitzka U, Licht R, Lund AH, Misiak B, Piotrowski P, Monteith S, Munoz R, Nakanotani T, Nielsen RE, O'Donovan C, Okamura Y, Osher Y, Reif A, Ritter P, Rybakowski JK, Sagduyu K, Sawchuk B, Schwartz E, Scippa AM, Slaney C, Sulaiman AH, Suominen K, Suwalska A, Tam P, Tatebayashi Y, Tondo L, Vieta E, Vinberg M, Viswanath B, Volkert J, Zetin M, Zorrilla I, Whybrow PC, Bauer M.. International multi-site survey on the use of online support groups in bipolar disorder. *Nordic Journal of Psychiatry .* 2017.06;
8. Kazuo Takiguchi, Akihito Uezato, Michio Itasaka, Hidenori Atsuta, Kenji Narushima, Naoki Yamamoto, Akeo Kurumaji, Makoto Tomita, Kazunari Oshima, Kosaku Shoda, Mai Tamaru, Masahito Nakataki, Mitsutoshi Okazaki, Sayuri Ishiwata, Yasuyoshi Ishiwata, Masato Yasuhara, Kunimasa Arima, Tetsuro Ohmori, Toru Nishikawa. Association of schizophrenia onset age and white matter integrity with treatment

- effect of D-cycloserine: a randomized placebo-controlled double-blind crossover study. *BMC Psychiatry*. 2017.07; 17(1); 249
9. Add-on treatment with mood stabilizer on schizophrenia 2017.07; 20(7); 837-839
 10. Kotaro Hatta, Yasuhiro Kishi, Ken Wada, Takashi Takeuchi, Shigeo Ito, Akiko Kurata, Kazunori Murakami, Manabu Sugita, Chie Usui, Hiroyuki Nakamura, . Preventive Effects of Suvorexant on Delirium: A Randomized Placebo-Controlled Trial. *J Clin Psychiatry*. 2017.08;
 11. Akihito Uezato, Mitsuhiro Enomoto, Meiyo Tamaoka, Mizue Hobo, Shusuke Inukai, Masayuki Hideshima, Yasunari Miyazaki, Toru Nishikawa, Kazuyoshi Yagishita. Effects of hyperbaric oxygen treatment on sleep: Potential prescription for sleep disorders. *Japanese Journal of Sports Psychiatry*. 2017.08; 14; 7-12
 12. Umino A, Ishiwata S, Iwama H, Nishikawa T. . Evidence for Tonic Control by the GABAA Receptor of Extracellular D-Serine Concentrations in the Medial Prefrontal Cortex of Rodents. *Front Mol Neurosci*.. 2017.08; (10); 240
 13. Shiwaku H, Umino A, Umino M, Nishikawa T. . Phencyclidine-induced dysregulation of primary cilia in the rodent brain. *Brain Res, Brain Res*.. 2017.08; (1674); 62-69
 14. Ishiwata S, Umino A, Nishikawa T. . Involvement of neuronal and glial activities in control of the extracellular D-serine concentrations by the AMPA glutamate receptor in the mouse medial prefrontal cortex. *Neurochem Int*.. 2017.09; in press;
 15. Akihito Uezato, Naoki Yamamoto, Daisuke Jitoku, Emiko Haramo, Eri Hiraaki, Yoshimi Iwayama, Tomoko Toyota, Masakazu Umino, Asami Umino, Yasuhide Iwata, Katsuaki Suzuki, Mitsuru Kikuchi, Tasuku Hashimoto, Nobuhisa Kanahara, Akeo Kurumaji, Takeo Yoshikawa, Toru Nishikawa. Genetic and molecular risk factors within the newly identified primate-specific exon of the SAP97/DLG1 gene in the 3q29 schizophrenia-associated locus. *Am. J. Med. Genet. B Neuropsychiatr. Genet*.. 2017.10;
 16. Takashi Takeuchi, Yasuyuki Okumura, Akihito Uezato, Toru Nishikawa. Clinical characteristics of suicidal behavior in an intensive care unit at a university hospital in Japan: a 7-year observational study. *Asian Journal of Psychiatry*. 2017.11; in press;
 17. Takagi S, Takeuchi T, Yamamoto N, Fujita M, Furuta K, Ishikawa H, Motohashi N, Nishikawa T.. Short- and long-term evaluation of cognitive functions after electroconvulsive therapy in a Japanese population. *Psychiatry Clin Neurosci*.. 2017.11; in press;
 18. Kobayashi M, Jitoku D, Iwayama Y, Yamamoto N, Toyota T, Suzuki K, Kikuchi M, Hashimoto T, Kanahara N, Kurumaji A, Yoshikawa T, Nishikawa T. . Association studies of WD repeat domain 3 and chitobiosyldiphosphodolichol beta-mannosyltransferase, genes with schizophrenia in a Japanese population. *PLoS One*.. 2017.12; in press;
 19. Umino M, Umino A, Nishikawa T. . Effects of a selective antagonist of the calcium-permeable AMPA receptor antagonist on phencyclidine- and methamphetamine-induced hyperactivity in the mouse. *J Neural Transm*.. 2017.12; in press;

[Misc]

1. Relationship between sunlight and the age of onset of bipolar disorder: An international multisite study 2017.04;

Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital staffs:

Takashi Sugawara, Kaoru Tamura, Takumi Kudo and Kazuhide Shimizu

Graduate Students: Masahumi Sasaki, Yoshiteru Obata, Yousuke Ishii,

Sakyo Hirai, Yasuhiro Ueda, Jun Karakama, Takahiro Ogishima, Shihori Hayashi, Kenji Yamada,

Shouko Hara, Satoka Hashimoto and Masataka Yoshimura

(1) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the central nervous system and spinal cord, which will directly benefit for the improvement of clinical results. Main educational purpose of neurosurgery in the graduate course is to provide students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

In the clinical practice, it is important to attach priority to the patients, considering their background. Also in surgery, it is important to preserve the normal brain functions by employing the cutting edge technique. In the research field, it is essential to introduce and develop the latest knowledge and technology by establishing the reciprocal relationship with the other laboratory institutions.

(2) Research

Brain tumors

1. Analysis of the mechanism of tumor proliferation and infiltration, and its application to treatment
2. Analysis of both proliferative and inhibitory cancer genes in cerebral and spinal tumors
3. Studies of photodynamic therapy, irradiation therapy, agents of chemotherapy, immunotherapy, and inhibition of angiogenesis
4. Development of the multi-modal navigation system integrated with anatomical, hemodynamic, and functional information for brain tumor surgery and evaluate its efficacy.

Vascular diseases in the central nervous system and spinal cord

1. Analysis of pathogenesis of vasospasm after subarachnoid hemorrhage and its application to treatment
2. Studies of circulatory disturbance in ischemic and hemorrhagic diseases, and reversibility of the brain tissue
3. Investigations of pathology of Moyamoya disease and the effects of indirect surgical anastomosis on this entity
4. Solutions of problems in the development of endovascular surgery

Neurotrauma

1. Analysis of cell damage and its reversibility, dynamic simulation in cerebrospinal injury
2. Animal experiments concerning treatment of cerebrospinal injury

Functional neurosurgery

1. Pathological analysis and treatment of temporal lobe epilepsy
2. Analysis of intracellular signal transductions

Others

1. Studies of human cerebral circulation, metabolism, and functions using PET, MRI/S, and MEG
2. Studies of receptors in the central nervous system using PET
3. Experiments of brain diseases using animal model MRI and PET

(3) Clinical Services & Other Works

Neurosurgery is a clinical department dealing with various diseases of central nervous system and spinal cord including tumors, vascular diseases, trauma, congenital malformation, functional disorders, and infection.

(4) Publications**[Original Articles]**

1. Wakabayashi T, Iuchi T, Tsuyuguchi N, Nishikawa R, Arakawa Y, Sasayama T, Miyake K, Nariai T, Narita Y, Hashimoto N, Okuda O, Matsuda H, Kubota K, Ito K, Nakazato Y, Kubomura K. . Diagnostic performance and safety of positron emission tomography using 18F-fluciclovine in patients with clinically suspected high- and low-grade gliomas: A multicenter phase IIb trial. *Asia Oceanian J Nucl Med Biol.* 2017; 5;
2. Takahiro Ogishima, Kaoru Tamura, Daisuke Kobayashi, Motoki Inaji, Shihori Hayashi, Reina Tamura, Tadashi Nariai, Kenji Ishii, Taketoshi Maehara. ATRX status correlates with 11 C-methionine uptake in WHO grade II and III gliomas with IDH1 mutations. *Brain Tumor Pathol.* 2017.01; 34(1); 20-27
3. S Hara, Y Tanaka, Y Ueda, S Hayashi, M Inaji, K Ishiwata, K Ishii, T Maehara, T Nariai. Noninvasive Evaluation of CBF and Perfusion Delay of Moyamoya Disease Using Arterial Spin-Labeling MRI with Multiple Postlabeling Delays: Comparison with (15)O-Gas PET and DSC-MRI. *AJNR Am J Neuroradiol.* 2017.02;
4. Taishi Nakamura, Satoshi Yamashita, Kazutaka Fukumura, Jun Nakabayashi, Kazuhiro Tanaka, Kaoru Tamura, Kensuke Tateishi, Manabu Kinoshita, Shintaro Fukushima, Hirokazu Takami, Kohei Fukuoka, Kai Yamazaki, Yuko Matsushita, Makoto Ohno, Yasuji Miyakita, Soichiro Shibui, Atsuhiko Kubo, Takashi Shuto, Sylvia Kocialkowski, Shoji Yamanaka, Akitake Mukasa, Takashi Sasayama, Kazuhiko Mishima, Taketoshi Maehara, Nobutaka Kawahara, Motoo Nagane, Yoshitaka Narita, Hiroyuki Mano, Toshikazu Ushijima, Koichi Ichimura. Genome-wide DNA methylation profiling identifies primary central nervous system lymphoma as a distinct entity different from systemic diffuse large B-cell lymphoma. *Acta Neuropathol.* 2017.02; 133(2); 321-324
5. Shintaro Fukushima, Satoshi Yamashita, Hisato Kobayashi, Hirokazu Takami, Kohei Fukuoka, Taishi Nakamura, Kai Yamazaki, Yuko Matsushita, Hiromi Nakamura, Yasushi Totoki, Mamoru Kato, Tomonari Suzuki, Kazuhiko Mishima, Takaaki Yanagisawa, Akitake Mukasa, Nobuhito Saito, Masayuki Kanamori, Toshihiro Kumabe, Teiji Tominaga, Motoo Nagane, Toshihiko Iuchi, Koji Yoshimoto, Masahiro Mizoguchi, Kaoru Tamura, Keiichi Sakai, Kazuhiko Sugiyama, Mitsutoshi Nakada, Kiyotaka Yokogami, Hideo Takeshima, Yonehiro Kanemura, Masahide Matsuda, Akira Matsumura, Kazuhiko Kurozumi, Keisuke Ueki, Masahiro Nonaka, Akio Asai, Nobutaka Kawahara, Yuichi Hirose, Tatusya Takayama, Yoichi Nakazato, Yoshitaka Narita, Tatsuhiro Shibata, Masao Matsutani, Toshikazu Ushijima, Ryo Nishikawa, Koichi Ichimura, . Genome-wide methylation profiles in primary intracranial germ cell tumors indicate a primordial germ cell origin for germinomas. *Acta Neuropathol.* 2017.03; 133(3); 445-462
6. Xiaoshu Dong, Kaoru Tamura, Daisuke Kobayashi, Noboru Ando, Kazutaka Sumita, Taketoshi Maehara. Erratum to: LAPTM4B-35 is a novel prognostic factor for glioblastoma. *J. Neurooncol.* 2017.04; 132(2); 305-306
7. Xiaoshu Dong, Kaoru Tamura, Daisuke Kobayashi, Noboru Ando, Kazutaka Sumita, Taketoshi Maehara. LAPTM4B-35 is a novel prognostic factor for glioblastoma. *J. Neurooncol.* 2017.04; 132(2); 295-303
8. Shimpei Baba, Yuji Sugawara, Kengo Moriyama, Motoki Inaji, Taketoshi Maehara, Toshiyuki Yamamoto, Tomohiro Morio. Amelioration of intractable epilepsy by adjunct vagus nerve stimulation therapy in a girl with a CDKL5 mutation. *Brain Dev.* 2017.04; 39(4); 341-344

9. Sakyo Hirai, Motoki Inaji, Yoji Tanaka, Shoko Hara, Tadashi Nariai, Taketoshi Maehara. Correlation between Clinical Presentations and Hemodynamic Parameters Measured by Dynamic Susceptibility Contrast Magnetic Resonance Imaging in Adult Patients with Moyamoya Disease. *J Stroke Cerebrovasc Dis.* 2017.08;
10. Jiro Aoyama, Tadashi Nariai, Maki Mukawa, Motoki Inaji, Yoji Tanaka, Taketoshi Maehara. Case of Familial Moyamoya Disease Presenting 10 Years After Initial Negative Magnetic Resonance Screening in Childhood. *World Neurosurg.* 2017.09; 105; 1035.e1-1035.e4
11. Sung Hugh Choi, Daniel W Stuckey, Sara Pignatta, Clemens Reinshagen, Jasneet Kaur Khalsa, Nicolaas Roozendaal, Jordi Martinez-Quintanilla, Kaoru Tamura, Erhan Keles, Khalid Shah. Tumor Resection Recruits Effector T Cells and Boosts Therapeutic Efficacy of Encapsulated Stem Cells Expressing IFN β in Glioblastomas. *Clin. Cancer Res.* 2017.11; 23(22); 7047-7058
12. Kei Wagatsuma, Keiichi Oda, Kenta Miwa, Motoki Inaji, Muneyuki Sakata, Jun Toyohara, Kiichi Ishiwata, Masayuki Sasaki, Kenji Ishii. O-labeled gas. The image quality with the neck shield was similar to that without the neck shield. *Radiol Phys Technol.* 2017.12; 10(4); 422-430
13. 3. Ishii Y, Tanaka Y, Momose T, Yamashina M, Sato A, Wakabayashi S, Maehara T, Nariai T. . Chronological evaluation of cerebral hemodynamics by dynamic susceptibility contrast magnetic resonance imaging after indirect bypass surgery for moyamoya disease. *World Neurosurgery.* 2017.12; 108; 427-435

[Misc]

1. Sato K, Nariai T, Momose-Sato Y, Kamino K.. Intraoperative intrinsic optical imaging of human somatosensory cortex during neurosurgical operations. *Neurophotonics.* 2017.03; 4(3); 031205

[Conference Activities & Talks]

1. Yukika Arai, Jun Karakama, Kazutoku Miki, Yoshikazu Yoshino, Shigeru Nemoto. A case of a IC-Pcom aneurysm. ABC-WIN seminar 2017.01.19
2. Sumita K, Tanaka Y, Takei T, Kudo T, Tamura K, Sugawara T, Inaji M, Nariai T, Maehara T . The effectiveness of color doppler for distal ACA aneurysms. 2017.03.04
3. Hara S, Hori M, Ueda R, Tanaka Y, Maehara T, Ishii K, Nariai T, Aoki S. Correlation of Intravoxel Incoherent Motion and ^{15}O -gas PET in patients with Moyamoya disease. 5th International Congress on Magnetic Resonance Imaging (ICMRI 2017) and 22nd Scientific Meeting of KSMRM 2017.03.23 Seoul, Korea
4. Hara S, Hori M, Murata S, Ueda R, Nakazawa M, Tanaka Y, Maehara T, Aoki S, Nariai T. NODDI revealed the brain microstructural damage in patients with moyamoya NODDI revealed the brain microstructural damage in patients with moyamoya disease. ISMRM 25th Annual Meeting & Exhibition 2017.04.25 Hawaii, U.S.A.
5. Maehara T, Inaji M, Hashimoto S, Kakita A, Ikeda A,. AMED Study Group of epilepsy and glia. Multi-institutional AMED study of epilepsy and glia in patients with intractable focal epilepsy. –a case presentation. 10th Epilepsy Colloquium 2017.06.17
6. Sugawara T, Inaji M, Tanaka Y, Nariai T, Maehara T.. Surgical Technique for Neck Clipping of Internal Carotid Artery Supraclinoid Segment Aneurysm -importance of complete exposure of the aneurysm. EANS 2017 2017.10.01
7. Kudo T, Sumita K, Maehara T, . RASSF3 functions as a tumor suppressor via p53 in glioblastoma. . EANS 2017. 2017.10.02 Venetia, Italy
8. Noninvasive ASL-MRI using two postlabeling delays can evaluate cerebral hemodynamics of moyamoya disease. 2017.10.13
9. A case of Female Neurosurgeon in Department of Neurosurgery, Tokyo Medical and Dental University. 50th Anniversary of Department of Neurosurgery, Tokyo Medical and Dental University 2017.11.11 Tokyo

10. Hara S, Hori M, Inaji M, Maehara T, Ishii K, Aoki S, Nariai T. . Correlation between brain microstructure revealed by Neurite Orientation Dispersion and Density Imaging and cerebral hemodynamics and metabolism measured with positron emission tomography in patients with moyamoya disease. . Society for Neuroscience 2017 2017.11.15
11. Shimizu K, Hara S, Tazawa T, Hori M, Tanaka Y, Maehara T, Aoki S, Nariai T.. Neurite orientation dispersion and density imaging (NODDI) study in patients with transient global amnesia (TGA). Neuroscience 2017 2017.11.15 Washington D.C., U.S.A
12. Hara S, Hori M, Inaji M, Maehara T, Ishii K, Aoki S, Nariai T. Correlation between brain microstructure revealed by Neurite Orientation Dispersion and Density Imaging and cerebral hemodynamics and metabolism measured with positron emission tomography in patients with moyamoya disease. Neuroscience 2017 2017.11.15 Washington D.C., U.S.A.
13. Shimizu K, Hara S, Tazawa T, Hori M, Tanaka Y, Maehara T, Aoki S, Nariai T. Neurite orientation dispersion and density imaging (NODDI) study in patients with transient global amnesia (TGA). Neuroscience 2017 2017.11.15
14. Chizuko Nagamori, Keiko Hara, Katsuya Ohta, Miho Akaza, Taketoshi Maehara, Motoki Inaji, Yuki Sumi. Knowledges and experiences concerning epilepsy can affect evaluation of social ability of people with epilepsy in Japan: comparison between in 2013 and in 2017. American Epilpsy Society Annual Meeting 2017 2017.12.01
15. Hashimoto S, Maeda J, Kumata K, Takado Y, Inaji M, Ming-Rong Zhang, Suhara T, Maehara T, Higuchi M. Altered tryptophan metabolism can accelerate epileptogenesis. American Epilpsy Society Annual Meeting 2017 2017.12.01

[Awards & Honors]

1. ICMRI2017 Scholarship, ICMRI2017 Organizing Committe, 2017.03

Endovascular Surgery

Professor Shigeru Nemoto
Associate Professor Kazutaka Sumita
Assistant Professor Kazunori Miki
Clinical Fellow Jun Karakama
Secretary Yoko Yanagida, Hitomi Kuwahara

(1) Outline

There are various attracting subjects in the field of clinical or basic research. It is essential to acquire the sufficient knowledge and insight into the pathological conditions as well as normal functions of the vascular system, which will directly benefit for the improvement of clinical results. Main educational purpose of Endovascular Surgery in the graduate course is to provide physicians/students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

(2) Research

Our experimental research program is objected to elucidate unsolved questions derived from daily clinical experience. To treat vascular diseases of central nervous system, facial and head-neck legions, we need to understand detailed vascular anatomy, accurate function of these organs and exact pathophysiology of each disease. Our essential research target is the hemodynamics in the vascular diseases of these lesions. Especially we are interested in the integration of the fluid engineering technology into the endovascular field in an effort to open a new frontier of surgical treatment.

(3) Education

Course objects of Endovascular Surgery in the graduate course is to acquire the proper technique as well as the basic knowledge of neuroendovascular surgery.

(4) Lectures & Courses

Main educational purpose of Endovascular Surgery in the graduate course is to provide students the proper technique as well as the basic knowledge of neuroendovascular surgery.

(5) Clinical Services & Other Works

Our major clinical and extracurricular activities are as follows. 1. Endovascular surgery for diseases of central nervous system, facial and head-neck legions. 2. Analysis of cerebrovascular diseases using computational fluid dynamics (CFD). 3. Development of integrated training system for the endovascular surgery.

(6) Clinical Performances

Endovascular Surgery is a clinical department dealing with various vascular diseases of central nervous system, spinal cord, facial and head-neck lesions including tumors, congenital malformation, and functional disorders.

(7) Publications**[Original Articles]**

1. Xiaoshu Dong, Kaoru Tamura, Daisuke Kobayashi, Noboru Ando, Kazutaka Sumita, Taketoshi Maehara. LAPTM4B-35 is a novel prognostic factor for glioblastoma. *J. Neurooncol.* 2017.04; 132(2); 295-303

[Conference Activities & Talks]

1. Shigeru Nemoto. Characteristics and problems of clot retrieving devices —study with artificial clot and endovascular simulation system. ABCWIN Seminar 2017 Anatomy-Biology-Clinical Correlations (ABC) / Working Group of Interventional Neuroradiology (WIN) 2017.01.18 Val d'Isere France
2. Sumita K, Tanaka Y, Takei T, Kudo T, Tamura K, Sugawara T, Inaji M, Nariai T, Maehara T . The effectiveness of color doppler for distal ACA aneurysms. 2017.03.04
3. Miki K, Karakama J, Yoshino Y, Nemoto S. Three cases of dual antiplatelet therapy resistance in patients undergoing carotid artery stenting and stent assisted coil embolization.. XXIII World Congress of Neurology 2017.09.16 Kyoto, Japan
4. Shigeru Nemoto. Endovascular revascularization of chronic total occlusion of the internal carotid artery. The 14th congress of WFITN 2017.10.16 Hungary

NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Hiroshi KUNUGI
Collaborative Professor	Takashi HANAKAWA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Associate Professor	Yoshitsugu AOKI

(1) Research

1) **Investigation of the molecular machinery underlying brain development.**

(Mikio Hoshino; Department of Biochemistry and Cellular Biology, National Institute of Neuroscience, NCNP)

We are investigating molecular machinery underlying nervous system development, especially focusing on neuron-subtype specification, nervous system regionalization and neuronal migration. We are also interested in human diseases/disorders caused by disorganized development of the nervous system.

We analyzed the relationship between cell division angles and daughter cell fates of cerebellar granule cell precursors (Miyashita et al) and roles of Meis1 in granule cell development (Owa et al).

2) **Molecular genetic and genomic study for intellectual disability in Japan.**

(Yu-ichi Goto, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, NCNP)

One of the major causes of intellectual disability (ID) is based on mutations in the related genes, which are timely and locally expressed in concert with one another in central nervous system. ID is a phenotype derived from the inappropriate expression of these genes. Recent advances in molecular genetics and genome medicine have pushed us on with systematic analysis of ID patients, especially on X-linked MR. In 2013, we investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and diseases with cortical and white matter dysplasia. We detected somatic mutations in surgically dissected brains of cortical dysplasia (Hanai S, et al. Am J Pathol, 2017), and novel causing gene of Arima syndrome which is similar to Joubert syndrome (Itoh M, et al. Brain Dev, 2018) and we studied a recovery effect of low-dose resveratrol on defect of differentiation of iPS cells from mitochondrial disease

(Mizuguchi Y, et al. Mitochondrion, 2017).

3) Clinical research on mood disorders and schizophrenia

(Hiroshi Kunugi, Department of Mental Disorder Research, National Institute of Neuroscience, NCNP)

The pathogenesis and physiology of mood disorders and schizophrenia remain elusive, and their biomarkers have not yet been established. Our department, which is in collaboration with the National Center of Neurology and Psychiatry Hospital, is trying to develop objective diagnostic markers for these diseases, employing omics approach, brain imaging, and physiological studies. We also aim to develop new treatment on the basis of key molecules and nutrition. In this year, we reported that dopamine metabolite could be a state-dependent marker for depressive disorder (J Clin Psychiatry, 2017). We used novel imaging method (diffusion kurtosis) and elucidated altered neural network in depressive disorder (J Psychiatr Res, 2018). As a nutritional approach, we reported that l-theanine a characteristic ingredient in the green tea has a anxiolytic-like effect and enhances regional glucose metabolism of the brain (Psychopharmacology, 2017).

4) Noninvasive study on pathophysiology of human higher brain function.

(Takashi Hanakawa, Department of Advanced Neuroimaging, Integrative Brain Imaging Center, NCNP)

We aim at revealing neural mechanisms underlying higher brain functions including sensory, motor, thought, emotion, and decision making functions in humans, by integrating innovative brain imaging techniques. Translational approach based on this methodological development is to find imaging biomarkers related to the pathophysiology of neuro-psychiatric disorders and to develop new diagnostic tools using the biomarkers. We also develop new rehabilitation methods using non-invasive brain stimulation and brain-machine interface.

In 2017, we clarified both brain and non-brain signal sources in near-infrared spectroscopy (NIRS), which is now widely applied to the diagnosis of psychiatric disorders (Moriguchi et al. Hum Brain Mapp). We also evaluated and developed methods for resting-state fMRI (Togo et al. Front Neurosci; Ogata et al. Front Neurosci). For studies on pathophysiology of neurological disorders, we discovered the involvement of the parallel cortico-basal ganglia circuits in both bradykinesia and bradyphrenia in patients with Parkinson's disease.

5) Primate Social brains: their development, anatomy, physiology and

patho-physiology.

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

We are aiming to elucidate the neural circuit mechanisms of primate social brain using Common Marmoset, new primate model animal. Emphases are on their development, anatomy, physiology and patho-physiology.

This year, we studied mechanisms of material perception, especially glossy materials at medial temporal sulcus (Miyawaka and Banno et al., Front Neural Circuits, 2017).

6) Molecular pathogenesis and gene therapies for neuromuscular diseases

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our research group focuses on genetic neuromuscular diseases including fatal Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS). Our lab integrates molecular, pharmacologic, proteomic and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic therapies for the diseases. Especially, we are dedicated to the development of antisense-oligonucleotides based drugs for the diseases in collaboration with Profs. Matthew Wood, Oxford, Kevin Talbot, Oxford, Toshifumi Yokota, Alberta, Fazel Shabanpoor, Melbourne and Samir El-Andaloussi, Karolinska Institutet.

During the academic year 15/16, we have discovered a fundamentally disturbed molecular pathway in C9orf72-related ALS and frontotemporal dementia that identifies a novel extracellular vesicle trafficking, determines the molecular mechanisms and for the first time links ALS pathogenesis with extracellular vesicle biogenesis (Aoki et al., BRAIN, 2017). The goal of the laboratory is a better understanding and improved treatment of fatal and currently untreated neuromuscular diseases.

(2) Education

The nervous system is a very fine and complex organ to elicit the higher brain function and its malfunction causes a variety of neurological and psychiatric disorders in humans. In this course, students learn the structure, development and function of the normal nervous and muscle systems as well as pathology of developmental disorders, psychiatric disorders, neurological diseases and muscle diseases. Students also study the latest progress of advanced remedy for neuromuscular diseases.

(3) Publications

[Original Articles]

1. Owa T, Taya S, Miyashita S, Yamashita M, Adachi T, Yamada K, Yokoyama M, Aida S, Nishioka T, Inoue YU, Goistuka R, Nakamura T, Inoue T, Kaibuchi K, Hoshino M: Meis1 coordinates cerebellar granule cell development by regulation Pax6 transcription, BMP signaling and Atoh1 degradation. *J. Neurosci.* 38, 1277-1294, 2018
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[Review Articles • Books]

1. Hori K, [Hoshino M](#): Neuronal Migration and AUTS2 Syndrome. *Brain Sci*. 2017 May 14;7(5). pii: E54.
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Immune Regulation

Professor Hajime Karasuyama, M.D., Ph.D.
 Associate Professor Yoshinori Yamanishi, M.D., Ph.D.
 Assistant Professor Yohei Kawano, Ph.D.
 Assistant Professor Soichiro Yoshikawa, Ph.D.
 Specially Appointed Assistant Professor Kensuke Miyake, M.D., Ph.D.

(1) Research

- 1) Role of basophils in immune disorders such as allergy
- 2) Role of basophils in protective immunity against infections
- 3) in vivo imaging of basophil-mediated immune responses

(2) Education

Main objective of the immunology course for undergraduate students is to provide them the basic ideas how the immune system works and is regulated in various physiological and pathological settings including infections, cancer, autoimmune and allergic disorders, and organ transplantation. In the immunology course for graduate students, they study molecular mechanisms underlying the development of immune diseases including allergy and parasitic infection, by employing advanced technology in molecular biology, biochemistry, cellular biology and developmental engineering.

(3) Publications

[Original Articles]

1. Kensuke Miyake, Nozomu Shiozawa, Toshihisa Nagao, Soichiro Yoshikawa, Yoshinori Yamanishi, Hajime Karasuyama. Trogocytosis of peptide-MHC class II complexes from dendritic cells confers antigen-presenting ability on basophils. *Proc. Natl. Acad. Sci. U.S.A.*. 2017.01; 114(5); 1111-1116
2. Hidemitsu Tsutsui, Yoshinori Yamanishi, Hiromi Ohtsuka, Shingo Sato, Soichiro Yoshikawa, Hajime Karasuyama. The Basophil-specific Protease mMCP-8 Provokes an Inflammatory Response in the Skin with Microvascular Hyperpermeability and Leukocyte Infiltration. *J. Biol. Chem.*. 2017.01; 292(3); 1061-1067
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4. Kaori Mukai, Hajime Karasuyama, Kenji Kabashima, Masato Kubo, Stephen J Galli. T Cells and ILC2 Cells in Primary and Secondary Immunity to *Strongyloides venezuelensis*. *Infect. Immun.*. 2017.04; 85(5);
5. Kumi Izawa, Akie Maehara, Masamichi Isobe, Yuka Yasuda, Makoto Urai, Yasutaka Hoshino, Keigo Ueno, Toshihiro Matsukawa, Mariko Takahashi, Ayako Kaitani, Emiko Shiba, Ayako Takamori, Shino Uchida, Koichiro Uchida, Keiko Maeda, Nobuhiro Nakano, Yoshinori Yamanishi, Toshihiko Oki, David Voehringer, Axel Roers, Susumu Nakae, Junko Ishikawa, Yuki Kinjo, Toshiaki Shimizu, Hideoki Ogawa,

- Ko Okumura, Toshio Kitamura, Jiro Kitaura. Disrupting ceramide-CD300f interaction prevents septic peritonitis by stimulating neutrophil recruitment. *Sci Rep.* 2017.06; 7(1); 4298
6. Sumika Toyama, Naoko Okada, Akio Matsuda, Hideaki Morita, Hirohisa Saito, Takao Fujisawa, Susumu Nakae, Hajime Karasuyama, Kenji Matsumoto. Human eosinophils constitutively express a unique serine protease, PRSS33. *Allergol Int.* 2017.07; 66(3); 463-471
 7. Tomoyuki Bando, Setsuko Fujita, Naoko Nagano, Soichiro Yoshikawa, Yoshinori Yamanishi, Masashi Minami, Hajime Karasuyama. Differential usage of COX-1 and COX-2 in prostaglandin production by mast cells and basophils. *Biochem Biophys Rep.* 2017.07; 10; 82-87
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 9. Barbara Dema, Yasmine Lamri, Christophe Pellefigues, Emeline Pacreau, Fanny Saidoune, Caroline Bidault, Hajime Karasuyama, Karim Sacré, Eric Daugas, Nicolas Charles. Basophils contribute to pristane-induced Lupus-like nephritis model. *Sci Rep.* 2017.08; 7(1); 7969
 10. Takuya Ohta, Soichiro Yoshikawa, Yuya Tabakawa, Kayoko Yamaji, Kenji Ishiwata, Hiroshi Shitara, Choji Taya, Masatsugu Oh-Hora, Yohei Kawano, Kensuke Miyake, Yoshinori Yamanishi, Hiromichi Yonekawa, Naohiro Watanabe, Hirotaka Kanuka, Hajime Karasuyama. Skin CD4+ Memory T Cells Play an Essential Role in Acquired Anti-Tick Immunity through Interleukin-3-Mediated Basophil Recruitment to Tick-Feeding Sites. *Front Immunol.* 2017.10; 8; 1348

[Misc]

1. Kensuke Miyake, Hajime Karasuyama. Emerging roles of basophils in allergic inflammation. *Allergol Int.* 2017.07; 66(3); 382-391
2. Yoshinori Yamanishi, Kensuke Miyake, Misako Iki, Hidemitsu Tsutsui, Hajime Karasuyama. Recent advances in understanding basophil-mediated Th2 immune responses. *Immunol. Rev.* 2017.07; 278(1); 237-245
3. Hajime Karasuyama, Kensuke Miyake, Soichiro Yoshikawa, Yoshinori Yamanishi. Multifaceted roles of basophils in health and disease. *J. Allergy Clin. Immunol.* 2017.12;

[Conference Activities & Talks]

1. Hajime Karasuyama. Basophils in immune-mediated disease. Third International Symposium on IgG4-RD and Fibrosis 2017.02.16 Hawaii, USA
2. Yoshinori Yamanishi, Misako Iki, Kensei Tanaka, Hayato Deki, Mio Fujimaki, Shingo Sato, Soichiro Yoshikawa, Hajime Karasuyama. Basophil tryptase mMCP-11 plays a crucial role in the IgE-mediated chronic allergic inflammation.. The 66th Annual Meeting of Japanese Society of Allergology 2017.06.15 Tokyo, Japan
3. Yohei Kawano, Georg Petkau, Christina Stehle, Pawel Durek, Gitta Anne Heinz, Kousuke Tanimoto, Hajime Karasuyama, Mir-Farzin Mashreghi, Chiara Romagnani, Fritz Melchers. Stable lines and clones of long-term proliferating normal, genetically unmodified murine common lymphoid progenitors.. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai, Japan
4. Soichiro Yoshikawa, Masatsugu Oh-hora, Kensuke Miyake, Yohei Kawano, Yoshinori Yamanishi, Hajime Karasuyama. Prolonged Ca²⁺ influx via STIM2 is essential for cytokine-induced IL-4 production in basophil. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai, Japan
5. Sho Shibata, Kensuke Miyake, Soichiro Yoshikawa, Yohei Kawano, Yoshinori Yamanishi, Hajime Karasuyama. Monocyte-derived macrophages in the lung contribute to the development of pulmonary emphysema through MMP12 production in a mouse model of COPD. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai, Japan
6. Hajime Karasuyama. Emerging roles of basophils in allergic inflammation and immune regulation. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai, Japan

7. Takahiro Adachi, Soichiro Yoshikawa, Hajime Karasuyama. Intravital imaging of Ca²⁺ signals in lymphocytes of the Ca²⁺ biosensor YC3.60 transgenic mice. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
8. Kensuke Miyake, Nozomu Shiozawa, Toshihisa Nagao, Soichiro Yoshikawa, Yoshinori Yamanishi, Hajime Karasuyama. Basophils exert antigen presentation via trogocytosis-mediated acquisition of peptide-MHC class II complexes from dendritic cells (DCs). The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
9. Hidemitsu Tsutsui, Yoshinori Yamanishi, Hiromi Ohtsuka, Shingo Sato, Soichiro Yoshikawa, Hajime Karasuyama. The basophil-specific protease mMCP-8 provokes an inflammatory response in the skin with microvascular hyperpermeability and leukocyte infiltration. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
10. Yuya Tabakawa, Takuya Ohta, Soichiro Yoshikawa, Kayoko Yamaji, Kenji Ishiwata, Yohei Kawano, Yoshinori Yamanishi, Naohiro Watanabe, Hiroshi Ohtsu, Hirotaka Kanuka, Hajime Karasuyama. Histamine plays a critical role in acquired protective immunity against tick infestation. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
11. Takuya Ohta, Soichiro Yoshikawa, Kayoko Yamaji, Kenji Ishiwata, Yuya Tabakawa, Yohei Kawano, Yoshinori Yamanishi, Naohiro Watanabe, Hirotaka Kanuka, Hajime Karasuyama. Skin-resident memory CD4⁺ T cells play an essential role in acquired tick resistance through IL-3-mediated basophil recruitment. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
12. Toshihisa Nagao, Mio Teranishi, Kensuke Miyake, Soichiro Yoshikawa, Yohei Kawano, Yoshinori Yamanishi, Hajime Karasuyama. Sugar modification of carrier protein confers ability on allergen to induce IgE- and basophil-mediated allergic inflammation. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
13. Tomoyuki Bando, Setsuko Fujita, Naoko Nagano, Soichiro Yoshikawa, Yoshinori Yamanishi, Masashi Minami, Hajime Karasuyama. Differential usage of COX-1 and COX-2 in prostaglandin production by mast cells and basophils. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
14. Toshiyuki Kojima, Soichiro Yoshikawa, Yoshinori Yamanishi, Hajime Karasuyama. Novel CD200 homologues iSEC1 and I SEC2 are gastrointestinal secretory cell-specific ligands of inhibitory receptor CD200R. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
15. Taro Watabe, Takashi Nagaishi, Akinori Hosoya, Nisha Jose, Naoya Tsugawa, Yudai Kojima, Soichiro Yoshikawa, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. Analysis of ileocecal immune response in an experimental colitis model using intra-vital imaging. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan
16. Naoya Tsugawa, Takashi Nagaishi, Taro Watabe, Akinori Hosoya, Nisha Jose, Yudai Kojima, Soichiro Yoshikawa, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. Verification of immunoglobulin A regulation of mucosal microflora and homeostasis. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai, Japan

[Awards & Honors]

1. The Best Presentation Award for RIKEN IMS Summer Program 2017 (Kensuke Miyake) , RIKEN IMS , 2017.06
2. Best presentation award, The 46th Annual Meeting of The Japanese Society for Immunology (Kensuke Miyake), The Japanese Society for Immunology, 2017.12

Molecular Virology

Professor : Shoji YAMAOKA
Junior Associate Professor : Hiroaki TAKEUCHI
Project Junior Associate Professor: Takaya HAYASHI
Assistant Professor: Takeshi YOSHIDA
Momoe ITSUMI
Medical Technologist : Yoshio INAGAKI
Secretary : Kumiko THORPE-MATSUI

-Students-

Ph.D. course: Miho OHTSUKA
Hideki SAITO
Hirona ICHIKAWA
Naoto SUZUKI
NDZINU JERRY KWAME
AZIATI ISHMAEL DZIGBORDI KWASI
MXWELL MAMFE SAKYIAMAH
Kosuke SAITO
RELEASE DELETSU
ADIZA ABASS
Master course: Chie MASAKI
Saki HASHIMOTO
Takuya HYODO
Haruka YAMAGUCHI
Masanori KITAMURA

(1) Outline

Microbiology covers several aspects of bacteriology, immunology and virology. Through the studies on various microbes it is expected to understand host-parasite relationship and mechanisms of pathogenicity. Unlike the past, microbiology has rapidly been drawn to the center of the biological stage.

Our laboratory mainly deals with viral oncogenesis and immunodeficiency in humans. Several projects are carried out with particular emphasis on investigation into the mechanisms of viral replication and pathogenesis induced by human retroviruses (HIV-1 and HTLV-I) and human herpes viruses. The purpose of many of the studies being undertaken is to identify critical events and molecules responsible for the efficient replication of these viruses, and in case of human retroviruses, those for transformation or destruction of normal lymphocytes. Virological, immunological and molecular approaches are being applied for this purpose.

(2) Research

The following studies have been extensively carried out in our laboratory with various biological and molecular biological techniques:

- Pathogenesis of HIV and HTLV (mutation, virulence, apoptosis, polymorphism).
- Studies on signal transduction pathways targeted by viral proteins.
- Molecular cloning by genetic approaches of components essential for virus replication in mammalian cells.

(3) Education

We are engaged in the lectures and practices on the basic aspects of infections for the 2nd year medical students and in the pre-clinical clerkship for the 4th year medical students. Students are also accepted in the Project Semester Program. Graduate course students carry out research on virology and oncology in the laboratory and join seminars and progress meetings.

(4) Lectures & Courses

Students can learn the structure, replication, function and genetics of micro-organisms as well as the host-pathogen interactions based on the front-line molecular and microbiological sciences.

(5) Publications**[Original Articles]**

1. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Direct and label-free influenza virus detection based on multisite binding to sialic acid receptors. *Biosensors and Bioelectronics*. 2017.02; 92; 234-240
2. Honami Takada, Ken-Ichi Imadome, Haruna Shibayama, Mayumi Yoshimori, Ludan Wang, Yasunori Saitoh, Shin Uota, Shoji Yamaoka, Takatoshi Koyama, Norio Shimizu, Kouhei Yamamoto, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. EBV induces persistent NF- κ B activation and contributes to survival of EBV-positive neoplastic T- or NK-cells. *PLoS ONE*. 2017.03; 12(3); e0174136
3. M Shiota, N Fujimoto, M Itsumi, A Takeuchi, J Inokuchi, K Tatsugami, A Yokomizo, S Kajioka, T Uchiyumi, M Eto. Gene polymorphisms in antioxidant enzymes correlate with the efficacy of androgen-deprivation therapy for prostate cancer with implications of oxidative stress. *Ann. Oncol.* 2017.03; 28(3); 569-575
4. Wenfeng Hai, Tatsuro Goda, Hiroaki Takeuchi, Shoji Yamaoka, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Specific Recognition of Human Influenza Virus with PEDOT Bearing Sialic Acid-Terminated Trisaccharides. *ACS Appl Mater Interfaces*. 2017.04; 9; 14162-14170
5. Tak W Mak, Melanie Grusdat, Gordon S Duncan, Catherine Dostert, Yannic Nonnenmacher, Maureen Cox, Carole Binsfeld, Zhenyue Hao, Anne Brüstle, Momoe Itsumi, Christian Jäger, Ying Chen, Olaf Pinkenburg, Bärbel Camara, Markus Ollert, Carsten Bindslev-Jensen, Vasilis Vasiliou, Chiara Gorrini, Philipp A Lang, Michael Lohoff, Isaac S Harris, Karsten Hiller, Dirk Brenner. Glutathione Primes T Cell Metabolism for Inflammation. *Immunity*. 2017.04; 46(4); 675-689
6. Hiroaki Takeuchi, Hideki Saito, Takeshi Noda, Tadashi Miyamoto, Tomokazu Yoshinaga, Kazutaka Terahara, Hiroshi Ishii, Yasuko Tsunetsugu-Yokota, Shoji Yamaoka. Phosphorylation of the HIV-1 capsid by MELK triggers uncoating to promote viral cDNA synthesis. *PLoS Pathog.* 2017.07; 13(7); e1006441
7. Hideki Saito, Hiroaki Takeuchi, Takao Masuda, Takeshi Noda, Shoji Yamaoka. N-terminally truncated POM121C inhibits HIV-1 replication. *PLoS ONE*. 2017.09; 12(9); e0182434

8. Nicholas Israel Nii-Trebi, James Ashun Mensah Brandful, Shiro Ibe, Wataru Sugiura, Jacob Samson Barnor, Patrick Owiredu Bampoh, Shoji Yamaoka, Tetsuro Matano, Kazuhisa Yoshimura, Koichi Ishikawa, William Kwabena Ampofo. Dynamic HIV-1 genetic recombination and genotypic drug resistance among treatment-experienced adults in northern Ghana. *J. Med. Microbiol.* 2017.11; 66(11); 1663-1672
9. Takeshi Yoshida, Akiko Hamano, Asuka Ueda, Hiroaki Takeuchi, Shoji Yamaoka. Human SMOOTHENED inhibits human immunodeficiency virus type 1 infection. *Biochem. Biophys. Res. Commun.* 2017.11; 493(1); 132-138

[Conference Activities & Talks]

1. Momoe Itsumi, Kazuhiro Iwai, Shoji Yamaoka. Role for linear ubiquitination in the growth of HTLV-I-infected cells. 18th International Conference on Human Retrovirology : HTLV and Related Viruses 2017.03.07 Tokyo
2. Hiroaki Takeuchi. The timing and triggering of uncoating in an early stage of HIV-1 infection: the essential role of MELK for optimal capsid core disassembly. Special AMR seminar at St. Vincent's Centre of Applied Medical Research 2017.09.27 Sydney, Australia
3. Hirona Ichikawa , Shoji Yamaoka , Shunichi Kajioka Momoe Itsumi. EPAC1 suppresses migration of bladder cancer cells. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.28 Yokohama
4. Kenzo Tokunaga, Weitong Yao, Takuya Tada, Yanzhao Zhang, Shoji Yamaoka. Two Different mechanism by which MARCH8 inhibits viral infection. The 65th Annual Meeting of the Japanese Society for Virology. 2017.10.24 Osaka
5. Weitong Yao, Yanzhao Zhang, Hideaki Fujita, Shoji Yamaoka, Kenzo Tokunaga. CRISPR-mediated activation of endogenous BST-2 expression blocks wildtype HIV-1 production. The 65th Annual Meeting of the Japanese Society for Virology. 2017.10.24 Osaka
6. Saki Hashimoto, Takeshi Yoshida, Hiroaki Takeuchi, Shoji Yamaoka. Species-specificity and Mechanism of viral protein U (Vpu) expressed by primate immunodeficiency viruses . 2017.11.24

Immunotherapeutics

Professor: Mari KANNAGI

Associate Professor: Takao MASUDA

Assistant Professor: Atsuhiko HASEGAWA (Lecturer)

Assistant Professor: Yoshiko NAGANO

Visiting Researcher:: Sayaka ITO

Graduate Student: Yoko SATO, Satomi ANDO, Tatsuro TAKAHATA, Yuji MURAKAMI, Leila SAWADA, Riho KOGA, Yu-Lun HUANG

(1) Outline

Our research area is in between clinical and basic science, involving immunology, microbiology, and oncology. Persistent viral infection causes various diseases by inducing immunodeficiency, malignancy, autoimmunity, and inflammation. Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS), and Human T-cell leukemia virus type-I (HTLV-I) causes adult T-cell leukemia (ATL) and various chronic inflammatory autoimmune-like diseases. To understand mechanisms of these diseases, investigation on host immunity is indispensable. Immune responses are usually protective but sometimes harmful for the host, and are important determinants for disease manifestation. The goal of our research is elucidation of the role of host immunity in the diseases in order to develop effective immunotherapy. We also investigate intracellular mechanisms of viral replication to target direct molecules for therapy.

Research Subjects

1. Analysis of immunological risks for ATL development in HTLV-I-carriers.
2. Development of anti-tumor vaccine against ATL.
3. Immunological and molecular mechanism of HTLV-1-induced leukemogenesis.
4. Molecular mechanism of HIV replication especially related to HIV-1 integrase.
5. Experiments based on gene therapy to suppress HIV-1 replication.

(2) Research

① Development and clinical study of anti-ATL vaccine therapy with Tax peptide-pulsed autologous dendritic cells.

Adult T-cell leukemia/lymphoma (ATL) is a human T-cell leukemia virus type-I (HTLV-I)-infected T-cell malignancy with poor prognosis. We developed a novel therapeutic vaccine designed to augment an HTLV-I Tax-specific cytotoxic T lymphocyte (CTL) response that has been implicated in anti-ATL effects, and conducted a pilot study to investigate its safety and efficacy in collaboration of Tokyo Medical and Dental University, National Kyushu Cancer Center, and Kyushu University. The vaccine consists of autologous dendritic cells pulsed with Tax peptides corresponding to the CTL epitopes. Two of three patients administered with the vaccine achieved partial and complete remission without severe side effects. The clinical outcomes of this pilot study indicate that the Tax peptide-pulsed DC vaccine is a safe and promising immunotherapy for ATL (Suehiro, Y., Hasegawa, A., et al. *Brit J Haematol.* 169: 356-367, 2015. doi: 10.1111/bjh.13302) .

② Involvement of innate immune response in HTLV-1 pathogenesis.

The constitutive activation of NF κ B plays an important role in leukemogenesis of adult T-cell leukemia/lymphoma

(ATL) caused by human T-cell leukemia virus type-1 (HTLV-1). Although HTLV-1 Tax is known to activate NF κ B, ATL cells exhibit NF κ B activities even in the absence of Tax expression, the mechanism of which has been a long-puzzling question. We demonstrate that both double-stranded RNA-dependent protein kinase (PKR) and anti-sense HTLV-1 transcripts are involved in the constitutive NF κ B activation in Tax-negative ATL cells. Our findings elucidate a novel Tax-independent mechanism of NF κ B activation underlying HTLV-1 leukemogenesis in which host antiviral responses are involved (Kinpara, S., et al. *Leukemia*, 29:1425-1444, 2015. doi: 10.1038/leu.2015.1).

(3) Education

① For under graduate students of the medical school, we participate in education of basic immunology I, and II, the project semester, and the preclinical clerkship.

② Graduate students are trained for basic skills in the field of immunology and virology to handle biohazard materials. We provide the opportunity to research for mechanisms of the retro-virus-mediated diseases and development of immunological therapeutics. All the staffs and students participate in maintenance of the laboratory and periodical seminars to discuss about their own studies and keep up with the latest knowledge and information in the area.

(4) Lectures & Courses

We always think of the clinical significance of the results of basic research. We try to find an effective therapy by approaching from basic research to understand the disease mechanisms and solve the problem. The disease mechanisms that we study include leukemogenesis, inflammation, immunosuppression, and autoimmunity in persistent virus infection. Through these studies, we contribute to clinical therapies as well as medical sciences.

(5) Clinical Services & Other Works

We developed an anti-ATL immunotherapy (Tax peptide-pulsed dendritic cell vaccine), which is under clinical studies in collaboration with National Kyushu Cancer Center and Kyushu University. We evaluate anti-tumor and anti-virus T-cell responses in HTLV-1-infected patients with or without various therapies including the immunotherapy and hematopoietic stem cell transplantation, in response to requests from clinical doctors.

(6) Publications

[Original Articles]

1. Ando S, Hasegawa A, Murakami Y, Zeng N, Takatsuka N, Maeda Y, T. Masuda, Y. Suehiro, and M. Kannagi.. HTLV-1 Tax-Specific CTL Epitope-Pulsed Dendritic Cell Therapy Reduces Proviral Load in Infected Rats with Immune Tolerance against Tax. *J. Immunol.* . 2017; 198; 1210-1219
2. Tatsuro Takahata, Eri Takeda, Minoru Tobiume, Kenzo Tokunaga, Masaru Yokoyama, Yu-Lun Huang, Atsuhiko Hasegawa, Tatsuo Shioda, Hironori Sato, Mari Kannagi, Takao Masuda. Critical Contribution of Tyr15 in the HIV-1 Integrase (IN) in Facilitating IN Assembly and Nonenzymatic Function through the IN Precursor Form with Reverse Transcriptase. *Journal of Virology*. 2017.01; 91(1);
3. Satomi Ando, Atsuhiko Hasegawa, Yuji Murakami, Na Zeng, Natsuko Takatsuka, Yasuhiro Maeda, Takao Masuda, Youko Suehiro, Mari Kannagi. HTLV-1 Tax-Specific CTL Epitope-Pulsed Dendritic Cell Therapy Reduces Proviral Load in Infected Rats with Immune Tolerance against Tax. *J. Immunol.*. 2017.02; 198(3); 1210-1219
4. Murakami, Y., A. Hasegawa, S. Ando, R. Tanaka, T. Masuda, Y. Tanaka, and M. Kannagi.. A novel mother-to-child HTLV-1 transmission model for investigating the role of maternal anti-HTLV-1 antibodies using orally infected mother rats. *J Gen Virol* . 2017.02;

5. Yuji Murakami, Atsuhiko Hasegawa, Satomi Ando, Reiko Tanaka, Takao Masuda, Yuetsu Tanaka, Mari Kannagi. A novel mother-to-child HTLV-1 transmission model for investigating the role of maternal anti-HTLV-1 antibodies using orally infected mother rats. *J. Gen. Virol.*. 2017.04;
6. Chie Sugimoto, Kristen M Merino, Atsuhiko Hasegawa, Xiaolei Wang, Xavier A Alvarez, Hiroshi Wakao, Kazuyasu Mori, Woong-Ki Kim, Ronald S Veazey, Elizabeth S Didier, Marcelo J Kuroda. Critical Role for Monocytes/Macrophages in Rapid Progression to AIDS in Pediatric Simian Immunodeficiency Virus-Infected Rhesus Macaques. *J. Virol.*. 2017.08; 91(17);
7. Hideki Saito, Hiroaki Takeuchi, Takao Masuda, Takeshi Noda, Shoji Yamaoka. N-terminally truncated POM121C inhibits HIV-1 replication. *PLoS ONE*. 2017.09; 12(9); e0182434
8. Leila Sawada, Yoshiko Nagano, Atsuhiko Hasegawa, Hikari Kanai, Kai Nogami, Sayaka Ito, Tomoo Sato, Yoshihisa Yamano, Yuetsu Tanaka, Takao Masuda, Mari Kannagi. IL-10-mediated signals act as a switch for lymphoproliferation in Human T-cell leukemia virus type-1 infection by activating the STAT3 and IRF4 pathways. *PLoS Pathog.*. 2017.09; 13(9); e1006597
9. Leila Sawada, Yoshiko Nagano, Atsuhiko Hasegawa, Hikari Kanai, Kai Nogami, Sayaka Ito, Tomoo Sato, Yoshihisa Yamano, Yuetsu Tanaka, Takao Masuda, Mari Kannagi. IL-10-mediated signals act as a switch for lymphoproliferation in Human T-cell leukemia virus type-1 infection by activating the STAT3 and IRF4 pathways. *PLoS Pathogens*. 2017.09; 13(9); e1006597
10. Sawada L, Nagano Y, Hasegawa A, Kanai H, Nogami K, Ito S, Sato T, Yamano Y, Tanaka Y, Masuda T, Kannagi M.. IL-10-mediated signals act as a switch for lymphoproliferation in Human T-cell leukemia virus type-1 infection by activating the STAT3 and IRF4 pathways. *PLoS Pathog.*. 2017.09; 13(9); e1006597
11. Sugimoto C, Merino KM, Hasegawa A, Wang X, Alvarez XA, Wakao H, Mori K, Kim WK, Veazey RS, Didier ES, Kuroda MJ. Correction for Sugimoto et al., "Critical Role for Monocytes/Macrophages in Rapid Progression to AIDS in Pediatric Simian Immunodeficiency Virus-Infected Rhesus Macaques". *Journal of virology*. 2017.11; 91(22);
12. Hasegawa Atsuhiko, Suehiro Youko, Kannagi Mari. Pathogen infection and host responses Potential prophylactic vaccine to protect against ATL development via induction of functional HTLV-1-specific CD8+ T cell responses *Proceedings of the Japanese Society for Immunology*. 2017.12; 46(Proceedings); S4-3

[Conference Activities & Talks]

1. Sawada L, Nagano Y, Hasegawa A, Ito S, Sato T, Yamano Y, Tanaka Y, Masuda T, ○ Kannagi M.. IL-10-mediated signals as a switch to proliferation in HTLV-1-infected T cells.. 18th International Conference on Human Retrovirology HTLV-1 and related viruses 2017.03.10 Tokyo
2. Takao Masuda, Tatsuro Takahata, Yu-Lun Huang, Atsuhiko Hasegawa, Mari Kannagi. . Non-enzymatic role of HIV-1 Integrase through RT-IN precursor form. . The 65th Annual Meeting of the Japanese Society for Virology 2017.10.24 Osaka
3. Undrakh Ganbaatar, Satomi Ando, Takao Masuda, Mari Kannagi, Atsuhiko Hasegawa. Selective dysfunction of HTLV-1-specific T cells in orally infected rats. The 65th Annual Meeting of the Japanese Society for Virology 2017.10.24 Osaka
4. Kannagi M, Sawada L, Nagano Y, Kinpara S, Hasegawa A.. Involvement of antiviral innate responses in HTLV-1 leukemogenesis.. The 76th Annual Meeting of the Japanese Cancer Association 2017.10.25 Yokohama
5. Takao Masuda. Molecular basis for non-enzymatic role of HIV-1 Integrase. 2017.11.24 Tokyo

[Awards & Honors]

1. Quality Award in Basic Science, 18th International Conference on Human Retrovirology , 2017.03

Cellular and Environmental Biology

Associate Professor Masayuki HARA

(1) Research

Research Subjects

- 1) Reaction mechanisms of cellular protection systems against environmental oxidation stresses.
- 2) Modifying mechanisms in higher order structure of chromatin in cellular differentiation.
- 3) Shifting mechanisms in proteome profiles of cell organelle between pre and post conditions in environment, cell differentiation, disease, or drug exposure.

(2) Education

Living organisms were influenced their life by environment and adapted themselves to it, however, they formed environment and affected it. In other words, the species that cannot fit the changing environment were fallen and replaced by the new species which could adapt itself to. The organisms are as a part of the global environment, so it is thought that the individual structure and working of them are necessary environmental measures for their survival. It may be said that it is excessive suddenness of the change that human activity is environmentally-impacted now.

Main objective of cellular and environmental biology in the graduate course is to provide students opportunity to study the reaction and adaptation of the organisms for the environmental change at cellular level, to consider hazardous property, toxicity, or physiological activity of environmental (or man-made) factor, and to mention the biotechnical action to the environmental problems.

(3) Publications

[Conference Activities & Talks]

1. A. Noto, H. Yokota, K. Nomura, M. Hara. Measurement of dose distribution in the cell culture chamber used to evaluate cell damage in low dose exposure.. 50th Annual Meeting of Japan Health Physics Society, 16th Annual Meeting of Japanese Society of Radiation Safety Management in Oita 2017.06.28
2. NOTO, Akio; AOSHIMA, Akihiro; MATSUSITA, Yoji; AOSHIMA, Keiichi; YOKOTA, Hiratsugu; NOMURA, Kiyoshi; HARA, Masayuki. A study about cleansing properties of various types of cleaners against radioactive-contamination materials for reconstruction 2. The 54th Annual Meeting on Radioisotopes and Radiation Researches 2017.07.05
3. Kiyoshi Nomura, Akira Yunoki, Yuko Morito, Chiaki Terashima, Akira Fujishima, Masayuki Hara, Yuya Koike. Development of a flexible gamma-ray detector using a liquid scintillator light guide (LSLG). The 54th Annual Meeting on Radioisotopes and Radiation Researches 2017.07.05
4. Masayuki Hara, Kiyoshi Nomura, Akio Noto, and Hiratsugu Yokota. Numerical Interpretation of the Radiation Effects Based on Ionization of Intracellular Water Molecules.. 13th International Workshop on Ionizing Radiation Monitoring (IWIRM) 2017.12.03

Biodefense Research

Professor Toshiaki Ohteki
 Junior Associate Professor (fm Jan.16) Taku Sato
 Adjunct Lecturer Nobuyuki Onai
 Assistant Professor (fm June.1st) Masashi Kanayama
 Assistant Professor (to March.31) Yusuke Nakanishi
 Junior Assistant Professor Jumpei Asano
 Junior Assistant Professor Mihoko Kajita
 Project Researcher Shunpike Kawamura
 Research Fellow (SONY) Tomohiko Nakamura
 Research Fellow (SONY) (fm Sept.1) Yasuharu Yamauchi
 Graduate Student Minako Inazawa
 Graduate Student Kana Minamide
 Graduate Student Miwako Sase
 Graduate Student Shuhei Imamura
 Graduate Student Shun Ishikawa
 Graduate Student Hirona Yamamoto
 Graduate Student Yuta Izumi
 Research Technician Shoko Kuroda
 Research Technician Kisho Shiseki
 Research Technician (fm April.1st) Minako Hanabusa
 Secretarial Assistant Hisako Kamioka

(1) Outline

Our research projects focus on understanding the dynamic maintenance and transfiguration of homeostasis in the living body. Our goal is to define the homeostasis mechanism under conditions of health and disease. To accomplish this goal, we are trying to clarify the molecular basis of induction and failure of homeostasis by focusing on immune cells in particular mononuclear phagocytes (dendritic cells and macrophages), tissue stem cells, and their functional interplay in the immunological and non-immunological organs, such as skin and intestine. On the basis of our findings, we will further pursue our research in the hope of developing new rational therapies for prevention and treatment of disease.

(2) Research

1. Research on mononuclear phagocytes

1) Discovery of a novel source of mononuclear phagocytes

In 1968, Drs. Ralph van Fruth and Zanvil A. Cohn proposed a concept of mononuclear phagocytes that include monocytes and macrophages. In 1973, Dr. Ralph Steinman discovered dendritic cells (DCs), thereby redefining the mononuclear phagocytes as a population consisting of monocytes, macrophages and also DCs. It has been recently continuing epoch-making discoveries in the field of mononuclear phagocytes and their functions are now beyond classical Immunology and rather extend to broad life phenomenon, e.g. tissue development/regeneration, wound-healing, and establishment of various inflammatory diseases.

DCs consist of conventional DCs (cDCs) and plasmacytoid DCs (pDCs), both of which play critical regulatory roles in the immune system. cDCs exhibit prominent antigen-presenting ability, whereas pDCs are characterized

by their capacity to produce large amounts of type I interferons (IFNs). We have discovered the DC progenitors in the mouse bone marrow, and named common DC progenitors (CDPs) (Immunity 2013; Nat Immunol 2007). Interestingly, CDPs are divided into 2 subpopulations. One is M-CSF receptor (R)+ CDPs mainly producing cDCs, and the other M-CSFR-CDPs producing a large number of pDCs. In addition to CDPs, common monocyte/macrophage progenitors, cMoP, identified in the mouse bone marrow and spleen by other group in 2013.

Based on these achievements in mouse, we have been trying to identify human progenitors of mononuclear phagocytes, and most recently succeeded to identify human cMoP (in revision). Human cMoP gives rise to only monocytes but not other hematopoietic cells including DCs. Given that monocytes and monocyte-derived macrophages cause a variety of inflammatory disorders, including metabolic syndromes and tumor development, our studies shed light on possible therapeutic applications for infectious diseases, cancers and autoimmune diseases.

2) Roles of mononuclear phagocytes in inflammatory bowel disease

Breakdown of the intestinal epithelial layer's barrier function results in the inflow of commensal flora and improper immune responses against the commensal flora, leading to inflammatory bowel disease (IBD) development. Using a mouse dextran sodium sulfate (DSS)-induced colitis model, we showed that commensal Gram-positive bacteria trigger the mobilization of inflammatory monocytes and macrophages into the colon (Mucosal Immunol 2015). TNF- α , a representative cytokine that aggravates colitis and a promising therapeutic target, was predominantly produced by monocytes/macrophages. Among macrophage subpopulations, Ly6c+ macrophages were a major colitogenic subset producing TNF- α . In addition, IFN- γ -Stat1 pathway was required for histone acetylation at the promoter regions of the Tnf loci in macrophages, indicating that IFN- γ -dependent epigenetic regulation instructs the development of colitogenic macrophages. Our study may provide new therapeutic targets, e.g. inhibition of acetyl transferase in macrophage, for treating IBD and colon cancer (in revision).

2. Research on tissue stem cells

1) Understanding of tissue homeostasis and its breakdown on the basis of immune cell-tissue stem cell interplay

We found that type I IFNs induce proliferation and exhaustion in hematopoietic stem cells (HSCs), and that interferon regulatory factor-2 (IRF2), a transcriptional suppressor of type I IFN signaling, preserves the self-renewal and multi-lineage differentiation capacity of HSCs (Nat Med 2009). Based on this finding, we show that type I IFN preconditioning, without irradiation or DNA alkylating agents, significantly enhanced the HSC engraftment efficiency in wild type (WT) recipient mice (Blood 2013). Based on these achievements, we have further found that physiological levels of type I IFN signaling also affect other tissue stem cells, e.g. intestinal stem cells (ISCs) and hair follicle stem cells (HFSCs). Elucidation of detailed mechanisms is currently in progress.

3. Collaborative research with other institutes

In collaboration with RIKEN, Institute of Physical and Chemical Research, we performed microbiota analysis by 16S rRNA sequencing, and found that there is no significant change in the feces of mice with excess IFN signals specifically in intestinal epithelial cells. As the mice showed defective regeneration capacity of ISCs, we concluded that it is unlikely due to the altered commensal composition (manuscript in preparation).

(3) Education

Immunology lectures in Faculty of Medicine, Masters Degree, and Doctoral Programs, Graduate School Seminar in other universities as a adjunct lecturer, and educational and research guidance for individual graduate students.

(4) Publications

[Original Articles]

1. Shunsuke Kawamura, Nobuyuki Onai, Fuyuki Miya, Taku Sato, Tatsuhiko Tsunoda, Kazutaka Kurabayashi, Satoshi Yotsumoto, Shoko Kuroda, Katsuto Takenaka, Koichi Akashi, Toshiaki Ohteki. Identification of a Human Clonogenic Progenitor with Strict Monocyte Differentiation Potential: A Counterpart of Mouse cMoPs. *Immunity*. 2017.05; 46(5); 835-848.e4

2. Jumpei Asano, Taku Sato, Shizuko Ichinose, Mihoko Kajita, Nobuyuki Onai, Shigeomi Shimizu, Toshiaki Ohteki. Intrinsic Autophagy Is Required for the Maintenance of Intestinal Stem Cells and for Irradiation-Induced Intestinal Regeneration. *Cell Rep.* 2017.08; 20(5); 1050-1060
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[Conference Activities & Talks]

1. P13K-Akt pathway enhances type 1 regulatory T cell differentiation induced by IL-27. 2017.12.12

[Awards & Honors]

1. Best Presentation Award, 2017.12

Pathological Cell Biology

Professor : Shigeomi SHIMIZU

Associate Professor : Norio SHIMIZU

Junior Associate Professor : Satoko ARAKAWA

Project Associate Professor : Masatsune TSUJIOKA, Satoshi TORII

Assistant Professor : Shinya HONDA

Project Assistant Professor : Hirofumi YAMAGUCHI,

Michiko MUROHASHI, Nobuhiro FUJIKAKE, Hajime SAKURAI, Minkyon SHIN

Postdoctoral fellow (PD2) : Go Yoshida

Secretary : Hitomi Fukabori, Setsu TAMAI

Research Assistant : Ikuyo YOSHINO, Ikuko NAKANOMYO, Naomi KOJIMA,

Hikari SHIMADA, Yuta YUNOMAE

Graduate Student : Yuna SUGIMOTO, Toyokazu SEKI, Tomoyo YOSHIDA, Saori NOGUCHI, Miyuki NAKAI,

Hatuki ENDO, Ryo OKUNO

(1) Outline

- 1) Analysis of apoptosis mechanism
- 2) Analysis of non-apoptotic cell death (autophagic cell death)
- 3) Physiological and pathological roles of cell death in mammals
- 4) Analysis of alternative macroautophagy mechanism
- 5) Physiological and pathological roles of autophagy in mammals
- 6) Development of novel EBV infection animal models using the hNOG mice
- 7) Development of an exhaustive pathogenic microbe screening system

(2) Research

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.

(3) Education

Main objective in the graduate course is to provide students opportunity to study the molecular mechanisms of cell death and autophagy, the cell death-related diseases, the physiological and pathological roles of autophagy, and the development mechanism of Epstein-Barr virus (EBV) infection, the employment of immunodeficiency animals for the creation of virus research models and development of an exhaustive pathogenic microbial screening system.

(4) Publications

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[Patents]

1. METHOD FOR DETECTING MYCOPLASMA, Announcement Number : 3192878

Pediatrics and Developmental Biology

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Department of Pediatrics, Neonatal and Maternal Medicine

Professor: Shozaburo DOI

Associate Professor: Kohsuke IMAI, Masatoshi TAKAGI

Department of Lifecourse Clinical Immunology

Professor: Masaaki MORI

Project Assistant Professor: Akihiro HOSHINO

(1) Outline

Our department is providing advanced medical service for infants, children, adolescents and young adults. The specialties cover most pediatric diseases, including hematology-oncology, immunology, cardiology, neurology, endocrinology, nephrology, neonatology, allergy and rheumatology. On the other hand, our scientific and academic activities encompass a wide spectrum, from basic to clinical research. By focusing on innovative strategies for clarifying pathogenesis, diagnostic tests, and therapeutic interventions, we are looking at comprehensive resolution of the child's health problems, improving their future.

(2) Research

Our research covers many specialties of pediatric diseases, and the researches are based on from bench to bedside. Our current main projects are

1. Identification of responsible genes for primary immunodeficiency (PID).
2. Development of therapeutic approach for PID
3. Research in autoimmune lymphoproliferative syndrome (ALPS) and RAS-associated ALPS like syndrome
4. Quality assessment of iPS cells for clinical application
5. Regulation of granulocyte activation and apoptosis
6. Development of innovative techniques for ex vivo cell therapy after hematopoietic stem cell transplantation.
7. Elucidating the pathogenesis of glomerulosclerosis formation and identifying the precise function of podocytes.
8. Identifying the pathological mechanisms of compromised immune-function caused by refractory nephrotic syndrome
9. Clarifying the mechanisms of immunological pathology of pediatric idiopathic nephrotic syndrome.
10. Effect of dexmedetomidine on pulmonary hypertension

11. Role of Pannexin-1, a heart mechanosensor, in the right ventricular remodeling induced by pulmonary hypertension
12. Identifying the pathological mechanisms of periventricular leukomalacia and pulmonary damage using model rats
13. Elucidating the molecular mechanisms of gonadal development
14. Molecular pathology of congenital adrenal diseases and disorder of sex development
15. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
16. Elucidating the role of ATM in cellular differentiation
17. Identifying pathological mechanisms of neurological diseases caused by defective DNA damage response
18. Investigation of molecule marker determine the prognosis of infant leukemia
19. Development of therapeutic strategy targeting homologous recombination repair
20. Genetic background of leukemia development
21. Genetic analysis and development of therapeutic approach for epilepsy syndrome
22. Developing data base of JIA (juvenile inflammatory arthritis), CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan)
23. Clarifying immunological profiles of the patients with autoimmune diseases
24. Developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, Istituto Nazionale Tumori (Dr. D. Delia), University of Queensland (Prof. Peter Koopman), Erasmus University (Prof. Jacques van Dongen), Yonsei University (Profs. H. Kim, and SK Lee), Sony Life Science Laboratories, National Institute for Longevity Sciences, National Research Institute for Child Health and Development, RIKEN Center for Integrative Medical Science, Kazusa DNA Research Institute, Tokyo Metropolitan Institute for Medical Science, Juntendo University, and many other laboratories.

● Hematology/Oncology/Immunology Group (Basic Research)

Hematology/Oncology/Immunology group includes 9 staff members, 3 medical staff, 12 graduate students (including 1 graduate student of society), collaborating researchers, and several technical assistants.

Identifying the pathophysiology of primary immunodeficiency (PID)

We perform whole exome sequencing using the next generation sequencer to identify novel PID candidate genes, and identified novel PID responsible genes, IKZF1 (Ikaros) and TNFAIP 3 (A20) (Kanegane, Takagi). We also investigate the etiology of PAPA syndrome, PID associated lymphoma susceptibility, and alveolar proteinosis and PID with immunoglobulin class switch dysregulation (Morio, Kanegane and Imai). For RAS-related ALPS-like diseases, we established iPS cells in collaboration with a group of Associate Professor Otsu of the University of Tokyo Medical Research Institute and started drug screening for therapeutic drug development (Takagi).

In the clinical setting, viral infection is one of a critical factor that affect the outcome of hematopoietic stem cell transplantation. To overcome this disadvantage, we have been starting the generation of multi virus specific cytotoxic T cell. This research expand to virus specific T cell therapy for intractable viral infection as a clinical trial (Morio and Yanagimachi).

We are planning to introduce of neonatal massscreening for PID by using TREC / KREC tests (Imai).

Regenerative medicine

Dr. Morio organized research group to evaluate the quality of clinical use iPS cell. Comprehensive microbe monitoring system has been developing collaborate with Dr. Shimizu at TMDU Medical research institute, and non-invasive genomic alteration detection system has been developing collaborate with Dr. Inazawa at TMDU Medical research institute and Dr. Ohara at Kazusa genome institute.

Oncology

We are focusing on identifying the mechanisms that suppress oncogenic transformation by DNA damage response. In addition, development of therapeutics targeting DNA damage and repair pathway is conducted. Comprehensive genome research for leukemia has been conducted. These researches will be lead to identification of novel therapeutic approaches for pediatric leukemia and neuroblastoma. The research was expanded to Phase I clinical trial of Olaparib for refractory solid tumor.

● Cardiology Group

Pannexin-1 (PANX1) was identified as a mechano-sensor in remodeling of the left ventricle. By exploiting model

mice of pulmonary hypertension, we are investigating the role of PANX1 in right ventricle remodeling. This project is carried out by collaborating with Prof. Furukawa (Department of Bio-informational Pharmacology). Evaluating the effect of Dexmedetomidine for pulmonary hypertension is another ongoing project.

● Neurology Group

Ataxia-telangiectasia (AT) is one of the major neurodegenerative diseases, and we established iPS cell lines from AT patients for elucidating the neuropathological mechanism. Further, we are exploring to discover unidentified genetic diseases with DNA repair-deficiency disorders using next-generation sequencing technology.

We aim to identify the pathological mechanisms of a disease associated with ER (Endoplasmic Reticulum) stress, Marinesco-Sjögren syndrome at the cellular level. We expect our research would provide therapeutic approach to the disease.

In collaborating with other research institutes, we have identified the adverse effect of BZDs on a mouse model of inflammation-induced status epilepticus. We showed that MDZ therapy significantly increased the risk for neurological sequelae in immature mice (collaboration with Haruo Okado, Tokyo Metropolitan Institute of Medical Science).

Elucidating immunological roles of the purinergic receptor signal for microglial inflammatory reaction is another target of our research. We have established P2RY12 KO microglial cell line that enabled us to investigate purinergic receptor signals on inflammatory cytokine production from microglia (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

● Endocrinology Group

Molecular mechanisms of gonadal development

We are trying to elucidate the molecular mechanisms of gonadal development, especially, focusing on elucidating transcriptional network of gonadal development and gonadal cell differentiation. Our projects also include identifying the precise function of transcription factors, such as NR5A1 (SF1), FOXL2 and SOX9.

Elucidating the mechanisms of de-methylation during primordial germ cells differentiation

This project is carried out in collaboration with Prof. Ishino (XXXX).

Molecular analysis of pathological mechanisms in congenital adrenal hyperplasia (CAH)

Including the relationships between genotype and phenotype, we are trying to elucidate the pathological mechanisms of the disease.

Identifying novel molecules of congenital endocrinological diseases

Including insulin resistance, we are aiming to identify novel molecules that is responsible for congenital endocrinological diseases. Current ongoing projects will be integrated systematically, and will be applicable to develop innovative approach for the treatment of congenital endocrine disorder, including regenerative medicine.

● Nephrology Group

Elucidating the pathological mechanisms of glomerulosclerosis and nephrotic syndrome

We carry out the project in collaborating with Division of Nephrology, Department of Internal Medicine, Juntendo University.

● Collagen/Rheumatoid disease group

We are establishing an evidence based guideline of pediatric rheumatoid diseases including juvenile idiopathic arthritis: JIA. Developing a novel database system, CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan), clarifying immunological profiles of the patients with autoimmune diseases, and developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker are other our current projects.

● Neonatology group

Using mesenchymal stem cells derived from umbilical cord blood cells, we are investigating a novel therapeutic approach for treating periventricular leukomalacia. We are exploiting a rat model of intrauterine infection, and the project is carried out in cooperation with the division of Cellular Physiological Chemistry and Nanomedicine (DNP) in TMDU.

● Allergy Group

One of our main project goals is to elucidate the immunological mechanisms of food allergy such as that against milk and eggs.

In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we are conducting several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma.

(3) Education

Block Lecture

The lecture of clinical medicine are proposed systematic lectures with Pediatrics, Obstetrics and Gynecology as “Reproduction and Development Block”. From this year, we introduced “active learning” at 9 lectures. Four fundamental education of medicine and odontology and 2 team based learning (TBL) were also provided.

Project semester

This provides the opportunities of basic research for the 4th grade students for a half years. This year, no student was committed to the research of our department.

Pre-clinical clerkship (PCC).

We proposed 6 programs providing the opportunities to learn the logical skills of clinical practice.

After the curriculum, The students undertake the examination of clinical practice, i.e., OSCE, CBT.

Clinical clerkship (CC)

The practical training of medicine, and every month, approximately 10 students have the training in our department. The students involved in each group of subspecialty (Hematology, Oncology, Immunology, Cardiology, Neurology, Nephrology, Rheumatology, Endocrinology, Neonatology). In addition to our university hospital, the students visit the satellite hospitals for the training of common diseases.

Once a week, the students round the pediatric ward of the hospital with the professor to learn the physical examination skills.

Training of junior clinical fellows

We provide clinical training courses in cooperation with satellite hospitals (Musashino Red Cross Hospital, Soka Municipal Hospital or North Tokyo Medical Center). Depending on the individuals, they could select the advanced training at the pediatric ward in The University Hospital for two to eight months.

(4) Lectures & Courses

Primary care of pediatrics covers wide spectrum of health care and clinical problems in children, and all pediatricians should be well trained in those subjects. Further, Medical and Dental University is one of the top ranked national medical university in Japan, and achieving cutting edge research is another social responsibility. For students, we provide educational programs to learn primary pediatric care, management of the diseases in every organ during neonatal period childhood, and basic science. For residents, our educational program is mainly focused on producing physician scientists who possess the skills of pediatrician for primary care, of physician specialist and of basic researcher.

(5) Clinical Services & Other Works

● Hematology/Oncology/Immunology Group

Treating children with primary immunodeficiency, hematological malignancies, hematological disorders, and malignant solid tumors.

Collaboration with other professional facilities including St. Luke’s International Hospital and Juntendo University Hospital. Joint clinical conference and trainee exchange program are regularly held in the collaborating system.

Medical care

By collaborating with national co-operative clinical research group, such as the Tokyo Children’s Cancer Study Group (TCCSG) and Japanese Children’s Cancer Study Group (JCCG), we offer our patients opportunities to participate in the latest clinical trials, contributing to establishment of both standard and novel therapies for childhood cancers and other non-malignant diseases.

In 2017, we performed HCT for 13, and 10 cases were for PID patients. Our experience of HCT exceeds 193

cases including more than 92 cases with primary immunodeficiency diseases, so far.

Clinical trials

Three doctor-initiated clinical trials led by pediatric department of Tokyo Medical and Dental University are on going.

"Phase I Clinical Study of Oral Olaparib in Pediatric Patients with Refractory Solid Tumors "

" Multi-virus (Cytomegalovirus, EB virus, Adenovirus, BK virus, and HHV-6) specific Cytotoxic T-Lymphocytes from HLA-haploidentical or more HLA-matched relative donor to persistent viral infection after hematopoietic cell transplantation (multi-center, prospective phase I/II study) "

" Clinical Phase II Study of hematopoietic stem cell transplantation for ataxia telangiectasia and related diseases " is carried out.

● Cardiology Group

We provide medical care in a wide range of pediatric cardiovascular diseases. Especially, our department is one of the major hospitals providing medical care of pediatric pulmonary hypertension.

In 2017, the number of inpatients was 127 (CHD: 57, acquired heart diseases:14, cardiac arrhythmias: 14, Kawasaki diseases (KD): 21)

Cardiac catheterizations were performed in 64 patients

Cardiac surgery was performed in 13 CHD patients (8 VSDs, 4 ASDs, 1 cTGA, 1 PAPVR, and one PDA)

● Neurology Group

We provide medical care in a wide range of pediatric neurologic diseases.

In particular, collaborating with the department of neurosurgery, we run an epilepsy center, providing advanced medical care for pediatric patients with intractable epilepsy.

The medical services in our department are long-term video EEG monitoring, high magnetic field MRI/PET, ACTH therapy, ketogenic diet, vagus nerve stimulation and surgical operation, such as focal brain resection and callosotomy.

● Endocrinology Group

We provide highly specific diagnostic approach and therapy in a wide range of pediatric endocrine disorders.

Among many pediatric endocrine disorders, we are directing our effort at the disorders of adrenal gland and sex development (DSD), and diabetes mellitus. We are looking at establishing the clinical center for those patients with pediatric-urologist and other co-medical staffs.

● Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with various kidney diseases. We perform kidney biopsy (30/year) and imaging examination.

We performed peritoneal dialysis for low-body-weight children and provided acute hemodialysis for children who developed acute kidney injury and for children with collagen diseases.

● Neonatology group

Our institute is registered on a board of Perinatal Cooperation Hospital in Tokyo running a transferring system of newborns who require neonatal care. Currently we accept newborn patients from the whole area in Tokyo, contributing the emergency network system for neonatal care in Tokyo.

We are treating low birth weight (> 1500g) and premature (> 28w) neonates.

● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in affiliated hospitals of our university, where not only the standard medical services following clinical guidelines for allergic diseases are provided, but also highly advanced treatment such as oral immunotherapy for food allergy as well.

(6) Clinical Performances

● Hematology-Oncology/ Immunology Group

Hematology-Oncology/ Immunology Group provides diagnosis, treatment and pathological analysis of hematological malignancies and primary immunodeficiency diseases. We perform hematopoietic stem cell transplan-

tation for refractory diseases. Especially, we treat the largest number of primary immunodeficiency disease patients in Japan. We participate in multi-center cooperative clinical research to establish both standard and novel therapies for childhood cancers, and also participate in industry-based clinical trials for drug, such as anticancer drug, approval.

● Cardiology Group

Cardiology group perform diagnosis, evaluation of treatment or decision of treatment strategy for PH patients. We positively treat by up-front combination therapy (uCT) with three kinds of disease targeted drugs and continuous venous infusion of epoprostenol. Worthy of special mention, surgical operation in children with congenital heart diseases was restarted after about 30 years blank.

● Neurology Group

Neurology group provide highly specialized diagnostic approach and medical care for neurological disorders such as intractable epilepsy, cerebellar ataxia, involuntary movement, immune-mediated neurological disease, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease and neuromuscular disorder.

● Endocrinology Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat many CAH (21-OHD) patients and performed couples of clinical studies. We also focus on disorder of sex development (DSD) and long-term follow-up for childhood cancer survivors (CSS). We are managing a Type 1 DM patients' association (Wakamatsu-kai) and organize the summer camp every year.

● Nephrology Group

We treat various pediatric kidney diseases, such as congenital nephrotic syndrome, refractory nephrotic syndrome, IgA nephropathy, etc. Kidney biopsy is performed to more than 40 patients. We provide acute hemodialysis treatment and peritoneal dialysis for low-body-weight patients (under 10kg) in cooperation with department of blood purification.

● Collagen/Rheumatoid disease group

Clinically, our target is not only pediatric collagen and rheumatic disease, but also inflammatory diseases which require biopharmaceutical medicine, such as periodic fever unknown origin, and repeated arthritis affecting multiple joints. Further, for developing a therapeutic approach, we are planning to register international clinical trials of a novel biopharmaceutical medicine, such as belimumab for pediatric SLE.

● Neonatology Group

Our NICU (Neonatal Intensive Care Unit) provides intensive care for preterm infants and critically ill newborns. As a designated Perinatal Cooperation Hospital in Tokyo, we accept newborn patients from various areas in Tokyo by collaborating with comprehensive reproductive medicine.

● Allergy Group

We focus on clinical care of severe and complicated allergic diseases such as food allergy-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, food protein-induced enterocolitis syndrome and oral allergy syndrome induced by cross-reactivity between food, inhalant and contact allergens. We extensively perform food challenge tests not only for correct diagnosis of food allergy but for preparation of oral immunotherapy in cooperation with the affiliated hospitals.

(7) Publications

[Original Articles]

1. Maki Igarashi, Kei Takasawa, Akiko Hakoda, Junko Kanno, Shuji Takada, Mami Miyado, Takashi Baba, Ken-Ichirou Morohashi, Toshihiro Tajima, Kenichiro Hata, Kazuhiko Nakabayashi, Yoichi Matsubara, Ryohei Sekido, Tsutomu Ogata, Kenichi Kashimada, Maki Fukami. Identical NR5A1 Missense Mutations in Two Unrelated 46,XX Individuals with Testicular Tissues. *Hum. Mutat.*. 2017.01; 38(1); 39-42
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8. Kaori Hisa, Masakatsu D Yanagimachi, Takuya Naruto, Takako Miyamae, Masako Kikuchi, Rhoki Hara, Tomoyuki Imagawa, Shumpei Yokota, Masaaki Mori. PADI4 and the HLA-DRB1 shared epitope in juvenile idiopathic arthritis. *PLoS ONE.* 2017.02; 12(2); e0171961
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4. Cell and Gene Therapy for Hematological Disorders. The 8th JSH International Symposium 2017 2017.05.01 Miyazaki, Japan
5. Masatoshi Takagi. Primary immunodeficiency and leukemia/lymphoma. 28th Annual Meeting of the International BFM-Study Group 2017.05.10 Jerusalem, Israel
6. Kuniko Kohyama, Ayuko Igarashi, Tomonori Suzuki, Taiki Shima, Hiroshi Sakuma.. The rapid and quantitative anti-MOG autoantibody assay using flow cytometry.. 14th Asian and Oceanian Congress of Child Neurology 2017.05.11 Fukuoka, Japan
7. Tomonori Suzuki, Kuniko Kohyama, Masaharu Hayashi, Hiroshi Sakuma.. Clinical features and cerebrospinal fluid cytokine/chemokine profiles of anti-NMDAR encephalitis in children.. 14th Asian and Oceanian Congress of Child Neurology 2017.05.11 Fukuoka, Japan
8. Yuji Sugawara, Hisako Ishiwata, Ayako Kashimada, Koji Takahashi, Kei Murayama, Mitsuhiro Kato, Hiroto Saito, Mitsuko Nakashima, Naomichi Matsumoto, Tomohiro Morio.. MRI findings in infantile fulminant SSADH deficiency. . 14th Asian and Oceanian Congress of Child Neurology 2017.05.11 Fukuoka, Japan
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11. Doi S. Prostacyclin Treatment. World Congress of Pediatric Cardiology and Cardiac Surgery 2017.07.17 Barcelona Spain
12. Doi S. Evaluation of the child with PAH. World Congress of Pediatric Cardiology & Cardiac Surgery 2017 2017.07.17 Barcelona Spain
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31. A 7-year-old girl who maintain complete remission after multiple hematopoietic cell transplantation for frequent relapse of infant leukemia. 2017.11.11
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Rheumatology

Professor	Hitoshi KOHSAKA
Professor emeritus	Nobuyuki MIYASAKA
Professor	Masaaki MORI (1) Tetsuo KUBOTA (2) Kazuki TAKADA (3) Ryuji KOIKE (2)
Junior Associate Professor	Hideyuki IWAI (5)
Assistant Professor	Fumitaka MIZOGUCHI, Tetsuya SAITO, Naoki KIMURA, Hisanori HASEGAWA, Natsuka UMEZAWA, Waka YOKOYAMA, Fumio HIRANO (1), Shoko KASAI (4), Yoko YOSHIHASHI (3)
Visiting Lecturer	Nobuyuki MIYASAKA, Hiroyuki HAGIYAMA, Makoto SOEJIMA, Tatsuhiko SUGIHARA, Fumihiko SUZUKI, Akito TAKAMURA, Kaori IMAI, Reiko TSUBATA, Jyunko NISHIO,
Graduate Student	Hirokazu SASAKI, Akio YAMAMOTO, Tatsuhiko SHINOHARA, Yasuhiro TAGAWA, Mari Kamiya, Fumiaki KONDO, Seiji NODA, Taku HONDA
Resident Physician	Wakako KAWASAKI, Yuriko YAGYU, Nao TANAKA, Yoichi IMAI, Motohiko SATO, Seiya OBA
Office Administrator	Kaori KONNO, Shoko AIBA, Minako WATANABE, Tomoko TAKAHASHI (1)
Technical Staff	Hidemi KASAHARA, Kazuko YAMAZAKI

(1) Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
(3) Curricular Management Division, Institute of Education, (4) Clinical Research Center, (5) Faculty of Medicine

(1) Research

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

- 1) Investigation of mechanism and development of new therapeutics for the treatment of rheumatoid arthritis and dermato/polymyositis.
 - 2) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies.
- We collaborate with department of lifetime clinical immunology and pediatrics.

(2) Education

We have provided medical students and graduates with the opportunity to obtain the ability to identify important clinical problems and to solve them by clinical reasoning through their active participation into the diagnosis and management of various rheumatic diseases.

(3) Clinical Services & Other Works

We have provided care to many patients with diverse rheumatic diseases. We have aimed to practice evidence-based medicine and to provide care that is in accordance with the global standard. We have contributed to the development of potential new drugs and treatments through participation into industry- as well as investigator-initiated clinical trials for chemical and biological agents. We have also contributed to the refinement of the care of rheumatic disease patients through the conduct of various pharmacovigilance studies.

We cooperate with department of lifetime clinical immunology and pediatrics.

(4) Publications**[Original Articles]**

1. Utsunomiya M, Dobashi H, Odani T, Saito K, Yokogawa N, Nagasaka K, Takenaka K, Soejima M, Sugihara T, Hagiyaama H, Hirata S, Matsui K, Nonomura Y, Kondo M, Suzuki F, Tomita M, Kihara M, Yokoyama W, Hirano F, Yamazaki H, Sakai R, Nanki T, Koike R, Kohsaka H, Miyasaka N, Harigai M. . Optimal regimens of sulfamethoxazole-trimethoprim for chemoprophylaxis of Pneumocystis pneumonia in patients with systemic rheumatic diseases: results from a non-blinded, randomized controlled trial *Arthritis Res Ther.* 2017.01; 19(1); 7
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- structural outcomes in a real-world clinical setting under a treat-to-target strategy. *Mod Rheumatol.* 2017.09; 27(5); 811-819
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 15. Matteo Bottai, Anna Tjärnlund, Giola Santoni, Victoria P Werth, Clarissa Pilkington, Marianne de Visser, Lars Alfredsson, Anthony A Amato, Richard J Barohn, Matthew H Liang, Jasvinder A Singh, Rohit Aggarwal, Snjolaug Arnardottir, Hector Chinoy, Robert G Cooper, Katalin Danko, Mazen M Dimachkie, Brian M Feldman, Ignacio García-De La Torre, Patrick Gordon, Taichi Hayashi, James D Katz, Hitoshi Kohsaka, Peter A Lachenbruch, Bianca A Lang, Yuhui Li, Chester V Oddis, Marzena Olesinka, Ann M Reed, Lidia Rutkowska-Sak, Helga Sanner, Albert Selva-O'Callaghan, Yeong Wook Song, Jiri Vencovsky, Steven R Ytterberg, Frederick W Miller, Lisa G Rider, Ingrid E Lundberg, . EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups: a methodology report. *RMD Open.* 2017.11; 3(2); e000507
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[Misc]

1. CD4+ and CD8+ CD28null T cells are cytotoxic to autologous muscle cells in patients with polymyositis RHEUMATOLOGY. 2017.07; 58(1); 109-116

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3. Natsuka Umezawa, Kimito Kawahata, Naoki Kimura, Yoko Yoshihashi-Nakazato, Hitoshi Kohsaka. Interleukin-23 as a therapeutic target for inflammatory myopathy.. 7th East Asian Group of Rheumatology 2017.06.07 Tokyo
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5. Natsuka Umezawa, Kimito Kawahata, Naoki Kimura, Yoko Yoshihashi- Nakazato, Hitoshi Kohsaka. Interleukin-23 as a therapeutic target for inflammatory myopathy. 7th East Asian Group of Rheumatology 2017.07.07
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7. Yoshiya Tanaka , Hideto Kameda, Kazuyoshi Saito, Yuko Kaneko, Eiichi Tanaka, Shinsuke Yasuda, Naoto Tamura, Keishi Fujio, Takao Fujii, Toshihisa Kojima, Tatsuhiko Anzai, Chikuma Hamada, Yoshihisa Fujino, Shinya Matsuda, Hitoshi Kohsaka. Improvement in Overall Work Productivity among Biologic-naïve Patients with Rheumatoid Arthritis Treated with Tocilizumab Subcutaneous Injection: A Prospective, Real World, Observational Study in Japan.. The 2017 ACR/ARHP Annual Meeting 2017.11.03 SanDiego
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11. Hitoshi Kohsaka. Treatment consensus of polymyositis and dermatomyositis in Japan. IMACS and JDM Working Group Annual Meeting 2017.11.05

Dermatology

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Associate Professor: Takeshi NAMIKI

Junior Associate Professor: Tsukasa UGAJIN, Makiko NISHIDA

Project Junior Associate Professor: Kaoru TAKAYAMA

Assistant Professor: Shown TOKORO, Takashi HASHIMOTO,

Minako INAZAWA, Yuki OHTSUKI

Senior Resident: Shinji OGAWA, Keiko INUI, Michiko NAKAMURA, Miho SHIMOKATA

Resident: Takuya WAKASA, Yutaro IWAMOTO

Doctoral Student: Rie YU, Sayaka KIKUCHI, Minako INAZAWA, Aiko FURUI, Kohei NOJIMA, Kohei KATO, Sally ESHIBA, Rumi SUZUKI, Takahiro ISHIKAWA, Al-Busani Hind Abdullah Ahmed,

Yutaro HANDA, Hazuki IJIMA

Technical Assistant: Chiyako MIYAGISHI, Ayumi FUJIKAWA

Staff Assistant: Masae SAKATA, Mayuko HAYASHI, Yu KAWAMURA

(1) Outline

Dermatology is a department of medical science which educates students to make a diagnosis and treatment for skin diseases. Main objective of Dermatology in the graduate course is to provide students opportunity to study advanced Immunodermatology, physiology, pathology and allergology, and also to study making diagnosis of skin diseases and operation techniques. Students are also taught on skin oncology (melanoma, angiosarcoma) and its related laboratory technology depending on their research project.

(2) Research

- 1) Mechanisms of contact hypersensitivity
- 2) Pathological etiology of atopic dermatitis
- 3) Mechanisms of eosinophil recruitment to the skin
- 4) Roles of basophils in human skin diseases
- 5) Functional roles of PGD₂ and its receptors in allergic inflammation
- 6) Therapeutic approach for skin diseases by stable form of galectin-9
- 7) Analysis of pathological mechanisms of hyperhidrosis
- 8) Investigation of mediators for itch
- 9) Pathological etiology of chronic prurigo
- 10) Therapeutic approach for angiosarcoma with HVJ-E.
- 11) To establish the in vitro diseases model of dermatological disorders using human induced pluripotent stem cell
- 12) Murine food allergy model with transcutaneous sensitization

(3) Clinical Performances

Dermatology clinic provides an advanced treatment for skin diseases; skin tumors, infectious diseases, skin allergy, collagen diseases and psoriasis. Recently, we established the gene therapies (STAT6 decoy ODN) for

severe atopic dermatitis in the clinic.

(4) Publications

[Original Articles]

1. Sone Y, Namiki T, Nojima K, Hashimoto T, Hanafusa T, Tokoro S, Miura K, Yokozeki H. . Kikuchi's disease: cutaneous involvement and dermoscopic features. *Eur J Dermatol.* 2017.01;
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5. Namiki T, Nojima K, Tokoro S, Hanafusa T, Yokozeki H. Microcystic adnexal carcinoma (syringomatous carcinoma and sclerosing sweat duct carcinoma) as an extensive sclerotic erythematous plaque with telangiectasia over the face. *Br J Dermatol.* 2017.06;
6. Ueno M, Namiki T, Hanafusa T, Miura K, Yokozeki H.. IgA-mediated leukaemic vasculitis in a patient with rapid progression of myelodysplastic syndrome to acute myeloid leukaemia. *Eur J Dermatol.* . 2017.06;
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14. Furuya A, Namiki T, Takayama K, Amano M, Ueno M, Nojima K, Hanafusa T, Miura K, Yokozeki H.. Dermales Melanom in großem kongenitalen, plaqueartigen blauen Naevus. *J Dtsch Dermatol Ges.* . 2017.08;
15. Nojima K, Namiki T, Hanafusa T, Miura K, Yokozeki H.. Pigmented squamous cell carcinoma of the right thumb: longitudinal melanonychia and dermoscopic features. *Eur J Dermatol.* . 2017.10;
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18. Komura Y, Kogure T, Kawahara K, Yokozeki H.. Economic assessment of actual prescription of drugs for treatment of atopic dermatitis: Differences between dermatology and pediatrics in large-scale receipt data. *J Dermatol.* 2017.11;
19. Namiki T, Hashimoto T, Nishida M, Uga, jin T, Miura K, Yokozeki H.. A case of peripheral T-cell lymphoma, not otherwise specified, with rapid progression to erythroderma. *Eur J Dermatol.* 2017.11;
20. Kato K, Namiki T, Nojima K, Hashimoto T, Ueno M, Hanafusa T, Miura K, Yokozeki H. . Case of subungual tumoral melanosis: The detection of melanoma cells and dermoscopic features. *J Dermatol.* 2017.12;
21. Omigawa C, Hashimoto T, Hanafusa T, Namiki T, Igawa K, Yokozeki H.. Modified method for applying Mohs' paste. *J Dermatol.* 2017.12;
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[Conference Activities & Talks]

1. Takashi Hashimoto, Takahiro Satoh, and Hiroo Yokozeki. Basophils release amphiregulin and may contribute to murine models of prurigo reaction and MC903-induced atopic dermatitis-like skin inflammation.. 2017 Society for investigative dermatology Annual meeting 2017.04.26 Oregon
2. Nojima K, Hayashi M, Funazumi M, Ishikawa M, Kaneko Y, Kawaguchi M, Suzuki T, Tanemura A, Katayama I, Mori T, Yamazaki N, Yokozeki H, Hearing VJ, Namiki T. NUA2 is over-expressed and DNA copy number is increased in acral melanoma: its significance on the survival of patients.. 47TH Annual Meeting of the European Society for Dermatologic Research 2017.09.27 SALZBURG
3. Uga, jin T, Shibama S, Yamaguchi T, Yokozeki H. Bilirubin oxidation is associated with the disease severity of atopic dermatitis in adults.. 47TH Annual Meeting of the European Society for Dermatologic Research 2017.09.27 SALZBURG
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NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Associate Professor	Satoshi FUJII
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Koji OKAMOTO
Visiting Lecturer	Takashi KOHNO
Visiting Lecturer	Michihiro MUTOH
Graduate Students	D3 Kasumi OTSUBO, Yuki YAMAMOTO
	D1 Tomoko WATANABE
	M2 Marina HENMI, Hidenobu SUZUKI, Taichi IJIMA
	M1 Yamato OGIWARA, Maiko TAKAHASHI, Naoki TSUKIMATA, Miyu YOSHIDA

(1) Research

1. Carcinogenesis and molecular mechanism
2. Functions of cancer-associated genes and their alterations
3. Genomic, epigenomic and proteomic analysis of cancer and personalized medicine
4. Tumor microenvironment
5. Cancer stem cells/non-coding RNA/signaling pathway
6. Molecular target/drug delivery/diagnosis and therapy

(2) Education

To learn knowledge and skill for cancer research, students attend lectures and seminars, and attend and/or practice research meeting, journal club, scientific meeting, etc. These practices will enable students to develop an ability to conduct their studies as an

independent cancer researcher in the future. To obtain good skills to carry out experiments that are required for cancer research, students belong to one of our research groups, and conduct their own studies under the guidance of the instructor and/or staff. Students perform various experiments involved in genetics, gene technology, biochemistry, cellular biology, molecular biology, physiology, experimental animal, pathology, genomic/epigenomic/proteomic analysis, imaging, next generation sequencing, etc.

(3) Publications

[Original Articles]

1. Tsuneki M, Kinjo T, Mori T, Yoshida A, Kuyama K, Ohira A, Miyagi T, Takahashi K, Kawai A, Chuman H, Yamazaki N, Masuzawa M, Arakawa H. Survivin: A novel marker and potential therapeutic target for human angiosarcoma. *Cancer Sci.* 108: 2295-2305, 2017.
2. Ishibashi M, Neri S, Hashimoto H, Miyashita T, Yoshida T, Nakamura Y, Udagawa H, Kirita K, Matsumoto S, Umemura S, Yoh K, Niho S, Tsuboi M, Masutomi K, Goto K, Ochiai A, Ishii G. CD200-positive cancer associated fibroblasts augment the sensitivity of Epidermal Growth Factor Receptor mutation-positive lung adenocarcinomas to EGFR Tyrosine kinase inhibitors. *Sci Rep.* 7: 46662, 2017.
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4. Yoshioka Y, Suzuki T, Matsuo Y, Tsurita G, Watanabe T, Dohmae N, Nakamura Y, Hamamoto R. Protein lysine methyltransferase SMYD3 is involved in tumorigenesis through regulation of HER2 homodimerization. *Cancer Med.* 6: 1665-1672, 2017.

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7. Higaki E, Yanagi S, Gotohda N, Kinoshita T, Kuwata T, Nagino M, Ochiai A, Fujii S. Intraoperative peritoneal lavage cytology offers prognostic significance for gastric cancer patients with curative resection. *Intraoperative peritoneal lavage cytology offers prognostic significance for gastric cancer patients with curative resection.* *Cancer Sci.* 108: 978-986, 2017.
8. Fujii S, Yamashita S, Yamaguchi T, Takahashi M, Hozumi Y, Ushijima T, Mukai H. Pathological complete response of HER2-positive breast cancer to trastuzumab and chemotherapy can be predicted by HSD17B4 methylation. *Oncotarget.* 8: 19039-19048, 2017.
9. Dendo K, Yugawa T, Nakahara T, Ohno S I, Goshima N, Arakawa H, Kiyono T. Induction of non-apoptotic programmed cell death by oncogenic RAS in human epithelial cells and its suppression by MYC overexpression. *Carcinogenesis.* 39: 202-213, 2018.
10. Yamamoto Y, Nagasato M, Rin Y, Henmi M, Ishikawa Y, Yachida S, Ohki E, Hiraoka N, Tagawa M, Aoki K. Strong antitumor efficacy of a pancreatic tumor-targeting oncolytic adenovirus for neuroendocrine tumors. *Cancer Med.* 6: 2385-2397, 2017.
11. Nagasato M, Rin Y, Yamamoto Y, Henmi M, Hiraoka N, Chiwaki F, Matsusaki

K, Tagawa M, Sasaki H, Aoki K. A tumor-targeting adenovirus with high gene transduction efficiency for primary pancreatic cancer and ascites cells.

Anticancer Res. 37: 3599-3506, 2017.

12. Miyamoto S, Komiya M, Fujii G, Hamoya T, Nakanishi R, Fujimoto K, Tamura S, Kurokawa Y, Takahashi M, Ijichi T, Mutoh M. Preventive effects of heat-killed *Enterococcus faecalis* strain EC-12 on mouse intestinal tumor development. *Int J Mol Sci.* 18: 826, 2017.

[Reviews Articles]

1. Nakamura Y, Arakawa H. Discovery of Mieap-regulated mitochondrial quality control as a new function of tumor suppressor p53. *Cancer Sci.* 108: 809-17, 2017.
2. Yasunaga M, Manabe S, Tsuji A, Furuta M, Ogata K, Koga Y, Saga T, Matsumura Y. Development of antibody–drug conjugates using DDS and molecular imaging. *Bioengineering.* 4: 78, 2017.
3. Yamamoto Y, Nagasato M, Yoshida T, Aoki K. Recent advances in genetic modification of adenovirus vectors for cancer treatment. *Cancer Sci.* 108: 831-837, 2017.

[Conference Activities & Talks]

1. Nakamura Y, Tsuneki M, Yamamoto M, Arakawa H. Mieap, the mitochondria-eating protein induces cell death by eating unhealthy mitochondria. AACR Annual Meeting 2017, (Washington, D.C, USA), April, 2017.
2. Maida Y*, Sakurai M*, Shiromoto Y*, Yasukawa M, Ghilotti M, Ariyoshi K, Nishikura K, Masutomi K. (*Equal contribution) A novel interaction of TERT with RNA editing. Cold Spring Harbor Laboratory Meeting “Telomere and Telomerase” Cold Spring Harbor, (NY, USA) May, 2017.
3. Maida Y*, Sakurai M*, Shiromoto Y*, Yasukawa M, Ghilotti M, Ariyoshi K,

- Masutomi K, Nishikura K. (*Equal contribution) RNA-mediated interaction between ADAR and TERT. 2017 Gordon Research Conference on RNA editing Ventura,(CA, USA), March, 2017.
4. Vassiliki Saloura, Theodore Vougiouklakis, Makda Zewde, Xiaolan Deng, Kazuma Kiyotani, Jae-Hyun Park, Yo Matsuo, Mark Lingen, Naoshi Dohmae, Takehiro Suzuki, Ryuji Hamamoto and Yusuke Nakamura. WHSC1L1-mediated EGFR mono-methylation enhances the cytoplasmic and nuclear oncogenic activity of EGFR in head and neck cancer, AACR Annual Meeting 2017, (Washington, D.C, USA), April, 2017.
 5. Masahiro Yasunaga, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikazu Koga and Yasuhiro Matsumura. Visualisation of EPR effect and active targeting by using microscopic mass spectrometry. AACR Annual Meeting, (Washington, DC, USA), April, 2017.
 6. Chie Kudo-Saito, Yamato Ogiwara, Kazunori Aoki. Blocking FSTL1 ameliorates immunity against osteosarcoma. AACR Annual Meeting 2017, (Washington, DC, USA), April, 2017.

Human Pathology

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Laboratory Technician: Asuka FURUKAWA

Technical Assistant: Yuki ISHIGE

Graduate Students:

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Tomohisa OGAWA, Tomohito AYABE, Nobuyasu AWANO,
Tomoya KAKEGAWA, Yuji SEKINE, Kurara YAMAMOTO,
Masahiro YAMAMOTO

(MD-PhD course) Yuriko WADA

(Master's Program) Madoka Yoshizaki

Reserch Student: Yuka HIROTA

Secretary: Miho IWAMITSU, Mayako TOKUNAGA

(1) Outline

Pathology in a medical department used to be the general study field about human disease. Later, Microbiology and Parasitology had been separated from the field of Pathology. Lately, interdisciplinary of traditional study field had been advanced and new specific academic disciplines are developed. Pathology is currently under the same trend. Basic divisions such as Experimental and Cell Biological pathology are becoming independent from the clinicopathological field. Thus, Human Pathology has become the main category of pathology.

The principles of Human Pathology are to educate clinical pathologists with accurate pathological diagnosis skills of human disease, to research theses that are directly related to human disease, and to educate pathological researchers with ability to perform such research.

(2) Research

- 1) Endogenous infection (diseases caused by indigenous microorganisms in susceptible hosts)
- 2) Cancer research (histopathology, carcinogenesis, prognostic factors, and so on)

(3) Education

In the course, they usually spend the first two years for anatomical pathology training, searching for their own research theme and another two years for researches and thesis-writing.

(4) Lectures & Courses

Department of Human Pathology provides a graduate course for future pathologists to train the skills and knowledge of anatomical pathology and develop the abilities for medical researches. Graduate students are

educated to associate their researches with problems in diagnosis and treatment of diseases and etiologies of the diseases of unknown causes.

(5) Clinical Performances

After the Meiji Era, the department of Human Pathology in medical faculty belonged under the basic medical sciences; however, Pathology in the existing hospitals is essentially the clinical medicine. Diagnosis of patients in each clinical department is done by taking the biopsy of diseased tissues or collecting the cell samples by either endoscope or surgery. Then, the lesions are analyzed with the microscope, and pathological diagnosis is reported to the clinical departments. The samples of organs and tissues taken from the surgery are used to study the spread of the lesion and its characteristics, and also to examine the adequacy of surgery. It is also used to determine future treatment policy. During the course of patients' treatments, sample tissues are taken periodically and are analyzed pathologically to see therapeutic effect. If a patient has unfortunately joined the majority, morbid anatomy is done by the pathologists along with the patient's attending physician. They study the resulting effects of laboratory findings and choice of treatment, and improve the future diagnosis and treatments. The department of Human Pathology and Surgical Pathology technically work as one although they are separated in this university's organizational structure. Human Pathology does not directly work with the patients; however, it is involved directly with the diagnosis as well as the treatments. Strong cooperation between clinicians and pathologists is essential for the best practice, and is required for the university hospital as an "advanced treatment hospital." Therefore, doctors of Human Pathology study, research and practice pathology to be the great pathologists so-called the "doctor of doctors.

(6) Publications

[Original Articles]

1. Takahiro Ogishima, Kaoru Tamura, Daisuke Kobayashi, Motoki Inaji, Shihori Hayashi, Reina Tamura, Tadashi Nariai, Kenji Ishii, Taketoshi Maehara. ATRX status correlates with 11 C-methionine uptake in WHO grade II and III gliomas with IDH1 mutations. *Brain Tumor Pathol.* 2017.01; 34(1); 20-27
2. Toshiyuki Yamamoto, Akiko Nishibu, Yoshinobu Eishi. Transepidermal elimination of sarcoidal granuloma in the lesional skin of psoriasiform sarcoidosis. *J. Dermatol.* 2017.01; 44(1); 100-101
3. Tomoya Kakegawa, Yuan Bae, Takashi Ito, Keisuke Uchida, Masaki Sekine, Yutaka Nakajima, Asuka Furukawa, Yoshimi Suzuki, Jiro Kumagai, Takumi Akashi, Yoshinobu Eishi. Frequency of Propionibacterium acnes Infection in Prostate Glands with Negative Biopsy Results Is an Independent Risk Factor for Prostate Cancer in Patients with Increased Serum PSA Titers. *PLoS ONE.* 2017.01; 12(1); e0169984
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5. Jessica L Werner, Sylvia G Escolero, Jeff T Hewlett, Tim N Mak, Brian P Williams, Yoshinobu Eishi, Gabriel Núñez. Induction of Pulmonary Granuloma Formation by Propionibacterium acnes Is Regulated by MyD88 and Nox2. *Am. J. Respir. Cell Mol. Biol.* 2017.01; 56(1); 121-130
6. Kazumasa Soga, Kinya Ishikawa, Tokuro Furuya, Tadatsune Iida, Tetsuo Yamada, Noboru Ando, Kiyobumi Ota, Hiromi Kanno-Okada, Shinya Tanaka, Masayuki Shintaku, Yoshinobu Eishi, Hidehiro Mizusawa, Takanori Yokota. Gene dosage effect in spinocerebellar ataxia type 6 homozygotes: A clinical and neuropathological study. *J. Neurol. Sci.* 2017.02; 373; 321-328
7. Yamanishi, E., Hasegawa, K., Fujita, K., Ichinose, S., Yagishita, S., Murata, M., Tagawa, K., Akashi, T., Eishi, Y., Okazawa, H.. A novel form of necrosis, TRIAD, occurs in human Huntington's disease. *Acta Neuropathologica Communications.* 2017.03; 5(19);
8. Yumi Sakakibara, Yoshimi Suzuki, Toshihide Fujie, Takumi Akashi, Tadatsune Iida, Yasunari Miyazaki, Yoshinobu Eishi, Naohiko Inase. Radiopathological Features and Identification of Mycobacterial Infections in Granulomatous Nodules Resected from the Lung. *Respiration.* 2017.03; 93(4); 264-270

9. Tsuyoshi Shirai, Haruhiko Furusawa, Asuka Furukawa, Yuki Ishige, Keisuke Uchida, Yasunari Miyazaki, Yoshinobu Eishi, Naohiko Inase. Protein antigen of bird-related hypersensitivity pneumonitis in pigeon serum and dropping. *Respir. Res.* 2017.04; 18(1); 65
10. Xiaoshu Dong, Kaoru Tamura, Daisuke Kobayashi, Noboru Ando, Kazutaka Sumita, Taketoshi Maehara. LAPTM4B-35 is a novel prognostic factor for glioblastoma. *J. Neurooncol.* 2017.04; 132(2); 295-303
11. Yamada I, Yoshino N, Hikishima K, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using 3-T high-spatial-resolution quantitative T2 mapping and its correlation with histopathologic findings. *Magn Reson Imaging.* 2017.05; 38(1); 174-181
12. Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Shuji Hibiya, Nobukatsu Horita, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Satoshi Motoya, Yoshiaki Takeuchi, Reiko Kunisaki, Ken Fukunaga, Shiro Nakamura, Naoki Yoshimura, Masakazu Takazoe, Bunei Iizuka, Yasuo Suzuki, Masakazu Nagahori, Mamoru Watanabe. Caudal type homeobox 2 expression induced by leukocytapheresis might be associated with mucosal healing in ulcerative colitis. *J. Gastroenterol. Hepatol.* 2017.05; 32(5); 1032-1039
13. Nobuyasu Awano, Minoru Inomata, Soichiro Ikushima, Daisuke Yamada, Masatoshi Hotta, Shunji Tsukuda, Toshio Kumasaka, Tamiko Takemura, Yoshinobu Eishi. Histological analysis of vasculopathy associated with pulmonary hypertension in combined pulmonary fibrosis and emphysema: comparison with idiopathic pulmonary fibrosis or emphysema alone. *Histopathology.* 2017.05; 70(6); 896-905
14. Atsushi Oba, Atsushi Kudo, Keiichi Akahoshi, Mitsuhiro Kishino, Takumi Akashi, Eriko Katsuta, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Yoshinobu Eishi, Ukihide Tateishi, Minoru Tanabe. A simple morphological classification to estimate the malignant potential of pancreatic neuroendocrine tumors. *J. Gastroenterol.* 2017.05;
15. Megumu Enjoji, Katsuya Sanada, Ryota Seki, Takashi Ito, Masato Maeda. Adrenal Rest Tumor of the Liver Preoperatively Diagnosed as Hepatocellular Carcinoma. *Case Rep Surg.* 2017.06; 2017; 8231943
16. Shohei Tomii, Takumi Akashi, Noboru Ando, Tomoki Tamura, Akira Sakurai, Asami Terada, Asuka Furukawa, Yoshimi Suzuki, Kou Kayamori, Kei Sakamoto, Hironori Ishibashi, Yoshinobu Eishi. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology.* 2017.07; 84(4); 171-183
17. Naoya Asakawa, Keisuke Uchida, Mamoru Sakakibara, Kazunori Omote, Keiji Noguchi, Yusuke Tokuda, Kiwamu Kamiya, Kanako C Hatanaka, Yoshihiro Matsuno, Shiro Yamada, Kyoko Asakawa, Yuichiro Fukasawa, Toshiyuki Nagai, Toshihisa Anzai, Yoshihiko Ikeda, Hatsue Ishibashi-Ueda, Masanori Hirota, Makoto Orii, Takashi Akasaka, Kenta Uto, Yasushige Shingu, Yoshiro Matsui, Shin-Ichiro Morimoto, Hiroyuki Tsutsui, Yoshinobu Eishi. Immunohistochemical identification of Propionibacterium acnes in granuloma and inflammatory cells of myocardial tissues obtained from cardiac sarcoidosis patients. *PLoS ONE.* 2017.07; 12(7); e0179980
18. Guillaume Ghislain Aubin, Grâce Ada Da Silva, Yoshinobu Eishi, Cédric Jacqueline, Frédéric Altare, Stéphane Corvec, Karim Asehnoune. Immune discrepancies during in vitro granuloma formation in response to Cutibacterium (formerly Propionibacterium) acnes infection. *Anaerobe.* 2017.08; 48; 172-176
19. Jiro Akimoto, Kenta Nagai, Daisuke Ogasawara, Yujiro Tanaka, Hitoshi Izawa, Michihiro Kohno, Keisuke Uchida, Yoshinobu Eishi. Solitary tentorial sarcoid granuloma associated with Propionibacterium acnes infection: case report. *J. Neurosurg.* 2017.09; 127(3); 687-690
20. Natsu Yamaguchi, Yoshimi Suzuki, M H Mahbub, Hidekazu Takahashi, Ryosuke Hase, Yasutaka Ishimaru, Hiroshi Sunagawa, Rie Watanabe, Yoshinobu Eishi, Tsuyoshi Tanabe. The different roles of innate immune receptors in inflammation and carcinogenesis between races. *Environ Health Prev Med.* 2017.10; 22(1); 70
21. Kenji Nagata, Yoshinobu Eishi, Keisuke Uchida, Kazuhito Yoneda, Hiroki Hatanaka, Toru Yasuhara, Maho Nagata, Chie Sotozono, Shigeru Kinoshita. Immunohistochemical Detection of Propionibacterium acnes in the Retinal Granulomas in Patients with Ocular Sarcoidosis. *Sci Rep.* 2017.11; 7(1); 15226

22. Hiroshi Goto, Yoshihiko Usui, Akihiko Umazume, Keisuke Uchida, Yoshinobu Eishi. Propionibacterium acnes as a possible pathogen of granuloma in patients with ocular sarcoidosis. Br J Ophthalmol. 2017.11; 101(11); 1510-1513
23. Sakiko Itaya, Yasuhiro Ueda, Zen Kobayashi, Hiroyuki Tomimitsu, Daisuke Kobayashi, Shuzo Shintani. Bilateral Frontal Lobe Vasogenic Edema Resulting from Hypertrophic Pachymeningitis due to Granulomatosis with Polyangiitis. Intern. Med.. 2017.12; 56(24); 3353-3355
24. Haruo Homareda, Masahiro Otsu, Sachiko Yamamoto, Makoto Ushimaru, Sayaka Ito, Toshiyuki Fukutomi, Taeho Jo, Yoshinobu Eishi, Yukichi Hara. A possible mechanism for low affinity of silkworm Na⁺/K⁺-ATPase for K. J. Bioenerg. Biomembr.. 2017.12; 49(6); 463-472

[Conference Activities & Talks]

1. Yoshinobu EISHI. Etiology of sarcoidosis as an allergic endogenous infection caused by Propionibacterium acnes. Institution at the University Hospital of Essen 2017.07.19 Essen, Germany
2. Yoshinobu EISHI. Etiology of sarcoidosis as an allergic endogenous infection caused by Propionibacterium acnes. Institute of Pathology at the University of Freiburg 2017.07.20 Freiburg, Germany

Physiology and Cell Biology

Junior associate professor: Shingo Sato

Assistant professor: Hiroki Ochi

Assistant professor: Satoko Sunamura

(1) Outline

Recent progress in molecular biology and genetics advanced our understanding of molecular basis of physiological function and pathophysiological mechanisms of various diseases. Besides, signal transduction system using intercellular, intersystem, and inter-organ networks has been shown to be essential for whole-body homeostatic function. In our department, we are studying on the inter-organ regulatory networks of metabolism, especially between bone and the other organs.

(2) Research

1. Studies on the regulatory network of metabolism between bone and the other internal organs: It had been believed that bone is controlled by local environment through the action of hormones and cytokines, independently of the other organs. However, our discovery that leptin regulates bone formation through the central nervous system shed light on a new regulatory system of bone metabolism, i.e., neuronal control (Takeda S, *Cell*, 2002, Nature, 2005). In addition, we have also demonstrated that neuromedin U, an anorexigenic neuropeptide, regulates bone formation through the central nervous system (Sato S, *Nat Med*, 2007). Moreover, recent studies have revealed that FGF23 or osteocalcin, which is secreted by bone, regulates the metabolism of kidney or pancreas. Thus, bone is now considered as a major player for whole-body homeostasis, and forms a regulatory network of metabolism together with the other organs. We are now conducting further experiments to clarify a comprehensive network between bone and the other organs.

2. Studies on the regulation of bone metabolism by sensory nerves: We have recently revealed that sensory nerves inside bones have a crucial role in regulating bone mass, and that the penetration of sensory nerves into bones is necessary for normal bone development or fracture healing (Fukuda T, *Nature*, 2013). Based on these findings, we are now conducting further experiments to develop novel therapeutic approaches to osteoporosis.

3. Studies on the regulation of bone metabolism and bone metastasis by microRNA: microRNA (miRNA) is a small non-coding RNA molecule, and regulates various developmental and homeostatic events in vertebrates and invertebrates. Aberrant expression of miRNA has been implicated in numerous disease states, and miRNA-based therapies are under investigation. We have previously demonstrated the physiological role of miRNA in osteoblast differentiation (PNAS, 2009). We also investigated the role of miRNA in bone metastatic microenvironment and recently demonstrated that bone metastatic lesions could be regulated by miRNAs secreted by cancer cells (Sato S, Hashimoto K, *PNAS*, 2018). We are now conducting further experiments to identify novel miRNAs regulating bone metabolism or bone metastasis and to develop new diagnostic or therapeutic approaches.

4. Studies on the mechanical regulation of musculoskeletal system: In Japan, the number of patients with osteoporosis or sarcopenia have rapidly increased. Mechanical stress is known to be essential for the maintenance of bone volume or muscle strength. However, the mechanism of the mechanical regulation remains elusive. We are now elucidating the role of gravity on bone or muscle homeostasis as well as on neurovascular formation in

bone or muscle tissues by utilizing a tail suspension mouse model.

5. Studies on the mechanism in the development of bone and soft tissue sarcomas: Sarcomas are malignancies derived from mesenchymal tissues such as bone, muscle, fat, and cartilage. Molecular mechanisms in the occurrence and growth of sarcomas have yet to be elucidated. Even the cell of origin for most sarcomas still remains unclear. We have recently established a novel mouse model for osteosarcoma and also demonstrated that sarcomas could be derived from pericytes with mutations of crucial genes. Based on these findings, we are now conducting further experiments to elucidate the detailed mechanism of sarcoma development.

(3) Education

We give lectures and laboratory teachings about physiology to sophomore medical students. We also teach experimental techniques to undergraduate students to develop young basic scientists. PhD students are required to join our research team and learn various experimental techniques including molecular biology, cellular biology, and physiology.

(4) Lectures & Courses

All students are expected to understand the background of the research field and bring up relevant scientific questions to verify the hypothesis. They are also expected to develop their scientific thinking with effective questions and cultivate their abilities to analyze obtained results objectively, discuss them logically and scientifically, and present them effectively.

(5) Publications

[Original Articles]

1. A Sato, H Ochi, Y Harada, T Yogo, N Kanno, Y Hara. Bone morphogenetic protein 4 and bone morphogenetic protein receptor expression in the pituitary gland of adult dogs in healthy condition and with ACTH-secreting pituitary adenoma. *Domest. Anim. Endocrinol.*. 2017.01; 58; 126-133
2. Mukaihara K, Tanabe Y, Kubota D, Akaike K, Hayashi T, Mogushi K, Hosoya M, Sato S, Kobayashi E, Okubo T, Kohsaka S, Saito T, Kaneko K, Suehara Y.. Cabozantinib and dastinib exert anti-tumor activity in alveolar soft part sarcoma. *PLoS One.* . 2017.01; 12(9); e0185321
3. Daiei Takahashi, Takayasu Mori, Eisei Sohara, Miyako Tanaka, Motoko Chiga, Yuichi Inoue, Naohiro Nomura, Moko Zeniya, Hiroki Ochi, Shu Takeda, Takayoshi Suganami, Tatemitsu Rai, Shinichi Uchida. WNK4 is an Adipogenic Factor and Its Deletion Reduces Diet-Induced Obesity in Mice. *EBioMedicine.* 2017.04; 18; 118-127
4. Hirakawa H, Gatanaga H, Ochi H, Fukuda T, Sunamura S, Oka S, Takeda S, Sato S. Antiretroviral therapy containing HIV protease inhibitors enhances fracture risk by impairing osteoblast differentiation and bone quality *JOURNAL OF INFECTIOUS DISEASES* . 2017.05; 215(12); 1893-1897

[Misc]

1. Sato S. Mouse models for bone and soft tissue sarcoma *Bone Joint Nerve.* 2017.07; 7(3); 375-383
2. Hiroki Ochi, Paul Baldock, Shu Takeda. Central Neuronal Control of Bone Remodeling Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 9th Edition. 2017.09;

[Conference Activities & Talks]

1. Shingo Sato. The role of orthopaedic surgeons in the management of bone metastasis patients. The 45th Kyoto Orthopaedic Seminar 2017.03.07 Kyoto
2. Sato S. Reduction in the frequency of pathological fracture by medical and dental combined treatment system for bone metastasis. The 43rd Annual Meeting of the Japanese Society for Fracture Repair 2017.07.08 Fukushima

3. Sato S. The osteoblastic phenotype of bone metastasis can be induced by microRNA secreted from cancer cells. The 50th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2017.07.14 Tokyo
4. Sato S. The effect of early treatment for bone metastasis by medical and dental combined multidisciplinary treatment approach. The 50th Annual Musculoskeletal Tumor Meeting of the Japanese Orthopaedic Association 2017.07.14 Tokyo
5. Kyoko Hashimoto, Satoko Sunamura, Hiroki Ochi, Toru Fukuda, Atsushi Okawa, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer cell-derived microRNA induces osteoblastic phenotype in bone metastasis microenvironment. 14th Meeting of Bone Biology Forum 2017.08.18 Cross wave Makuhari, Chiba
6. Kyoko Hashimoto, Satoko Sunamura, Hiroki Ochi, Toru Fukuda, Atsushi Okawa, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer cell-derived microRNA induces osteoblastic phenotype in bone metastasis microenvironment. American Society of Bone and Mineral Research 2017 Annual Meeting 2017.09.08 Denver, USA
7. Sato S. The effect of early treatment for bone metastasis by medical and dental combined multidisciplinary treatment approach. The 66th Annual Meeting of the Eastern Japan Association of Orthopaedics and Traumatology 2017.09.15 Tokyo
8. Kyoko Hashimoto, Hiroki Ochi, Satoko Sunamura, Toru Fukuda, Kenta Yao, Yo Mabuchi, Atsushi Okawa, Chihiro Akazawa, Mitsuru Futakuchi, Shu Takeda, Shingo Sato. Cancer-secreted hsa-miR-940 induces osteoblastic phenotype in the bone metastatic microenvironment via targeting ARHGAP1 and FAM134A. ERATO/AMED-CREST/PRESTO Joint International Symposium 2017.12.04 International Institute for Advanced Studies, Kyoto

Molecular Cellular Cardiology

Professor	Tetsushi Furukawa
Assistant professor	Kensuke Ihara
Post-doc (RPD)	Masami Kodama
Post-doc (PD)	Yoshitake Higashijima
Post-doc	Masahiro Yamazoe
D2	Xiaoki Yang
D2(Department of Pediatrics)	Yohei Yamaguchi
D1(Department of Dental Anesthetics)	Keiko Abe
M2	Shuhei Ishii
M2	Sun Yihan
Technician	Reiko Kimura
Secretary	Yukiko Takakura

(1) Outline

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

(2) Research

1. Pathogenesis of atrial fibrillation (AF)

Combining discovery panel and replication panel, we performed GWAS in 113,00 AF cases and 153,676 controls in Japanese population, and identified total 14 AF-sensitive SNPs. We calculated weighed genetic risk score (wGRS) and divided them into quartiles; the highest quartile group (top 25%) had 7.58-fold higher incidence of AF compared to the lowest quartile group (bottom 25%) (integrated odds ratio) (Nat. Genet. 2017;70:180-184). In order to carry out personalized medicine involving medical intervention, we require odds ratio up to around 50. Thus, to raise odds ratio from less than 10 to about 50 is the bottle-neck to materialize personalized medicine. Since most SNPs with high odds ratio have been identified through 3 rounds of GWAS, it is impossible by increasing sample numbers for genetic analysis to overcome this bottle-neck. Then, we searched for AF-sensitive biomarkers, and identified 4 AF biomarker candidates. We compared circulating miRNA between serum from 100 AF patients and those from 100 controls with miRNA array. We also compared circulating miRNA between AF mice and non-AF mice in 2 mouse AF models, a pressure-overload model and a high-fat-diet model. We found 4 circulation miRNAs (miR-99a-5p, miR-192-5p, miR-214-3p, miR-342-5p), which showed significant difference between AF and non-AF both in human and mouse. Combining 4 miRNAs, we could segregate AF from non-AF with 76% sensitivity and 80% selectivity.

2. Pannexin for ischemic preconditioning

Pannexin is a member of gap-junction channel, which is not involved in the formation of gap-junction channels between cells, but provides hemi-channels on the surface of the membrane and transport small molecules between cytosol and extracellular space. Pannexin functions as chloride channels in the basal condition and as ATP-release channels after mechanical stimuli. Being suffered from myocardial infarction, hearts with prior ischemic

events (angina) develop reduced size infarcted size compared with those without prior ischemic events. The effect of prior ischemic events is referred as “ischemic pre-conditioning”. Though extracellular ATP is known to play an important role for ischemic pre-conditioning, the source of ATP is not known. Using pannexin-1 (a major isoform of pannexin in hearts) KO mouse, we found that ATP released during hypoxia was much lower in KO mice than in WT mice. Ischemic pre-conditioning reduced the infarcted area in WT mice, which was almost abolished in KO mice. Taken together, we conclude that hypoxia-activated pannexin provides extracellular ATP, which is required for the ischemic pre-conditioning.

Next, we have proposed the working hypothesis that pannexin activators would work as a potential new drugs against ischemia heart diseases. Then, we performed screening of chemical library present in the TMDU chemical screening center. We found 2 small molecules that could activate pannexin-1. We would try to confirm their potential as new ischemia drug seeds in in vivo study.

3. Electrophysiological Assessment of Murine heart with High-Resolution Optical Mapping

Conventional optical mapping of murine heart, especially of its atria, has some critical problems due to its small size. To overcome them, we developed the novel electrophysiological assessment method for elucidating the underlying mechanism of arrhythmogenesis using murine heart by combining high spatial and temporal resolution optical mapping system and precise electrophysiological study (J. Vis. Exp 2018 in press). This novel method will contribute to assessing the onset and maintenance mechanism of arrhythmias precisely in various mouse models.

4. Sex specific mRNAs/miRNAs expression in human/murine heart diseases

Sexual dimorphisms in various heart diseases; ex ICM, MI and DCM are well known. However, the questions why these diseases onset in men/males are higher than in women/females remain unsolved. Here, we show that the transcriptional profiles of mRNAs and miRNAs between men/males and women/females from left ventricles in heart development, their failures and MI models. In this profile, mRNA and miRNA transcriptome of normal and disease heart show significant sex differences, which might impact the cardiac homeostasis (Tsuji et al., PLoS One 2017). Especially, we identified 2 miRNAs; miR2861, miR-139-5p, which have unique expression patterns during heart development and its disease by in silico analysis and GO analysis. Together this study provides the first comprehensive picture of the genome-wide program underlying the heart sexual dimorphisms, laying the foundation for gender specific treatment strategies.

(3) Education

School of Medicine

2nd grade Introduction to Neurophysiology (2 units)

2nd grade Physiology (6 units)

3rd grade Cardiology (1 unit)

4th grade Project semester

School of Dentistry

3rd grade Pharmacology III(2 units)

3rd grade Practice for Pathophysiological Sciences (2 units)

School of Health Care Medicine

3rd/4th grade Cardiac physiology (8 units)

(4) Publications

[Original Articles]

1. Kimura Y, Aiba T, Sasano T, Furukawa T, Kusano K, Shimizu W. IRX3 variant as a modifier of Brugada syndrome with frequent ventricular fibrillation. *Heart Rhythm Case Report*. 2017;
2. Kuroda Y, Yuasa S, Watanabe Y, Ito S, Egashira T, Seki T, Hattori T, Ohno S, Kodaira M, Suzuki T, Hashimoto H, Okata S, Tanaka A, Aizawa Y, Murata M, Aiba T, Makita N, Furukawa T, Shimizu W, Kodama I, Ogawa S, Kokubun N, Horigome H, Hoerir M, Kamiya K, Fukuda K. Flecainide ameliorates arrhythmogenicity through NCX flux in Andersen-Tawil syndrome-iPS cell derived cardiomyocytes *Biochemical Biophysical Reports*. 2017.01; 9; 245-256

3. Liu L, Ebana Y, Nitta J, Takahashi Y, Miyazaki S, Tanaka T, Komura M, Isobe M, Furukawa T. Genetic variants associated with susceptibility to atrial fibrillation in Japanese population *Canadian Journal of Cardiology*. 2017.04; 33; 443-449
4. Li M, Kanda Y, Ashihara T, Sasano T, Nakai Y, Kodama M, Hayashi E, Sekino Y, Furukawa T, Kurokawa J. Overexpression of KCNJ2 in induced pluripotent stem cell-derived cardiomyocytes for the assessment of QT-prolonging drugs *Journal of Pharmacological Science*. 2017.06; 134(2); 75-85
5. Low SK, Takahashi A, Ebana Y, Ozaki K, Christophersen IE, Ellinor PT; AFGen Consortium., Ogishima S, Yamamoto M, Satoh M, Sasaki M, Yamaji T, Iwasaki M, Tsugane S, Tanaka K, Naito M, Wakai K, Tanaka H, Furukawa T, Kubo M, Ito K, Kamatani Y, Tanaka . Identification of six new genetic loci associated with atrial fibrillation in the Japanese population *Nature Genetics*. 2017.06; 49(6); 953-958
6. Zaw KTT, Sato N, Ikeda S, Thu KS, Mieno MN, Arai T, Mori S, Furukawa T, Sasano T, Sawabe M, Tanaka M, Muramatsu M. Association of ZFHX3 gene variant with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study *Journal of Cardiology*. 2017.08; 70(2); 180-184
7. Ebana Y, Ozaki K, Liu L, Hachiya H, Hirao K, Isobe M, Kubo M, Tanaka T, Furukawa T. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25 *Journal of Cardiology*. 2017.10; 70(4); 366-373
8. Miyazaki S, Ebana Y, Liu L, Nakamura H, Hachiya H, Taniguchi H, Takagi T, Kajiyama T, Watanabe T, Igarashi M, Kusa S, Niida T, Iesaka Y, Furukawa T. Chromosome 4q25 variants and recurrence after second-generation cryoballoon ablation in patients with paroxysmal atrial fibrillation *International Journal of Cardiology*. 2017.10; 244; 151-157
9. Yusuke Ebana, Kouichi Ozaki, Lian Liu, Hitoshi Hachiya, Kenzo Hirao, Mitsuaki Isobe, Michiaki Kubo, Toshihiro Tanaka, Tetsushi Furukawa. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25. *J Cardiol*. 2017.10; 70(4); 366-373
10. Yoshioka K, Kuroda S, Takahashi K, Sasano T, Furukawa T, Matsumura A. Calcification of joints and arteries with novel NT5E mutations with involvement of upper extremity arteries *Vascular Medicine*. 2017.12; 22(6); 541-543

[Books etc]

1. Tetsushi Furukawa. How to interpret ECG from its basic. 2017.10 (ISBN : 978-4-88378-656-5)

[Misc]

1. Tetsushi Furukawa. Arrhythmias originating from localized areas of the heart SEITAI NO KAGAKU. 2017.12; 68(6); 564-568

[Conference Activities & Talks]

1. Lian Liu, Yusuke Ebana, Jun-ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Common genetic variants indicate the risk of atrial fibrillation in Japanese population. The 63th Annual Meeting of the Japanese Heart Rhythm Society 2017.07.16 .Sapporo
2. Sekigawa M, Satoh A, Nitta J, Sato Y, Honda Y, Kuroda S, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Effect of SNP on 9q22 (rs6479562) on the progression from paroxysmal atrial fibrillation to persistent atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
3. Sato Y, Satoh A, Nitta J, Honda Y, Kuroda S, Sekigawa M, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Impact of SNP on IL6R (rs7514452) for age at onset of atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
4. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPSCs. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

5. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPS cells. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

Stem Cell Regulation

Professor Tetsuya TAGA
Associate Professor Ikuo NOBUHISA
Assistant Professor Kouichi TABU
Technical Assistant/Administrative Assistant Kazuko INOUE

(1) Outline

Research in this department has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. Particular attention is given to cell-external cues (such as cytokines) and cell-intrinsic programs (including epigenetic modification), taking cross-interactions of transcriptional regulatory signals into consideration.

(2) Research

Research Subjects in this department are as follows:

- 1) Molecular basis for the maintenance of neural stem cells
- 2) Regulation of the neural stem cell fate
- 3) Characterization of hematopoietic stem cells in fetal hematopoietic organs
- 4) Characterization of cancer stem cells and their niche
- 5) Epigenetic regulation of neural development

(3) Education

Our education has been conducted to elucidate the mechanisms by which stem cells are regulated. The major focus has been on neural stem cells, hematopoietic stem cells, and cancer stem cells. The study is aimed to understand development, maintenance, and regeneration of the central nervous system and the hematopoietic system, and to obtain a clue to tackle the problem of cancer recurrence. The projects have been performed, for instance by elucidation of stem cell characteristics, analysis of transcriptional regulatory signaling pathways, and identification of niche signals.

(4) Lectures & Courses

Under our education program, students will learn the molecular basis of stem cell regulation in view of cell-extrinsic signals and cell intrinsic-programs during tissue development, maintenance, and regeneration from molecular to whole-body levels. Students will receive exposure to cutting edge concepts and research technologies, and study regulatory mechanisms in neural, hematopoietic, and cancer stem cells. With emphasis also on physiological and pathological conditions surrounding the stem cells, we aims to improve student's understanding of stem cells from multiple viewpoints.

(5) Publications**[Original Articles]**

1. Wang W, Tabu K, Hagiya Y, Sugiyama Y, Kokubu Y, Murota Y, Ogura SI, and Taga T. Enhancement of 5-aminolevulinic acid-based fluorescence detection of side population-defined glioma stem cells by iron chelation. *Sci Rep.* 2017.02; 7; 42070
2. Harada K, Nobuhisa I, Anani M, Saito K, Taga T. Thrombopoietin contributes to the formation and the maintenance of hematopoietic progenitor-containing cell clusters in the aorta-gonad-mesonephros region. *Cytokine.* 2017.07; 95; 32-42

[Conference Activities & Talks]

1. Tabu K and Taga T. Self-maintenance strategies of glioma stem cells (GSCs) involving GSC-induced protumoral macrophages. 11th International Symposium of The Institute Network 2017.01.27 Tokushima University, Tokushima, Japan
2. Murota Y, Schmidt S, Tabu K, Ito H, Tanaka S, Bradley M and Taga T. Screening for human pancreatic cancer stem cell niche mimicry by using synthetic polymer microarrays. The 15th Stem Cell Research Symposium 2017.05.27 Tokyo University, Tokyo, Japan
3. Taga T, Takayanagi H, Takeuchi T. Comprehensive perspectives of systemic and organ specific inflammatory responses (Opening Remarks by T. Taga).. 13th World Congress on Inflammation: Symposium on "Comprehensive perspectives of systemic and organ specific inflammatory responses" (organized by T. Taga, H. Takayanagi, and T. Takeuchi). 2017.07.08 Hilton London Metropole, London, United Kingdom
4. Taga T and Tabu K. Glioma progression by intrinsic capacities of glioma stem cells to organize a self-advantageous microenvironment niche for their maintenance and expansion. The 38th Annual Meeting of the Japanese Society of Inflammation and Regeneration, Symposium "Diseases and Stem Cells" 2017.07.18 Osaka International Convention Center, Osaka
5. Tabu K, Wang W, Murota Y and Taga T. Self-expanding strategies of glioma stem cells that involves macrophages to adapt to iron-deprivation stress. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.28 Pacifico Yokohama, Yokohama, Japan
6. Murota Y, Wenqing GY, Tabu K, and Taga T. Establishment of glioma mouse model by transducing oncogenic H-RasV12 gene into the p53 deficient astrocytes. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.30 Pacifico Yokohama, Yokohama, Japan
7. Saito K, Nobuhisa I, and Taga T. The mechanism of maintaining the undifferentiated state of hematopoietic stem cell by Sox17 and TET family members. The 40th Annual Meeting of the Molecular Biology Society of Japan 2017.12.07 Kobe International Conference Center, Kobe, Japan
8. Murota Y, Schmidt S, Tabu K, Ito H, Tanaka S, Bradley M, and Taga T. Screening for pancreatic cancer stem cell niche-mimicking synthetic polymers. Consortium of Biological Sciences 2017 2017.12.07 Pacifico Yokohama, Yokohama, Japan
9. Tabu K, Tatsumi R, and Taga T. Glioma stem cells exploit host monocytes/macrophages to adapt to iron deprivation stress: a mechanism for the development of their own niche. Consortium of Biological Sciences 2017 2017.12.08 Pacifico Yokohama, Yokohama, Japan
10. Matsunaga H, Tabu K, and Taga T. Roles of autophagic-like cell death by glioma stem cells in educating host macrophages. Consortium of Biological Sciences 2017 2017.12.08 Pacifico Yokohama, Yokohama, Japan
11. Nobuhisa I, Takahashi S, Saito K, and Taga T. Role of adhesion molecules induced by a transcription factor Sox17 in intra-aortic hematopoietic cell cluster formation in midgestation mouse embryos. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai International Center, Sendai, Japan

Molecular Pharmacology

Professor: Masaki Noda, M.D., Ph.D.

Associate Professor: Yoichi Ezura, M.D., Ph.D.

Assistant Professor: Yayoi Izu, DVM, Ph.D.

Research Assistant Professor: Smriti Aryal A.C., DDS, Ph.D.

(1) Outline

In order to contribute to the establishment of therapy and prevention for osteoporosis and the other calcium-related disorders, we are elucidating molecular mechanisms underlying regulation of calcium metabolism with emphases on bone formation and resorption. Skeletal system is the largest storage site for calcium in a living body and its metabolism is conducted by a complex cell society consisting of bone-forming osteoblasts and bone-resorbing osteoclasts as well as stromal cells and chondrocytes. In our department, we take molecular and cellular biological approaches to study the mechanisms underlying regulation of development, differentiation, and function of these cells.

(2) Research

Bone is the major organ for calcium metabolism in our body. The regulation of bone metabolism is mediated by a balance between osteoblastic bone formation and osteoclastic bone resorption. These activities are maintained in balance and called bone remodeling. Imbalance of the remodeling results in development of bone disorders, such as osteoporosis. Osteoblasts are differentiated from mesenchymal stem cells. These cells are under the regulation by local and systematical factors, such as growth factors and hormones. These factors activate intracellular signaling, which promotes transcription factors thereby delineates cell differentiation. In our laboratory, we are studying the process from various aspects of bone cell regulation including transcription factors, cytokines and hormones. To promote our study, knockout and transgenic mice, gene introduction via virus, global analysis of gene expression, and genome database analysis are used. Our study will provide the basic understandings of bone homeostasis, which will contribute the development of measures for diagnosis and treatment of bone disorders.

Stem Cell Biology

Professor : Emi Nishimura, M.D., Ph.D.

Associate Professor: Daisuke Nanba, Ph.D

Assistant Professor : Hiroyuki Matsumura, Ph.D.

Project Assistant Professor :Yasuaki Mohri, Ph.D.

Hironobu Morinaga, Ph.D.

Kyosuke Asakawa, Ph.D.

Researcher:Yasuko Kato

Gu jie

(1) Outline

Stem cell systems play fundamental roles in tissue turnover and homeostasis. Our goal is to understand the mechanisms of tissue homeostasis driven by stem cell systems and to apply the knowledge to better understand the mechanisms underlying specific tissue decline by aging, cancer development and other diseases associated with aging. We further aim to apply this knowledge to drug discovery and regenerative medicine using somatic stem cells and the prevention and treatment of age-associated diseases.

(2) Research

1) Identification of stem cells in the skin

The skin is the largest organ in the body. Hair follicles in the skin constantly renew themselves by alternate phases of growth, regression and rest. During this process, mature melanocytes (pigment cells) in hair follicles are replaced by a new cell population every hair cycle. We previously identified the source of those melanocytes, “melanocyte stem cells” (McSC), which are located in the hair follicle bulge and supply mature melanocytes required for hair and skin pigmentation (Nishimura EK et al. Nature 2002). We currently identified McSCs in eccrine sweat glands in non-hair-bearing skin areas as well (Okamoto N et al.PCMR, 2014). Also we are currently searching for the prospective method for identification of epidermal keratinocyte stem cells in mouse and human skin.

2) Mechanisms of stem cell maintenance

The underlying mechanisms of stem cell maintenance is a fundamental issue in stem cell biology and medicine. We previously demonstrated that the niche microenvironment plays dominant role in melanocyte stem cell fate determination (Nishimura EK et al. 2002). We then revealed that hair follicle stem cells (HFSC), which surround McSCs in the hair follicle bulge-subbulge area, serve as a functional niche for McSC maintenance through transforming growth factor β (TGF- β)(Nishimura EK et al. Cell Stem Cell, 2010)(Tanimura S et al. Cell Stem Cell 2011). As intrinsic defects in stem cells such as caused by Mitf or Bcl2 deficiency also induces McSC depletion which leads to the progressive expression of hair graying phenotype, incomplete maintenance of McSCs either by defective signaling from the stem cell niche or by intrinsic defects in stem cells induces the progressive hair graying phenotype.

3) Mechanisms for stem cell aging and tissue/organ aging

Physiological hair graying is the most obvious outward sign of aging in mammals, yet it has been unclear what causes the incomplete maintenance of MsSCs during the course of aging (Nishimura EK et al. Science 2005). We have found that genotoxic stress abrogates renewal of McSCs by triggering their differentiation without in-

ducing stem cell apoptosis nor cellular senescence. Our findings indicated that a “stem cell renewal checkpoint” exists to maintain the quality of the melanocyte stem cell pool (Inomata K, Aoto T et al. Cell 2009). Similar checkpoint has been found in other somatic stem cell systems as well and we recently found that HFSCs also have similar checkpoint mechanism. We are currently studying the underlying molecular mechanism.

4) Hair follicle aging is driven by stem cell-centric aging program

Hair thinning/loss is a prominent aging phenotype but has an unknown mechanism. We show that hair follicle stem cell (HFSC) aging causes the stepwise miniaturization of hair follicles and eventual hair loss in wild-type mice and in humans. In vivo fate analysis of HFSCs revealed that the DNA damage response in HFSCs causes proteolysis of Type XVII Collagen (COL17A1/BP180), a critical molecule for HFSC maintenance, to trigger HFSC aging, characterized by the loss of stemness signatures and by epidermal commitment. Aged HFSCs are cyclically eliminated from the skin through terminal epidermal differentiation, thereby causing hair follicle miniaturization. The aging process can be recapitulated by Col17a1-deficiency and prevented by the forced maintenance of COL17A1 in HFSCs, demonstrating that COL17A1 in HFSCs orchestrates the stem cell-centric aging program of the epithelial mini-organ (Matsumura H et al. Science 2016).

5) Development of skin regeneration technology with human skin stem cells and/or stem cell-targeted small molecules

Human epidermal keratinocyte stem cells can be cultivated under suitable conditions, and generate a progeny large enough to entirely reconstitute the epidermis of an adult human. This has enabled the autologous transplantation of cultured epidermal sheets onto patients with extensive burns. However, the cultured keratinocytes can regenerate only the epidermis and cannot suppress dermal scarring. To develop novel skin regeneration technology, we have investigated human epidermal keratinocytes and found that human epidermal keratinocyte stem cells can be identified in situ by analyzing cell motion during their cultivation (Nanba et al., J. Cell Biol., 2015). The identification of keratinocyte stem cells by image analysis is a valid parameter for quality control of cultured keratinocytes for transplantation, and improves the clinical outcome of cell therapy and the efficiency of cell manufacturing for regenerative medicine. Finally, the treatment of skin ulcer and decubitus is an urgent problem in this aging society. We are currently trying to establish the screening system for small molecules that activate stem cells in the wound edge.

(3) Publications

[Original Articles]

1. Matsumura H., Mohri Y., Nguyen T., Morinaga H., Fukuda M., Ito M., Kurata S., Hoeijmakers J., Nishimura E. K.. Defective maintenance of hair follicle stem cells through COL17A1 loss orchestrates the hair follicle aging program JOURNAL OF INVESTIGATIVE DERMATOLOGY. 2017.10; 137(10); S235
2. Nanba D., Toki F., Matsumura H., Toki H., Nishimura E. K.. Locomotive ability of human keratinocyte stem cells is an intrinsic property for stem cell expansion and epidermal reconstruction JOURNAL OF INVESTIGATIVE DERMATOLOGY. 2017.10; 137(10); S310
3. Nanba D., Toki F., Matsumura H., Toki H., Nishimura E. K.. Locomotive ability of human keratinocyte stem cells is an intrinsic property for stem cell expansion and epidermal reconstruction JOURNAL OF INVESTIGATIVE DERMATOLOGY. 2017.10; 137(10); S310

[Conference Activities & Talks]

1. Emi Nishimura. Stem cell aging: the core to orchestrates tissue aging. Aging Science:from Molecules to Society-Aging Biology- 2017.05.09 Tohoku University
2. Emi K. Nishimura. Tissue aging program based on stem cell aging in hair follicle. KEYSTONE SYM-POSIA on Molecular and Cellular Biology -Aging and Mechanisms of Aging-Related Disease- 2017.05.15 Pacifico YOKOHAMA, Kanagawa, Japan
3. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. International Society for Stem Cell Research 2017 Annual Meeting 2017.06.14 Boston, USA
4. Emi K. Nishimura. Melanocyte stem cells in eccrine sweat glands: a potential original of acral melanoma. IPCC2017 2017.08.26 Denver, USA
5. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. WCHR2017(10th World Congress for Hair Research) 2017.10.01 Kyoto, Japan
6. Daisuke Nanba. Analysis of human epidermal keratinocyte stem cell behavior. The 26th Research Council Meeting of Japan Society of Plastic and Reconstructive Surgery 2017.10.20
7. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. WCHR2017(10th World Congress for Hair Research) 2017.11.03 Kyoto, Japan
8. Emi K. Nishimura. The mechanism of aging-associated hair graying and hair thinning:toward the discovery of pharmacological targets. WCHR2017(10th World Congress for Hair Research) 2017.11.03 Kyoto, Japan
9. Emi K. Nishimura. Stem cells orchestrates hair follicle aging program. Stem Cell in Disease Modeling and Therapeutics 2017.11.13 Tokyo, Japan
10. Nanba D, Morhi Y, Okamoto S, Matsumura H, Usami T, Aida T, Tanaka K, Nishimura EK. Targeting melanocyte stem cells with Dct locus by cloning-free CRISPR/Cas9 technology. The 42nd Annual Meeting of the Japanese Society for Investigative Dermatology. 2017.12.16

[Awards & Honors]

1. Myron Gordon Award, International federation of Pigment Cell Societies(IFPCS), 2017.08

Respiratory Medicine

Professor: Naohiko INASE

Junior Associate Professor: Toshihide FUJIE

Assistant Professor: Tomoya TATEISHI, Haruhiko FURUSAWA, Masahiro MASUO, Tsuyoshi SHIRAI

Graduate Students: Mayuko TAO, Yuta ADACHI, Ken UCHIBORI,

Yu KUSAKA, Rie SAKAKIBARA, Manabu SEMA, Tomoko TERADA, Yoshihisa NUKUI, Takayuki HONDA,

Takahiro MITSUMURA, Sho SHIBATA, Yukihisa INOUE, Hiroaki SAITOH, Satoshi HANZAWA,

Naoki NISHIYAMA, Takashi YAMANA

(1) Outline

Respiratory Medicine deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders.

(2) Research

- 1) Pathogenesis of hypersensitivity pneumonitis and detection of environmental causative antigen
- 2) Airway remodeling in bronchial asthma model
- 3) Acute exacerbation in pulmonary fibrosis
- 4) Proteomics of pulmonary fibrosis
- 5) Pathogenesis of pulmonary fibrosis and emphysema

(3) Education

Main objective in the graduate course is to provide students to study specific diagnostic modalities as well as basic scientific findings regarding the pathogenesis of pulmonary diseases. Students are also taught on basic science and its related laboratory technology depending upon their research subject.

(4) Lectures & Courses

Students should try to understand a variety of pulmonary diseases in terms of scientific aspect and make an appropriate plan to examine unsolved research questions.

(5) Clinical Services & Other Works

Our clinic provides a full spectrum of diagnosis and treatment of a variety of pulmonary diseases. Consultant system is open to all departments in this hospital and daily clinical conference regarding inpatients is organized by professors of the department. In outpatient clinic, chemotherapy, home oxygen therapy, management of sleep apnea, and arrange of clinical studies are provided.

(6) Clinical Performances

We have immunological tools to examine hypersensitivity pneumonitis including antigen inhalation challenge test, specific antibody against causative antigen, and lymphocyte proliferation test. Many patients with interstitial lung diseases in Japan are referred to our clinic.

(7) Publications**[Original Articles]**

1. Chiba S, Tsuchiya K, Ogata T, Imase R, Yagi T, Mishima Y, Jinta T, Saito K, Isogai S, Jinn Y, Kawasaki T, Natsume I, Miyashita Y, Takagiwa J, Ishiwata N, Chiaki T, Kishi M, Tsukada Y, Yamasiki M, Inase N. Treatment of asthma in the elderly: questionnaire survey in Japan. *Int J Clin Med* . 2017; 8; 236-247
2. Chiba S, Okayasu K, Tsuchiya K, Tamaoka M, Miyazaki Y, Inase N, Sumi Y. The C-jun N-terminal kinase signaling pathway regulates cyclin D1 and cell cycle progression in airway smooth muscle cell proliferation. *Int J Clin Exp Med* . 2017; 10(2); 2252-2262
3. Sakakibara Y, Suzuki Y, Fujie T, Akashi T, Iida T, Miyazaki Y, Eishi Y, Inase N. Radiopathological features and identification of Mycobacterial infections in granulomatous nodules resected from the lung. *Respiration*. 2017.02;
4. Shirai T, Furusawa H, Furukawa A, Ishige Y, Uchida K, Miyazaki Y, Eishi Y, Inase N. Protein antigen of bird-related hypersensitivity pneumonitis in pigeon serum and dropping. *Respir Res*. 2017.03; 20(18); 65
5. Uchibori K, Inase N, Araki M, Kamada M, Sato S, Okuno Y, Fujita N, Katayama R. Brigatinib combined with anti-EGFR antibody overcomes osimertinib resistance in EGFR-mutated non-small-cell lung cancer. *Nat Commun*. 2017.03; 13(8); 14768
6. Sakakibara R, Inamura K, Tambo Y, Ninomiya H, Kitazono S, Yanagitani N, Horiike A, Ohyanagi F, Matsuura Y, Nakao M, Mun M, Okumura S, Inase N, Nishio M, Motoi N, Ishikawa Y. EBUS-TBNA as a promising method for the evaluation of tumor PDL-1 expression in lung cancer. *Clin Lung Cancer*. 2017.09; 18(5); 527-534
7. Adachi Y, Watanabe K, Kita K, Kitai H, Kotani H, Sato Y, Inase N, Yano S, Ebi H.. Resistance mediated by alternative receptor tyrosine kinases in FGFR1-amplified lung cancer. *Carcinogenesis*. 2017.10; 38(11); 1063-1072
8. Furusawa H, Sugiura M, Mitaka C, Inase N. Direct hemoperfusion with polymyxin B-immobilized fibre treatment for acute exacerbation of interstitial pneumonia. *Respirology*. 2017.10; 22(7); 1357-1362

[Conference Activities & Talks]

1. Furuei W, Endo J, Otani Y, Nakamura Y, Akaza M, Sasano T, Miyazaki Y, Inase N, Sumi Y. Reference values of MostGraph measures for healthy Japanese adults.. The 57th Annual Meeting of The Japanese Respiratory Society 2017.04.22 Tokyo
2. Koike F, Otani Y, Oyama S, Furuei W, Endo J, Nakamura Y, Akaza M, Sasano T, Inase N, Sumi Y. Cluster analysis of cough variant asthma using MostGraph.. The 57th Annual Meeting of The Japanese Respiratory Society 2017.04.22 Tokyo
3. Sema M, Miyazaki Y, Inase N. Measurement of avian antigen in household dust for measurement of chronic bird-related hypersensitivity pneumonitis.. ATS International Conference 2017.05.21 Washington DC
4. Kusaka Y, Kajiwara C, Miyazaki Y, Inase N, Tateda K. Effects of neutrophil depletion on M1/M2 macrophage polarization and lethality of mice with Legionella pneumophila pneumonia. . ATS International Conference 2017.05.21 Washington DC
5. Saito H, Miyazaki Y, Furusawa H, Yamamoto Y, Yamamoto H, Inase N. A role of RAGE and HMGB-1 in chronic hypersensitivity pneumonitis.. ATS International Conference 2017.05.21 Washington DC
6. Furusawa H, Saito H, Sema M, Miyazaki Y, Inase N. Bronchoalveolar lavage in chronic hypersensitivity pneumonitis and IPF.. ATS International Conference 2017.05.23 Washington DC
7. Ishizuka M, Miyazaki Y, Inase N. Validation of new prediction score in inhalation provocation test for chronic hypersensitivity pneumonitis.. ATS International Conference 2017.05.23 Washington DC
8. Tateishi T, Fujie T, Saito H, Miyazaki Y, Inase N. Serum angiopoietin-2 can be a biomarker in acute exacerbation of interstitial pneumonia. . ATS International Conference 2017.05.23

9. Shota Hayashi, Masayuki Hideshima, Naoki Ishihara, Tomohiro Kurashima, Shusuke Inukai, Yuuko Mitsuma, Shuhei Nakamura, Toshihide Fujie, Yasunari Miyazaki, Meiyo Tamaoka. Conversion from continuous positive airway pressure therapy to oral appliance therapy for obstructive sleep apnea in Tokyo Medical and Dental University Hospitals. 16th the Japanese Academy of Dental Sleep Medicine 2017.11.04 Yamaguchi, Japan

Gastroenterology and Hepatology

Professor Mamoru WATANABE

Professor Yasuhiro ASAHINA (Department for Hepatitis Control)
Kazuo OHTSUKA (Department of Endoscopic Diagnosis and Therapeutics)
Ryuichi OKAMOTO (Center for Stem Cell and Regenerative Medicine)
Tetsuya NAKAMURA
(Department of Advanced Therapeutics in Gastrointestinal Diseases)

Associate Professor

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Sei KAKINUMA (Department for Hepatitis Control)
Kiichiro TSUCHIYA (Gastroenterology and Hepatology)
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Yoichi NIBE, Syuji HIBIYA, Taro WATABE, Yuka MATSUMOTO, Ayako WATANABE,
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Yuka MATSUMOTO, Kohei SUZUKI, Akinori HOSOYA, Yu ASANO,
Shintaro AKIYAMA, Fumiaki ISHIBASHI, Emi INOUE, Ami KAWAMOTO,
Masato MIYOSHI, Tomoyuki TSUNODA, Yuria TAKEI, JOSE Nisha, Sho ANZAI,
Tomoaki SHIRASAKI, Shohei TANAKA, Reiko KUNO, Kana OTSUBO, Ayako Sato,
Sho WARANABE, Maiko MOTOHASHI, Konomi KUWABARA, Hiroki MATSUDA,
Takehito ASAKAWA, Ai MINAMIDATE, Ryo MORIKAWA, Emi AONUMA, Mao KAWAI,
Jyunichi TAKAHASHI, Naoya TSUGAWA, Yuta KOJIMA, Minami HAMA

(1) Outline

Research project is selected from the clinical problems in the Gastroenterology and Hepatology to understand the research policy, as clinical science that the results of research project finally should be restored to clinical medicine.

The purpose of this course is the understanding the situation of inflammatory bowel disease (IBD) in Japan and the problems about the pathogenesis and intractable cause of IBD. In addition, the understanding the pathogenesis and problems about the liver diseases such as viral hepatitis, cirrhosis and hepatocellular carcinoma is the purpose of this course.

(2) Research

Basic Research Projects

Systemic Organ Regulation

- Elucidating the pathophysiology of inflammatory bowel diseases and development of treatment by disease-specific immune-regulation.
- Development of novel therapeutics for inflammatory and allergic diseases based on gut-specific mucosal immune regulation.
- Basic research and clinical application of regenerative medicine in gastrointestinal diseases.
- Analysis of interferon-resistant hepatitis C virus.
- Comprehensive analysis of susceptibility genes for various gastrointestinal diseases.
- Crosstalk of the signaling pathways in intestinal epithelial cells.
- Functional analysis of the intestine using primary cell culture in vitro.

(3) Education

We believe that the central role of clinical departments in the graduate school is to establish basis for the innovative medicine / medical treatment in the next generation. Basic research lead by clinical concepts, and development of novel therapeutics established upon basic research are both critically required to achieve our mission. Therefore, our primary goal is set to train highly educated and experienced clinician-researchers in the field of gastroenterology and hepatology.

In the clinical area, we pursue development and application of highly advanced technologies, including novel endoscopic procedures, for sophisticated diagnosis and treatment of gastrointestinal and liver diseases. In basic research, our principle is to achieve "clinical science", a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice. Based on these principals, we are running research projects to 1) develop novel therapy for refractory inflammatory bowel diseases, 2) prevent progression of liver failure in chronic hepatitis patients and 3) improve anti-cancer therapy for the treatment of gastrointestinal malignancies, by expanding our distinct basic research findings in the area of mucosal immunology, liver immunology, regenerative medicine and virology, to various clinical settings. Moreover, we promote both intra- and inter-national exchanges of researchers, and provide good opportunities to study abroad. The final goal of our education is to promote students to become a well-developed clinician researcher, and also a leading expert in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Research Conference	every Tuesday 18:00 19:30
Journal Club	every Tuesday 18:00 19:30

(5) Clinical Services & Other Works

Expert Areas in Clinical Practice

- Immune-regulation based treatment of inflammatory bowel diseases.

- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.
- Clinical trial of innovative treatment for hepatocellular cancer.
- Diagnosis and treatment of small intestinal diseases by balloon enteroscopy and capsule enteroscopy.
- Advanced diagnosis and treatment of colonic diseases by colonoscopy.
- Development of minimally-invasive diagnostic modalities for gastrointestinal diseases (i.e. MR enteroclysis).
- Improved chemotherapy for gastric and pancreatic malignancies.

(6) Clinical Performances

Therapeutics of inflammatory bowel diseases by corrections of immunological disfunctions.

Diagnostic and interventional gastrointestinal endoscopy

Antiviral therapies against chronic viral hepatitis and preventions of hepatic malignancy novel interventions of hepatic malignancy.

(7) Publications

[Original Articles]

1. Makoto Naganuma, Shigeo Okuda, Tadakazu Hisamatsu, Katsuyoshi Matsuoka, Kiyoto Mori, Naoki Hosoe, Yoshihiro Nakazato, Haruhiko Ogata, Takanori Kanai. Findings of ulceration and severe stricture on MRE can predict prognosis of Crohn's disease in patients treated with anti-TNF treatment. *Abdom Radiol (NY)*. 2017.01; 42(1); 141-151
2. Shinta Mizuno, Kosaku Nanki, Katsuyoshi Matsuoka, Keiichiro Saigusa, Keiko Ono, Mari Arai, Shinya Sugimoto, Hiroki Kiyohara, Moeko Nakashima, Kozue Takeshita, Makoto Naganuma, Wataru Suda, Masahira Hattori, Takanori Kanai. Single fecal microbiota transplantation failed to change intestinal microbiota and had limited effectiveness against ulcerative colitis in Japanese patients. *Intest Res*. 2017.01; 15(1); 68-74
3. Shinichiro Shinzaki, Katsuyoshi Matsuoka, Hideki Iijima, Shinta Mizuno, Satoshi Serada, Minoru Fujimoto, Norimitsu Arai, Noriyuki Koyama, Eiichi Morii, Mamoru Watanabe, Toshifumi Hibi, Takanori Kanai, Tetsuo Takehara, Tetsuji Naka. Leucine-rich Alpha-2 Glycoprotein is a Serum Biomarker of Mucosal Healing in Ulcerative Colitis. *J Crohns Colitis*. 2017.01; 11(1); 84-91
4. Toru Nakata, Hiromichi Shimizu, Sayaka Nagata, Go Ito, Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Reiko Kuno, Sho Anzai, Tatsuro Murano, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Mamoru Watanabe, Ryuichi Okamoto. Indispensable role of Notch ligand-dependent signaling in the proliferation and stem cell niche maintenance of APC-deficient intestinal tumors. *Biochem. Biophys. Res. Commun.* 2017.01; 482(4); 1296-1303
5. Erika Kuwahara, Yoshitaka Murakami, Takahiro Nakamura, Nagamu Inoue, Masakazu Nagahori, Toshiyuki Matsui, Mamoru Watanabe, Yasuo Suzuki, Yuji Nishiwaki. Factors associated with exacerbation of newly diagnosed mild ulcerative colitis based on a nationwide registry in Japan. *J. Gastroenterol.* 2017.02; 52(2); 185-193
6. Toru Nakata, Hiromichi Shimizu, Sayaka Nagata, Go Ito, Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Reiko Kuno, Sho Anzai, Tatsuro Murano, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Mamoru Watanabe, Ryuichi Okamoto. Data showing proliferation and differentiation of intestinal epithelial cells under targeted depletion of Notch ligands in mouse intestine. *Data Brief*. 2017.02; 10; 551-556
7. Shinya Sugimoto, Makoto Naganuma, Yasushi Iwao, Katsuyoshi Matsuoka, Masayuki Shimoda, Shuji Mikami, Shinta Mizuno, Yoshihiro Nakazato, Kosaku Nanki, Nagamu Inoue, Haruhiko Ogata, Takanori Kanai. Endoscopic morphologic features of ulcerative colitis-associated dysplasia classified according to the SCENIC consensus statement. *Gastrointest. Endosc.* 2017.03; 85(3); 639-646.e2
8. Sayako Chiba, Tadakazu Hisamatsu, Hiroaki Suzuki, Kiyoto Mori, Mina T Kitazume, Katsuyoshi Shimamura, Shinta Mizuno, Nobuhiro Nakamoto, Katsuyoshi Matsuoka, Makoto Naganuma, Takanori Kanai. Glycolysis regulates LPS-induced cytokine production in M2 polarized human macrophages. *Immunol. Lett.* 2017.03; 183; 17-23

9. Kosuke Fujimoto, Makoto Kinoshita, Hiroo Tanaka, Daisuke Okuzaki, Yosuke Shimada, Hisako Kayama, Ryu Okumura, Yoki Furuta, Masashi Narazaki, Atsushi Tamura, Shigetsugu Hatakeyama, Masahito Ikawa, Kiichiro Tsuchiya, Mamoru Watanabe, Atsushi Kumanogoh, Sachiko Tsukita, Kiyoshi Takeda. Regulation of intestinal homeostasis by the ulcerative colitis-associated gene RNF186. *Mucosal Immunol.* 2017.03; 10(2); 446-459
10. Chiaki Maeyashiki, Shigeru Oshima, Kana Otsubo, Masanori Kobayashi, Yoichi Nibe, Yu Matsuzawa, Michio Onizawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. HADHA, the alpha subunit of the mitochondrial trifunctional protein, is involved in long-chain fatty acid-induced autophagy in intestinal epithelial cells. *Biochem. Biophys. Res. Commun.* 2017.03; 484(3); 636-641
11. Susumu Tazuma, Michiaki Unno, Yoshinori Igarashi, Kazuo Inui, Kazuhisa Uchiyama, Masahiro Kai, Toshio Tsuyuguchi, Hiroyuki Maguchi, Toshiyuki Mori, Koji Yamaguchi, Shomei Ryozaawa, Yuji Nimura, Naotaka Fujita, Keiichi Kubota, Junichi Shoda, Masami Tabata, Tetsuya Mine, Kentaro Sugano, Mamoru Watanabe, Tooru Shimosegawa. Evidence-based clinical practice guidelines for cholelithiasis 2016. *J. Gastroenterol.* 2017.03; 52(3); 276-300
12. Jorg Mahlich, Katsuyoshi Matsuoka, Rosarin Sruamsiri. Shared Decision Making and Treatment Satisfaction in Japanese Patients with Inflammatory Bowel Disease. *Dig Dis.* 2017.04; 35(5); 454-462
13. Yoshimoto Nomura, Taro Yamashita, Naoki Oishi, Kouki Nio, Takehiro Hayashi, Mariko Yoshida, Tomoyuki Hayashi, Tomomi Hashiba, Yasuhiro Asahina, Hikari Okada, Hajime Sunagozaka, Hajime Takatori, Masao Honda, Shuichi Kaneko. De Novo Emergence of Mesenchymal Stem-Like CD105(+) Cancer Cells by Cytotoxic Agents in Human Hepatocellular Carcinoma. *Transl Oncol.* 2017.04; 10(2); 184-189
14. Masakazu Nagahori, Shuji Kochi, Hiroyuki Hanai, Takayuki Yamamoto, Shiro Nakamura, Soji Omuro, Mamoru Watanabe, Toshifumi Hibi, . Real life results in using 5-ASA for maintaining mild to moderate UC patients in Japan, a multi-center study, OPTIMUM Study. *BMC Gastroenterol.* 2017.04; 17(1); 47
15. Norie Yamada, Ryuichi Sugiyama, Sayuri Nitta, Asako Murayama, Minoru Kobayashi, Chiaki Okuse, Michihiro Suzuki, Kiyomi Yasuda, Hiroshi Yotsuyanagi, Kyoji Moriya, Kazuhiko Koike, Takaji Wakita, and Takanobu Kato. Resistance mutations of hepatitis B virus in entecavir-refractory patients HEPATOLOGY COMMUNICATIONS. 2017.04; 1(2); 110-121
16. Shuji Hibiya, Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Nobukatsu Horita, Sho Watanabe, Tomoaki Shirasaki, Ryu Nishimura, Natsuko Kimura, Tatsunori Nishimura, Noriko Gotoh, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term Inflammation Transforms Intestinal Epithelial Cells of Colonic Organoids. *J Crohns Colitis.* 2017.05; 11(5); 621-630
17. Kentaro Matsuura, Hiromi Sawai, Kazuho Ikeo, Shintaro Ogawa, Etsuko Iio, Masanori Isogawa, Noritomo Shimada, Atsumasa Komori, Hidenori Toyoda, Takashi Kumada, Tadashi Namisaki, Hitoshi Yoshiji, Naoya Sakamoto, Mina Nakagawa, Yasuhiro Asahina, Masayuki Kurosaki, Namiki Izumi, Nobuyuki Enomoto, Atsunori Kusakabe, Eiji Kajiwara, Yoshito Itoh, Tatsuya Ide, Akihiro Tamori, Misako Matsubara, Norifumi Kawada, Ken Shirabe, Eiichi Tomita, Masao Honda, Shuichi Kaneko, Sohji Nishina, Atsushi Suetsugu, Yoichi Hiasa, Hisayoshi Watanabe, Takuya Genda, Isao Sakaida, Shuhei Nishiguchi, Koichi Takaguchi, Eiji Tanaka, Junichi Sugihara, Mitsuo Shimada, Yasuteru Kondo, Yosuke Kawai, Kaname Kojima, Masao Nagasaki, Katsushi Tokunaga, Yasuhito Tanaka, . Genome-Wide Association Study Identifies TLL1 Variant Associated With Development of Hepatocellular Carcinoma After Eradication of Hepatitis C Virus Infection. *Gastroenterology.* 2017.05; 152(6); 1383-1394
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[Books etc]

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[Conference Activities & Talks]

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2. Watanabe M. Intestinal Epithelial Stem Cells for the Treatment of GI Disease. Digestive and Liver Diseases Conference, Special Lecture 2017.04.05 Dallas(USA)
3. Kawai-Kitahata F, Asahina Y, Kakinuma S, Murakawa M, Niita S, Nagata H, Kaneko S, Otani S, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Genetic differences in hepatocellular carcinoma among chronic persistent hepatitis B virus infection with or without viral suppression and prior hepatitis B virus infection. EASL The International Liver Congress 2017 2017.04.20 Amsterdam (Netherlands)
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8. Watanabe M. Recent Advances in Therapy of IBD. 2017 TSIBD Spring Forum 2017.05.27 Taipei
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22. Watanabe M. Being at the leading Edge in IBD Care and Research : Chair . AOCC2017 2017.06.17 Seoul (Korea)
23. Nagaishi T, Watabe T, Jose N, Hosoya A, Kojima Y, Tsugawa N, Adachi T, Watanabe M. Deficiency of IgA Induces Microflora Alteration and Ileal Inflammation. ICM1 2017 2017.07.21 Washington DC (USA)
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27. Watanabe M. **【Inflammatory Bowel Disease : Future Treatment Paradigm】** Chair. APDW2017 2017.09.25 (Hong Kong)
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34. Tanaka H, Kamata N, Yamada A, Fujii T, Endo K, Yoshino T, Bamba S, Sugaya T, Kawaguchi T, Ishii M, Shinzaki S, Toya Y, Yanai Y, Yokoyama Y, Umeno J, Okada T, Kobayashi T, Nojima M, Hibi T. Usefulness of combination therapy with adalimumab and immunomodulators in patients with crohn's disease: a large, multi-centre cohort study. UEGW2017 2017.10.31 Barcelona(Spain)
35. Shinzaki S, Fujii T, Bamba S, Kobayashi T, Tanaka T, Yoshino T, Yamada A, Kamata N, Hibi T. Safety and efficacy of Helicobacter pylori eradication in patients with inflammatory bowel disease. UEGW2017 2017.10.31 Barcelona(Spain)
36. Tsugawa N, Nagaishi T, Watabe T, Jose N, Hosoya A, Kojima Y, Adachi T, Blumberg R, Watanabe M. Verification of immunoglobulin a regulation of microflora and protection of intestinal mucosa. UEGW2017 2017.10.31 Barcelona(Spain)
37. Fujii T, Kitazume Y, Takenaka K, Kimura M, Saito E, Matsuoka K, Nagahori M, Ohtsuka K, Watanabe M. Simplified MR enterocolonography Classification Based on Endoscopic Findings for Activity Assessment of Crohn's Disease. UEGW2017 2017.11.01 Barcelona(Spain)
38. Ishibashi F, Shimizu H, Kawamoto A, Ito G, Nakata T, Fujii S, Suzuki K, Kuno R, Anzai S, Kuwabara K, Kawai M, Takahashi J, Hama M, Nagata S, Tsuchiya K, Nakamura T, Okamoto R, Watanabe M. Reprogrammed Atoh1+ intestinal epithelial cells contribute to regenerate damaged colonic mucosa in DSS-induced colitis. UEGW2017 2017.11.01 Barcelona(Spain)
39. Watanabe S, Tsuchiya K, Shirasaki T, Hibiya S, Ooshima S, Nakamura T, Nishimura R, Okamoto R, Watanabe M. TP53 mutation acquires higher malignant potential in human colon cancer cells. UEGW2017 2017.11.01 Barcelona(Spain)
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41. Chiba A, Nagaishi T, Miyake S. MAIT cells exacerbate the disease course of oxazolone-induced colitis. CD1-MR1 2017 2017.11.05 California (USA)
42. Watanabe M. Stem Cell Therapy for IBD: Promise and Challenge. GZDDW2017 2017.11.11 (China)
43. Watanabe M. 【Symposium 3 : Tissue-specific immune diseases】 Chair. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Miyagi (Japan)
44. Watabe T, Nagaishi T, Hosoya A, Jose N, Tsugawa N, Kojima Y, Yoshikawa S, Karasuyama H, Adachi T, Watanabe M . Analysis of ileocecal immune response in an experimental colitis model using intra-vital imaging. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Miyagi (Japan)
45. Watanabe M. 【Clinical Seminar】Chair. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Miyagi (Japan)
46. Tsugawa N, Nagaishi T, Watabe T, Hosoya A, Jose N, Kojima Y, Yoshikawa S, Karasuyama H, Adachi T, Watanabe M. Verification of immunoglobulin A regulation of mucosal microflora and homeostasis. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Miyagi (Japan)

Specialized Surgeries

< Division of Specialized Surgeries >

Professor: Hiroyuki UETAKE

Associate Professor: Toshifumi KUDO, Toshiaki ISHIKAWA

Junior Associate Professor: Tsuyoshi NAKAGAWA, Kentaro OKAMOTO

Assistant Professor: Takahiro TOYOFUKU, Mai KASAHARA

Attending staff:

Masato NISHIZAWA, Yohei YAMAMOTO, Tsuyoshi ICHINOSE

< Department of Translational Oncology >

Associate Professor: Megumi ISHIGURO

< Facility of Medical Informatics >

Junior Associate Professor: Goshi ODA

(1) Outline

Division of Specialized Surgeries have been launched in April 2015, which consists of 4 clinical departments in the Medical Hospital:

- Division of Chemotherapy and Oncosurgery
- Division of Vascular Surgery
- Division of Breast Surgery
- Division of Pediatric surgery

(2) Research

Main themes of our research activities

- Identification of prognostic factors and the predictive factors for chemo-responsiveness in gastrointestinal and breast cancer, by molecular biological technique and immuno-histochemical approach
- Micro circulation in severe ischemic extremity
- Relation between vascular disease and periodontitis
- Development of new device for evaluating hemodynamics
- Development of safety central venous catheterization
- Establishment of telemedicine

(3) Education

Main objective in the graduate course is to bring up the well-rounded surgeons who has international and scientific feelings.

(4) Publications

[Original Articles]

1. Stremitzer S, Berghoff AS, Volz NB, Zhang W, Yang D, Stintzing S, Ning Y, Sunakawa Y, Yamauchi S, Seboi A, Matsusaka S, Okazaki S, Hanna D, Parekh A, Mendez A, Berger MD, El-Khoueiry R, Birner P, Preusser M, Lenz HJ.. Genetic variants associated with colorectal brain metastases susceptibility and survival. *Pharmacogenomics J.* 2017.01; 17(1); 29-35
2. Yoshino T, Uetake H, Tsuchihara K, Shitara K, Yamazaki K, Oki E, Sato T, Naitoh T, Komatsu Y, Kato T, Yamanaka K, Iwasaki K, Soeda J, Hihara M, Ymanaka T, Ochiai A, Muro K.. Rationale for and design of the PARADIGM Study: Randomized phase III study of mFOLFOX6 plus bevacizumab or panitumumab in chemotherapy- naïve patients with RAS (KRAS/NRAS) wild-type, metastatic colorectal cancer. *Clin Colorectal Cancer.* 2017.01; 16(2); 158-163
3. Yamamoto Y, Ichinose T, Nakamura M, Nishizawa M, Igari K, Toyofuku T, Kudo T, Inoue Y.. Successful complete surgical resection of a large venous malformation of the lower extremity: A case report. *Ann Vasu Dis.* 2017.01; 10(1); 59-62
4. Tomii C, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. TPX2 expression is associated with poor survival in gastric cancer *World J Surg Oncol.* 2017.01; 15(1);
5. Iwata N, Ishikawa T, Okazaki S, Mogushi K, Baba H, Ishiguro M, Kobayashi H, Tanaka H, Kawano T, Sugihara K, Uetake H. Clinical Significance of Methylation and Reduced Expression of the Quaking Gene in Colorectal Cancer. *Anticancer Res..* 2017.02; 37(2); 489-498
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10. Matsusaka S, Wu AH, Cao S, Hanna DL, Chin K, Yang D, Zhang W, Ning Y, Stintzing S, Sebio A, Sunakawa Y, Stremitzer S, Yamauchi S, Okazaki S, Berger MD, Parekh A, Miyamoto Y, Mizunuma N, Lenz HJ.. Prognostic impact of FOXF1 polymorphisms in gastric cancer patients. *Pharmacogenomics J.* 2017.04; [Epub ahead of print] ;
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[Conference Activities & Talks]

1. Shinozaki E, Ishiguro M, Nakatani E, Yamaguchi T, Nakamura M, Miyamoto Y, Ojima H, Honma Y, Gotoh M, Ishikawa T, Takahashi K, Shimada Y, Yoshida K, Mizunuma N, Muro K, Komatsu Y, Yamaguchi K, Nakano H, Koike J, Sugihara K.. A phase II study of panitumumab with FOLFOX or FOLFIRI as 1st line chemotherapy for KRAS-wild type metastatic colorectal cancer;the PaFF-J study.. American Society of Clinical Oncology 2018 Gastrointestinal Cancers Symposium (ASCO-GI) 2017.01.21 San Francisco (USA)
2. Kudo T. Chair: Presentation Award 8. Japan Endovascular Treatment Conference (JET) 2017. 2017.02.18 Tokyo
3. Yamauchi S, Okazaki S, Kikuchi A, Ishiguro M, Ishikawa T, Uetake H, Yasuno M, Sugihara K.. Prognostic factor of lower rectal cancer with lateral pelvic lymph node metastasis treated with lateral lymph node dissection.. Society of Surgical Oncology (SSO) 2017 Annual Meeting 2017.03.16 Seattle (USA)
4. Hanaoka M, Ishikawa T, Ishiguro M, Tokura M, Yamauchi S, Kikuchi A, Yasuno M, Uetake H, Kawano T. ATF6, a UPR related gene, expression in malignant conversion and progression of Ulcerative colitis (UC)-associated and non-UC-associated colorectal cancer. Society of Surgical Oncology (SSO) 2017 Annual Meeting 2017.03.16 Seattle (USA)
5. Uetake H. The Current Statue of Treatment for Metastatic Colorectal Cancer: Firt-Line and Beyond. The 2017 Annual Meeting & 50th Anniversary of Taiwan Surgical Association (Lunch Seminar) 2017.03.19 Taipei
6. Igari K, Kudo T, Toyofuku T, Inoue Y. The chimney graft placement in the inferior mesenteric artery in endovascular aneurysm repair . 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.25 Seoul (Korea)
7. Kudo T, Yamamoto Y, Ichinose T, Nishizawa M, Igari K, Toyohuku T, Inoue Y.. Multiple recurrent pseudoaneurysms after EVAR in a patient with Behçet' s disease.. The 10th Korea-Japan Joint Meeting for Vascular Surgery 2017.04.14 Busan (Korea)
8. Kudo T, Ichinose T, Yamamoto Y, Nishizawa M, Igari K, Toyohuku T, Inoue Y.. Emergency endovascular repair for ruptured abdominal aortic and iliac aneurysms.. The 10th Korea-Japan Joint Meeting for Vascular Surgery 2017.04.15 Busan (Korea)

9. Igari K, Kudo T, Toyofuku T, Inoue Y. The relationship between inflammatory biomarkers and ischemic severity of patients with peripheral arterial disease. 85th EAS Congress 2017.04.24 Prague (Czech Republic)
10. Igari K, Kudo T, Toyofuku T, Inoue Y. The endovascular procedures of abdominal aortic aneurysms with challenging neck anatomy. 66th ESCVS 2017.05.14 Thessaloniki (Greece)
11. Ishikawa T, Ishiguro M, Nakatani E, Uetake H, Ueno H, Murotani K, Matsui S, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Teramukai S, Sugihara K.. Prognostic impact of MSI in stage II colon cancers: An additional translational study of the SACURA trial.. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
12. Ishiguro M, Nakatani E, Ueno H, Ishikawa T, Uetake H, Shimada Y, Takahashi K, Kotake K, Watanabe M, Tomita N, Mochizuki H, Teramukai S, Sugihara K.. Recurrence risk factors and outcome stratification stage II colon cancer patients: A subanalysis of the SACURA trial.. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
13. Ueno H, Ishiguro M, Nakatani E, Ishikawa T, Uetake H, Murotani K, Matsui S, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Teramukai S, Sugihara K.. Prognostic impact of tumor budding in Stage II colon cancer: A Prospective study(SACURA trial).. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
14. Ishiguro M, Nakatani E, Yamaguchi Y, Takahashi K, Shimada Y, Yoshida K, Mizunuma N, Muro K, Komatsu Y, Sugihara K . Impact of early tumor shrinkage (ETS) and depth of response (DoR) on survival: A phase II study of the 1st line therapy with panitumumab for KRAS-wild type metastatic colorectal cancer (the PaFF-J study). The 55th Annual Meeting of Japan Society of Clinical Oncology 2017.10.22 Yokohama
15. Yamauchi S, Yasuno M, Takaoka A, Matsumiya Y, Seki R, Orita F, Sasaki M, Miura T, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Sugihara K.. Clinical significance of extended lateral lymph node dissection for lower rectal cancer.. Asian Surgical Association 21st Asian Congress of Surgery 2017.11.12 Tokyo
16. Miura T, Yamauchi S, Takaoka A, Seki R, Matsumiya Y, Orita F, Sasaki M, Tokura M, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Yasuno M.. Negative pressure wound therapy for closure of ileostomy and colostomy.. The 1st International Conference of Surgical Infection Society Asia-Pacific 2017.11.29 Tokyo

Cardiovascular Medicine

Professor

Kenzo Hirao

Endowed Professor

Takashi Ashikaga

Associate Professor

Masahiko Goya

Tetsuo Sasano (Graduate School of Health Care Sciences,
Biofunctional Informatics)

Kiyoshi Nobori (Clinical Research Center)

Junior Associate Professor

Yasuhiro Maejima, Mihoko Kawabata, Yusuke Ebana (Medical Research Institute
Bio-informational Pharmacology)

Assistant Professor

Takanobu Yamamoto, Yoshihide Takahashi, Taro Sasaoka,,

Yu Hatano, Hidenori Arima, Masanori Konishi

Specially-Appointed Professor

Shingo Maeda, Kentaro Takahashi

Endowed Assistant Professor

Tomoyuki Umemoto

Joint Research Assistant Professor

Atsuhiko Yagishita

Graduate Student

Yusuke Ito, Kei Takayama, Ryota Iwatsuka, Tatsuya Fujinami, Osamu Inaba, Rena Nakamura, Riri Watanabe, Naoyuki Miwa, Tomoyuki Umemoto, Takashi Nakagawa, Yasuaki Tanaka, Tetsumin Lee, Yukihiro Inamura, Mie Ochida, Tomomasa Takamiya, Kensuke Hirasawa, Yuki Osaka, Ohnishi Kentaro, Mituhisa Asano, Nobutaka Kato, Yasuhiro Shirai, Naohiko Kawaguchi, Shinsuke Iwai, Shunsuke Kuroda, Nobuyuki Kagiya, Takuro Nisimura, Junji Matuda, Makoto Araki, Shigeki Kusa, Kazuya Yamao, Takamitsu Takagi, Yoshihisa Kanaji, Sho Nagamine, Rei Masuda, Eisuke Usui, Naoko Kato, Takashi Niida, Akira, Mizukami, Masakazu Kaneko, Tatsuhiko Hirao, Takakatu Yoshitake, Taku Fukushima, Yuichiro Sagawa, Tadashi Fukuda

(1) Outline

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University aims to elucidate the cause of the cardiovascular diseases, including ischemic heart diseases, arrhythmia and heart failure, and to develop their novel therapeutic strategies by assessing both basic and clinical research approaches.

We encourage young doctors to be well-balanced physicians who focus on medical therapy as well as on research. Students are encouraged and being trained to take an active role at global level, as well. We strive to make high contributions in the area of cardiovascular medicine within Japan.

(2) Research

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, thereby developing novel technologies for diagnosis and treatment. For that purpose we investigate clinical cases and experimental animal models. Our faculty members pursue a wide variety of basic research, ranging from investigations on the molecular mechanism of heart failure to the development of novel interventional devices for patients with angina pectoris. Current strengths of the program include molecular cardiology under Yasuhiro Maejima MD, PhD. We also actively investigate immunocardiology, the molecular mechanism of pulmonary hypertension and periodontitis-associated cardiovascular diseases.

- 1) System of origin with tachyarrhythmias (particularly supraventricular tachycardia) (Hirao)
- 2) Medical therapy and ablation for tachyarrhythmias (Hirao)
- 3) Research for the conduction of atrio-ventricular node (Hirao)
- 4) Research and Therapy for arrhythmia by using cardioendoscopy (Hirao)
- 5) Research of atrial fibrillation from origin of pulmonary vein (Hirao)
- 6) Research of genetic factor with atrial fibrillation (Hirao)
- 7) Research of ablation for atrial fibrillation (Hirao, Goya)
- 8) Clinical study for treatment of acute coronary syndrome (Ashikaga, Yamamoto, Umemoto, Sasaoka, Hatano)
- 9) Molecular mechanism and treatment of myocardial ischemia and reperfusion injury (Maejima, Hatano)
- 10) Molecular mechanism and treatment of coronary restenosis and vascular disease (Maejima, Hatano)
- 11) Treatment of heart failure and cardiomyopathy by myocardial regeneration (Maejima)
- 12) Regulation of arteriosclerosis by targeting transcription factors (Maejima)
- 13) Diagnostic imaging of aortitis (Tezuka)
- 14) Assessment by imaging of coronary artery and cardiac function (Tezuka)
- 15) Molecular mechanism and treatment of aortitis (Maejima)
- 16) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia (Maejima)
- 17) Application in gene therapy for heart failure and cardiomyopathy (Maejima)
- 18) Molecular system of myocardial remodeling in heart failure and ventricular hypertrophy (Maejima)

There are many fruitful collaborative efforts between our department and other departments with the TMDU, such as the Department of Bio-informational Pharmacology, Medical Research Institute. Collaborations with other institutions are also common. Especially, we closely collaborate with the Department of Cell Biology and Molecular Medicine, Rutgers-New Jersey Medical School (Newark, NJ, USA; Junichi Sadoshima MD, PhD). Our cardiologists continuously contribute to establish evidence-based cardiovascular medicine through clinical researches. So far, we are engaged in over ten clinical studies. The targets of our clinical research include heart failure, ischemic heart disease, arrhythmia, cardiac imaging and Takayasu arteritis.

(3) Education

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University (TMDU) primarily aims at offering patient-centered care for every person who suffer from cardiovascular diseases, including ischemic heart diseases, arrhythmia, heart failure, valvular disorders and vasculitis. Our cardiologists are experts in electrophysiology, interventional cardiology, heart failure, and cardiac imaging who make full use of state-of-the-art diagnostic tests and therapeutic procedures to provide high-quality care for every patient. We also actively engage in basic and clinical research to elucidate the mechanism of heart & vessel disorders for providing novel therapeutic strategies to the patients of cardiovascular diseases. In addition to high-quality patient care and innovative research, our faculty members are vigorously involved in the education and training to the young physicians and researchers specializing in cardiovascular medicine. Thus, we are continuously making every effort to serve the highest quality of patient care, education and innovative research of cardiovascular medicine.

(4) Clinical Services & Other Works

Our clinical training program provides the trainee with outstanding skills in clinical cardiology. The trainees will develop their clinical knowledge, clinical judgment, procedural skills and interpersonal skills required as a specialist in cardiovascular diseases. The program provides clinical cardiology training not only at the University Hospital but also at our outstanding affiliate hospitals (N=22), including Kameda General Hospital, Musashino Red-Cross Hospital, Tsuchiura Kyodo Hospital and Yokosuka Kyosai Hospital. Our training program for re-

search emphasizes developing academic cardiologists who will become leaders in cardiovascular research. The program offers training of basic, clinical and translational researches not only at the Graduate School of our department but also at other departments with the TMDU and at other institutions described above.

(5) Publications

[Original Articles]

1. Takigawa M, Takahashi A, Kuwahara T, Okubo K, Takahashi Y, Watari Y, Nakashima E, Nakajima J, Yamao K, Takagi K, Tanaka Y, Fujino T, Kimura S, Hikita H, Hirao K, Isobe M. . Long-term outcome after catheter ablation of paroxysmal atrial fibrillation: Impact of different atrial fibrillation foci. *Int J Cardiol.* . 2017.01; 227; 407-412
2. Takigawa M, Takahashi A, Kuwahara T, Okubo K, Takahashi Y, Watari Y, Nakashima E, Nakajima J, Yamao K, Takagi K, Tanaka Y, Fujino T, Kimura S, Hikita H, Hirao K, Isobe M. . Long-term outcome after catheter ablation of paroxysmal atrial fibrillation: Impact of different atrial fibrillation foci. *Int J Cardiol.* . 2017.01; 227; 407-412
3. Miyazaki S, Taniguchi H, Kusa S, Nakamura H, Hachiya H, Hirao K, Iesaka Y. . Five-year follow-up outcome after catheter ablation of persistent atrial fibrillation using a sequential biatrial linear defragmentation approach: What does atrial fibrillation termination during the procedure imply? *Heart Rhythm.* . 2017.01; 14(1); 34-49
4. Yagishita A, Yamauchi Y, Miyamoto T, Hirao K.. Electrophysiological evidence of localized reentry as a trigger and driver of atrial fibrillation at the junction of the superior vena cava and right atrium. *HeartRhythm Case Rep.* . 2017.01; 3(3); 164-166
5. Ohtani H, Kimura S, Sugiyama T, Hishikari K, Misawa T, Mizusawa M, Hayasaka K, Yamakami Y, Kojima K, Sagawa Y, Hikita H, Ashikaga T, Takahashi A, Isobe M. . Comparison of vascular responses after different types of second-generation drug-eluting stents implantation detected by optical coherence tomography. *Int J Cardiovasc Imaging.* . 2017.02; 33(2); 177-186
6. Yagishita A, Yamauchi Y, Sato H, Yamashita S, Hirao T, Miyamoto T, Hirao K, Isobe M.. Improvement in the Quality of Life and Exercise Performance in Relation to the Plasma B-Type Natriuretic Peptide Level After Catheter Ablation in Patients With Asymptomatic Persistent Atrial Fibrillation. *Circ J.* 2017.03; 81(4); 444-449
7. Kagiya N, Hayashida A, Toki M, Fukuda S, Ohara M, Hirohata A, Yamamoto K, Isobe M, Yoshida K. . Insufficient Leaflet Remodeling in Patients With Atrial Fibrillation: Association With the Severity of Mitral Regurgitation. *Circ Cardiovasc Imaging.* . 2017.03; 10(3); e005451
8. Tao S, Otomo K, Ono Y, Osaka Y, Hirao T, Koura K, Manno T, Ueshima D, Shimizu S, Isobe M, Hirao K. . Efficacy and safety of uninterrupted rivaroxaban taken preoperatively for radiofrequency catheter ablation of atrial fibrillation compared to uninterrupted warfarin. *J Interv Card Electrophysiol.* 2017.03; 48(2); 167-175
9. Ryo Watanabe, Jun-Ichi Suzuki, Kouji Wakayama, Yasuhiro Maejima, Munehisa Shimamura, Hiroshi Koriyama, Hironori Nakagami, Hidetoshi Kumagai, Yuichi Ikeda, Hiroshi Akazawa, Ryuichi Morishita, Issei Komuro, Mitsuaki Isobe. A peptide vaccine targeting angiotensin II attenuates the cardiac dysfunction induced by myocardial infarction. *Sci Rep.* 2017.03; 7; 43920
10. Takahashi Y, Iwai S, Yamashita S, Masumura M, Suzuki M, Yabe K, Sato Y, Hirao K, Isobe M. . Novel Mapping Technique for Localization of Focal and Reentrant Activation During Atrial Fibrillation. *J Cardiovasc Electrophysiol.* . 2017.04; 28(4); 375-382
11. Kawabata M, Goya M, Sasaki T, Maeda S, Yagishita A, Shirai Y, Kaneko M, Shiohira S, Isobe M, Hirao K. . Surface Electrocardiogram Screening for Subcutaneous Implantable Cardioverter-Defibrillators in Japanese Patients With and Without Brugada Syndrome. *Circ J.* 2017.04; 81(5); 645-651
12. Iwai S, Takahashi Y, Masumura M, Yamashita S, Doi J, Yamamoto T, Sakakibara A, Nomoto H, Yoshida Y, Sugiyama T, Oumi T, Ohno M, Sato Y, Hirao K, Isobe M. . Occurrence of Focal Atrial Tachycardia During the Ablation Procedure Is Associated With Arrhythmia Recurrence After Termination of Persistent Atrial Fibrillation. *J Cardiovasc Electrophysiol.* 2017.05; 28(5); 489-497

13. Miyazaki S, Nakamura H, Taniguchi H, Hachiya H, Takagi T, Igarashi M, Kajiyama T, Watanabe T, Niida T, Hirao K, Iesaka Y. . Gastric hypomotility after second-generation cryoballoon ablation-Unrecognized silent nerve injury after cryoballoon ablation. *Heart Rhythm.* . 2017.05; 14(5); 670-677
14. Miyazaki S, Kusa S, Hachiya H, Taniguchi H, Niida T, Ichijo S, Hirao K, Iesaka Y. . Electrical superior vena cava isolation using a novel pace-and-ablate technique under diaphragmatic electromyography monitoring. *Heart Rhythm.* . 2017.05; 14(5); 678-684
15. Shirai Y, Goya M, Ohno S, Horie M, Doi S, Isobe M, Hirao K. . Elimination of Ventricular Arrhythmia in Catecholaminergic Polymorphic Ventricular Tachycardia by Targeting "Catecholamine-Sensitive Area": A Dominant-Subordinate Relationship between Origin Sites of Bidirectional Ventricular Premature Contractions. *Pacing Clin Electrophysiol.* 2017.05; 40(5); 600-604
16. Ohigashi H, Tamura N, Ebana Y, Harigai M, Maejima Y, Ashikaga T, Isobe M. . Effects of immunosuppressive and biological agents on refractory Takayasu arteritis patients unresponsive to glucocorticoid treatment. *J Cardiol.* 2017.05; 69(5); 774-778
17. Ueshima D, Ashikaga T, Yoshikawa S, Sasaoka T, Hatano Y, Kurihara K, Maejima Y, Isobe M. . Effect of over-2-year dual antiplatelet therapy on the rate of major adverse cardiac and cerebral events for everolimus-eluting stent implantation: The landmark analysis from Tokyo-MD PCI registry. *J Cardiol.* . 2017.06; 69(6); 815-822
18. Shiohira S, Sasaki T, Maeda S, Kawabata M, Goya M, Hirao K. . Bronchogenic cyst of the atrioventricular septum presenting with ventricular fibrillation. *HeartRhythm Case Rep.* . 2017.06; 3(8); 389-391
19. Inaba O, Satoh Y, Isobe M, Yamamoto T, Nagao K, Takayama M. . Factors and values at admission that predict a fulminant course of acute myocarditis: data from Tokyo CCU network database. *Heart Vessels.* . 2017.08; 32(8); 952-959
20. Hirasawa K, Izumo M, Sasaoka T, Ashikaga T, Suzuki K, Harada T, Isobe M, Akashi YJ. . Effect of aortic regurgitant jet direction on mitral valve leaflet remodeling: a real-time three-dimensional transesophageal echocardiography study. *Sci Rep.* 2017.08; 7(1); 8884
21. Hirasawa K, Izumo M, Sasaoka T, Ashikaga T, Suzuki K, Harada T, Isobe M, Akashi YJ. . Effect of aortic regurgitant jet direction on mitral valve leaflet remodeling: a real-time three-dimensional transesophageal echocardiography study. *Sci Rep.* 2017.08; 7(1); 8884
22. Takigawa M, Takahashi A, Kuwahara T, Okubo K, Nakashima E, Watari Y, Yamao K, Nakajima J, Tanaka Y, Takagi K, Kimura S, Hikita H, Hirao K, Isobe M. . Airway support using a pediatric intubation tube in adult patients with atrial fibrillation: A simple and unique method to prevent heart movement during catheter ablation under continuous deep sedation. *J Arrhythm.* . 2017.08; 33(4); 262-268
23. Inaba O, Nagata Y, Yamauchi Y, Miyamoto T, Goya M, Hirao K. . Verapamil-sensitive atrial tachycardia with a slow conduction zone near the noncoronary aortic sinus and His bundle. *Clin Case Rep.* . 2017.08; 5(10); 1623-1627
24. Taku Fukushima, Takashi Ashikaga, Shunji Yoshikawa, Yu Hatano, Daisuke Ueshima, Takanobu Yamamoto, Yasuhiro Maejima, Mitsuaki Isobe. Effect of drug-coated balloon on stent restenosis, neointimal proliferation, and coronary dissection: an optical coherence tomography analysis. *Coron. Artery Dis.* 2017.09;
25. Tamura N, Maejima Y, Tezuka D, Takamura C, Yoshikawa S, Ashikaga T, Hirao K, Isobe M. . Profiles of serum cytokine levels in Takayasu arteritis patients: Potential utility as biomarkers for monitoring disease activity. *J Cardiol.* . 2017.09; 70(3); 278-285
26. Yagishita A, Hirao K. . Efficacy of Familial Screening After Sudden Cardiac Death in Young Adults Irrespective of Postmortem Analysis: Implication of a Pharmacological Challenge as a First Step of Screening. *Circ Arrhythm Electrophysiol.* 2017.09; 10(9); e005710
27. Yagishita A, Hirao K. . Efficacy of Familial Screening After Sudden Cardiac Death in Young Adults Irrespective of Postmortem Analysis: Implication of a Pharmacological Challenge as a First Step of Screening. *Circ Arrhythm Electrophysiol.* 2017.09; 10(9); e005710

28. Ebana Y, Ozaki K, Liu L, Hachiya H, Hirao K, Isobe M, Kubo M, Tanaka T, Furukawa T. . Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25. *J Cardiol.* . 2017.10; 70(4); 366-373
29. Nakamura T, Okishige K, Kanazawa T, Yamashita M, Kawaguchi N, Kato N, Aoyagi H, Yamauchi Y, Sasano T, Hirao K.. Incidence of silent cerebral infarctions after catheter ablation of atrial fibrillation utilizing the second-generation cryoballoon. *Europace.*. 2017.10; 19(10); 1681-1688
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31. Aoyama N, Suzuki JI, Kobayashi N, Hanatani T, Ashigaki N, Yoshida A, Shiheido Y, Sato H, Kumagai H, Ikeda Y, Akazawa H, Komuro I, Minabe M, Izumi Y, Isobe M. Japanese Cardiovascular Disease Patients with Diabetes Mellitus Suffer Increased Tooth Loss in Comparison to Those without Diabetes Mellitus -A Cross-sectional Study. *Intern. Med.*. 2017.11; epub;

[Misc]

1. Anindita Das, Flávio Reis, Yasuhiro Maejima, Zhiyou Cai, Jun Ren. mTOR Signaling in Cardiometabolic Disease, Cancer, and Aging. *Oxid Med Cell Longev.* 2017.07; 2017; 6018675
2. Sebastiano Sciarretta, Yasuhiro Maejima, Daniela Zablocki, Junichi Sadoshima. The Role of Autophagy in the Heart. *Annu. Rev. Physiol.*. 2017.10;

[Conference Activities & Talks]

1. Maejima Yasuhiro. The critical role of autophagy in the Progression of Heart Failure. 2017.03.15
2. Maejima Yasuhiro. TXNIP accumulation caused by single nucleotide polymorphism of MLX gene enhances inflammasome formation, thereby promoting the development of Takayasu Arteritis. The 18th International Vasculitis and ANCA Workshop 2017.03.27 Tokyo, Japan
3. Yasuhiro Maejima, Yusuke Ito, Natsuko Tamura, Masanori Konishi, Mitsuaki Isobe. Factor Xa Deteriorates Atherosclerosis by Facilitating Inflammasome Formation via PAR-2-mediated Autophagy Suppression. AHA Basic Cardiovascular Sciences 2017 2017.07.10 Portland, Oregon, USA
4. Yasuhiro Maejima, Yusuke Ito, Natsuko Tamura, Masanori Konishi, Mitsuaki Isobe. Blood coagulation factor Xa promotes the progression of atherosclerosis by enhancing inflammasome formation as a consequence of PAR2-mediated autophagy inhibition. ESC Congress 2017 2017.08.26 Barcelona, Spain

Anesthesiology

Professor: Tokujiro Uchida

Junior Associate Professor: Jiro Kurata

Assistant Professor: Akio Masuda, Yusuke Ito, Atsushi Ito, Hiroto Yamamoto, Hiroki Yamamoto, Ken Shinoda, Takafumi Omori, Aya Takemoto, Kunio Suzuki, Akiko Kitajo, Hitomi Kanamori, Sayomi Tsukada, Arisa Fukagawa,

Staff: Tomoko Ishibasi, Koji Kido, Yudai Yamamoto,

Mayumi Echizen, Mamiko Yoshida, Akiko Suzuki

Resident: Junpei Shibata, Hiromichi Suzuki, Shiho Tanaka,

Mizuki Motomura, Sayaka Yamashita, Sho Watanabe, Saki Hagiwara,

Hironobu Katsuyama, Marina Goto, Shoko Imamura, Yoriko Yamada

Postgraduate Student: Hiroyuki Kobinata, Eri Ikeda, Tomoko Ishibashi, Hiroto Yamamoto,

Yudai Yamamoto, Zhang Shuo, Tianjiao Li, Tsuyoshi Kanma, Hirotsugu Ota

(1) Outline

A comprehensive understanding of research trends, research methods, and analysis of results by introducing the latest papers published in prestigious journals related to anesthesiology.

(2) Research

- 1) Discovering most effective ventilation methods for injury lungs.
- 2) Therapeutic mechanism of mesenchymal stem cell for lung injury (rat and mouse model)
- 3) Studies on the central nervous system effects of general anesthetics by human electrocorticogram and functional neuroimaging.
- 4) Studies on the mechanisms of cerebral pain processing and pain chronification by human functional magnetic resonance imaging and positron emission tomography.
- 5) Studies on the effects of protective one-lung ventilation on ventilatory mechanics.
- 6) Epidemiologic studies to identify incidence of, and risk factors for postoperative acute kidney injury in patients undergoing liver resection.

(3) Publications

[Original Articles]

1. Effectiveness of the regional anesthesia for open abdominal colectomy in patients with low pulmonary function 2017.02; 41(2); 157-160
2. Odaka M., Nagata M., Mizuno T., Uchida T., Takahashi H., Makita K., Arai H., Echizen H., Yasuhara M.. EFFECT OF CARDIOPULMONARY BYPASS SURGERY ON UNBOUND FRACTION OF CEFAZOLIN IN PLASMA CLINICAL PHARMACOLOGY & THERAPEUTICS. 2017.02; 101(S1); S81
3. Ishikawa S, Akune T, Ishibashi T, Makita K.. A case of unexpected impaired oxygenation due to intraoperative pneumothorax: an adverse event associated with respiratory management with spontaneous

respiration in a patient with esophagobronchial fistulae. *Journal of Anesthesia Clinical Reports*. 2017.05; 3(1); 31

4. Hideaki Kaneko, Shuo Zhang, Miho Sekiguchi, Takuya Nikaido, Koshi Makita, Jiro Kurata, Shin-Ichi Konno. Dysfunction of Nucleus Accumbens Is Associated With Psychiatric Problems in Patients With Chronic Low Back Pain: A Functional Magnetic Resonance Imaging Study. *Spine*. 2017.06; 42(11); 844-853
5. Yohei Matsuo, Jiro Kurata, Miho Sekiguchi, Katsuhiro Yoshida, Takuya Nikaido, Shin-Ichi Konno. Attenuation of cortical activity triggering descending pain inhibition in chronic low back pain patients: a functional magnetic resonance imaging study. *Journal of Anesthesia*. 2017.08; 31(4); 523-530
6. Hiroyuki Kobinata, Eri Ikeda, Shuo Zhang, Tianjiao Li, Koshi Makita, Jiro Kurata. Disrupted offset analgesia distinguishes patients with chronic pain from healthy controls. *Pain*. 2017.10; 158(10); 1951-1959

[Books etc]

1. Lohser J, Ishikawa S. Chapter 6, Clinical management of one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 83-101..
2. Lohser J, Ishikawa S. Chapter 5, Physiology of the lateral decubitus position, open chest, and one-lung ventilation. Slinger P Ed., Principles and practice of anesthesia for thoracic surgery. Springer, 2011, pp 71-82..

[Conference Activities & Talks]

1. Jiro Kurata. Pain in the brain. Winter Scientific Meeting London, Association of Anaesthetists of Great Britain and Ireland 2017.01.13
2. Jiro Kurata. Anaesthesia – Too Little of Too Much?. Winter Scientific Meeting London (Association of Anaesthetists of Great Britain and Ireland) 2017.01.13
3. Li T, Ikeda E, Kobinata H, Zhang S, Makita K, Kurata J. Functional connectivity modulations in resting state and offset analgesia in chronic pain patients: an fMRI study. *Euroanaesthesia 2017* 2017.06.04 Geneva, Switzerland
4. Uchida T, Mitaka K. Treatment of Acute Kidney Injury: Atrial Natriuretic Peptide. The 64th Annual Meeting of the Japanese Society of Anesthesiologists 2017.06.08 Kobe, Hyogo, Japan
5. Jiro Kurata. Cerebral signatures of pain chronification. 10th International Symposium on Memory and Awareness in Anaesthesia 2017.06.21
6. Kido K, Ito H, Uchida T. Protective Effects of Coenzyme Q10 on Cytotoxicity of Propofol in Human-induced Pluripotent Stem Cell-derived Cardiomyocytes. *Anesthesiology 2017* 2017.10.23 Boston, MA, USA
7. Jiro Kurata. Neural mechanisms of offset analgesia. 7th Asian Pain Symposium 2017.10.27

[Awards & Honors]

1. Best Abstract Award First Prize, European Society for Anaesthesiologists, 2017.06
2. Best Abstract Award, The 51st Annual Meeting of the Japanese Society of Pain Clinicians, 2017.07

Cardiovascular Surgery

Professor: Hirokuni ARAI

Associate Professor: Tomohiro MIZUNO

Junior Associate Professor: Keiji OI

Assistant Professor: Masafumi YASHIMA, Tsuyoshi HACHIMARU, Eiki NAGAOKA(sabbatical leave from July), Hidehito KUROKI(from July), Tatsuki FUJIWARA, Masashi TAKESHITA

Graduate Student: Tatsuki FUJIWARA, Hidehito KUROKI, Dai TASAKI, Kenji SAKAI, Ryoji KINOSHITA(from April)

Hospital Staff: 4

Department of Advanced Surgical Technology Research and Development

Associate Professor: Katsuhiko OUCHI

(1) Research

- 1) Developing safe and high quality surgical strategy in coronary artery bypass grafting surgery.
- 2) Developing new surgical technique for ischemic heart disease
- 3) Developing new surgical technique for beating mitral valve surgery
- 4) Clinical research for artificial heart
- 5) Research for new regenerative therapy for failing heart to recover cardiac function

(2) Education

Cardiovascular Surgery is a branch of surgery which deals with heart and vascular (mainly aortic) disease. Main objective of our department in the graduate course is to provide medical students an opportunity to study surgical anatomy, pathophysiology, pharmacology, and advanced surgical treatment for heart and aortic disease. Students are also taught basic research for the surgical treatment for heart and aortic disease. We also provide clinical training program for young surgeon to obtain Japanese cardiovascular surgical board.

(3) Clinical Performances

Our department provides well-advanced surgical treatment of heart and aortic surgery. We perform off-pump coronary artery bypass grafting for more than 90% of patients with coronary artery disease, mitral valve repair, not valve replacement, for almost all patients with mitral valve regurgitation. New surgical reconstruction technique is provided for patients with functional mitral regurgitation due to severe heart failure. For elderly patients, we offer minimally invasive aortic surgery such as thoracic endovascular aortic repair (TEVAR) and hybrid aortic surgery without cardiopulmonary bypass for aortic arch and thoracoabdominal aortic disease.

(4) Publications

[Original Articles]

1. Ryoji Kinoshita, MD, Tomohiro Mizuno, MD, PhD, Tsuyoshi Hachimaru, MD, Keiji Oi, MD, PhD, Masafumi Yashima, MD, Eiki Nagaoka, MD, PhD, Tatsuki Fujiwara, MD, Hidehito Kuroki, MD, Dai Tasaki, MD, and Hirokuni Arai, MD, PhD. Antineutrophil Cytoplasmic Antibody—Associated Multiple Giant Saccular Aortic Aneurysms The Annals of Thoracic Surgery. 2017.02; 103(2); e153-e155
2. Tomomi Hasegawa, Munetaka Masuda, Meinoshin Okumura, Hirokuni Arai, Junjiro Kobayashi, Yoshikatsu Saiki, Kazuo Tanemoto, Hiroshi Nishida, Noboru Motomura. Trends and outcomes in neonatal cardiac surgery for congenital heart disease in Japan from 1996 to 2010. Eur J Cardiothorac Surg. 2017.02; 51(2); 301-307
3. Tomohiro Mizuno, Koso Egi, Kenji Sakai, Keiji Oi, Tsuyoshi Hachimaru, Tohru Makita, Kiyotoshi Oishi, Hirokuni Arai. Minimally Circulatory-Assisted On-Pump Beating Coronary Artery Bypass Grafting for Patients With Complex Conditions for Off-Pump Surgery. Artif Organs. 2017.03; 41(3); 233-241
4. Munetaka Masuda, Hiroyuki Kuwano, Meinoshin Okumura, Hirokuni Arai, Shunsuke Endo, Yuichiro Doki, Junjiro Kobayashi, Noboru Motomura, Hiroshi Nishida, Yoshikatsu Saiki, Fumihiro Tanaka, Kazuo Tanemoto, Yasushi Toh, Hiroyasu Yokomise. Erratum to: Thoracic and cardiovascular surgery in Japan during 2013 : Annual report by The Japanese Association for Thoracic Surgery. Gen Thorac Cardiovasc Surg. 2017.03; 65(3); 182-186
5. Tomohiro Mizuno, Masahiko Goya, Kenzo Hirao, Hirokuni Arai. Implantable epicardial cardioverter-defibrillator-induced localized constrictive pericarditis. Interact Cardiovasc Thorac Surg. 2017.08; Epub;
6. Arimura S., Seki M., Sasaki K., Takai H., Matsuhama M., Kunihara T., Okita Y., Takanashi S., Komiya T., Yaku H., Okabayashi H., Takemura H., Arai H., Sawazaki M., Matsui Y., Shiiya N.. A nationwide survey of aortic valve surgery in Japan: current status of valve preservation in cases with aortic regurgitation Gen Thorac Cardiovasc Surg. 2017.08; 65(8); 429-434
7. Tatsuki Fujiwara, Daisuke Sakota, Katsuhiko Ohuchi, Shu Endo, Tomoki Tahara, Tomotaka Murashige, Ryo Kosaka, Keiji Oi, Tomohiro Mizuno, Osamu Maruyama, Hirokuni Arai. Optical Dynamic Analysis of Thrombus Inside a Centrifugal Blood Pump During Extracorporeal Mechanical Circulatory Support in a Porcine Model. Artif Organs. 2017.10; 41(10); 893-903

[Conference Activities & Talks]

1. Arai H. Seeing for Optimum Exposure in OPCAB. Tentacles for CABG 2017.03.22 Seoul, Korea
2. Arai H. Ultrasonic Intraoperative Surgical Guidance and Quality Assessment to improve outcomes after CABG. The 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.23 Seoul, Korea
3. Takeshita M, Arai H, Mizuno T, Oi K, Yashima M, Hachimaru T, Nagaoka E, Kuroki H, Tasaki D, Fujiwara T, Kinoshita R. Left atrioventricular valve repair in adult partial atrioventricular septal defect cases. The 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.24 Seoul, Korea
4. Ryoji Kinoshita, Tomohiro Mizuno, Tsuyoshi Hachimaru, Keiji Oi, Masafumi Yashima, Eiki Nagaoka, Tatsuki Fujiwara, Hidehito Kuroki, Dai Tasaki, Masashi Takeshita, Hirokuni Arai. Surgical Strategies for Multiple Inflammatory Thoracic Aortic Aneurysms due to Vasculitis. the 25th Annual meeting of Asian Society for Cardiovascular and Thoracic Surgery (ASCVTS2017) 2017.03.24 Seoul, Korea
5. Arai H. (Moderator) Coronary Artery Bypass Grafting: Total Arterial Revascularization for Ischemic Heart Disease. The 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.24 Seoul, Korea
6. Arai H. Coronary Artery Bypass Grafting: Total Arterial Revascularization for Ischemic Heart Disease. The 25th Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery 2017.03.24 Seoul, Korea
7. Arai H. Mitral valve repair: State of Art. Master of Surgery 2017 2017.03.31 Bangkok, Thailand

8. Arai H. How to improve outcomes of CABG. Master of Surgery 2017 2017.03.31 Bangkok, Thailand
9. Tomohiro Mizuno. Patient Selection Case Studies. International MCS Advanced Workshop 2017.04.03 San Diego, USA
10. Takeshita M, Yashima M, Mizuno T, Oi K, Hachimaru T, Nagaoka E, Kuroki H, Tasaki D, Fujiwara T, Kinoshita R, Arai H. Successful Mitral Valve Repair involving Division of Bridging Tissue in a Patient with Double Orifice Mitral Valve. AATS Mitral Conclave 2017 2017.04.27 New York, NY, USA
11. Ryoji Kinoshita, Hirokuni Arai. Septal Leaflet Augmentation for Severe Tricuspid Regurgitation Caused by Pacemaker/Intracardiac Defibrillator Leads. AATS Mitral Conclave 2017 2017.04.27 New York, USA
12. Ryoji Kinoshita. Early to Mid-Term Results of Mitral Valve Repair with Autologous Pericardial Patch for Active Infective Endocarditis with Extensive Leaflet Destruction. AATS Mitral Conclave 2017 2017.04.27 New York, USA
13. E. Nagaoka, T. Mizuno, K. Oi, M. Yashima, T. Hachimaru, H. Kuroki, D. Tasaki, T. Fujiwara, M. Takeshita, R. Kinoshita, H. Arai. Efficacy of Subvalvular Procedures for Ischemic Mitral Regurgitation . AATS Mitral Conclave 2017 2017.04.27 New York, United States
14. Arai H. New Pathology Oriented Repair Technique for Posterior Mitral Leaflet Prolapse: “Mt. Fuji” Repair Technique.. AATS Mitral Conclave 2017 2017.04.27 New York, USA
15. Arai H. Repair Strategies for Functional TR. AATS Mitral Conclave 2017 2017.04.27 New York, USA
16. Tomohiro Mizuno, Kenji Sakai, Eiki Nagaoka, Daiju Watanabe, Keiji Oi, Tsuyoshi Hachimaru, Masafumi Yashima, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Masashi Takeshita, Ryoji Kinoshita, Hirokuni Arai. (Poster) Off pump Intraabdominal Rerouting of Patent Gastroepiploic Arterial Grafts at the Time of Laparotomy after Coronary Artery Bypass Grafting. ISMICS Annual Scientific Meeting 2017.06.07 Rome, Italy
17. Hidehito Kuroki, Smith Srisont, Hirokuni Arai. Development of a New Sternal Fixation Device; An Uncalcined Hydroxyapatite Poly-L-Lactide Corrugated Sheet. International Society for Minimally Invasive Cardiothoracic Surgery 2017 Annual Scientific Meeting 2017.06.07 Rome, Italy
18. Nagaoka E., Mizuno T., Goya M., Oi K., Yashima M., Hachimaru T., Kuroki H., Tasaki D., Fujiwara T., Takeshita M., Kinoshita R., Arai H. Hybrid Approach for Intravenous Lead Extraction. 17 ISMICS Annual Scientific Meeting 2017.06.07 Rome, Italy
19. Tatsuki Fujiwara, Hirokuni Arai, Tomohiro Mizuno, Keiji Oi, Masafumi Yashima, Tsuyoshi Hachimaru, Eiki Nagaoka, Hidehito Kuroki. Minimally Circulatory-assisted On-pump Beating Coronary Artery Bypass Grafting For Patients With Complex Conditions For Off-pump Surgery. 2017 International Coronary Congress 2017.08.18 New York
20. Arai H. GEA: Which Targets? Free Graft or In-Situ?. 2017 International Coronary Congress 2017.08.18 New York, USA
21. Tomohiro Mizuno, Keiji Oi, Masafumi Yashima, Tsuyoshi Hachimaru, Eiki Nagaoka, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Masashi Takeshita, Ryoji Kinoshita, Hirokuni Arai. How to select Proximal Anastomotic Devices and Procedures to avoid Perioperative Stroke in CABG. International Coronary Congress 2017.08.19 New York
22. Tomohiro Mizuno, Kenji Sakai, Eiki Nagaoka, Daiju Watanabe, Keiji Oi, Tsuyoshi Hachimaru, Masafumi Yashima, Hidehito Kuroki, Dai Tasaki, Tatsuki Fujiwara, Masashi Takeshita, Ryoji Kinoshita, Hirokuni Arai. (Poster) Intraabdominal Off-pump Rerouting Procedure of Patent Gastroepiploic Arterial Grafts for Pancreaticoduodenectomy. International Coronary Congress 2017.08.19 New York
23. Arai H. High Frequency Ultrasound Interrogation of Anastomoses. 2017 International Coronary Congress 2017.08.19 New York, USA
24. Arai H. Coronary Shunting and Other Adjuncts to OPCABG. 2017 International Coronary Congress 2017.08.19 New York, USA
25. Arai H. Innovative Approach for treatment of FMR. 4th Heart Care Heart International Symposium (Pre-congress) 2017.08.24 Bangkok, Thailand

26. Arai H. Pathology Oriented Resection in MV Repair : Mount Fuji's Technique. 4th Heart Care Heart International Symposium 2017.08.25 Bangkok, Thailand
27. Arai H. B. Papillary Muscle Relocation. 4th Heart Care Heart International Symposium 2017.08.26 Bangkok, Thailand
28. Kosaka R, Sakota D, Fujiwara T, Murashige T, Nishida M, Tahara T, Ohuchi K, Orai H, Maruyama O.. Evaluation of hemocompatibility of a hydrodynamically levitated centrifugal blood pump using hyperspectral imaging in acute animal studies. 44th ESAO and 7th IFAO Congress 2017.09.06 Vienna, Austria
29. Arai H. Non-invasive quantification of blood flow in epicardial coronary arteries, coronary artery graft and anastomosis – Can this change graft patency in minimally invasive CABG?. 2nd Annual Conference of Society of Minimally Invasive Cardiovascular and Thoracic Surgeons of India 2017.09.10 Jaipur, India
30. Arai H. (Moderator) SESSION XIII - CORONARY SURGERY PART II. The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.22 Iasi, Romania
31. Arai H. Papillary Muscle Relocation for Functional Mitral Regurgitation. The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.22 Iasi, Romania
32. Arai H. Impact of Intraoperative Imaging during Cardiac surgery using High Frequency Epicardial Ultrasound. The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.22 Iasi, Romania
33. Arai H. LMT ostial plasty using superficial femoral artery patch in Takayasu. The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.23 Iasi, Romania
34. Arai H. A new pathology oriented repair technique for posterior mitral leaflet “Mt. Fuji Repair Technique” (video presentation in AATS Mitral Conclave 2017). The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.23 Iasi, Romania
35. Arai H. OPCAB Technique using multi-suction heart positioner „ TENTACLESTM” . The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.23 Iasi, Romania
36. Arai H. (Moderator) SESSION XVII– VIDEO PRESENTATION. The Euro-Asian Bridge Society 13th International Meeting on Cardiac Surgery 2017.09.23 Iasi, Romania
37. Keiji Oi, Tomohiro Mizuno, Tsuyoshi Hachimaru, Eiki Nagaoka, Hidehito Kuroki, Tatsuki Fujiwara, Ryoji Kinoshita, Hirokuni Arai. Long-term outcome of triple arterial graft CABG. 31st EASTS Annual Meeting 2017.10.10 Vienna,Austria
38. D. Sakota, T. Fujiwara, K. Ohuchi, K. Kuwana, H. Yamazaki, R. Kosaka, H. Arai, O. Maruyama. Quantitative and real-time monitoring of thrombus formation on the pivot bearing of an extracorporeal centrifugal blood pump. The 2017 ISMCS Conference 2017.10.16 Tucson, Arizona, USA
39. Arai H. Current CABG in Japan. The 16th Annual Meeting of Taiwan Association of Thoracic & Cardiovascular Surgery 2017.10.28 Taipei, Taiwan
40. Arai H. Intraoperative Ultrasonic Quality Assessment and Surgical Guidance to Improve Outcomes after CABG. The 16th Annual Meeting of Taiwan Association of Thoracic & Cardiovascular Surgery 2017.10.28 Taipei, Taiwan
41. Keji Oi, Eiki Nagaoka, Tomohiro Mizuno, Tsuyoshi Hachimaru, Masafumi Yashima, Hidehito Kuroki, Tatsuki Fujiwara, Masashi Takeshita, Kenji Yokoyama, Hironobu Sakurai, Hirokuni Arai. Mitral Valve Repair With Intervention to Subvalvular Apparatus Has a Potential to Improve the Outcome for Functional Mitral Regurgitation. American Heart Association Scientific Sessions 2017 2017.11.13 California,USA
42. Arai H.. Current Trends in CABG in Japan. 23rd PATACSI Annual Convention 2017.12.02 Manila, Philippine
43. Arai H.. Intra-operative Ultrasonic Quality Assessment and Surgical Guidance to Improve CABG Outcomes. 23rd PATACSI Annual Convention 2017.12.02 Manila, Philippine

Nephrology

Professor:

Shinichi UCHIDA

Tatemitsu RAI (Dept. of Nephrology and Regional Medicine (Ibaraki))

Associate Professor:

Tomokazu OKADO (Dept. of Blood Purification)

Eisei SOHARA

Junior Associate Professor:

Shotaro NAITO

Assistant Professor:

Naohiro NOMURA

Soichiro IIMORI (Dept. of Blood Purification)

Takayasu MORI (Dept. of Blood Purification)

Kiyoshi ISOBE (Dept. of Nephrology and Regional Medicine (Ibaraki))

Fumiaki ANDO (Project Assistant Professor)

Graduate Student:

Yohei ARAI, Yuri KASAGI, Emi SASAKI

Shintaro MANDAI, Sayaka YOSHIDA, Wang Yuan Long

Hiroaki KIKUCHI, Wakana SHODA, Hiroko HASHIMOTO

Takuya FUJIMARU, Taisuke FURUSHO, Yoshiaki MATSUURA

Naohiro TAKAHASHI, Tamami FUJIKI

Hospital Staff:

Seiko ISHIKAWA, Yuto TOMA, Noriyuki TOSHIMA

Takashi MIYAZAKI, Saki KUBO

Shunsuke INABA, Shota SAKASHITA, Takanori MIYAZAKI

Technician:

Chieko IJIMA, Motoko CHIGA

Secretary:

Asa MURANO, Yukiko ITO

(1) Outline

The policy of the Department of Nephrology is to accomplish trustworthy medicine and to educate excellent academic scientists and nephrologists. Our department is one of the initial institutes that started the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases.

We are now investigating pathophysiological mechanisms of various kidney diseases including genetic renal diseases. Furthermore, we are taking a proactive stance in developing innovative therapy. We hope new young scientists and physicians join us for future science and nephrology.

(2) Research

The theme of our study is "to investigate the mechanisms of maintaining blood pressure and body fluids homeostasis regulated by the kidney and to clear the pathophysiology caused by their failure, and to develop novel strategies for their treatment." This would lead to the development of kidney disease therapy itself and

would also lead to studying for multiple organ failure caused by chronic kidney disease (CKD).

In 2017, our 14 presentations, including 2 oral presentations, were adopted in the annual meeting of American society of nephrology (ASN KIDNEY WEEK). Moreover, our research manuscripts were published in several high impact journals such as EBioMedicine, open access Elsevier journal supported by Cell Press and The Lancet, Kidney International (IF: 7.68), Molecular and Cellular Biology (IF: 4.4), or Scientific Reports (IF: 4.3). We published 26 reports and four of them were presented in "press release".

In addition to them, a lot of our members have got prizes in various medical meetings regardless of whether they are in or out of the country. Further, comprehensive diagnosis of inherited kidney diseases using next generation sequencer (NGS) and clinical studies on genome information are now on track and is contributing to various genetic diagnosis of many patients. Genetic diagnosis were carried out for more than 200 cases a year. CKD-ROUTE study, which is the clinical cohort study with 1,000 subjects we take the initiative have been finished the observation period of 3 years, which enabled us to publish 7 clinical research papers (3 in Clin Exp Nephrol., 1 inNephrology and others).

(3) Education

"Undergraduate education"

(Systematic lecture)

For third grade medical students, we are conducting lectures organized in a three-week 'block form' together with urology and pathology sections. Under the name of "Body Fluid Regulation and Urology" Block, the students can learn intensively about kidney and urologic diseases during a period of three weeks. In this lecture, we incorporate PBL (Problem-Based Learning) lectures and lectures held by actual patients, so that the students will be able to study independently and bi-directionally.

(Project semester)

We accept several students every year in the project semester, in which they are expected to participate in the forefront research with the assistance of graduate students.

(Clinical clerkship)

For fifth grade students who finished the systematic lectures and project semester, we provide the Pre-Clinical Clerkship (PCC) lectures for ten weeks, which are more practical and comprehensive than that the previous lectures held in the classroom. After PCC, the students will undergo Clinical Clerkship (CC), in which they will actually take charge of patients in the hospital ward, and study about kidney diseases while developing their clinical skills. They will be in charge of one new inpatient each week, make a presentation about their patient at the medical conference every week, and are expected to learn about the pathophysiology of various kidney diseases in depth.

"Postgraduate education"

After the two-year initial training after graduation, postgraduate doctors will be engaged in clinical training as nephrologists either in the University Hospital or affiliated hospitals as senior trainees, and during this period, we teach them so that they can be aware about unsolved clinical problems. We are planning to bring them up as "academic doctors".

Research activities in the graduate school are quite active, and by carrying out the state-of-the-art research as described above, we are training doctors to be able to excel in both basic and clinical works.

(4) Clinical Services & Other Works

Our department is one of the initial institutes that started the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases. We have close coordination with our 19 affiliated hospitals, and are performing CKD-ROUTE clinical cohort study stated above in cooperation with 15 hospitals of the 19, which enabled us to publish 7 clinical research papers. We continue to make an effort to reveal the pathophysiology of CKD patients. We have been actively adopting the "educational admission" for CKD patients and it has been showing the significant inhibitory effect on progression of kidney disease. For end-stage renal disease patients, vascular access surgery, peritoneal dialysis-related surgery, and induction of dialysis are consistently carried out in our department.

Our hemopurification center is one of the biggest institutions among 42 hospitals belonging to national uni-

versities. In 2017, the number of newly started dialysis patients was in 1st place, the total number of blood purifications, hemodialysis, and plasma exchanges was in 2nd place. Furthermore, we developed diagnostic panel for comprehensive genetic diagnosis for hereditary kidney diseases like nephrogenic diabetes insipidus, pseudohypoaldosteronism type II, Liddle syndrome, and Polycystic kidney diseases. Currently, we receive requests of genetic tests from all over the country. Genetic screening using next-generation sequencing technology enables definite diagnosis for rare hereditary diseases.

(5) Publications

[Original Articles]

1. Yokote Koutaro, Chanprasert Sirisak, Lee Lin, Eirich Katharina, Takemoto Minoru, Watanabe Aki, Koizumi Naoko, Lessel Davor, Mori Takayasu, Hisama Fuki M, Ladd Paula D, Angle Brad, Baris Hagit, Cefle Kivanc, Palanduz Sukru, Ozturk Sukru, Chateau Antoinette, Deguchi Kentaro, Easwar T K M, Federico Antonio, Fox Amy, Grebe Theresa A, Hay Beverly, Nampoothiri Sheela, Seiter Karen, Streeten Elizabeth, Pina-Aguilar Raul E, Poke Gemma, Poot Martin, Posmyk Renata, Martin George M, Kubisch Christian, Schindler Detlev, Oshima Junko. WRN Mutation Update: Mutation Spectrum, Patient Registries, and Translational Prospects. *Hum Mutat.* 2017.01; 38(1); 7-15
2. Yui Naofumi, Sasaki Sei, Uchida Shinichi. Aquaporin-2 Ser-261 phosphorylation is regulated in combination with Ser-256 and Ser-269 phosphorylation. *Biochem Biophys Res Commun.* 2017.01; 482(4); 524-529
3. Nagata Soichiro, Ikegaya Naoki, Ogino Shuhei, Uchida Shinichi, Itaya Mikiko, Momita Aoi, Shinozaki Shingo, Ohura Masaharu, Kuriki Ken, Kono Satoshi, Miyajima Hiroaki, Hishida Akira. The Resection of Thyroid Cancer Was Associated with the Resolution of Hyporesponsiveness to an Erythropoiesis-stimulating Agent in a Hemodialysis Patient with Aceruloplasminemia. *Intern Med.* 2017.01; 56(7); 805-810
4. Purizaca-Rosillo Nelson, Mori Takayasu, Benites-Condor Yamali, Hisama Fuki M, Martin George M, Oshima Junko. High incidence of BSCL2 intragenic recombinational mutation in Peruvian type 2 Berardinelli-Seip syndrome. *Am J Med Genet A.* 2017.02; 173(2); 471-478
5. Mori Takayasu, Hosomichi Kazuyoshi, Chiga Motoko, Mandai Shintaro, Nakaoka Hirofumi, Sohara Eisei, Okado Tomokazu, Rai Tatemitsu, Sasaki Sei, Inoue Ituro, Uchida Shinichi. Comprehensive genetic testing approach for major inherited kidney diseases, using next-generation sequencing with a custom panel. *Clin Exp Nephrol.* 2017.02; 21(1); 63-75
6. Mandai Shintaro, Kanda Eiichiro, Iimori Soichiro, Naito Shotaro, Noda Yumi, Kikuchi Hiroaki, Akazawa Masanobu, Oi Katsuyuki, Toda Takayuki, Sohara Eisei, Okado Tomokazu, Sasaki Sei, Rai Tatemitsu, Uchida Shinichi. Association of serum chloride level with mortality and cardiovascular events in chronic kidney disease: the CKD-ROUTE study. *Clin Exp Nephrol.* 2017.02; 21(1); 104-111
7. Shintaro Mandai, Eiichiro Kanda, Soichiro Iimori, Shotaro Naito, Yumi Noda, Hiroaki Kikuchi, Masanobu Akazawa, Katsuyuki Oi, Takayuki Toda, Eisei Sohara, Tomokazu Okado, Sei Sasaki, Tatemitsu Rai, Shinichi Uchida. Association of serum chloride level with mortality and cardiovascular events in chronic kidney disease: the CKD-ROUTE study. *Clin. Exp. Nephrol.* 2017.02; 21(1); 104-111
8. Wakana Shoda, Naohiro Nomura, Fumiaki Ando, Yutaro Mori, Takayasu Mori, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Calcineurin inhibitors block sodium-chloride cotransporter dephosphorylation in response to high potassium intake. *Kidney Int.* 2017.02; 91(2); 402-411
9. Eriko Takehara, Shintaro Mandai, Satomi Shikuma, Wataru Akita, Motoko Chiga, Takayasu Mori, Takashi Oda, Michio Kuwahara, Shinichi Uchida. Post-infectious Proliferative Glomerulonephritis with Monoclonal Immunoglobulin G Deposits Associated with Complement Factor H Mutation. *Intern. Med.* 2017.04; 56(7); 811-817
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[Conference Activities & Talks]

1. Soichiro Iimori, Shotaro Naito, Hidehiko Sato, Naohiro Nomura, Eisei Sohara, Tomokazu Okado, Shinichi Uchida, Tatemitsu Rai. Effects of proteinuria reduction on kidney function, mortality and cardiovascular risk in newly visiting CKD patients in Japan : the CKD-ROUTE study. The 6th CKD Frontier Meeting 2017.02.25 Nagoya, Japan
2. Seiko Ishikawa, Hidehiko Sato, Soichiro Iimori, Shotaro Naito, Naohiro Nomura, Eisei Sohara, Eiichiro Kanda, Tomokazu Okado, Shinichi Uchida, Kiyohide Fushimi, Tatemitsu Rai. Relationship between Hospital Volume and In-hospital Mortality in Patients with Rapidly Progressive Glomerulonephritis. The 6th CKD Frontier Meeting 2017.02.25 Nagoya, Japan
3. Sayaka Yoshida, Eisei Sohara, Yuya Araki, Yuri Kasagi, Emi Sasaki, Koichiro Susa, Takayasu Mori, Yuichi Inoue, Kiyoshi Isobe, Tatemitsu Rai, Shinichi Uchida. Decreased protein expression of KLHL3 is involved in the pathogenesis of PHAII caused by CUL3 mutation in vivo.. The 60th Annual Meeting Japanese Society of Nephrology 2017.05.26 Sendai
4. Takuya Fujimaru, Eisei Sohara, Takayasu Mori, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi , Fumiaki Ando, Yutaro Mori, Naohiro Nomura, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Shinichi Uchida. Development of a customized diagnostic panel for targeted exome sequencing of cystic kidney diseases. The 60th Annual Meeting of the Japanese Society of Nephrology 2017.05.27
5. Yuri Kasagi, Eisei Sohara, Tomomi Aida, Daiei Takahashi, Hidenori Nishida, Naohiro Nomura, Moko Zeniya, Takayasu Mori, Emi Sasaki, Fumiaki Ando, Tatemitsu Rai, Shinichi Uchida. KLHL2 promotes WNK4 degradation in mouse kidneys.. The 60th Annual Meeting of the Japanese Society of Nephrology 2017.05.28

6. Sohara Eisei. WNK kinase signalling to cation chloride transporters. Symposium, INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCE, 38th World Congress 2017.08.05 Rio de Janeiro, Brazil
7. Naohiro Nomura, Wakana Shoda, Yuanlong Wang, Daiei Takahashi, Moko Zeniya, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Role of ClC-K and Barttin in Low-Potassium induced Sodium-Chloride Cotransporter Activation and Hypertension in Mouse Kidney. Bunkyo Jin Kenkyukai 2017.10.26 Tokyo
8. Kiyoshi Isobe, Viswanathan Raghuram, Hyun Jun Jung, Chin-Rang Yang, Maurice B. Burg, Mark A. Knepper. Global Identification of Protein Phosphorylation Changes Following CRISPR/Cas9-Deletion of cAMP-Dependent Protein Kinase (PKA) in Collecting Duct Cells. The 50th Annual Meeting of the American Society of Nephrology 2017.10.31 New Orleans, USA
9. Takayasu Mori, Motoko Chiga, Takuya Fujimaru, Shintaro Mandai, Shota Watanabe, Yasuhisa Nakamura, Takehiro Morishita, Osamu Uemura, Eri Imai, Shuzo Kaneko, Yusuke Tsukamoto, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. We propose single heterozygous mutation in ATP6V0A4 as novel genetic cause of dRTA. The 50th Annual Meeting of the American Society of Nephrology 2017.11.02 New Orleans, LA.
10. Shinichi Uchida. Translational researches in the field of water and electrolyte disorders. The annual meeting of the American Society of Nephrology 2017.11.02 New Orleans, USA
11. Hiroaki Kikuchi, Eiichiro Kanda, Fumiaki Ando, Hidehiko Sato, Kiyoshi Isobe, Takayasu Mori, Soichiro Iimori, Naohiro Nomura, Shotaro Naito, Eisei Sohara, Tomokazu Okado, Shinichi Uchida, Kiyohide Fushimi and Tatemitsu Rai. Association between Body Mass Index and In-hospital Mortality in Emergently Hospitalized Dialysis-Independent CKD Patients; A Nationwide Retrospective Cohort Study in Japan. 2017.11.02 New Orleans, LA.
12. Naohiro Nomura, Wakana Shoda, Yuanlong Wang, Daiei Takahashi, Moko Zeniya, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Role of ClC-K and Barttin in Low-Potassium induced Sodium-Chloride Cotransporter Activation and Hypertension in Mouse Kidney. The 50th Annual Meeting of the American Society of Nephrology 2017.11.02 New Orleans, USA
13. Takuya Fujimaru, Takayasu Mori, Akinari Sekine, Shintaro Mandai, Motoko Chiga, Hiroaki Kikuchi , Fumiaki Ando, Yutaro Mori, Naohiro Nomura, Shotaro Naito, Tomokazu Okado, Tatemitsu Rai, Junichi Hoshino, Yoshifumi Ubara, Shinichi Uchida, Eisei Sohara. Genomic background of adult polycystic kidney disease patients without a family history. Kidney Week 2017 2017.11.03 New Orleans, LA
14. Yuri Kasagi, Daiei Takahashi, Tomomi Aida, Hidenori Nishida, Naohiro Nomura, Moko Zeniya, Takayasu Mori, Emi Sasaki, Fumiaki Ando, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Generation and Analysis of KLHL2 Knockout Mice. 2017.11.04
15. Daiei Takahashi, Shinichi Uchida. WNK4 Deletion Inhibits Adipogenesis In Vitro and In Vivo. The 50th Annual Meeting of the American Society of Nephrology 2017.11.04
16. Yohei Arai, Shinichi Uchida et al.. A High Salt Diet Suppressed CXCL9 and CXCL10 in Proximal Tubules through the IFN γ -JAK1-STAT1 Signaling Pathway. The 50th Annual Meeting of the American Society of Nephrology 2017.11.04
17. Sayaka Yoshida, Yuya Araki, Takayasu Mori, Emi Sasaki, Yuri Kasagi, Kiyoshi Isobe, Koichiro Susa, Yuichi Inoue, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara.. Decreased protein expression of KLHL3 is involved in the pathogenesis of PHAII caused by CUL3 mutation in vivo.. The 51th Annual Meeting of American Society of Nephrology. 2017.11.04 New Orleans, LA

Comprehensive Reproductive Medicine

Professor : Naoyuki MIYASAKA
Associate Professor : Satoshi OBAYASHI
Project Professor : Masakazu TERAUCHI
Junior Associate Professor : Naoyuki YOSHIKI, Kimio WAKANA
Project Junior Associate Professor: Tomonori ISHIKAWA, Makiko EGAWA
Assistant Professor : Yuki IWAHARA, Noriko OSHIMA- SUDO, Shiro HIRAMITSU, Nobuyuki KIDERA,
Takashi NAKASUJI, kotoi TSURANE, Asuka HIROSE, Reiko NAKAMURA
Project Assistant Professor : Ayako FUDONO, kazuki SAITO
HospitalStaff :hiroshi YOMOGITA, Noriko KUROSAKA, Kiyoko ISHIZUKA
Graduate Student :Reiko SHIRAI, Kiyotaka KAWAI, Kazuki SAITO, Akiko FURUSAWA, Takuto MATSUURA,
Rie OI, Takayuki TATSUMI, Masaki SEKIGUCHI, Tamami ODAI, Kenta TAKAHASHI,
Mayumi KOBAYASHI, AsamiHIRATA, Shiho YAUCHI, Misako IWATA,
Nobuyuki KIDERA, Ayako FUDONO, Misaki MASUYAMA

(1) Research

Research divisions :

- 1) Research in physiology, endocrinology and metabolism in the reproductive medicine
- 2) Research of female physical and mental change with aging
- 3) Pathophysiological examination of gynecological malignant tumor
- 4) Clinical research and basic research in perinatal medicine

Available scientific procedures :

- 1, Cell culture technique of ovarian granulosa cells, endometrial cells, malignant cells, osteoblast and so on.
- 2, Determination of intracellular calcium (by Fura 2 method and patch clamp)
- 3, Measurement of intra-cellular IP3
- 4, Hormonal assay in plasma, urine, follicular fluid (RIA & EIA)
- 5, Immunohistochemistry with ABC method
- 6, Analysis of micro-structure with electrical microscopy
- 7, Determination with molecular biological technique.
- 8, Physiological determination with isometric tension change
- 9, Determination of cerebral blood flow with MRI in cerebral infarction
- 10, Analysis of protein expression with flow cytometry

(2) Education

CRM (OB/GY) department has an obligation to offer medical services, education, research as one of the clinical departments in national graduate school, and has duty on making a mutual cooperation with local gynecological institutions.

Our main objectives are

- 1, Investigation for a new progress in treatment technique
- 2, Acquisition of medical knowledge and procedure
- 3, Providing systemic lecture about women's physiological and pathological change during adolescence through senescence.

Aims of research works are focusing on reproductive medicine, perinatal medicine and oncology.

Educational intention in medical doctor course and nursing course includes systemic lectures, clinical conferences and special lecture by many extramural speakers. During Bed-Side Learning period, students should be treated as one of medical stuffs, attend all of deliveries and be present at gynecological procedure. Several OB/GY institutions will be provided as an extramural drills.

(3) Clinical Performances

For intractable sterilization, satisfactory results are obtained with endoscopic examinations and IVF-ET methods. Health care unit for menopausal women was established, where inspections for atherosclerosis, osteoporosis (DEXA), autonomic nervous system are performed, and postmenopausal managements are provided including HRT, mental care and counseling.

After construction of LDR(labor, delivery, recovery) unit, cure for complicated pregnancies is now carried out, and cases of deliveries are rising now.

Malignant gynecological tumor is also an important aim of this department, for which surgery, chemotherapy and radiotherapy with complete cure are applied to patients. For benign tumor and endometriosis, laparoscopic operations are aggressively performed, whose number is now increasing.

(4) Publications

[Original Articles]

1. Takashi Nakasuji, Narumi Ogonuki, Tomoki Chiba, Tomomi Kato, Kumiko Shiozawa, Kenji Yamatoya, Hiromitsu Tanaka, Tadashi Kondo, Kenji Miyado, Naoyuki Miyasaka, Toshiro Kubota, Atsuo Ogura, Hiroshi Asahara. Complementary Critical Functions of Zfy1 and Zfy2 in Mouse Spermatogenesis and Reproduction. *PLoS Genet.* 2017.01; 13(1); e1006578
2. T Tatsumi, S C Jwa, A Kuwahara, M Irahara, T Kubota, H Saito. No increased risk of major congenital anomalies or adverse pregnancy or neonatal outcomes following letrozole use in assisted reproductive technology. *Hum. Reprod.* 2017.01; 32(1); 125-132
3. Saito K, Miyado K, Yamatoya K, Kuwahara A, Inoue E, Miyado M, Fukami M, Ishikawa T, Saito T, Kubota T, Saito H.. Increased incidence of post-term delivery and Cesarean section after frozen-thawed embryo transfer during a hormone replacement cycle. *Journal of Assisted Reproduction and Genetics.* 2017.01; 34; 465-470
4. Masaki Sekiguchi, Aiko Sasaki, Seiji Wada, Nobuaki Ozawa, Haruhiko Sago. Impact of the introduction of Non-invasive prenatal genetic testing on invasive tests A single-center study in Japan *Congenital Anomalies* 2017. 2017.01; 57(1); 35-36
5. Asuka Hirose, Masakazu Terauchi, Miho Hirano, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. Higher intake of cryptoxanthin is related to low body mass index and body fat in Japanese middle-aged women. *Maturitas.* 2017.02; 96; 89-94
6. Makiko Egawa, Kohsuke Imai, Masaaki Mori, Naoyuki Miyasaka, Tetsuo Kubota. Placental Transfer of Canakinumab in a Patient with Muckle-Wells Syndrome. *J. Clin. Immunol.* 2017.04;
7. Yamatoya K, Saito K, Saito T, Kang W, Nakamura A, Miyado M, Kawano N, Miyamoto Y, Umezawa A, Miyado K, Saito H. Birthweights and Down syndrome in neonates that were delivered after frozen-thawed embryo transfer: The 2007-2012 Japan Society of Obstetrics and Gynecology National Registry data in Japan. *Reproductive Medicine and Biology.* 2017.04;
8. Irahara M, Kuwahara A, Iwasa T, Ishikawa T, Ishihara O, Kugu K, Sawa R, Banno K and Saito H.. Assisted reproductive technology in Japan: a summary report of 1992–2014 by the Ethics Committee, Japan Society of Obstetrics and Gynecology *Reproductive Medicine and Biology.* 2017.04; 16; 126-132

9. Yamada I, Yoshino N, Hikishima K, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using 3-T high-spatial-resolution quantitative T2 mapping and its correlation with histopathologic findings. *Magn Reson Imaging*. 2017.05; 38(1); 174-181
10. Egawa M, Imai K, Mori M, Miyasaka N, Kubota T.. Placental Transfer of Canakinumab in a Patient with Muckle-Wells Syndrome. *J Clin Immunol.* 2017.05;
11. M Terauchi, A Hirose, M Akiyoshi, K Kato, N Miyasaka. Feelings of unattractiveness in peri- and postmenopausal women are associated with depressed mood, poor memory and unsatisfactory sexual relationships. *Climacteric*. 2017.06; 20(3); 228-232
12. M Miyado, K Yoshida, K Miyado, M Katsumi, K Saito, S Nakamura, T Ogata, M Fukami.. Knockout of Murine Mamld1 Impairs Testicular Growth and Daily Sperm Production but Permits Normal Postnatal Androgen Production and Fertility. *International Journal of Molecular Sciences*. 2017.06;
13. T Tatsumi, S C Jwa, A Kuwahara, M Irahara, T Kubota, H Saito. Pregnancy and neonatal outcomes following letrozole use in frozen-thawed single embryo transfer cycles. *Hum. Reprod.* 2017.06; 32(6); 1244-1248
14. Nakamura S, Miyado M, Saito K, Katsumi M, Nakamura A, Kobori Y, Tanaka Y, Ishikawa H, Yoshida A, Okada H, Hata K, Nakabayashi K, Okamura K, Ogata H, Matsubara Y, Ogata T, Nakai H, Fukami M. Next-generation sequencing for patients with non-obstructive azoospermia: implications for significant roles of monogenic/oligogenic mutations *Andrology*. 2017.07; 5(4); 824-831
15. Fusegi Atsushi, Nakamura Reiko, Oshima Noriko, Ishikawa Tomonori, Wakana Kimio, Yoshiki Naoyuki, Miyasaka Naoyuki. Port site recurrence and diffuse subcutaneous metastasis of the early stage ovarian cancer after laparoscopic surgery *Japan Society of Gynecologic and Obstetric Endoscopy and Minimally Invasive Therapy*. 2017.08; 33(Suppl.I); 1280
16. Kazuki Saito, Maki Fukami, Mami Miyado, Ichiro Ono, Keiji Sumori. A case of heterotopic cervical pregnancy and total placenta accreta after artificial cycle frozen-thawed embryo transfer *Reproductive Medicine and Biology*. 2017.10;
17. Komaki M, Numata Y, Morioka C, Honda I, Tooi M, Yokoyama N, Ayame H, Iwasaki K, Taki A, Oshima N, Morita I. Exosomes of human placenta-derived mesenchymal stem cells stimulate angiogenesis. *Stem Cell Res Ther*. 2017.10; 8(1); 219
18. Rina Komazaki, Sayaka Katagiri, Hirokazu Takahashi, Shogo Maekawa, Takahiko Shiba, Yasuo Takeuchi, Yoichiro Kitajima, Anri Ohtsu, Sayuri Udagawa, Naoki Sasaki, Kazuki Watanabe, Noriko Sato, Naoyuki Miyasaka, Yuichiro Eguchi, Keizo Anzai, Yuichi Izumi. Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism *Scientific Reports*. 2017.10;
19. Takekuma M, Mori K, Iida T, Kurihara K, Saitou M, Tokunaga H, Kawana K, Ikeda M, Satoh T, Saito T, Miyagi E, Nagai Y, Furusawa A, Kawano Y, Kawano K, Tabata T, Ota Y, Hayase R, Mikami M, Sugiyama T.. The concept of platinum sensitivity could be applied to recurrent cervical cancer: a multi-institutional retrospective study from the Japanese Gynecologic Oncology Group. *Cancer Chemother Pharmacology*. 2017.10; 80(4);
20. Rina Komazaki, Sayaka Katagiri, Hirokazu Takahashi, Shogo Maekawa, Takahiko Shiba, Yasuo Takeuchi, Yoichiro Kitajima, Anri Ohtsu, Sayuri Udagawa, Naoki Sasaki, Kazuki Watanabe, Noriko Sato, Naoyuki Miyasaka, Yuichiro Eguchi, Keizo Anzai, Yuichi Izumi. Periodontal pathogenic bacteria, *Aggregatibacter actinomycetemcomitans* affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. *Sci Rep*. 2017.10; 7(1); 13950
21. Nakamura R., Furusawa A., Oshima N., Wakana K., Miyasaka N.. COMORBIDITIES AND COMPLICATIONS OF ELDERLY PATIENTS WITH CERVICAL CANCER *INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER*. 2017.11; 27; 837
22. Oshima N., Nakamura R., Furusawa A., Toba M., Wakana K., Miyasaka N.. RETROSPECTIVE ANALYSIS OF RADICAL RADIOTHERAPY FOR ENDOMETRIAL CANCER *INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER*. 2017.11; 27; 1175

23. Saito H, Jwa SC, Kuwahara A, Saito K, Ishikawa T, Ishihara O, Kugu K, Sawa R, Banno K, Irahara M. Assisted reproductive technology in Japan: a summary report for 2015 by The Ethics Committee of The Japan Society of Obstetrics and Gynecology Reproductive Medicine and Biology. 2017.12;
24. Sekiguchi M, Miyoshi Y, Kikuchi N, Sago H1. Pregnancy outcomes in female childhood cancer survivors: Nationwide survey in Japan *Pediatr Int*. 2017.12;

[Misc]

1. Naoyuki Yoshiki. Review of transvaginal natural orifice transluminal endoscopic surgery in gynecology. *Gynecol Minim Invasive Ther*. 2017.02; 6(1); 1-5

[Conference Activities & Talks]

1. Kimio Wakana, Naoyuki Miyasaka. Endometrial cancer treatment up-to-date. *Shoheizaka radiology* 2017.03.17
2. K. Kawai, M. Kawahara, N. Kidera, K. Teraoka, A. Yamamoto, K. Ohuchi, Y. Iwahara, T. Ishikawa, T. Harada, N. Miyasaka. EFFICACY OF LUTEAL PHASE (LP) -COS AND FOLLICULAR AND LUTEAL PHASE OVARIAN STIMULATION DURING THE SAME MENSTRUAL CYCLE (DUOSTIM) IN BREAST CANCER PATIENTS . 7th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE 2017) 2017.03.31
3. Miyuki Nonaka, Tomonori Ishikawa, Sachi Murakata, Nobuyuki Kidera, Atsushi Yamamoto, Yuki Iwahara, Naoyuki Miyasaka.. Piezo ICSI improves fertilization rate and good-quality day3 embryo as compared with conventional ICSI. . 7th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE 2017) 2017.04.01
4. K. Hiraoka, M. Saito, A. Kuga, T. Kaji, A. Ichihashi, T. Suhara, M. Ibayashi, T. Tamaki, K. Miyata, Y. Ohtsuka, K. Ohuchi, T. Ishikawa, T. Harada, K. Kawai. IMPACT OF MOVING SPEED OF ICSI NEEDLE INSIDE THE OOCYTE ON SURVIVAL AND FERTILIZATION IN HUMAN ICSI . 7th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE 2017) 2017.04.01
5. Miyuki Nonaka, Tomonori Ishikawa, Sachi Murakata, Kenichiro Hiraoka, Atsushi Yamamoto, Yuki Iwahara, Naoyuki Miyasaka. PIEZO-ICSI IMPROVES FERTILIZATION RATE AS COMPARED WITH CONVENTIONAL-ICSI. The 7th Congress of the Asia Pacific Initiative on Reproduction 2017.04.01 Kuala Lumpur
6. Akiko Furusawa, Jun Inoue, Hitoshi Tsuda, Naoyuki Miyasaka, Johji Inazawa. Differential requirement of amino acids on cell survival of ovarian cancer cells. *AACR Annual Meeting 2017* 2017.04.03 Washington, D.C
7. Fusegi Atsushi, Furusawa Akiko, Ooshima Noriko, Toba Mikayo, Wakana Kimio, Terauchi Masakazu, Obayashi Satoshi, Miyasaka Naoyuki. The impact of p53 in predicting clinical outcome of type II endometrial carcinoma: a retrospective analysis. *69th Annual Congress of the Japan Society of Obstetrics and Gynecology* 2017.04.16 Hiroshima
8. Asuka Hirose, Masakazu Terauchi, Miho Hirano, Mihoko Akiyoshi, Kiyoko Kato, Naoyuki Miyasaka. HIGHER INTAKE OF CRYPTOXANTHIN IS RELATED TO LOW BODY MASS INDEX AND BODY FAT IN JAPANESE MIDDLE-AGED WOMEN. *6th Scientific Meeting of the Asia Pacific Menopause Federation* 2017.04.22 Singapore
9. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Kiyoko Kato, Naoyuki Miyasaka. MUSCLE AND JOINT PAINS IN MIDDLE-AGED WOMEN ARE ASSOCIATED WITH INSOMNIA AND LOW GRIP STRENGTH. *6th Scientific Meeting of the Asia Pacific Menopause Federation* 2017.04.22 Singapore
10. Noriko Oshima, Ken-ichi Nakahama, Satoshi Obayashi, Naoyuki Miyasaka, Ikuo Morita. Tissue engineered lymphatic microvessels using cell-printing technology. *The 7th Scientific Meeting of the Asia Pacific Menopause Federation* 2017.04.22
11. Asuka Hirose, Masakazu Terauchi, Miho Hirano, Mihoko Akiyoshi, Kiyoko Kato, Naoyuki Miyasaka. Higher intake of cryptoxanthin is related to low body mass index and body fat in Japanese middle-aged women. *The 6th Scientific Meeting of the Asia Pacific Menopause Federation* 2017.04.22 Singapore

12. Saito K, Matsuzaki T, Ogata T, Kubota T, Irahara M, Fukami M. Multiple androgen biosynthesis pathways are operating in women with polycystic ovary syndrome. 2017 ACOG Annual Clinical and Scientific Meeting 2017.05.07 San Diego
13. Asuka Hirose, Masakazu Terauchi, Yurika Osaka, Mihoko Akiyoshi, Kiyoko Kato, Naoyuki Miyasaka. Effect of soy lecithin on menopausal symptoms: a randomized, double-blind, placebo-controlled study. The 11th European Congress on Menopause and Andropause 2017.05.23 Amsterdam
14. Masakazu Terauchi, Asuka Hirose, Mihoko Akiyoshi, Kiyoko Kato, Naoyuki Miyasaka. Muscle and joint pains in middle-aged women are associated with insomnia and low grip strength. 11th European Congress on Menopause and Andropause 2017.05.24 Amsterdam, Netherlands
15. Kazuki Saito, Kiyotaka Kawai, Kenichi Tatsumi, Mami Miyado, Momori Katsumi, Shigeru Nakamura, Tomonori Ishikawa, Naoyuki Miyasaka, Maki Fukami. POR mutations as novel genetic causes of female infertility due to partial 17 alpha hydroxylase deficiency . ESHRE 2017 annual meeting 2017.07.05 Geneva
16. Makiko Egawa, Naoyuki Miyasaka, Ayako Fudono, Mayumi Yokota, Asuka Hirose, Kohsuke Imai, Masaaki Mori and Tetsuo Kubota. The first case of canakinumab administration during pregnancy for cryopyrin associated periodic syndrome. 21st International Conference on Prenatal Diagnosis and Therapy 2017.07.10
17. TOBA, M. MORIWAKI, M. OHSHIMA, N. WAKANA, K. OBAYASHI, S. MIYASAKA, N. FUSHIMI, K.. Calculation of inpatient mortality after total hysterectomies using a nationwide administrative database.. The International Forum on Quality and Safety in Healthcare 2017.08.25 Kuala Lumpur
18. TOBA, M. MORIWAKI, M. OBAYASHI, S. FUSHIMI, K. Comparison of healthcare safety indicators among acute care hospitals in Japan using a nationwide administrative database. The International Forum on Quality and Safety in Healthcare 2017.08.25 Kuala Lumpur
19. Takashi Nakasuji, Tomonori Ishikawa, Yasumasa Sega, Naoyuki Miyasaka. Laparoscopic surgery of peritoneal inclusion cyst for ovum pick up. 18th APAGE Annual Congress 2017.09.07 Okayama
20. Eri Inoue, Rie Oi, Takahiro Yamashita, et al.. Fetal right aortic arch can be screener with three vessels view in the second or third trimester ultrasound screening. International Society of Ultrasound in Obstetrics and Gynecology 2017.09.17 Vien, Austria
21. Masaki Iwamoto, Satoko Yazaki, Tomonori Ishikawa, Kiyotaka Kawai, Kenichiro Hiraoka. Effects of different sperm immobilization method on the in vitro development of porcine ICSI embryos. World Congress of Reproductive Biology 2017 2017.09.27 Okinawa
22. Akiko Furusawa, Jun Inoue, Hitoshi Tsuda, Naoyuki Miyasaka, Johji Inazawa. Differential requirement of amino acids on cell survival of ovarian cancer cells. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.28 Yokohama
23. K. Hiraoka, Y. Otsuka, T. Ishikawa, K. Kawai, T. Harada. Effect the sperm selection magnification (400x vs 1,200x) on fertilization results and embryo development in human Piezo-ICSI. ASRM 73 r d Scientific Congress 2017.10.28 San Antonio
24. N. Oshima, R. Nakamura, A. Furusawa, M. Toba, K. Wakana, N. Miyasaka. Retrospective analysis of radical radiotherapy for endometrial cancer. The 20th international meeting of the European Society of Gynaecological Oncology 2017.11.05
25. R. Nakamura, A. Furusawa, N. Oshima, M. Toba, K. Wakana, N. Miyasaka. Comorbidities and complications of elderly patients with cervical cancer. The 20th international meeting of the European Society of Gynaecological Oncology 2017.11.05
26. Akiko Furusawa, Jun Inoue, Hitoshi Tsuda, Naoyuki Miyasaka, Johji Inazawa. Differential requirement of amino acids on cell survival of ovarian cancer cells. The 62nd Annual Meeting of the Japan Society of Human Genetics 2017.11.17 Kobe
27. K. Kawai, M. Kawahara, N. Kidera, K. Teraoka, A. Yamamoto, K. Ohuchi, Y. Iwahara, T. Ishikawa, T. Harada, N. Miyasaka. EFFICACY OF LUTEAL PHASE (LP) -COS AND FOLLICULAR AND LUTEAL PHASE OVARIAN STIMULATION DURING THE SAME MENSTRUAL CYCLE (DUOSTIM) IN BREAST CANCER PATIENTS . the 7th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE 2017) 2017.11.19 Kuala Lumpur

28. Kimio Wakana, Mikayo Toba, Reiko Nakamura, Akiko Furusawa, Noriko Oshima, Naoyuki Miyasaka. Postoperative mortality rate and complications after surgery for ovarian cancer: A retrospective study using a national inpatient database in Japan. The 5th Biennial Meeting of Asian Society of Gynecologic Oncology 2017.11.30 Tokyo

[Awards & Honors]

1. 6th Scientific Meeting of the Asia Pacific Menopause Federation Best Oral Award (Masakazu Terauchi), Asia Pacific Menopause Federation, 2017.04

Urology

Professor and Chairman: Yasuhisa Fujii

Associate Professor: Kazutaka Saito

Junior Associate Professor: Yoh Matsuoka,

Junichiro Ishioka (Department of Insured Medical Care Management), Minato Yokoyama

Assistant Professor: Soichiro Yoshida, Toshiki Kijima, Masaya Ito (- March), Masaharu Inoue (- May), Hajime Tanaka (April - September), Yosuke Yasuda (June -), Sho Uehara (October -)

Hospital Staff: Hajime Tanaka (-March), Takayuki Nakayama (-March), Yosuke Yasuda (- May), Sho Uehara (April - September), Yuma Waseda, Shohei Fukuda (October -), Masahiro Toide (October -), Shugo Yajima, Keita Izumi (- June), Takashi Tamiya (April - September),

Kohei Chino (April - September), Takahiko Soma (August -), Yuichi Fukuda (August -)

Resident: Takahiko Soma (- July), Yuichi Fukuda (- July)

Graduate Student: Saori Araki, Yosuke Yasuda, Sho Uehara, Yuma Waseda, Hiroshi Fukushima, Shingo Moriyama

Project professor: Kazunori Kihara

(1) Outline

Our mission is to establish and provide the best urological care to all patients in the super aging society which all over the world is facing.

Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices based on the evidences of the clinical and translational research which we commit under the concept of “Bed to Bench, Feedback to Bed” .

To realize the mission, we have been developing various procedures.

1. Gasless Single-Port RoboSurgeon urological surgery which can be applied to most of patients with urological tumors is a safe and educational minimally invasive surgery satisfying no CO2 gas insufflation, no peritoneal injury, no multiple ports, and no high cost.
2. Bladder sparing treatment consisting of transurethral resection of bladder tumor, low-dose chemoradiotherapy and Gasless Single-Port RoboSurgeon partial cystectomy with pelvic lymph node dissection can preserve urinary and sexual function without compromising curability in carefully selected patients with muscle-invasive bladder cancer for which radical cystectomy with urinary diversion is the standard treatment.
3. Gasless Single-Port RoboSurgeon clampless partial nephrectomy for kidney cancer potentially preserves maximal renal function with minimal invasiveness especially in patients with single kidney or impaired renal function.
4. Focal brachytherapy for localized prostate cancer precisely diagnosed by MRI and meticulous biopsy can provide cure without deteriorating urinary and sexual function.

The continuous commitment to clinical and translational research is reflected to publications in international journals, presentations at international meetings and awards.

(2) Research

Clinical Research

- 1) Innovation and establishment of a minimally invasive surgery, Gasless Single-Port RoboSurgeon urological surgery

- 2) Development of optimal MRI-ultrasonography fusion prostate needle biopsy
- 3) Sequential combination therapy to prolong survival of advanced prostate cancer patients
- 4) Development and establishment of curative and minimally invasive bladder preservation using low-dose chemoradiotherapy plus Gasless Single-Port RoboSurgeon partial cystectomy against muscle-invasive bladder cancer
- 5) Development and establishment of Gasless Single-Port RoboSurgeon clampless partial nephrectomy against kidney cancer
- 6) Development and establishment of focal brachytherapy against localized prostate cancer
- 7) Sequential combination therapy to prolong survival of advanced kidney cancer patients, starting with immunotherapy combined with multiple molecular targeted agents
- 8) Application of diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
- 9) Application of serum C-reactive protein as a prognostic biomarker of urological malignancies and as a marker for surgical invasiveness
- 10) Development of prognostic prediction model for non-muscle-invasive bladder cancer

Translational Research

- 1) Development of differentiation-inducing therapy against hormone-resistant prostate carcinomas
- 2) Investigation on molecular mechanisms, in particular deregulation of the NO system, underlying voiding and erectile dysfunction to develop rational therapy
- 3) Overcoming therapeutic resistance to chemo- and/or radiotherapy against urological malignancies using novel molecular targeted agents
- 4) Investigation on functional roles of p63 protein in urothelial carcinomas

(3) Lectures & Courses

Our top priority is to establish the best urological practice in the super aging society which all over the world is facing. We are committed to offering educational programs to facilitate the development of outstanding academic urologists of the next generation. We believe that one of our missions is to educate students, residents and fellows in the art and science of urology and thereby to train the future leaders in the field. The continuous commitment to clinical and translational research is reflected to publications in international journals, presentations at international meetings and awards.

(4) Clinical Performances

Our mission is to provide the best urological care to all patients. Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices. The Gasless Single-Port RoboSurgeon urological surgery, which we have innovated its concept and developed surgical techniques specific to all urological organs, has been officially approved as medical services provided by the Japanese Governmental Health Insurance System in April 2008. These minimally invasive surgical techniques can be fundamentally applied to all patients having urological malignancies, even those having locally advanced disease and previous histories of abdominal surgery.

(5) Publications

[Original Articles]

1. Yuki Nakamura, Soichiro Yoshida, Hiroshi Tanaka, Masaharu Inoue, Masaya Ito, Toshiki Kijima, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Potential Utility of Diffusion-Weighted Magnetic Resonance Imaging in Diagnosis of Residual Bladder Cancer before Second Transurethral Resection. *Urol. Int.*. 2017.03; 98(3); 298-303
2. Hajime Tanaka, Yasuhisa Fujii, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara. Absence of renal artery pseudoaneurysm on computed tomography after minimally-invasive partial nephrectomy using clampless and sutureless techniques. *Int. J. Urol.*. 2017.06; 24(6); 472-473

3. Toshinori Nishizawa, Soichiro Yoshida, Fumitaka Koga, Hiroshi Tanaka, Mihiro Kaga, Kotaro Watanabe, Hiroshi Fukushima, Yasukazu Nakanishi, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Standardization of the apparent diffusion coefficient value of bladder cancer across different centers: Applicability in predicting aggressive pathologic phenotypes. *Clin Imaging*. 2017.07; 44; 121-126
4. Hajime Tanaka, Yasuhisa Fujii, Hiroshi Tanaka, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Sho Uehara, Noboru Numao, Takeshi Yuasa, Shinya Yamamoto, Hitoshi Masuda, Junji Yonese, Kazunori Kihara. Stepwise algorithm using computed tomography and magnetic resonance imaging for diagnosis of fat-poor angiomyolipoma in small renal masses: Development and external validation. *Int. J. Urol.* 2017.07; 24(7); 511-517
5. Soichiro Yoshida, Tsuneo Fukuyo, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Real-time three-dimensional image angle rectification to improve hand-eye coordination in single-port laparoscopic surgery. *Int. J. Urol.* 2017.08; 24(8); 639-640
6. Yoh Matsuoka, Junichiro Ishioka, Hiroshi Tanaka, Tomo Kimura, Soichiro Yoshida, Kazutaka Saito, Yasuhisa Fujii, Kazunori Kihara. Impact of the Prostate Imaging Reporting and Data System, Version 2, on MRI Diagnosis for Extracapsular Extension of Prostate Cancer. *AJR Am J Roentgenol.* 2017.08; 209(2); W76-W84
7. Yuma Waseda, Soichiro Yoshida, Taro Takahara, Thomas Christian Kwee, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. Utility of computed diffusion-weighted MRI for predicting aggressiveness of prostate cancer. *J Magn Reson Imaging.* 2017.08; 46(2); 490-496
8. Masanori Murakami, Takano Yoshimoto, Kazuhiko Nakabayashi, Yujiro Nakano, Takahiro Fukaishi, Kyoichiro Tsuchiya, Isao Minami, Ryotaro Bouchi, Kohji Okamura, Yasuhisa Fujii, Koshi Hashimoto, Ken-Ichiro Hata, Kazunori Kihara, Yoshihiro Ogawa. Molecular characteristics of the KCNJ5 mutated aldosterone-producing adenomas. *Endocr. Relat. Cancer.* 2017.10; 24(10); 531-541
9. Hiroshi Fukushima, Madoka Kataoka, Yasukazu Nakanishi, Kazumasa Sakamoto, Kosuke Takemura, Hiroaki Suzuki, Masaya Ito, Ken-Ichi Tobisu, Yasuhisa Fujii, Fumitaka Koga. Posttherapeutic skeletal muscle mass recovery predicts favorable prognosis in patients with advanced urothelial carcinoma receiving first-line platinum-based chemotherapy. *Urol. Oncol.* 2017.10;
10. Yosuke Yasuda, Kazutaka Saito, Takeshi Yuasa, Sho Uehara, Naoko Kawamura, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Shinya Yamamoto, Tetsuo Okuno, Junji Yonese, Kazunori Kihara, Yasuhisa Fujii. Early response of C-reactive protein as a predictor of survival in patients with metastatic renal cell carcinoma treated with tyrosine kinase inhibitors. *Int. J. Clin. Oncol.* 2017.12; 22(6); 1081-1086

[Misc]

1. Soichiro Yoshida, Taro Takahara, Thomas C Kwee, Yuma Waseda, Shuichiro Kobayashi, Yasuhisa Fujii. DWI as an Imaging Biomarker for Bladder Cancer. *AJR Am J Roentgenol.* 2017.06; 208(6); 1218-1228
2. Kazutaka Saito, Yasuhisa Fujii. Antitumor Activity and Safety of Enzalutamide After Abiraterone Acetate: Seeking the Optimal Treatment Sequence for Castration-resistant Prostate Cancer Patients. *Eur. Urol.* 2017.10;
3. Yasuhisa Fujii. Prediction models for progression of non-muscle-invasive bladder cancer: A review. *Int. J. Urol.* 2017.12;

[Conference Activities & Talks]

1. Izumi Keita, Saito Kazutaka, Nakayama Takayuki, Fukuda Shohei, Fukushima Hiroshi, Uehara Sho, Koga Fumitaka, Yonese Junji, Kageyaam Yukio, Kihara Kazunori, Fujii Yasuhisa. Contact with renal sinus is a significant risk factor for metastasis in pT1 clear cell renal cell carcinoma. . 32nd Annual EAU Congress 2017.03.26 London, UK
2. Kawamura Naoko, Saito Kazutaka, Inoue Masaharu, Ito Masaya, Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Kihara Kazunori, Fujii Yasuhisa. Adherent perinephric fat in Asian patients: predictors, and impact on perioperative outcomes of partial nephrectomy. 32nd Annual EAU Congress 2017.03.27 London, UK

3. Kawamura Naoko, Yokoyama Minato, Nakayama Takayuki, Tanaka Hajime, Inoue Masaharu, Ito Masaya, Kijima Toshiki, Yoshida Soichiro, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Acute kidney injury after clampless partial nephrectomy: incidence, predictors, and its low impact on intermediate-term renal function . 32nd Annual EAU Congress 2017.03.27 London, UK
4. Matsuoka Yoh, Ishioka Junichiro, Tanaka Hiroshi, Kimura Tomo, Inoue Masaharu, Ito Masaya, Kijima Toshiki, Yoshida soichiro, Yokoyama Minato, Saito Kazutaka, Kihara Kazunori, Fujii Yasuhisa. Characteristics of MRI staging using PI-RADS version 2 and its predictive performance for biochemical recurrence after radical prostatectomy compared to PI-RADS version 1. 32nd Annual EAU Congress 2017.03.27 London, UK
5. Nakamura Yuki, Tanaka Hajime, Fujii Yasuhisa, Inoue Masaharu, Ito Masaya, Kijima Toshiki, Yoshida Soichiro, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Kihara Kazunori. Bladder-sparing protocol consisting of low-dose chemoradiotherapy and consolidative partial cystectomy against muscle-invasive bladder cancer: A comparison of oncological outcomes between primary and progressive diseases. . 32nd Annual EAU Congress 2017.03.27 London, UK
6. Junichiro Ishioka, Yoh Matsuoka, Masaya Itoh, Masaharu Inoue, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Kazutaka Saito, Kazunori Kihara, Hiroshi Tanaka, Tomo Kimura, and Yasuhisa Fujii. Computer-aided diagnosis of prostate cancer using a deep neural networks algorithm in pre-biopsy multiparametric MRI.. AUA Annual Meeting 2017 2017.05.12 Boston
7. Yosuke Yasuda¹, Kazutaka Saito¹, Naoko Kawamura¹, Sho Uehara², Takeshi Yuasa², Minato Yokoyama¹, Junichiro Ishioka¹, Yoh Matsuoka¹, Shinya Yamamoto², Shunji Takahashi³, Tetsuo Okuno⁴, Junji Yonese², Kazunori Kihara¹ and Yasuhisa Fujii¹. EARLY RESPONSE AT FOUR WEEKS OF C-REACTIVE PROTEIN PREDICTS SURVIVAL IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA TREATED WITH TYROSINE KINASE INHIBITORS. 2017.05.12 Boston
8. Yuma Waseda, Masaharu Inoue, Masaya Ito, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazutaka Saito, Kazunori Kihara, Yasuhisa Fujii. New predictive scoring model for recurrence incorporating bladder neck involvement in patients with non-muscle-invasive bladder cancer.. AUA Annual Meeting 2017 2017.05.13 Boston
9. Inoue M, Fujii Y, Ito M, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K.. Incidence and risk factors of postoperative hypertension after partial nephrectomy for renal tumors. AUA Annual Meeting 2017 2017.05.14 Boston
10. Yuma Waseda, Kazutaka Saito, Masaharu Inoue, Masaya Ito, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Junichiro Ishioka, Yoh Matsuoka, Kazunori Kihara, Yasuhisa Fujii. Predictive ability of renal cortex enhancement in dynamic CT for residual renal function after nephroureterectomy: Comparative study with renography.. AUA Annual Meeting 2017 2017.05.15 Boston
11. Yokoyama Minato, Koga Fumitaka, Otsuka Yukihiro, Tsukamoto Tetsuro, Okuno Tetsuo, Nagahama Katsushi, Kageyama Yukio, Noro Akira, Tsujii Toshihiko, Morimoto Shinji, Kitahara Satoshi, Kihara Kazunori, and Fujii Yasuhisa. Impact of chronic kidney disease and hypertension on decline in remaining kidney function after radical nephrectomy. AUA Annual Meeting 2017 2017.05.15 Boston, USA
12. Takayuki Nakayama, Toshiki Kijima, Soichiro Yoshida, Fumitaka Koga, Kazunori Kihara and Yasuhisa Fujii. Zoledronic acid sensitizes castration-resistant prostate cancer cells to radiotherapy and chemotherapy by downregulating STAT1. AUA Annual Meeting 2017 2017.05.15

Gastrointestinal Surgery

Professor

Yusuke Kinugasa

Project Professor

Masahiro TSUBAKI

Associate Professor

Masamichi YASHUNO, Mikito INOKUCHI, Yasuaki NAKAJIMA

Junior Associate Professor

Kenro KAWADA, Takuya OKADA

Assistant Professor

Yutaka TOKAIRIN, Akifumi KIKUCHI, Toshiro TANIOKA

Akihiro HOSHINO, Shinichi YAMAUCHI

Graduate Student

Yasunori SOMENO, Tairi RYOTOKUJI, Shunsuke OTA,

Masatoshi NAKAGAWA, Masafumi OKUDA, Yuichiro KUME,

Yutaka NAKAJIMA, Taichi OGOU, Michiyo TOKURA, Marie HANAOKA,

Toshihiro MATSUI, Tomoki ABURATANI, Chiharu TOMII,

Keisuke OKUNO, Kentaro GOKITA, Ryota SEKI, Fukuichiro ORITA,

Yudai KAWAMURA, Tomiyuki MIURA, Kazuya YAMAGUCHI,

Megumi SASAKI, Ayumi TAKAOKA, Emi KANEMOTO, Yuriko MATSUMIYA,

Rei GHO, Mora ANDRES, Yuya UMEBAYASHI

(1) Research

- 1) Development of esophageal surgery.
- 2) Development of gastric surgery.
- 3) Development of colorectal surgery.

(2) Education

The history of the department started as both the Department of Esophageal and General Surgery and the Department of Surgical Oncology of TMDU, and many surgeons and researchers in various specialties have gathered and have been keeping a high level of activities. Our main purposes of education are to make the post-graduate physicians grown up to excellent surgeons and to contribute in development of medical/surgical sciences. Surgeons with high-level medical knowledge and techniques are expected to grow up in this department. Moreover, making surgeons with matured humanity is one of the purposes. The department has a peaceful atmosphere and stands for active work in solving difficult problems.

(3) Clinical Performances

Main clinical services are diagnosis and treatment for esophageal, gastric and colorectal diseases. Post-graduate students learn and study general surgery and sub-specialty, e.g. esophageal surgery, gastric surgery and colorectal surgery. The territory of clinics is wide and the department provides a full spectrum of standard and special technologies such as minimally invasive surgery and extended radical surgery for malignancies.

(4) Publications

[Original Articles]

1. Okada T, Nakajima Y, Nishikage T, Ryotokuji T, Miyawaki Y, Hoshino A, Tokairin Y, Kawada K, Nagai K, Kawano T.. A prospective study of nutritional supplementation for preventing oral mucositis in cancer patients receiving chemotherapy. *Asia Pac J Clin Nutr.* 2017.01; 26(1); 42-48
2. Stremitzer S, Berghoff AS, Volz NB, Zhang W, Yang D, Stintzing S, Ning Y, Sunakawa Y, Yamauchi S, Seboi A, Matsusaka S, Okazaki S, Hanna D, Parekh A, Mendez A, Berger MD, El-Khoueiry R, Birner P, Preusser M, Lenz HJ.. Genetic variants associated with colorectal brain metastases susceptibility and survival. *Pharmacogenomics J.* 2017.01; 17(1); 29-35
3. Tomii C, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. TPX2 expression is associated with poor survival in gastric cancer *World J Surg Oncol.* 2017.01; 15(1);
4. Inokuchi M, Murase H, Otsuki S, Kawano T, Kojima K. Different clinical significance of FGFR1-4 expression between diffuse-type and intestinal-type gastric cancer *World J Surg Oncol.* 2017.01; 15(1);
5. Okada T, Nakajima Y, Nishikage T, Ryotokuji T, Miyawaki Y, Hoshino A, Tokairin Y, Kawada K, Nagai K, Kawano T.. A prospective study of nutritional supplementation for preventing oral mucositis in cancer patients receiving chemotherapy. *Asia Pac J Clin Nutr.* 2017.01; 26(1); 42-48
6. kawada k, Kawano T, Sugimoto T, Yamaguchi K, Kawamura Y, Matsui T, Okuda M, Ogo T, Kume Y, Nakajima Y, Andres Mora, Okada T, Hoshino A, Tokairin Y, Nakajima Y, Okada R, Kiyokawa Y, Nomura F, Asakage T, Shimoda R, Ito T. Case of Superficial Cancer Located at the Pharyngoesophageal Junction Which Was Dissected by Endoscopic Laryngopharyngeal Surgery Combined with Endoscopic Submucosal Dissection. *Case Rep Otolaryngol.* 2017.01;
7. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawada, Akihiro Hoshino, Takuya Okada, Taichi Ogo, Masafumi Okuda, Yuichiro Kume, Yutaka Nakajima, Toshihiro Matsui, Yudai Kawamura, Kazuya Yamaguchi, Kagami Nagai, Keiichi Akita, Tatsuyuki Kawano. A mediastinoscopic approach with bilateral cervicopneumomediastinum in radical thoracic esophagectomy *International Surg.* 2017.02; Epub ahead;
8. Iwata N, Ishikawa T, Okazaki S, Mogushi K, Baba H, Ishiguro M, Kobayashi H, Tanaka H, Kawano T, Sugihara K, Uetake H. Clinical Significance of Methylation and Reduced Expression of the Quaking Gene in Colorectal Cancer. *Anticancer Res.* 2017.02; 37(2); 489-498
9. Yuya Sato, Mikito Inokuchi, Sho Otsuki, Yoshitaka Fujimori, Kazuyuki Kojima. Risk Factor of Pancreatic Fistula after Radical Gastrectomy from the Viewpoint of Fatty Pancreas. *Dig Surg.* 2017.02;
10. Yamada I, Yoshino N, Hikishima K, Miyasaka N, Yamauchi S, Uekake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y.. Colorectal carcinoma: Ex vivo evaluation using 3-T high-spatial-resolution quantitative T2 mapping and its correlation with histopathologic findings. *Magn Reson Imaging.* 2017.03; 38; 174-181
11. Higuchi K, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. Cadherin 5 expression correlates with poor survival in human gastric cancer *J Clin Pathol.* 2017.03; 70; 217-221
12. Okazaki S, Baba H, Iwata N, Yamauchi S, Sugihara K.. Carcinoembryonic antigen testing after curative liver resection for synchronous liver metastasis of colorectal cancer: a Japanese multicenter analysis. *Surg Today.* 2017.04; [Epub ahead of print] ;
13. Matsusaka S, Wu AH, Cao S, Hanna DL, Chin K, Yang D, Zhang W, Ning Y, Stintzing S, Sebio A, Sunakawa Y, Stremitzer S, Yamauchi S, Okazaki S, Berger MD, Parekh A, Miyamoto Y, Mizunuma N, Lenz HJ.. Prognostic impact of FOXF1 polymorphisms in gastric cancer patients. *Pharmacogenomics J.* 2017.04; [Epub ahead of print] ;
14. Baongoc Nasri, Mikito Inokuchi, Toshiaki Ishikawa, Hiroyuki Uetake, Yoko Takagi, Sho Otsuki, Kazuyuki Kojima, Tatsuyuki Kawano. High expression of EphA3 (erythropoietin-producing hepatocellular A3) in gastric cancer is associated with metastasis and poor survival *BMC Clin Pathol.* 2017.04; 17;
15. Tomoki Aburatani, Kazuyuki Kojima, Sho Otsuki, Hideaki Murase, Keisuke Okuno, Kentaro Gokita, Chiharu Tomi, Toshiro Tanioka, Mikito Inokuchi. Double-tract reconstruction after laparoscopic proximal gastrectomy using detachable ENDO-PSD *Surg Endosc.* 2017.04; published online;

16. Keisuke Okuno, Kentaro Gokita, Toshiro Tanioka, Norihito Ogawa, Sho Otsuki, Mikito Inokuch, Toshio Takayama, Kazuyuki Kojima. Esophagojejunostomy Using the Purse-String Suturing Device After Laparoscopic Total or Proximal Gastrectomy for Gastric Cancer *World J Surg.* 2017.04; published online;
17. Berger MD, Yamauchi S, Cao S, Hanna DL, Sunakawa Y, Schirripa M, Matsusaka S, Yang D, Groshen S, Zhang W, Ning Y, Okazaki S, Miyamoto Y, Suenaga M, Lonardi S, Cremolini C, Falcone A, Heinemann V, Loupakis F, Stintzing S, Lenz HJ.. Autophagy-related polymorphisms predict hypertension in patients with metastatic colorectal cancer treated with FOLFIRI and bevacizumab: Results from TRIBE and FIRE-3 trials. *Eur J Cancer.* 2017.05; 77; 13-20
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21. Tomoki Aburatani, Mikito Inokuchi, Yoko Takagi, Toshiaki Ishikawa, Keisuke Okuno, Kentaro Gokita, Chiharu Tomii, Toshiro Tanioka, Hideaki Murase, Sho Otsuki, Hiroyuki Uetake, Kazuyuki Kojima, Tatsuyuki Kawano. High expression of P21-activated kinase 5 protein is associated with poor survival in gastric cancer. *Oncol Lett.* 2017.07; 14(1); 404-410
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25. Mikito Inokuchi, Toshiro Tanioka, Masatoshi Nakagawa, Keisuke Okuno, Kentaro Gokita, Kazuyuki Kojima. Laparoscopic Distal Gastrectomy is Feasible in Very Elderly Patients as Compared with Open Distal Gastrectomy. *JOURNAL OF INVESTIGATIVE SURGERY.* 2017.08; 1-7
26. Kenro Kawada, Takuya Okada, Taro Sugimoto, Kazuya Yamaguchi, Yuudai Kawamura, Toshihiro Matsui, Masafumi Okuda, Taichi Ogo, Yuuichiro Kume, Andres Mora, Akihiro Hoshino, Yutaka Tokairin, Yasuaki Nakajima, Ryuhei Okada, Yusuke Kiyokawa, Fuminori Nomura, Yosuke Ariizumi, Takahiro Asakage, Takashi Ito and Tatsuyuki Kawano. Observation of the Pharynx to the Cervical Esophagus Using Transnasal Endoscopy with Image-enhanced Endoscopy for Early Detection of Head and Neck Cancers *Journal of Gastrointestinal & Digestive System.* 2017.08; 7(4);
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31. M. Nakagawa, C. Tomii, M. Inokuchi, S. Otsuki, K. Kojima. Feasibility Of A Clinical Pathway With Early Oral Intake And Discharge For Laparoscopic Gastrectomy *Scandinavian journal of surgery.* 2017.12; Published online ;
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34. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. *Magnetic Resonance Imaging.*
35. Kobayashi K, Inokuchi M, Takagi Y, Otsuki S, Fujimori Y, Sato Y, Yanaka Y, Higuchi K, Aburatani T, Tomii C, Uetake H, Kojima K, Kawano T. Prognostic significance of PAK4 expression in gastric cancer. *J Clin Pathol.*
36. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget.*
37. Inokuchi M, Otsuki S, Murase H, Kojima K, Kawano T. Feasibility of laparoscopy-assisted gastrectomy for patients with poor physical status: A propensity-score matching study. *Int J Surg.*
38. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR Imaging of Gastric Carcinoma Ex Vivo: Correlation with Histopathologic Findings. *Magn Reson Med.*
39. Nakagawa M, Kojima K, Inokuchi M, Kato K, Sugita H, Otsuki S, Sugihara K. Identification of frequency, severity and risk factors of complications after open gastrectomy: Retrospective analysis prospectively collected database using the Clavien-Dindo classification. *J Med Dent Sci.*
40. Higuchi K, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. Cadherin 5 expression correlates with poor survival in human gastric cancer. *J Clin Pathol.*
41. Nishikawaji T, Akiyama Y, Shimada S, Kojima K, Kawano T, Eishi Y, Yuasa Y, Tanaka S. Oncofetal roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget.*

[Conference Activities & Talks]

1. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Norihito Ogawa, Mikito Inokuchi, Kazuyuki Kojima.. Roux-en-Y reconstruction after LDG - surgical technique and functional advantages . *China-Japan-Korea Laparoscopic gastrectomy* 2017.02.11
2. Yamauchi S, Okazaki S, Kikuchi A, Ishiguro M, Ishikawa T, Uetake H, Yasuno M, Sugihara K.. Prognostic factor of lower rectal cancer with lateral pelvic lymph node metastasis treated with lateral lymph node dissection.. *Society of Surgical Oncology (SSO) 2017 Annual Meeting* 2017.03.16 Seattle (USA)

3. Hanaoka M, Ishikawa T, Ishiguro M, Tokura M, Yamauchi S, Kikuchi A, Yasuno M, Uetake H, Kawano T. ATF6, a UPR related gene, expression in malignant conversion and progression of Ulcerative colitis (UC)-associated and non-UC-associated colorectal cancer. Society of Surgical Oncology (SSO) 2017 Annual Meeting 2017.03.16 Seattle (USA)
4. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Okada T, Okuda M, Ogo T, Kume Y, Kawamura Y, Yamaguchi K, Kawano T. Esophageal bypass surgery followed by definitive chemoradiotherapy can become an effective therapeutic strategy, improving the poor quality of life of patients with locally advanced esophageal carcinoma. SAGES2017 2017.03.23 Houston(USA)
5. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Mikito Inokuchi, Kazuyuki Kojima. Effect of postoperative complications on the long-term survival of patients with gastric cancer. 12th International Gastric Cancer Congress 2017.04.21
6. Keisuke Okuno, Kentaro Gokita, Toshiro Tanioka, Norihito Ogawa, Sho Otuki, Mikito Inokuchi, Kazuyuki Kojima. A study on gastroesophageal reflux disease after laparoscopic distal gastrectomy. 12th International Gastric Cancer Congress 2017.04.21
7. Masatoshi Nakagawai, Mikito Inokuchi, Sho Otuki, Norihito Ogawa, Toshiro Tanioka, Kazuyuki Kojima. Is laparoscopic approach an effective tool for total gastrectomy to obese patients. 12th International Gastric Cancer Congress 2017.04.22
8. Kenro Kawada. Observation of the pharynx to the cervical esophagus using transnasal endoscopy with image-enhanced endoscopy. 11th GLOBAL GASTROENTEROLOGISTS MEETING 2017.06.12 Rome(Italy)
9. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Okada T, Okuda M, Kume Y, Kawamura Y, Yamaguchi K, Kawano T. The therapeutic strategy for esophageal bypass surgery followed by definitive chemoradiotherapy for patients with locally advanced esophageal carcinoma. 52nd International Meeting of the European Society for Surgical Research (ESSR) 2017.06.16 Amsterdam(the Netherlands)
10. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Okada T, Kawano T. THE “LARYNX ROTATION METHOD” – A NOVEL SURGICAL PROCEDURE FOR LARYNX-PRESERVING CERVICAL ESOPHAGECTOMY. World Congress of Surgery (WCS) 2017 2017.08.16 Basel(Switzerland)
11. Kenro kawada, Yausaki Nakajima, Yutaka Tokairin, Akihiro Hoshino, Takuya Okada, Yudai Kawamura. Observation of the oral cavity of patients with esophageal cancer using trans-nasal esophagogastroduodenoscopy with image enhanced endoscopy.. OESO 14th World Conference, CICG (International Conference center of Geneva) 2017.09.03 Geneva(Switzerland)
12. Yudai Kawamura, Kawada Kenro. Endoscopic submucosal dissection for Barrett’ s adenocarcinoma observed in the esophageal remnant after a radical surgery for esophageal cancer: a case report. 14th OESO Conference 2017.09.04 Geneva(Switzerland)
13. Nakajima Y, Kawada K, Tokairin Y, Hoshino A, Okada T, Ryotokuji T, Okuda M, Kume Y, Kawamura Y, Yamaguchi K. Clinical outcomes of larynx-preserving surgery for resectable cervical esophageal carcinoma. APDW2017 2017.09.25 Hong Kong
14. K.Kojima, T.Tanioka, M.Inokuchi. Reconstruction after laparoscopic gastrectomy-Our procedure and clinical results-. Japan Digestive Disease Week 2017 (JDDW2017) 2017.10.13 Fukuoka
15. Y. Kinugasa. The surgical technique and outcome of robotic rectal cancer surgery. Japan Digestive Disease Week 2017 (JDDW2017) 2017.10.13 Fukuoka
16. Y. Kume, K. Kawada, N. Y Nakajima. Treatment strategy of superficial Barrett’s esophageal cancer. Japan Digestive Disease Week 2017 JDDW2017 2017.10.14 Fukuoka
17. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Masatoshi Nakagawa, Mikito Inokuchi, Kazuyuki Kojima. An Intraoperative Educational Annotation System for Endoscopic Surger. 103th Annual Clinical Congress of the American College of Surgeons(ACS2017) 2017.10.25 San Diego
18. Kume Yuichiro, Hoshino Akihiro, Yamaguchi Kazuya, Kawamura Yudai, Okuda Masafumi, Ryotokuji Tairo, Okada Takuya, Tokairin Yutaka, Kawada Kenro, Nakajima Yasuaki. Clinicopathological features of reconstructed gastric tube cancer after esophagectomy. ESDE Annual Meeting 2017 2017.11.08 Utrecht(the Netherlands)

19. Hoshino A, Nakajima Y, Kawada K, Tokairin Y, Okada T, Ryotokuji T, Kume Y, Okuda M, Kawamura Y, Yamaguchi K.. Strategies for initiating early oral ingestion in thoracoscopic esophagectomy.. The Congress of the European Society for Diseases of the Esophagus (ESDE) 2017 2017.11.08 Utrecht(the Netherlands)
20. Yamauchi S, Yasuno M, Takaoka A, Matsumiya Y, Seki R, Orita F, Sasaki M, Miura T, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Sugihara K.. Clinical significance of extended lateral lymph node dissection for lower rectal cancer.. Asian Surgical Association 21st Asian Congress of Surgery 2017.11.12 Tokyo
21. M Okuda, J Inoue, N Fujiwara, T Kawano, J Inazawa. Subcloning and characterization of highly metastatic cells derived from human esophageal squamous cell carcinoma KYSE150 cells by in vivo selection. IASGO World Congress 2017 2017.11.17 Lyon(France)
22. Tokairin Y, Kawada K, Hoshino A, Okada T, Okuda M, Nakajima Y, Akita K, Nakajima Y. Nontransthoracic radical esophagectomy using cervical and transhiatal approach under pneumomediastinum.. IASGO World Congress 2017 2017.11.17 Lyon(France)
23. Y.Nakajima, K.Kawada, Y.Tokairin, A.Hoshino, T.Okada, T.Ryotokuji, M.Okuda, Y.Kume, Y.Kawamura, K.Yamaguchi. A pilot of S1 and Paclitaxel in esophageal carcinoma pretreated by 5FU, CISPLATIN and docetaxel-Follow-up report. IASGO World Congress 2017 2017.11.17 Lyon(France)
24. Yusuke Kinugasa. The surgical technique and outcome of robotic rectal cancer surgery. 3rd Asian Congress of Robotic and Endoscopic Surgery (2017ACRES) 2017.11.25 Taipei
25. Miura T, Yamauchi S, Takaoka A, Seki R, Matsumiya Y, Orita F, Sasaki M, Tokura M, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Yasuno M.. Negative pressure wound therapy for closure of ileostomy and colostomy.. The 1st International Conference of Surgical Infection Society Asia-Pacific 2017.11.29 Tokyo
26. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryotokuji, Takuya Okada, Yutaka Miyawaki, Youichi Kumagai, Kagami Nagai, Tatsuyuki Kawano. . Efficacy of endoscopy for evaluating esophago-gastric anastomosis on post-esophagectomy day 1. . 14th World Congress of the International Society for Diseases of the Esophagus

[Awards & Honors]

1. 2017 Albert Nelson Marquis Lifetime Achievement Award (Kenro Kawada), 2017.04

Thoracic Surgery

Professor Kenichi Okubo	
Junior Associate Professor Hironori Ishibashi	
Assistant Professor Masashi Kobayashi	
Hospital assistant professor Chihiro Takasaki	
Graduate Student	Sachiko Imai
Graduate Student	Akiko Sugawara
Graduate Student	Ken Takahashi
Graduate Student	Katsutoshi Seto
Graduate Student	Ryo Wakejima
Graduate Student	Syunichi Baba
Graduate Student	Yasuhiro Nakashima
Graduate Student	Ayaka Asakawa
Graduate Student	Yuya Ishikawa

(1) Outline

Department of Thoracic Surgery deal with clinical management, basic and clinical research, and education of thoracic surgery, which includes surgical diagnosis and treatment of respiratory diseases.

(2) Research

- Minimally invasive surgery for lung cancer
- Multimodal treatments for thoracic malignancies
- Surgery for metastatic lung tumors
- Clinico-pathological studies on lung cancer

(3) Education

Department of Thoracic Surgery has a mission to educate medical post-graduates for expert thoracic surgeons. Thoracic surgeon requires the Board of Surgery and the Board of Thoracic Surgery to perform clinical cares as a specialist. We provide clinical specialty course for thoracic surgery and graduate course for thoracic surgery, and support to obtain the boards.

(4) Clinical Services & Other Works

Out-patient Clinic: Tuesday, Thursday, Friday
 Operative Day: Monday, Wednesday, Thursday, Friday
 Clinical Conference: Monday
 Chest Conference : Monday
 Clinico-pathological Conference: Wednesday
 Medical Round: every morning
 Professor's Round: Tuesday
 Journal Club: Tuesday (every other week)

Mortality & Morbidity Conference: Tuesday (every other week)

Lab Meeting: Tuesday (monthly)

Scientific Meeting: Japan Surgical Society, Japanese Association for Chest Surgery, Japanese Association for Thoracic Surgery, Japan Lung Cancer Society, Japan Society for Respiratory Endoscopy

(5) Clinical Performances

Thoracic Surgery deal with surgical treatment for lung, mediastinum, pleura and chest wall. We provide high-grade medical care as a university hospital. We offer less invasive surgery for early-stage lung cancers or benign diseases, and multimodality treatment for locally advanced thoracic malignancies.

(6) Publications

[Original Articles]

1. Sato M, Kuwata T, Yamanashi K, Kitamura A, Misawa K, Imashimizu K, Kobayashi M, Ikeda M, Koike T, Kosaka S, Fukai R, Sekine Y, Isowa N, Hirayama S, Sakai H, Watanabe F, Nagayama K, Aoyama A, Date H, Nakajima J. Safety and reproducibility of virtual-assisted lung mapping: a multicentre study in Japan. *European Journal of Cardio-Thoracic Surgery*. 2017.05; 51(5); 861-868
2. Tomii S, Akashi T, Ando N, Tamura T, Sakurai A, Terada A, Furukawa A, Suzuki Y, Kayamori K, Sakamoto K, Ishibashi H, Eishi Y. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology*. 2017.07; 84(4); 171-183
3. Yukinori Matsuo, Keiko Shibuya, Kenichi Okubo, Nami Ueki, Akihiro Aoyama, Makoto Sonobe, Mitsuhiro Nakamura, Takashi Mizowaki, Hiroshi Date and Masahiro Hiraoka. Long-term outcomes of intensity-modulated radiotherapy following extra-pleural pneumonectomy for malignant pleural mesothelioma *Acta Oncologica*. 2017.07; 56(7); 957-962

[Others]

1. Chylothorax post thoroscopic surgery for an anterior mediastinal tumor, 2017.11
General Thoracic and Cardiovascular Surgery, 2017.Nov.16.[Epub ahead of print]
Hironori Ishibashi, Yuya Ishikawa, Ayaka Asakawa, Sachiko Imai, Masashi, Kobayashi, Kenichi Okubo

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara

Visiting Professor Makoto Arai

Visiting Professor Masato Hasegawa

Visiting Professor Haruo Okado

Graduate Student Narumi Ikeda, Risa Kanda,
Kasumi Kori, Riichi Okuda, Yuna Takahashi
(April~), Maki Nakasone (April~), Takahiro
Mitsui (April~), Harumi Tabata (April~)

(1) Research

[Takahiko Hara] We attempt to elucidate how tissue stem cells (hematopoietic stem cells, skeletal muscle stem cells, etc.) are developed in embryos and maintained in adults by utilizing *in vitro* differentiation systems of ES/iPS cells and conditional KO mouse strains. In addition, we advance the molecular biology of CXCL14, which is involved in obesity-induced diabetes, carcinogenesis, feeding behavior, etc.

[Makoto Arai] Our research focuses on unraveling the pathophysiology of mental illnesses using molecular biology tools. Our ultimate goal is to identify new disease mechanisms, leading to the development of novel and more efficacious therapies. We perform genetic association studies, as well as metabolomics studies using samples from patients with mental disorders. Any abnormalities identified from patient samples are investigated further, using *in vitro* and *in vivo* systems, such as, cell culture assays to highlight functional alterations and behavioral studies in gene knockout mouse models.

[Masato Hasegawa] We investigate the molecular pathogenesis and progression of neurodegenerative diseases including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. We use biochemistry, immunohistochemistry and molecular biology in all our work of *in vitro*, cellular and animal models to find effective ways for clinical therapy.

[Haruo Okado] To discover the fundamental cause of various nervous diseases, e.g., brain tumors, brain malformations, and neurodevelopmental disorders, we will study the molecular mechanisms for the regulation of neural development in the cerebral cortex using gene-targeted mice, primary cultures, viral vectors, *in-utero*

electroporation, real-time imaging of slice culture, immunohistochemistry, and transcription analysis.

(2) Education

We will educate students for the purpose that they could investigate molecular mechanisms of life-threatening diseases such as cancer, diabetes, schizophrenia, amyotrophic lateral sclerosis, and brain malformations. Trained students will eventually help us to develop novel therapeutic strategies against them. In addition, they must learn the importance of good animal models (including genetically engineered mice), which faithfully reproduce symptom and progression of the diseases.

(3) Publications

[Original Articles]

1. K. Tanegashima, Y. Sato-Miyata, M. Funakoshi, Y. Nishito, T. Aigaki, and T. Hara. Epigenetic regulation of the glucose transporter gene *Slc2a1* by b-hydroxybutyrate underlies preferential glucose supply to the brain of fasted mice. *Genes Cells*, 22: 71-83, 2017.
2. H. Ohtsuka, T. Iguchi, M. Hayashi, M. Kaneda, K. Iida, M. Shimonaka, T. Hara, M. Arai, Y. Koike, N. Yamamoto, and K. Kasahara. SDF-1 α /CXCR4 signaling in lipid rafts induces platelet aggregation via PI3 kinase-dependent Akt phosphorylation. *PLoS ONE*, 12: e0169609, 2017.
3. K. Tanegashima, R. Takahashi, H. Nuriya, R. Iwase, N. Naruse, K. Tsuji, A. Shigenaga, A. Otaka, and T. Hara. CXCL14 acts as a specific carrier of CpG DNA into dendritic cells and activates Toll-like receptor 9-mediated adaptive immunity. *EBioMedicine*, 24: 247-256, 2017.
4. T. Shinohara, K. Kazuki, N. Ogonuki, H. Morimoto, S. Matoba, K. Hiramatsu, K. Honma, T. Suzuki, T. Hara, A. Ogura, M. Oshimura, M. Kanatsu-Shinohara, and Y. Kazuki. Transfer of mouse artificial chromosome into spermatogonial stem cells generates transchromosomic mice. *Stem Cell Rep.*, 9: 1180-1191, 2017.
5. K. Miyashita, K. Kitajima, S. Goyama, T. Kitamura, and T. Hara. Overexpression of *Lhx2* suppresses proliferation of human T cell acute lymphoblastic leukemia-derived cells, partly by reducing LMO2 protein levels. *Biochem. Biophys. Res. Commun.*, 495: 2310-2316, 2018. (Published on December 24, 2017)

6. Y. I. Ishida, T. Kayama, Y. Kibune, S. Nishimoto, S. Koike, T. Suzuki, Y. Horiuchi, M. Miyashita, M. Itokawa, M. Arai, and Y. Ogasawara. Identification of an argpyrimidine-modified protein in human red blood cells from schizophrenic patients: A possible biomarker for diseases involving carbonyl stress. *Biochem. Biophys. Res. Commun.*, 493: 573-577, 2017.
7. I. Kushima, B. Aleksic, M. Nakatochi, T. Shimamura, T. Shiino, A. Yoshimi, H. Kimura, Y. Takasaki, C. Wang, J. Xing, K. Ishizuka, T. Oya-Ito, Y. Nakamura, Y. Arioka, T. Maeda, M. Yamamoto, M. Yoshida, H. Noma, S. Hamada, M. Morikawa, Y. Uno, T. Okada, T. Iidaka, S. Iritani, T. Yamamoto, M. Miyashita, A. Kobori, M. Arai, M. Itokawa, M. C. Cheng, Y. A. Chuang, C. H. Chen, M. Suzuki, T. Takahashi, R. Hashimoto, H. Yamamori, Y. Yasuda, Y. Watanabe, A. Nunokawa, T. Someya, M. Ikeda, T. Toyota, T. Yoshikawa, S. Numata, T. Ohmori, S. Kunimoto, D. Mori, N. Iwata, and N. Ozaki. High-resolution copy number variation analysis of schizophrenia in Japan. *Mol. Psychiatry*, 22: 430-440, 2017.
8. D. Abe, M. Arai, and M. Itokawa. Music-evoked emotions in schizophrenia. *Schizophr. Res.*, 185: 144-147, 2017.
9. M. Hosokawa, H. Kondo, G.E. Serrano, T.G. Beach, A.C. Robinson, D.M. Mann, H. Akiyama, M. Hasegawa, and T. Arai: Accumulation of multiple neurodegenerative disease-related proteins in familial frontotemporal lobar degeneration associated with granulin mutation. *Sci. Rep.*, 7: 1513, 2017.
10. Y. Tanaka, G. Suzuki, T. Matsuwaki, M. Hosokawa, G. Serrano, T.G. Beach, K. Yamanouchi, M. Hasegawa, and M. Nishihara. Progranulin regulates lysosomal function and biogenesis through acidification of lysosomes. *Hum. Mol. Genet.*, 26: 969-988, 2017.
11. K. Eguchi, Z. Taoufiq, O. Thorn-Seshold, D. Trauner, M. Hasegawa, and T. Takahashi. Wild-type monomeric α -synuclein can impair vesicle endocytosis and synaptic fidelity via tubulin polymerization at the calyx of Held. *J. Neurosci.*, 37: 6043-6052, 2017.
12. A. Shimozawa, M. Ono, D. Takahara, A. Tarutani, S. Imura, M. Masuda-Suzukake, M. Higuchi, K. Yanai, S.-I. Hisanaga, and M. Hasegawa. Propagation of pathological α -synuclein in marmoset brain. *Acta Neuropathol. Commun.*, 5: 12, 2017.
13. T. Mano, K. Nagata, T. Nonaka, A. Tarutani, T. Imamura, T. Hashimoto, T. Bannai, K. Koshi-Mano, T. Tsuchida, R. Ohtomo, J. Takahashi-Fujigasaki, S. Yamashita, Y. Ohyagi, R. Yamazaki, S. Tsuji, A. Tamaoka, T. Ikeuchi, T. Saido, T. Iwatsubo, T. Ushijima, S. Murayama, M. Hasegawa, and A. Iwata. Neuron-specific methylome

- analysis reveals epigenetic regulation and tau-related dysfunction of BRCA1 in Alzheimer's disease. *Proc. Natl. Acad. Sci. U.S.A.*, 114: E9645-E9654, 2017.
14. T. Okada, K. Keino-Masu, S. Nagamine, F. Kametani, T. Ohto, M. Hasegawa, T. van Kuppevelt, S. Kunita, S. Takahashi, and M. Masu, Desulfation of Heparan Sulfate by Sulf1 and Sulf2 Is Required for Corticospinal Tract Formation. *Sci. Rep.*, 7: 13847, 2017.
 15. S. Hirai, K. Hotta, Y. Kubo, A. Nishino, S. Okabe, Y. Okamura, and H. Okado. AMPA glutamate receptors are required for sensory-organ formation and morphogenesis in the basal chordate. *Proc. Natl. Acad. Sci. U.S.A.*, 114: 3939-3944, 2017.
 16. S. Yokoi, T. Udagawa, Y. Fujioka, D. Honda, H. Okado, H. Watanabe, M. Katsuno, S. Ishigaki, and G. Sobue. 3'UTR length-dependent control of SynGAP isoform $\alpha 2$ mRNA by FUS and ELAV-like proteins promotes dendritic spine maturation and cognitive function. *Cell Rep.*, 20: 3071-3084, 2017.
 17. S. Ishigaki, Y. Fujioka, Y. Okada, Y. Riku, T. Udagawa, D. Honda, S. Yokoi, K. Endo, K. Ikenaka, S. Takagi, Y. Iguchi, N. Sahara, A. Takashima, H. Okano, M. Yoshida, H. Warita, M. Aoki, H. Watanabe, H. Okado, M. Katsuno, and G. Sobue. Altered Tau Isoform Ratio Caused by Loss of FUS and SFPQ Function Leads to FTLD-like Phenotypes. *Cell Rep.*, 18: 1118-1131, 2017.

[Review Articles]

1. M Miyashita, K Toriumi, Y Horiuchi, K Suzuki, M Itokawa, and M Arai. Peripheral Soluble RAGE Levels in Schizophrenia. *IMARS HIGHLIGHTS*, 12: 5-9, 2017.
2. R Mizutani, R Saiga, S Takekoshi, C Inomoto, N Nakamura, M Arai, K Oshima, M Itokawa, A Takeuchi, K Uesugi, Y Terada, and Y Suzuki. Estimating the resolution of real images. X-Ray Microscopy Conference 2016, *Proceedings, IOP Conf. Series: Journal of Physics: Conf. Series*, 849: 012042, 2017.
3. M. Hasegawa and G. Suzuki: Following the fate of endocytosed fibrils. *J. Biol. Chem.*, 292: 13498-13499. 2017.

[Books]

1. T. Nonaka and M. Hasegawa. TDP-43 prions. Prion Disease, *Cold Spring Harb. Perspect. Med.*, New York, 2017, pp451-460, Edited by S. Prusiner.

[Conference Activities & Talks]

1. Y Horiouchi, M Miyashita, K Toriumi, M Itokawa, and M Arai. Influence of carbonyl stress on neural cells derived from induced pluripotent cell. 5th Congress of Asian College of Neuropsychopharmacology (AsCNP), 2017.4.27, Nusa Dua Bali, Indonesia.
2. M Arai, K Toriumi, M Miyashita, Y Horiuchi, I Nohara, N Obata, G Konopka, M Itokawa, T Dan, and T Miyata. Administration of high-dose pyridoxamine to adult mice. WPA XVII WORLD CONGRESS OF PSYCHIATRY, 2017.10.9, Berlin.
3. M Miyashita, M Arai, T Dan, K Toriumi, Y Horiuchi, A Kobori, K Suzuki, M Itokawa, and T Miyata. Pyridoxamine, a novel treatment for negative symptoms of schizophrenia. WPA XVII WORLD CONGRESS OF PSYCHIATRY, 2017.10.9, Berlin.
4. K Toriumi, M Miyashita, Y Horiuchi, I Nohara, N Obata, G Konopka, M Itokawa, T Dan, T Miyata , and M Arai. Effect of deficiency of vitamin B6 on mouse behavior and monoaminergic system. WPA XVII WORLD CONGRESS OF PSYCHIATRY, 2017.10.11, Berlin.
5. M. Hasegawa. FTLD-TDP-43 and FTLD-FUS. Emerging Concepts in the Biology of Frontotemporal Lobar Degeneration, Alzheimer's Association International Conference (AAIC) 2017, 2017.7.18, London.
6. M. Hasegawa. α Synuclein. World Congress of Neurology (WCN2017), 2017.9.19, Kyoto.
7. M. Hasegawa. TDP-43 prions. Joint Meeting of PACTALS & Brain Protein Aging and Dementia Control, 2017.9.21, Kyoto.
8. M. Hasegawa. α Synuclein prions. Brain Protein Aging and Dementia Control”project, The 2nd International Symposium, 2017.11.2, Nagoya.

Clinical Anatomy

Professor Keiichi AKITA

Associate Professor Akimoto NIMURA (Department of Functional Joint Anatomy)

Junior Associate Professor Kumiko YAMAGUCHI

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Graduate Student Kazuhito SEKIZAWA, Keiko OKUMURA, Ryuhei OKADA, Eichirou KAGAWA,

Motoki TANAKA, Kotaro EGUCHI, Saya HORIUCHI, Pawaree NONTHASAEN, Natnicha KAMPAN,

Kentaro AMAHA, Yusuke UEDA, Yasunori TATARA, Shota HOSHIKA, Phichaya BARAMEE,

Atsuhiko OCHI, Souichi HATTORI, Kou MIWA, Satoru MURO, Suriyut JANARUK,

Syuusaku HOSONO (April ~), Haruka EISHI (April ~), Masahiro TSUTSUMI (April ~),

Wachirawit SIRIRAT (April ~)

Research Student Hirokazu SAKAMOTO, Mamiko SUZUKI,

(1) Outline

Department of Clinical Anatomy supports clinical medicine through formulation of human anatomical and developmental biological bases of diagnoses and surgical procedures. We handle the whole body in human anatomical researches. We think it is classic but important to represent human morphology for exactly what they are based on meticulous observations of human body structures regardless of diagnostic technics and surgical procedures. Our researches are aimed to share languages among all clinicians based on clinical anatomy by describing the results of observations in an accessible way for clinicians. In addition, we perform analyses using experimental embryological approaches and developmental biological approaches, because we think it is important to consider how human structures are constructed.

(2) Research

- 1) Clinical anatomic study of the shoulder joint and rotator cuff.
- 2) Clinical anatomic study of the anal region for the rectoanal surgery.
- 3) Cadaveric study of the female pelvis for the gynecologic oncology and colposcopy.
- 4) Analyses of the lamination in the masticatory muscles with special reference of nerve supply.
- 5) Embryological study of the differentiation of cloaca and surrounding muscles.

(3) Education

Clinical anatomy is generally considered as the practical application of anatomical knowledge to diagnosis and treatment, however we think that this course is a part of pure anatomical science based on the findings of the morphological observations of the human bodies. Main objective of Clinical anatomy in the graduate course is to make detailed anatomical data to answer the questions developed from clinical fields especially by surgeons and radiologists. We collaborate with many clinicians: ENT, orthopedics, gynecology, thoracic surgery, radiology and so on, and our projects have been broad areas. Students are expected to get fine dissection techniques of

human bodies and also learn techniques of histology and embryological experiments. By using these techniques, we study the spatial relationships of organs, vessels nerves, and also try to examine their developmental processes in various projects.

(4) Lectures & Courses

Theories and hypotheses of morphogenesis derived from descriptive anatomy and descriptive biology have been confirmed and modified by experimental biology. Furthermore, progresses of developmental biology identified molecules and signaling pathways involved in the morphogenesis. Progresses in the developmental biology also verified morphological hypotheses, and added revisions to the morphological models. The postulates of the morphological models which are currently investigated were built and completed by Anatomy. However, we find Anatomy is still not completed and has many obscure issues through careful dissection of human body. It might be thought that everything was done and there could be no new finding in the human anatomical field anymore because the anatomy employs the classic procedures such as the gross anatomy. However, there are still a lot of unclear anatomical topics, because they had not been focused and not investigated with their clinical significances.

(5) Publications

[Original Articles]

1. Hitomi Fujishiro, Sachiya Tsukada, Tomomasa Nakamura, Akimoto Nimura, Tomoyuki Mochizuki, Keiichi Akita. Attachment area of fibres from the horns of lateral meniscus: anatomic study with special reference to the positional relationship of anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc.* 2017.02; 25(2); 368-373
2. Keiko Okumura, Kumiko Yamaguchi, Tatsuya Tamaki, Kazuhiro Oinuma, Hikaru Tomoe, Keiichi Akita. Prospective analyses of female urinary incontinence symptoms following total hip arthroplasty. *Int Urogynecol J.* 2017.04; 28(4); 561-568
3. Tomoyasu Kato, Keiichi Akita. Abstracts presented at the 20th Japanese Research Society of Clinical Anatomy on November 12th 2016 at National Cancer Center Hospital. *Surg Radiol Anat.* 2017.05; 1029-1043
4. Luo Y, Fujita H, Nedelescu H, Biswas MS, Sato C, Ying S, Takahashi M, Akita K, Higashi T, Aoki I, Sugihara I. Lobular homology in cerebellar hemispheres of humans, non-human primates and rodents: a structural, axonal tracing and molecular expression analysis. *Brain Structure and Function.* 2017.05; 222(6); 2449-2472
5. Junichiro Hamada, Akimoto Nimura, Kunio Yoshizaki, Keiichi Akita. Anatomic study and electromyographic analysis of the teres minor muscle. *J Shoulder Elbow Surg.* 2017.05; 26(5); 870-877
6. Okada R, Muro S, Eguchi K, Yagi K, Nasu H, Yamaguchi K, Miwa K, Akita K. The extended bundle of the tensor veli palatini: Anatomic consideration of the dilating mechanism of the Eustachian tube. *Auris Nasus Larynx.* 2017.06;
7. Satoshi Usami, Mutsumi Okazaki, Tomohisa Nitta, Noriko Uemura, Tsutomu Homma, Keiichi Akita. Histological investigation of common insensate flaps obtained from the hand and forearm regions for use in fingertip reconstruction. *J Plast Surg Hand Surg.* 2017.06; 51(3); 182-186
8. Junya Imatani, Keiichi Akita. Volar Distal Radius Anatomy Applied to the Treatment of Distal Radius Fracture. *J Wrist Surg.* 2017.08; 6(3); 174-177
9. Kawada K, Kawano T, Sugimoto T, Yamaguchi K, Kawamura Y, Matsui T, Okuda M, Ogo T, Kume Y, Nakajima Y, Andres Mora, Okada T, Hoshino A, Tokairin Y, Nakajima Y, Okada R, Kiyokawa Y, Nomura F, Asakage T, Shimoda R, Ito T. Case of superficial cancer located at the pharyngoesophageal junction which was dissected by endoscopic laryngopharyngeal surgery combined with endoscopic submucosal dissection. *Case Rep Otolaryngol.* 2017.08;

10. kawada k, Kawano T, Okada T, Yamaguchi K, Kawamura Y, Matsui T, Okuda M, Ogo T, Kume Y, Nakajima Y, Anderes Mora, Hoshino A, Tokairin Y, Nakajima Y, Okada R, Kiyokawa Y, Nomura F, Ariizumi Y, Sugimoto T, Asakage T, Ito T. The usefulness of intra-oropharyngeal U-turm method using trans-nasal endoscopy for detecting superficial squamous cell carcinoma of the base of the tongue J Otolaryngol ENT Res. 2017.08; 8; 240
11. Minobu Kamo, Taiki Nozaki, Jay Starkey, Saya Horiuchi, Natsuka Muraishi, Kazunori Hattori, Keiichi Akita. The Peak Site of Stone Distribution in the Upper Ureter is Unlikely the Ureteropelvic Junction: Computed Tomography Analysis of Stone Lodging Site With Respect to a Newly Identified Area of Constriction. Urology. 2017.09; 107; 31-36
12. Yasuo Nakajima, Satoru Muro, Hisayo Nasu, Masayo Harada, Kumiko Yamaguchi, Keiichi Akita. Morphology of the region anterior to the anal canal in males: visualization of the anterior bundle of the longitudinal muscle by transanal ultrasonography. Surg Radiol Anat. 2017.09; 39(9); 967-973
13. Takamitsu Arakawa, Takahiro Kondo, Masahiro Tsutsumi, Yuko Watanabe, Toshio Terashima, Akinori Miki. Multiple muscular variations including tenuissimus and tensor fasciae suralis muscles in the posterior thigh of a human case. Anat Sci Int. 2017.09; 92(4); 581-584
14. Hisayo Nasu, Akimoto Nimura, Sara Sugiura, Hitomi Fujishiro, Hideyuki Koga, Keiichi Akita. An anatomic study on the attachment of the joint capsule to the tibia in the lateral side of the knee. Surg Radiol Anat. 2017.11;
15. Yusuke Ueda, Hiroyuki Sugaya, Norimasa Takahashi, Keisuke Matsuki, Morihito Tokai, Kazutomo Onishi, Shota Hoshika, Hiroshige Hamada. Arthroscopic Fragment Resection for Capitellar Osteochondritis Dissecans in Adolescent Athletes: 5- to 12-Year Follow-up. Orthop J Sports Med. 2017.12; 5(12); 2325967117744537

[Misc]

1. Yoshihiro Sakamoto, Norihiro Kokudo, Yoshikuni Kawaguchi, Keiichi Akita. Clinical Anatomy of the Liver: Review of the 19th Meeting of the Japanese Research Society of Clinical Anatomy. Liver Cancer. 2017.02; 6(2); 146-160

[Conference Activities & Talks]

1. Keiichi Akita. Clinical anatomy of Masticatory Muscles. Joint Educational Meeting 2017 of Society of Spanish Anatomy and Society of Portuguese Anatomy 2017.02.17 Madrid, Spain
2. Saya Horiuchi, Taiki Nozaki, Atsushi Tasaki, Sachiko Ohde, Jay Starkey, Deshpande Gautam, Yasuyo Teramura, Yasuyuki Kurihara, Hiroshi Yoshioka. Comparison of 3D isotropic fast spin-echo and conventional 2D shoulder MRI for the evaluation of rotator cuff. Annual Congress of the European Congress of Radiology 2017 2017.03.01 Vienna, Austria
3. Yusuke Ueda, Hiroyuki Sugaya, Norimasa Takahashi, Keisuke Matsuki, Morihito Tokai, Kazutomo Onishi, Shota Hoshika, Hiroshige Hamada. Mid to long term outcome after arthroscopic fragment resection for capitellar OCD lesions in adolescent athletes. Orthopaedic Research Society 2017 Annual Meeting 2017.03.16 San Diego, USA
4. M. Uomizu, T. Mochizuki, T. Ohara, J. Matsuda, N. Ozeki, K. Tsuji, A. Nimura, T. Miyamoto, M. Goto, I. Sekiya, T. Muneta. Synovium-derived MSCs promote the restoration of tensile strength of the rotator cuff tendon after repair in a rat model. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 San Diego, CA, USA
5. Daisuke Momma, Akimoto Nimura, Tadanao Funakoshi, Tomoyuki Mochizuki, Keiichi Akita, Norimasa Iwasaki. Anatomical Analysis of the Whole Articular Capsule from the Glenoid and the Humeral Attachment. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 San Diego, USA
6. Mari Uomizu, Tomoyuki Mochizuki, Toshiyuki Ohara, Junpei Matsuda, Nobutaka Ozeki, Kunikazu Tsuji, Akimoto Nimura, Takashi Miyamoto, Masafumi Goto, Ichiro Sekiya, Takeshi Muneta. Synovium-derived MSCs promote the restoration of tensile strength of the rotator cuff tendon after repair in a rat model. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 San Diego, USA

7. Kohtaro Eguchi, Masami Suzuki, Shota Ida, Keita Mori, Hisao Imai, Shigehiro Kudo, Ken Ando, Keiko Higuchi, Takeshi Ebara. Laryngopharyngeal reflux is a risk factor for radiation-induced mucositis in head and neck cancer. 5th Congress of Asian Society of Head & Neck Oncology 2017.03.25 Bali, Indonesia
8. Shouta Hoshika, Akimoto Nimura, Hiroyuki Sugaya, Norimasa Takahashi, Keiichi Akita . Stabilizing structures of the medial side of elbow joint: an anatomic study. 14th Association France Japon d'Orthopedie 2017.05.12 Nikko, Tochigi
9. Kentaro Amaha, Akimoto Nimura, Soichi Hattori, Reiko Yamaguchi, Keiichi Akita. Anatomic study regarding the medial side of the ankle based on the joint capsule. 14th Association France Japon d'Orthopedie 2017.05.12 Nikko, Tochigi
10. Yusuke Ueda, John G Costouros, Emilie Cheung. Deep shoulder infection: Prosthetic reimplantation or cement spacer retention?. The 62nd Annual LeRoy C. Abbott Society Scientific Program 2017.05.12 San Francisco, USA
11. Keiichi Akita. Surgical Anatomy of the pancreas with special reference to the nerves to the pancreas and the ligament of Treitz. Joint congress of 6th Asian-Pacific Hepato-Pancreato-Biliary Association and 29th Meeting of Japanese Society of Hepato-Biliary-Pancreatic Surgery 2017.06.09 Yokohama, Japan
12. Kenji Ibukuro, Masaya Mori. The Hepatic Capsular Arteries: Radiological and Anatomical Features. ESGAR2017 2017.06.19 Athens, Greece
13. Akimoto Nimura, Tetsuya Sato, Reiko Yamaguchi, Koji Fujita, Takashi Miyamoto, Keiichi Akita. Intramuscular tendons of the adductor pollicis and the thumb metacarpophalangeal joint capsule: an anatomic study with implications regarding Stener lesion. Eurohand 2017 2017.06.21 Budapest, Hungary
14. Satoru Muro, Yasuo Nakajima, Hisayo Nasu, Kumiko Yamaguchi, Keiichi Akita.. Anterior Region of the Anal Canal: Transanal Ultrasonography and Histological Study.. 34th Annual Meeting - American Association of Clinical Anatomists 2017.07.21 Minneapolis, USA
15. Yusuke Ueda, Hiroyuki Sugaya, Norimasa Takahashi, Keisuke Matsuki, Morihito Tokai, Kazutomo Onishi, Shota Hoshika, Hiroshige Hamada. Mid to long term outcome after arthroscopic fragment resection for capitellar OCD lesions in adolescent athletes. AOSSM 2017 2017.07.23 Toronto, Canada
16. Masayo Harada, Keiichi Akita. The spontaneous mutation (N143T) in mouse Fgf9 leads to thicker long bones. 14th International Conference on Limb Development and Regeneration 2017.07.24 Edinburgh, UK
17. Keiichi Akita. Surgical Anatomy of the pancreas with special reference to the nerves to the pancreas and the ligament of Treitz. Post graduate Seminar in Siriraj Hospital, Mahidol University 2017.08.28 Bangkok, Thailand
18. Yusuke Ueda, John G Costouros, Emilie Cheung. Low body mass index and young age are associated with inferior outcomes after reverse total shoulder arthroplasty. 1st AP Shoulder and Elbow Symposium 2017.10.07 Tokyo, Japan
19. Akimoto Nimura, Shota Hoshika, Hiroyuki Sugaya, Keiichi Akita. Anatomy of medial ligament complex in elbow. 1st AP Shoulder and Elbow Symposium 2017.10.08 Tokyo, Japan
20. Ryuhei Okada, Masaru Yokomura, Keiji Oi, Yosuke Ariizumi, Yusuke Kiyokawa, Fuminori Nomura, Akihisa Tasaki, Yumiko Tateishi, Susumu Kirimura, Takahiro Asakage. Medullary thyroid carcinoma detected based on elevated serum procalcitonin levels: A case report. 2nd Congress of Asia-Pacific Society of Thyroid Surgery 2017.11.02

Systems BioMedicine

Professor Hiroshi ASAHARA
Junior Associate Professor Masahiro SHINOHARA
Assistant Professor Tomoki CHIBA
Project Assistant Professor Takahide MATSUSHIMA, Ryouta KURIMOTO
Project Researcher Yoko TANAKA
Graduate Students
Kensuke KATAOKA, Yuki YANO, Hiroto YAMAMOTO,
Takahiro MITSUMURA, Takayuki MIYAZAKI, Kihou TAKADA
Yusuke MOCHIZUKI

(1) Research

We revealed that A-to-I RNA editing altered target genes of microRNAs using a reporter library.
The function and regulatory mechanisms of eIF2 gamma will be examined.
Search for novel regulator of microRNA by high throughput screening.
Established novel strategies for the osteoporosis by targeting molecules critical for the bone homeostasis.
Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.
Analyzed the bone phenotype of spaceflight mice.
Analyzed molecular mechanisms by which the bone tissue regulates the energy metabolism.
The Screening of novel Damage-associated molecular patterns proteins
Protein localization analysis by High-throughput microscope system
MiRNA which regulates cartilage homeostasis was identified.
We developed screening system for miRNA target genes using reporter vector library.
MicroRNA KO mice were generated using CRISPR/Cas9 system, and its function in skeletal pattern formation was analyzed.
Molecular mechanisms and in vivo roles of RNA-binding proteins and long non-coding RNAs in the context of inflammatory response

(2) Education

Under Graduate:

Conducting “Molecular Genetics”, which is a series of lectures to understand the gene expression machinery and human genetics and their application to current medicine and biology. Under graduate students can join the lab works to learn the skills for molecular biology and pathology.

Graduate School:

Organizing “Development and Regeneration” lecture series to understand the basis for regenerative medicine and reproduction at the level of molecular genetics.

Students can join the Lab to perform researches using various experimental techniques, such as microarray, cell-based high throughput screening etc. Using these techniques, core molecular network for tissue development and inflammatory diseases will be examined, which forms the basis of systems biomedicine.

(3) Publications**[Original Articles]**

1. Koda N, Sato T, Shinohara M, Ichinose S, Ito Y, Nakamichi R, Kayama T, Kataoka K, Suzuki H, Moriyama K, Asahara H. The transcription factor mohawk homeobox regulates homeostasis of the periodontal ligament. *Development*. 2017.01; 144(2); 313-320
2. Nakasuji T, Ogonuki N, Chiba T, Kato T, Shiozawa K, Yamatoya K, Tanaka H, Kondo T, Miyado K, Miyasaka N, Kubota T, Ogura A, Asahara H. Complementary critical functions of Zfy1 and Zfy2 in mouse spermatogenesis and reproduction. *PLoS Genetics*. 2017.01; 13(1); e1006578
3. Otero M, Peng H, El Hachem K, Culley KL, Wondimu EB, Quinn J, Asahara H, Tsuchimochi K, Hashimoto K, Goldring MB. ELF3 modulates type II collagen gene (COL2A1) transcription in chondrocytes by inhibiting SOX9-CBP/p300-driven histone acetyltransferase activity. *Connect Tissue Res*. 2017.01; 58(1); 15-26
4. Matsui-Hasumi A, Sato Y, Uto-Konomi A, Yamashita S, Uehori J, Yoshimura A, Yamashita M, Asahara H, Suzuki S, Kubo M. E3 ubiquitin ligases SIAH1/2 regulates hypoxia-inducible factor 1(HIF1)-mediated TH17 cell differentiation. *Int Immunol*. 2017.02; 29(3); 133-143
5. Hasei J, Teramura T, Takehara T, Onodera Y, Horii T, Olmer M, Hatada I, Fukuda K, Ozaki T, Lotz M, Asahara H. TWIST1 induces MMP3 expression through up-regulating DNA hydroxymethylation and promotes catabolic responses in human chondrocytes. *Sci Rep*. 2017.02; 7; 42990
6. Saito T, Hara S, Tamano M, Asahara H, Takada S. Deletion of conserved sequences in IG-DMR at Dlk1-Gtl2 locus suggests their involvement in expression of paternally expressed genes in mice. *J Reprod Dev*. 2017.02; 63(1); 101-109
7. Ohmae S, Noma N, Toyomoto M, Shinohara M, Takeiri M, Fuji H, Takemoto K, Iwaisako K, Fujita T, Takeda N, Kawatani M, Aoyama M, Hagiwara M, Ishihama Y, Asagiri M. Actin-binding protein coronin 1A controls osteoclastic bone resorption by regulating lysosomal secretion of cathepsin K. *Sci Rep*. 2017.03; 16(7); 41710
8. Emiko Sakaida, Takahiro Ebata, Shunichiro Iwasawa, Ryota Kurimoto, Sachiko Yonemori, Satoshi Ota, Yukio Nakatani, Ikuo Sekine, Yuichi Takiguchi. Potential Activity of Amrubicin as a Salvage Therapy for Merkel Cell Carcinoma. *Internal Medicine*. 2017.03; 56(5); 567-570
9. Kensuke Kataoka, Takahide Matsushima, Yoshiaki Ito, Tempei Sato, Shigetoshi Yokoyama, Hiroshi Asahara. Bhlha9 regulates apical ectodermal ridge formation during limb development. *J. Bone Miner. Metab.*. 2017.03;
10. Ito Y, Inoue A, Seers T, Hato Y, Igarashi A, Toyama T, Taganov K, Boldin M, Asahara H. Identification of targets of tumor suppressor microRNA-34a using a reporter library system. *Proc Natl Acad Sci U S A*. 2017.04; 114(15); 3927-3932
11. Yachie N, Robotic Biology Consortium, Natsume T. Robotic crowd biology with Maholo LabDroids. *Nat Biotech*. 2017.04; 35(4); 310-312
12. Kurimoto R, Iwasawa S, Ebata T, Ishiwata T, Tada Y, Tatsumi K, Takiguchi Y. Pirfenidone in reversion of the epithelial-to-mesenchymal transition in human lung adenocarcinoma. *Oncology Letters*. 2017.05; 14(1); 944-950
13. Yokoyama S, Furukawa S, Kitada S, Mori M, Saito T, Kawakami K, Izpisua Belmonte JC, Kawakami Y, Ito Y, Sato T, Asahara H. Analysis of transcription factors expressed at the anterior mouse limb bud. *PLoS One*. 2017.05; 12(5); e0175673
14. Oba A, Shimada S, Akiyama Y, Nishikawaji T, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Asahara H, Kaida A, Miura M, Tanabe M, Tanaka S. ARID2 modulates DNA damage response in human hepatocellular carcinoma cells. *J Hepato*. 2017.05; 66(5); 942-951
15. Ogino H, Hisanaga A, Kohno T, Kondo Y, Okumura K, Kamei T, Sato T, Asahara H, Tsuiji H, Fukata M, Hattori M. Secreted Metalloproteinase ADAMTS-3 Inactivates Reelin. *J Neurosci*. 2017.05; 37(12); 3181-3191

16. Miyata K, Naito M, Miyata T, Mokuda S, Asahara H*. Bisulfite Sequencing for DNA Methylation Analysis of Primary Muscle Stem Cells. *Methods Mol Biol.* 2017.08; (1668); 3-13
17. Asahara H*, Inui M*, Lotz M. Tendons and Ligaments: Connecting Developmental Biology to Musculoskeletal Disease Pathogenesis. 2017.09; 32(9); 1773-1782
18. Shiba D, Mizuno H, Yumoto A, Shimomura M, Kobayashi H, Morita H, Shimbo M, Hamada M, Kudo T, Shinohara M, Asahara H, Shirakawa M, Takahashi S.. Development of new experimental platform 'MARS'-Multiple Artificial-gravity Research System-to elucidate the impacts of micro/partial gravity on mice. *Sci Rep.* 2017.09; 7(1); 10837
19. kuda K, Kobayashi S, Fukaya M, Watanabe A, Murakami T, Hagiwara M, Sato T, Ueno H, Ogonuki N, Komano-Inoue S, Manabe H, Yamaguchi M, Ogura A, Asahara H, Sakagami H, Mizuguchi M, Manabe T, Tanaka T. CDKL5 controls postsynaptic localization of GluN2B-containing NMDA receptors in the hippocampus and regulates seizure susceptibility. *Neurobiol Dis.* 2017.10; 106; 158-170

[Books etc]

1. Ryota Kurimoto, Yuichi Takiguchi. Targeting Epithelial-Mesenchymal Transition and Cancer Stem Cell. 2017.01

[Misc]

1. Masahiro Shinohara. Osteoporosis in spaceflight and osteoclasts Kidney and Metabolic Bone Diseases. 2017.07; 30(3); 195-202
2. 1. Okamoto K, Nakashima T, Shinohara M, Negishi-Koga T, Komatsu N, Terashima A, Sawa S, Nitta T, Takayanagi H. Osteoimmunology: the conceptual framework unifying the immune and skeletal systems *Physiol Rev.* 2017.10; 97(4); 1295-1349

[Conference Activities & Talks]

1. Hiroshi Asahara. Tendon development and regeneration analyzed by Mxk KO Rat. The 291st IMEG Seminar 2017.02.24
2. Hiroshi Asahara. Identification of targets of tumor suppressor microRNA-34a using a reporter library system . RNA 2017—Prague 2017.05.25 Prague
3. Tomoki Chiba,Hiroshi Asahara. Regulation of inflammatory cytokine expression by long non-coding RNA LASC. The 43rd Naito Conference 2017.06.27
4. Hiroshi Asahara. miRNA in Cancer, Arthritis and Homeostasis. The 43rd Naito Conference 2017.06.29
5. Hiroshi Asahara. Transcription Factor Mxk Regulates Tendon Development, Homeostasis and Regeneration. Collagen Gordon Research Conference 2017.07.16 New London
6. Escort-1 regulates expression of inflammatory cytokines. 2017.07.19
7. Tomoki Chiba,Hiroshi Asahara. Regulation of inflammatory cytokine expression by long non-coding RNA LASC. RNA2017 2017.07.19
8. The Future of HiBiT Technology for Molecular Biological Analysis. 2017.12.07
9. Kensuke Kataoka,Tomoki Chiba,Yoshiaki Ito,Akira Nakamichi,Hiroshi Asahara. Stem cell applications of tendon regenerative medicine using Mxk and mechanobiology. The 3rd International Symposium on Mechanobiology 2017.12.11

Comprehensive Pathology

Professor

Masanobu KITAGAWA

Junior associate Professor

Morito KURATA

Assistant Professor

Kouhei YAMAMOTO, Iichiro ONISHI

Laboratory Technician

Miori INOUE

Technical Assistant

Sachiko ISHIBASHI, Masumi IKEDA,

Graduate Students

Yuko KINOWAKI, GULINISHA Aihemaiti, Masae Yanai,

Mariko Muto, Ryoko KATO, Naoko OZAWA, Norikazu MIYAMOTO, Risa Fusa,

Sumito Shingaki, Masanori Matsuda, Tan Wang, Akiko YAMAMOTO,

Miyaka Umemori, Jyunichiro SATO, Masahiro KATO, Msahiro KATO,

Noriaki FUKUHARA, Tomohiro YOKOUCHI, Shigeo TODA,

Jyunnosuke HAYASAKA, Tatsunori Mineo, Vilayvong Sulideyh,

Luangxay Thitsamay, Abudushalamu Muyashaer,

(1) Outline

Main objective of comprehensive pathology in the graduate course is to acquire the technique of clinical and basic pathology. This course provides students opportunity to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

(2) Research

- 1) Clinico-pathological study by morphological findings, immunohistochemistry, and electron microscope, etc.
- 2) Molecular analysis of leukomogenesis induced by Friend leukemia virus (FLV)
- 3) Enhancement of apoptosis by virus-derived protein and development of apoptosis-induction cancer therapy
- 4) Molecular pathology of the myelodysplastic syndromes (MDS)
- 5) Clarification of drug resistance mechanism for hematopoietic malignancies
- 6) Comprehensive research for aging focus on the decreased immune competence
- 7) Molecular biology of the cancer progression and metastasis

(3) Education

Main objective of comprehensive pathology in the graduate course is to acquire the techniques of clinical and basic pathology. This course provides students opportunities to study clinical pathology (for example, histological and cytological diagnosis, autopsy, clinico-pathologic conference) and also basic pathology (molecular pathology and molecular biology).

(4) Publications

[Original Articles]

1. Miyamoto K, Kurata M, Nagiri T, Yamamoto K, Onishi I, Kirimura S, Kitagawa M.. Differential expression of ACINUS variants in the bone marrow of myelodysplastic syndromes. *Int J Clin Exp Pathol.* 2017.01; (10); 4330-4338
2. Honami Takada, Ken-Ichi Imadome, Haruna Shibayama, Mayumi Yoshimori, Ludan Wang, Yasunori Saitoh, Shin Uota, Shoji Yamaoka, Takatoshi Koyama, Norio Shimizu, Kouhei Yamamoto, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. EBV induces persistent NF- κ B activation and contributes to survival of EBV-positive neoplastic T- or NK-cells. *PLoS ONE.* 2017.03; 12(3); e0174136
3. Kohei Kato, Takeshi Namiki, Makiko Ueno, Madoka Iikawa, Shown Tokoro, Aya Nishizawa, Kouhei Yamamoto, Keiko Miura, Hiroo Yokozeki. A Case of Primary Cutaneous Gamma-Delta T-Cell Lymphoma with Pautrier Microabscess. *Annals of Dermatology.* 2017.04; 29(2); 229-232
4. Keiichi Kinowaki, Yurie Soejima, Arisa Kumagai, Fukuo Kondo, Keiji Sano, Takeshi Fujii, Masanobu Kitagawa, Toshio Fukusato. Clinical and pathological significance of myeloid differentiation factor 88 expression in human hepatocellular carcinoma tissues. *Pathology international 東京医科歯科大学.* 2017.05; 67(5); 256-263
5. Ayano Imai, Hiroshi Takase, Ken-Ichi Imadome, Go Matsuda, Ichiro Ohnishi, Kouhei Yamamoto, Takumi Kudo, Yoji Tanaka, Takatoshi Maehara, Osamu Miura, Ayako Arai. Development of Extranodal NK/T-cell Lymphoma Nasal Type in Cerebrum Following Epstein-Barr Virus-positive Uveitis. *Intern. Med..* 2017.05; 56(11); 1409-1414
6. Naoki Kasahata, Tomohide Sato, Ichiroh Onishi, Masanobu Kitagawa, Toshiki Uchihara, Katsuike Hirokawa. Three-Repeat Tau with Grain-Like Structures and Distribution in an 83-Year-Old Man. *J. Alzheimers Dis..* 2017.06; 58(3); 681-685
7. Naoko Tsuyama, Seiji Sakata, Satoko Baba, Yuko Mishima, Noriko Nishimura, Kyoko Ueda, Masahiro Yokoyama, Yasuhito Terui, Kiyohiko Hatake, Masanobu Kitagawa, Naoki Ishizuka, Naoto Tomita, Kengo Takeuchi. BCL2 expression in DLBCL: reappraisal of immunohistochemistry with new criteria for therapeutic biomarker evaluation. *Blood.* 2017.07; 130(4); 489-500
8. Akira Toriihara, Ayako Arai, Masashi Nakadate, Kouhei Yamamoto, Ken-Ichi Imadome, Osamu Miura, Ukihide Tateishi. FDG-PET/CT findings of chronic active Epstein-Barr virus infection. *Leuk. Lymphoma.* 2017.10; 1-4
9. Honami Takada, Ken-Ichi Imadome, Haruna Shibayama, Mayumi Yoshimori, Ludan Wang, Yasunori Saitoh, Shin Uota, Shoji Yamaoka, Takatoshi Koyama, Norio Shimizu, Kouhei Yamamoto, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. Correction: EBV induces persistent NF- κ B activation and contributes to survival of EBV-positive neoplastic T- or NK-cells. *PLoS ONE.* 2017.10; 12(8); e0182682
10. Yae Ohata, Anna Tatsuzawa, Yoshio Ohyama, Ayako Ichikawa, Yumi Mochizuki, Sachiko Ishibashi, Yuri Itakura, Urara Sakurai, Kei Sakamoto, Tohru Ikeda, Masanobu Kitagawa, Kouhei Yamamoto. A distinctive subgroup of oral EBV+ B-cell neoplasm with polymorphous features is potentially identical to EBV+ mucocutaneous ulcer. *Hum. Pathol..* 2017.11; 69; 129-139

Molecular Oncology

Professor: Shinji TANAKA
Associate Professor: Yoshimitsu AKIYAMA
Associate Professor: Hiroshi FUKAMACHI
Assistant Professor: Shu SHIMADA
Laboratory Technician: Hiromi NAGASAKI
Graduate Student: Taketo NISHIKAWAJI
Graduate Student: Misaki SERIZAWA

(1) Outline

To understand the molecular mechanisms underlying carcinogenesis and malignant progression for clinical application of cancer prevention, diagnosis and treatment.

(2) Research

1. Molecular analysis of refractory malignancies including liver, pancreatic and scirrhus gastric cancers
2. Development of molecularly targeted therapy for refractory malignancies
3. Cancer epigenetics/epigenomics and clinical application in refractory malignancies
4. Research of cancer stem cells and targeted therapy
5. Development of regenerative medicine using stem cell research

(3) Education

Hygiene is our charge. The undergraduate curriculum of hygiene includes lectures, and laboratory studies. Topics of lectures consist of environmental pollution and human health, world-wide environmental problems, carcinogen and occupational cancer, smoking-related diseases, infectious diseases including AIDS and hepatitis, food poisoning, anoxia and heat-related diseases.

(4) Lectures & Courses

The graduate students pursue their own projects associated with one of researches being in progress in the division. Every student can learn the basic scientific techniques, such as genetic engineering, cell culture and biochemical procedures. There are also many special lectures on cancer, gene, cell biology and biochemistry for the graduate students. On weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

(5) Publications

[Original Articles]

1. Oze I, Shimada S, Nagasaki H, Akiyama Y, Watanabe M, Yatabe Y, Matsuo K, Yuasa Y.. Plasma miR-103, miR-107, and miR-194 levels are not correlated with human diffuse gastric cancer. *Journal of Cancer*

Research and Clinical Oncology. 2017.03; (143); 551-554

2. Oba A, Shimada S, Akiyama Y, Nishikawaji T, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Asahara H, Kaida A, Miura M, Tanabe M, Tanaka S . ARID2 modulates DNA damage response in human hepatocellular carcinoma cells. *Journal of Hepatology*. 2017.05; 66(5); 942-951
3. Keiichi Akahoshi, Takanori Ochiai, Ayumi Takaoka, Takuya Kitamura, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Emergency Cholecystectomy for Patients on Antiplatelet Therapy. *Am Surg*. 2017.05; 83(5); 486-490
4. Atsushi Oba, Atsushi Kudo, Keiichi Akahoshi, Mitsuhiro Kishino, Takumi Akashi, Eriko Katsuta, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Yoshinobu Eishi, Ukihide Tateishi, Minoru Tanabe. A simple morphological classification to estimate the malignant potential of pancreatic neuroendocrine tumors. *J. Gastroenterol.*. 2017.05; 52(10); 1140-1146
5. Ohata Y, Shimada S, Akiyama Y, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Tanabe M, Tanaka S . Acquired resistance with epigenetic alterations under long-term anti-angiogenic therapy for hepatocellular carcinoma. *Molecular Cancer Therapeutics*. 2017.06; 16(6); 1155-1165
6. Ueda H, Ban D, Akahoshi K, Mitsunori Y, Matsumura S, Ochiai T, Kudo A, Tanaka S, Tanabe M. Refractory long-term cholangitis after pancreaticoduodenectomy: a retrospective study *World Journal of Surgery*. 2017.07; 41(7); 1882-1889
7. Ishikawa Y, Ban D, Matsumura S, Mitsunori Y, Ochiai T, Kudo A, Tanaka S, Tanabe M. Surgical pitfalls of jejunal vein anatomy in pancreaticoduodenectomy *J Hepatobiliary Pancreat Sci*. 2017.07; 4(7); 394-400

[Books etc]

1. Fukamachi H. *Encyclopedia of Cancer*, 4th ed. Springer, 2017.04 (ISBN : 978-3-662-46874-6)

[Misc]

1. Gao D, Herman JG, Cui H, Jen J, Fuks F, Brock MV, Ushijima T, Croce C, Akiyama Y, Guo M.. Meeting Report of the Fifth International Cancer Epigenetics Conference in Beijing, China, October 2016. *Epigenomics*. 2017.07; 9(7); 937-941

[Conference Activities & Talks]

1. Ochiai T, Asano D, Yoshino J, Watanabe S, Ishikawa Y, Chiyonobu N, Mizuno Y, Sato T, Ueda H, Iwao Y, Ono H, Mitsunori Y, Matsumura S, Ban D, Kudo A, Tanaka S, Tanabe M. Surgical Strategy of Hepatic Resection with Inferior Vena Cava Resection for Liver Cancers. 12th Annual Academic Surgical Congress 2017.02.07 Las Vegas, USA
2. Tanaka S, Shimada S, Akiyama Y, Muramatu S, Mitsunori Y, Aihara A, Ochiai T, Ban D, Kudo A, Arii S, Tanabe M.. Significance of molecular subtypes and therapeutic resistance mechanisms in hepato-biliary-pancreatic malignancies for precision cancer medicine . The 117th Annual Congress of Japan Surgical Society 2017.04.27 Yokohama
3. Hiroaki Ono, Keiichi Akahoshi, Yasuhito Iwao, Satoshi Matsumura, Yusuke Mitsunori, Daisuke Ban, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical evaluation of lymph node metastasis after surgery of IPMN. 6th A-PHPBA 29th JSHBPS 2017.06.08 yokohama
4. Yusuke Mitsunori, Daisuke Ban, Hiroaki Ono, Keiichi Akahoshi, Yasuhito Iwao, Satoshi Matsumura, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Can we predict postoperative diabetes mellitus in patient with distal pancreatectomy?. 6th A-PHPBA & 29th JSHBPS 2017.06.08 yokohama
5. Atsushi Kudo, Daisuke Ban, Keiichi Akahoshi, Satoshi Matsumura, Yusuke Mitsunori, Yasuhito Iwao, Shinji Tanaka, Minoru Tanabe. How to manage liver metastases of pancreatic NET?. 6th A-PHPBA & 29th JSHBPS 2017.06.08 yokohama

6. Atsushi Kudo, Daisuke Ban, Keiichi Akahoshi, Yusuke Mitsunori, Shinji Tanaka, Minoru Tanabe. Systemic therapy may decide surgical indication for patients with Unresectable of Metastatic Pancreatic Neuroendocrine Tumor. 6th A-PHPBA & 29th JSHBPS 2017.06.08 yokohama
7. Shuichi Watanabe, Daisuke Ban, Yasuhito Iwao, Keiichi Akahoshi, Akihiro Ono, Yusuke Mitsunori, Satoshi Matsumura, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Study of the prognosis of recurrent pancreatic cancer: The significance of the solitary recurrence. 2017.06.08
8. Hiroki Ueda, Daisuke Ban, Atsushi Kudo, Takanori Ochiai, Shinji Tanaka, Minoru Tanabe . Refractory long-term cholangitis after pancreaticoduodenectomy: a retrospective study . 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
9. Ken-ichi Okada, Daisuke Ban, Keiichi Akahoshi, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Satoshi Matsumura, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The optimal pancreatic stump closure method of a laparoscopic distalpancreatectomy: wrapping and fibrin capping technique. 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
10. Takehiro Okabayashi, Daisuke Asano, Keiichi Akahoshi, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The optimal management depending on the features of CT imaging of borderline resectable pancreatic cancer. 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
11. Takehisa Yazawa, Hiroaki Ono¹, Yasuhito Iwao, Satoshi Matsumura, Yusuke Mitsunori, Daisuke Ban, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical significance of enhancing nodules in preoperative imaging studies of IPMN. 6th A-PHPBA & 29th JSHBPS 2017.06.10 yokohama
12. Fukamachi, H., Nishikawaji, T., Shimada, S., Akiyama, Y., Yuasa, Y., Tsuchiya, Kim, W. H., K., Tanaka, S.. Identification of a signal transduction pathway working in the genesis and progression of diffuse type gastric cancers. . Post-A3 Meeting 2017 Epigenetic Signature of Carcinogenesis 2017.07.03 Naha, Okinawa
13. Tanaka S, Oba A, Ogawa Y, Ono H, Mitunori Y, Ban D, Kudo A, Arie S, Tanabe M. . Personalized medicine to target the cancer stemness of hepato-biliary-pancreatic malignancies (Symposium).. The 72rd General Meeting of the Japanese Society of Gastroenterological Surgery 2017.07.22 Kanazawa
14. Shu Shimada, Yoshiteru Ohata, Yoshimitsu Akiyama, Shinji Tanaka. Acquired resistance with epigenetic alterations under long-term anti-angiogenic therapy for hepatocellular carcinoma. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.28 Yokohama
15. Fukamachi, H., Nishikawaji, T., Shimada, S., Akiyama, Y., Yuasa, Y., Tsuchiya, K., Tanaka, S. . Identification of signal transduction pathway in PDX-derived diffuse-type gastric tumor-initiating cells.. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.30 Yokohama
16. Akiyama Y, Nishikawaji T, Shimada S, Yuasa Y, Tanaka S.. Molecular mechanisms of SETDB2 histone methyltransferase overexpression in gastric cancer.. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.30 Yokohama

[Patents]

1. Dominant negative mutants of IRS-1 and uses there of (Tanaka S, Wands JR), Patent Number : United States Patent 6,528,479
2. Compositions and methods for detection and treatment of hepatocellular carcinoma (Tanaka S, MacDonald G), Application Number : US 61/811,360

Surgical Pathology

Professor : Masanobu KITAGAWA
Associate Professor : Takumi AKASHI
Assistant Professor : Emiko SUGAWARA, Susumu KIRIMURA,
Shohei TOMII, Atsuko KONTA
Hospital Staff Doctor : Keiko MIURA
Secretary : Ayako UENO

(1) Outline

Missions of diagnostic pathology are summarized to following 4 items. 1) participation to the medical treatment of the patients through anatomical diagnosis 2) assessment of medical treatment through autopsy examination 3) training of diagnostic pathologists 4) development of diagnostic methods by anatomical, immunohistochemical, microbiological and molecular technologies.

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides 1. diagnostic pathology services for the clinicians of the affiliated hospital 2. education of medical students and post-graduate students through both lectures and medical practice 3. development of new methods in diagnostic pathology.

(2) Research

1) Analysis of the pathophysiology of the disease, especially invasion mechanism of lung and gastrointestinal cancers by molecular biological technology.

2) Identification of epithelial neoplasms with chromosome translocation

3) Carcinogenesis of prostatic cancer in view of microbiology

(3) Education

Main object of surgical pathology in the course of graduate school is to provide medical students opportunity to study pathophysiology and diagnosis of core diseases, both neoplastic and non-neoplastic, through biopsy, surgical and autopsy cases. Another important mission is a training of pathology specialist in the post-graduate school through diagnostic services of surgical pathology, cytopathology and autopsy.

(4) Lectures & Courses

The initial purpose of this program is to acquire how to morphologically diagnose both neoplastic and non-neoplastic diseases. In addition, it is also very important to recognize the limitations and problems of morphological diagnosis and to learn the morphological and molecular methods which are necessary for the resolution of the problems. The ultimate purpose is to develop a new diagnostic method which can resolve the problems of morphological diagnosis.

(5) Clinical Services & Other Works

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides autopsy services (38 case in a year), cytopathology services (9,957 cases in a year) and surgical pathology (11,574 cases in a year) for the clinicians of the affiliated hospital. Diagnosis is mostly done by the organ-subspecialized staffs. Clinico-pathological conferences have been held about two hundred times in 2014.

(6) Clinical Performances

Department of diagnostic pathology participates in the medical treatment of the patients through anatomical diagnosis. In the era of molecule-targeted therapy, specialized information has been requested in the field of pathological diagnosis. In order to appropriately respond to a latest request of clinicians, we practice pathological diagnosis in cooperation with departments of human pathology and comprehensive pathology with latest techniques, such as immunohistochemistry, electron microscopy, and FISH.

(7) Publications**[Original Articles]**

1. Yamanishi, E., Hasegawa, K., Fujita, K., Ichinose, S., Yagishita, S., Murata, M., Tagawa, K., Akashi, T., Eishi, Y., Okazawa, H.. A novel form of necrosis, TRIAD, occurs in human Huntington's disease. *Acta Neuropathologica Communications*.. 2017.03; 5(19);
2. Yumi Sakakibara, Yoshimi Suzuki, Toshihide Fujie, Takumi Akashi, Tadatsune Iida, Yasunari Miyazaki, Yoshinobu Eishi, Naohiko Inase. Radiopathological Features and Identification of Mycobacterial Infections in Granulomatous Nodules Resected from the Lung. *Respiration*. 2017.03; 93(4); 264-270
3. Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Shuji Hibiya, Nobukatsu Horita, Mariko Negi, Eisaku Itoh, Takumi Akashi, Yoshinobu Eishi, Satoshi Motoya, Yoshiaki Takeuchi, Reiko Kunisaki, Ken Fukunaga, Shiro Nakamura, Naoki Yoshimura, Masakazu Takazoe, Bunei Iizuka, Yasuo Suzuki, Masakazu Nagahori, Mamoru Watanabe. Caudal type homeobox 2 expression induced by leukocytapheresis might be associated with mucosal healing in ulcerative colitis. *J. Gastroenterol. Hepatol.*. 2017.05; 32(5); 1032-1039
4. Atsushi Oba, Atsushi Kudo, Keiichi Akahoshi, Mitsuhiro Kishino, Takumi Akashi, Eriko Katsuta, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Yoshinobu Eishi, Ukihide Tateishi, Minoru Tanabe. A simple morphological classification to estimate the malignant potential of pancreatic neuroendocrine tumors. *J. Gastroenterol.*. 2017.05;
5. Shohei Tomii, Takumi Akashi, Noboru Ando, Tomoki Tamura, Akira Sakurai, Asami Terada, Asuka Furukawa, Yoshimi Suzuki, Kou Kayamori, Kei Sakamoto, Hironori Ishibashi, Yoshinobu Eishi. Cortical Actin Alteration at the Matrix-Side Cytoplasm in Lung Adenocarcinoma Cells and Its Significance in Invasion. *Pathobiology*. 2017.07; 84(4); 171-183
6. Ochi Junichi, Ohtani Yoshio, Takemura Tamiko, Akashi Takumi, Tateishi Tomoya, Miyazaki Yasunari, Inase Naohiko, Yoshizawa Yasuyuki. Histological variability and consequences in chronic bird-related hypersensitivity pneumonitis. *Respirology*. 2017.10; 22(7); 1350-1356

Experimental Animal Model for Human Disease

Professor	Masami Kanai-Azuma
Junior Associate Professor	Yoshikazu Hirate
Assistant Professor	Shu Endo
Assistant Professor	Hitomi Suzuki
Assistant Professor	Hinako M Takase

(1) Research

- 1)Molecular biological analysis of organ formation using knockout mice and knockout ES cells.
- 2)Application of Sox17 mutant mice as the animal model for human disease.
- 3)Analysis of molecular mechanisms using mice with implantation defects.
- 4)Analysis of folliculogenesis using disease-model mouse for premature ovarian insufficiency.
- 5)Study of the molecular events involved in the regulation of spermatogonial stem cells.

(2) Publications

[Original Articles]

1. Hiroki Higashiyama, Aisa Ozawa, Hiroyuki Sumitomo, Mami Uemura, Ko Fujino, Hitomi Igarashi, Kenya Imaimatsu, Naoki Tsunekawa, Yoshikazu Hirate, Masamichi Kurohmaru, Yukio Saijoh, Masami Kanai-Azuma, Yoshiakira Kanai. Embryonic cholecystitis and defective gallbladder contraction in the Sox17-haploinsufficient mouse model of biliary atresia. *Development*. 2017.05; 144(10); 1906-1917
2. Ryuichi Ohgaki, Takahiro Ohmori, Saori Hara, Saya Nakagomi, Masami Kanai-Azuma, Kazuko Kaneda-Nakashima, Suguru Okuda, Shushi Nagamori, Yoshikatsu Kanai. Essential Roles of L-Type Amino Acid Transporter 1 in Syncytiotrophoblast Development by Presenting Fusogenic 4F2hc. *Mol. Cell. Biol.* 2017.06; 37(11);
3. Kento Miura, Chiharu Murata, Kyoko Harikae, Hitomi Suzuki, Masami Kanai-Azuma, Masamichi Kurohmaru, Naoki Tsunekawa, Yoshiakira Kanai. Defects in the first wave of folliculogenesis in mouse XO ovaries. *J. Reprod. Dev.* 2017.06; 63(3); 333-338
4. Kasane Kishi, Aya Uchida, Hinako M Takase, Hitomi Suzuki, Masamichi Kurohmaru, Naoki Tsunekawa, Masami Kanai-Azuma, Stephen A Wood, Yoshiakira Kanai. Spermatogonial deubiquitinase USP9X is essential for proper spermatogenesis in mice. *Reproduction*. 2017.08; 154(2); 135-143

[Conference Activities & Talks]

1. Hirate Yoshikazu, Hayakawa Kana, Toyomura Yuga, Igarashi Hitomi, Miura Kento, Kanai Yoshiakira, Kanai-Azuma Masami. Sox17heterozygous mutant females are defective in implantation. Annual Meeting of the Japanese Society of Developmental Biologists 50th 2017.05.10 Tower Hall Funabori

2. Pattarapanawan M, Uemura M, Higashiyama H, Hiramatsu R, Tsunekawa N, Kurohmaru M, Kanai-Azuma M, Kanai Y.. Morphological change in hepatobiliary and related structures in postnatal and adult Sox17+/- mice. 6th congress-asian-veterinary-anatomists 2017.10.15 Malaysia

Signal Gene Regulation

Professor NAKAMURA Masataka
Associate Professor FUNATO Noriko
Assistant Professor MIZUGUCHI Mariko

(1) Research

- 1) Molecular mechanism of tumorigenesis by human T-cell leukemia virus type I (HTLV-I).
- 2) Roles of transcription factors in cell differentiation.
- 3) Implication of prostaglandin D2 receptor (CRTH2) in allergy reactions.

(2) Lectures & Courses

The aim of Human Gene Sciences Center is to provide laboratory equipment, room and information for researches in advanced molecular and cellular biology. In educational objectives in the graduate school, our Center gives lecture, seminar, training course and individual assistance in research fields of molecular genetics, immunology and virology.

(3) Publications

[Original Articles]

1. *Noriko Funato, Masataka Nakamura. Identification of shared and unique gene families associated with oral clefts. *Int J Oral Sci.* 2017.06; 9(2); 104-109

[Conference Activities & Talks]

1. Mariko Mizuguchi, Toshifumi Hara, Manami Yoshita-Takahashi, Yuetsu Tanaka, Takuya Fukushima, Masataka Nakamura. Expression of the Human Telomerase Reverse Transcriptase (hTERT) in Human T-cell Leukemia Virus Type 1 (HTLV-1)-Infected T-cells. The 18th International Conference on Human Retrovirology: HTLV and Related Viruses 2017.03.08 Tokyo
2. Taga Y, Kusubata M, Ogawa-Goto K, Hattori S, Funato N. Gelatin Hydrolysates Prepared Using Ginger Protease Promote Osteoblast Differentiation. The 65th Annual Meeting of Japanese Association for Dental Research 2017.11.18 Showa University, Tokyo
3. Funato N, Srivastava D, Yanagisawa H. Tbx1 knockout mice exhibit dysregulated expression of genes associated with cleft palate in humans. ASCB/EMBO 2017 Meeting 2017.12.05 Philadelphia, USA
4. Taga Y, Laurie LE, Kokubo H, Saga Y, Kusubata M, Ogawa-Goto K, Hattori S, Funato N. Role of HAND1 in collagen expression and post-translational modifications in the long bone. ASCB/EMBO 2017 Meeting 2017.12.05 Philadelphia, USA

Material Biofunctions

Keiji Itaka (Professor)
Akiko Nagai (Associate Professor)
Kosuke Nozaki (Assistant Professor)

(1) Outline

The mission of this lab is to develop innovative medical technologies based on the science of biomaterials, DDS, and molecular biology. We aim at regulating biofunctions of host cells and the biomaterials, obtaining proof-of-concept of the therapeutic strategies by animal studies, and pursuing their clinical applications in collaboration with hospitals and companies.

1. mRNA-based therapeutics: a new paradigm of gene therapy

Gene therapy is defined as introducing genetic information for therapeutic purposes. Besides the conventional strategy of protein replacement for congenital gene defects, gene therapy may have wide application, including vaccination against cancer and infectious diseases, regenerative medicine by in situ cell regulation by introducing “therapeutic” gene(s), and the ultimate goal of “gene” therapy by the technology of gene editing. In addition, cell therapy combined with ex vivo gene introduction is also a promising field. Messenger RNA (mRNA) is a new tool for introducing the genetic information. Direct delivery of mRNA into cells is highlighted as a safe and effective method without concerning the risk of random integration into the genome. Despite the fact that mRNA delivered in the body would be susceptible to highly active RNases that are ubiquitous in the extracellular space, we have established a drug delivery system (DDS) based on synthesized polymers, polyplex nanomicelle, to transport mRNA into target cells by preventing its degradation. We have already achieved in vivo mRNA administration for therapeutic purposes of various organs and tissues including brain, spinal cord, bone, articular cartilage, skeletal muscle, and liver. The mRNA-based therapy is indicated for treatment of various diseases including the fields of gene therapy, cell therapy, and regenerative medicine.

2. Generally-modified spheroid cell culture system for cell transplantation

Cell transplantation therapy is an attractive strategy for various medical fields. One serious problem is that the therapeutic effects may be limited by the death of transplanted cells or the decrease in cell activity due to unfavorable microenvironments such as ischemia, hypoxia, or inflammation. We established an injectable spheroid system for cell transplantation therapy, based on three-dimensional (3D) spheroid cell culture system for preserving cell-to-cell interaction using micropatterned plates coated with a thermosensitive polymer. In addition, the genetic modification of the cells using a biocompatible non-viral gene carrier, polyplex nanomicelle, was integrated for augmenting the therapeutic effects of cell transplantation. This system can be used for many applications of cell transplantation therapy.

3. Development of functional dental implants

Although dental implant treatment has already been clinically applied and excellent clinical progress has been reported, some cases demonstrate the unexpected disorder. Because natural teeth integrate the bone via periodontal ligament to exert their functions, the osseointegration, which is a healing form of current dental implant, is thought to be one of the causes. In this department, we are working on the development of periodontal ligament-bonded dental implant material, and we are trying to elucidate the mechanism of periodontal tissue homeostasis.

4. Interaction between biomaterials and the host tissues

To develop a new biomaterial for clinical applications, the material is requested to enhance biocompatibility and to decrease possible side effects in addition to its functionality. Biomaterials meet and interact with the living tissues at their interfaces. We evaluate phenomena of material-tissue interfaces and try to clarify the mechanism through material science and biological methods. These findings based on surface science contribute to develop new biomaterial designs.

(2) Education

The objective and principle of this graduate course is to educate students with materials knowledge demanded to medical and dental doctors who are leading medical professionals and bioscientists who are capable of carrying out their own research at an international level in the area of their special fields of science, respectively.

(3) Publications

[Original Articles]

1. Shen D, Horiuchi N, Miyashin M, Yamashita K, Nagai A. Synthesis and enhanced bone regeneration of carbonate substituted octacalcium phosphate Bio-med. Mater. Eng.. 2017;
2. Liza S, Hieda J, Akasaka H, Ohtake, N, Tsutsumi Y, Nagai A, Hanawa T. Deposition of boron doped DLC films on TiNb and characterization of their mechanical properties and blood compatibility Science and Technology of Advanced Materials. 2017; 18; 76-87
3. Norio Wada, Naohiro Horiuchi, Makoto Nishio, Miho Nakamura, Kosuke Nozaki, Akiko Nagai, Kazuaki Hashimoto, Kimihiro Yamashita. Crystallization of calcium phosphate in agar hydrogels in presence of polyacrylic acid under double diffusion conditions Crystal Growth & Design. 2017.01; 17(2); 604-611
4. Kazuki Igeta, Yuta Kuwamura, Naohiro Horiuchi, Kosuke Nozaki, Daichi Shiraishi, Mamoru Aizawa, Kazuaki Hashimoto, Kimihiro Yamashita, Akiko Nagai. Morphological and functional changes in RAW264 macrophage-like cells in response to a hydrated layer of carbonate-substituted hydroxyapatite. J Biomed Mater Res A. 2017.01;
5. Kazuhiro Kohata, Soichiro Itoh, Naohiro Horiuchi, Taro Yoshioka, Kimihiro Yamashita. Influences of osteoarthritis and osteoporosis on the electrical properties of human bones as in vivo electrets produced due to Wolff's law Bio-Medical Materials and Engineering. 2017.01; 28(1); 65-74
6. Kyoshi Matsukawa, Reina Nemoto, Kosuke Nozaki, Mariko Kubo, Tasuku Inagaki, Keiichi Yoshida, Hiroyuki Miura. The influence of the framework thickness on surface strain of the 3-unit Zirconia resin-bonded fixed dental prostheses under the functional loading Asian Pacific Journal of Dentistry. 2017.01; 17(1); 1-7
7. Naohiro Horiuchi, Yuki Iwasaki, Kosuke Nozaki, Miho Nakamura, Kazuaki Hashimoto, Akiko Nagai, Kimihiro Yamashita. A Critical Phenomenon of Phase Transition in Hydroxyapatite Investigated by Thermally Stimulated Depolarization Currents Journal of the American Ceramic Society. 2017.02; 100(2); 501-505
8. Federico Perche, Satoshi Uchida, Hiroki Akiba, Chin-Yu Lin, Masaru Ikegami, Anjaneyulu Dirisala, Toshihiro Nakashima, Keiji Itaka, Kohei Tsumoto, Kazunori Kataoka. Improved Brain Expression of Anti-Amyloid β scFv by Complexation of mRNA Including a Secretion Sequence with PEG-based Block Cationomer. Curr Alzheimer Res. 2017.03; 14(3); 295-302
9. N. Iwata, K. Nozaki, N. Horiuchi, K. Yamashita, Y. Tsutsumi, H. Miura, A. Nagai . Effects of Controlled Micro/Nano Surfaces on Osteoblast Proliferation Journal of Biomedical Matererials Research A. 2017.07; 105(9); 2589-2596
10. Risa Yamada, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Reina Nemoto, Hiroyuki Miura, Akiko Nagai. Ag nanoparticle-coated zirconia for antibacterial prosthesis. Mater Sci Eng C Mater Biol Appl. 2017.09; 78; 1054-1060

11. Satoshi Uchida, Naoto Yoshinaga, Kayoko Yanagihara, Eiji Yuba, Kazunori Kataoka, Keiji Itaka. Designing immunostimulatory double stranded messenger RNA with maintained translational activity through hybridization with poly A sequences for effective vaccination. *Biomaterials*. 2017.09;
12. Y Anraku, H Kuwahara, Y Fukusato, A Mizoguchi, T Ishii, K Nitta, Y Matsumoto, K Toh, K Miyata, S Uchida, K Nishina, K Osada, K Itaka, N Nishiyama, H Mizusawa, T Yamasoba, T Yokota, K Kataoka. Glycaemic control boosts glycosylated nanocarrier crossing the BBB into the brain. *Nat Commun*. 2017.10; 8(1); 1001
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[Books etc]

1. Akiko Nagai, Naohiro Horiuchi, Miho Nakamura, Norio Wada, Kimihiro Yamashita. *Handbook of Solid State Chemistry Volume 6: Functional Materials*. 2017.07 (ISBN : 978-3-527-32587-0)

[Conference Activities & Talks]

1. Inokoshi M, Shimizu H, Nozaki K, Takagaki T, Zhang, F, Vleugels J, Van Meerbeek B, Uo M, Minakuchi S. Crystallographic analysis of alumina sandblasted highly translucent dental zirconia. 95th General Session and Exhibition of the IADR 2017.03 San Francisco
2. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Interfacial polarization caused by proton conduction in hydroxyapatite and its application for electret formation. 20th International Conference on Solid State Ionics (SSI-21) 2017.06.20 Padova, Italy
3. Kosuke Nozaki, Takayuki Endo, Naohiro Horiuchi, Kimihiro Yamashita, Kazuaki Hashimoto, Keiji Itaka, Akiko Nagai. Electrical and structural evaluation of sodium ion doped beta-tricalcium phosphate. The Tenth International Conference on the Science and Technology for Advanced Ceramics (STAC-10) 2017.08.02
4. Inokoshi M, Nozaki K, Takagaki T, Van Meerbeek B, Minakuchi S. Initial curing characteristics of composite cements under ceramic restorations. CED-IADR/NOF Oral Health Research Congress 2017 2017.09.22 Vienna
5. K. Nozaki, K. Fujita, N. Horiuchi, K. Yamashita, H. Miura, A. Nagai, K. Itaka. Regulation of periodontal ligament-derived cell morphology by type III collagen-coated hydroxyapatite. 2nd International Symposium on Creation of Life Innovation Materials 2017.09.30

Genetic Regulation

Professor Akinori KIMURA
Associate Professor Takeharu HAYASHI
Assistant Professor Jianbo AN
Research Associate Taeko K. NARUSE

(1) Outline

Research and Education in the Department of Genetic Regulation are carried out by staff members of the Department of Molecular Pathogenesis, Medical Research Institute.

The main purpose of this Department is to decipher the genetic regulation involved in the pathogenesis of intractable diseases, including hereditary cardiovascular diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy and hereditary arrhythmia, autoimmune diseases such as rheumatoid arthritis, type I diabetes mellitus, autoimmune thyroid diseases (Graves disease and Hashimoto thyroiditis), inflammatory bowel diseases (Crohn disease and ulcerative colitis) and SLE, as well as infectious diseases including HIV/AIDS. We also investigate molecular pathogenesis of coronary heart disease (atherosclerosis) and intractable vascular diseases (Takayasu arteritis and Buerger disease).

(2) Research

- 1) Identification and functional analysis of disease-related genes for cardiovascular diseases including hereditary cardiomyopathy and arrhythmia
- 2) Identification and functional analysis of disease-related genes for autoimmune diseases including autoimmune thyroiditis and inflammatory bowel disease
- 3) Identification and functional analysis of disease-related genes for infectious diseases including HIV-1 infection
- 4) Structural, functional and evolutionary analyses of MHC and immune-related genes
- 5) Evolutionary medicine for human diseases

(3) Education

Structural and functional diversity of human genome, are involved in the etiology and pathogenesis of human diseases. Main objective of Genetic Regulation is to identify the gene mutations or polymorphisms and to decipher the molecular mechanisms involved in the etiology and pathogenesis of intractable diseases, in order to develop new strategies for diagnosis, treatment and/or prevention of the diseases. Current research is focused on the intractable cardiovascular diseases (e.g. idiopathic cardiomyopathy, idiopathic arrhythmia, and coronary heart disease), autoimmune diseases (e.g. Burger disease, Graves disease, and rheumatoid arthritis) and infectious diseases (e.g. HIV/AIDS). In addition, genome diversity in immune-related genes is investigated from the view-point of primate evolution.

(4) Lectures & Courses

Main purpose is to understand the molecular pathogenesis of various intractable diseases by methodologies in the fields of Human Genetics, Genome Medicine, Biochemistry and Cell Biology.

(5) Publications**[Original Articles]**

1. Eri Kikkawa, Masafumi Tanaka, Taeko K Naruse, Tomi T Tsuda, Michio Tsuda, Koichi Murata, Akinori Kimura. Diversity of MHC class I alleles in *Spheniscus humboldti*. *Immunogenetics*. 2017.02; 69(2); 113-124
2. John M Gregson, Daniel F Freitag, Praveen Surendran, Nathan O Stitzel, Rajiv Chowdhury, Stephen Burgess, Stephen Kaptoge, Pei Gao, James R Staley, Peter Willeit, Sune F Nielsen, Muriel Caslake, Stella Trompet, Linda M Polfus, Kari Kuulasmaa, Jukka Kontto, Markus Perola, Stefan Blankenberg, Giovanni Veronesi, Francesco Gianfagna, Satu Männistö, Akinori Kimura, Honghuang Lin, Dermot F Reilly, Mathias Gorski, Vladan Mijatovic, , Patricia B Munroe, Georg B Ehret, , Alex Thompson, Maria Uria-Nickelsen, Anders Malarstig, Abbas Dehghan, , Thomas F Vogt, Taishi Sasaoka, Fumihiko Takeuchi, Norihiro Kato, Yoshiji Yamada, Frank Kee, Martina Müller-Nurasyid, Jean Ferrières, Dominique Arveiler, Philippe Amouyel, Veikko Salomaa, Eric Boerwinkle, Simon G Thompson, Ian Ford, J Wouter Jukema, Naveed Sattar, Chris J Packard, Abdulla Al Shafi Majumder, Dewan S Alam, Panos Deloukas, Heribert Schunkert, Nilesh J Samani, Sekar Kathiresan, , Børge G Nordestgaard, Danish Saleheen, Joanna Mm Howson, Emanuele Di Angelantonio, Adam S Butterworth, John Danesh, . Genetic invalidation of Lp-PLA2 as a therapeutic target: Large-scale study of five functional Lp-PLA2-lowering alleles. *Eur J Prev Cardiol*. 2017.03; 24(5); 492-504
3. Teruki Sato, Chitose Sato, Ayumi Kadowaki, Hiroyuki Watanabe, Lena Ho, Junji Ishida, Tomokazu Yamaguchi, Akinori Kimura, Akiyoshi Fukamizu, Josef M Penninger, Bruno Reversade, Hiroshi Ito, Yumiko Imai, Keiji Kuba. ELABELA-APJ axis protects from pressure overload heart failure and angiotensin II-induced cardiac damage. *Cardiovasc. Res.*. 2017.06; 113(7); 760-769
4. Zhiyong Chen, Yan Wang, Masataka Kuwana, Xue Xu, Wei Hu, Xuebing Feng, Hong Wang, Akinori Kimura, Lingyun Sun. HLA-DRB1 Alleles as Genetic Risk Factors for the Development of Anti-MDA5 Antibodies in Patients with Dermatomyositis. *J. Rheumatol.*. 2017.09; 44(9); 1389-1393
5. Sayuri Seki, Takushi Nomura, Masako Nishizawa, Hiroyuki Yamamoto, Hiroshi Ishii, Saori Matsuoka, Teiichiro Shiino, Hironori Sato, Kazuta Mizuta, Hiromi Sakawaki, Tomoyuki Miura, Taeko K Naruse, Akinori Kimura, Tetsuro Matano. In vivo virulence of MHC-adapted AIDS virus serially-passaged through MHC-mismatched hosts. *PLoS Pathog.*. 2017.09; 13(9); e1006638
6. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K Naruse, Mamoru Watanabe, Akinori Kimura. MKL1 expressed in macrophages contributes to the development of murine colitis. *Sci Rep*. 2017.10; 7(1); 13650

Applied Gene Medicine

Professor Yoshio MIKI
Associate Professor Akira NAKANISHI
Assistant professor Miho TAKAOKA
Project Assistant Professor Ken MIYAGUCHI
Graduate Student Konuskan Ucar AYSE,
Shun ITO,
Maiko UMEGAKI,
Gen SATO
Naoko Otsuka

(1) Outline

Since 1981, cancer has been a top leading cause of death in our country and a novel action is an urgent social challenge. In Department of Molecular Genetics, we aim to study a basic biology underlying cancer and establish novel diagnostic and therapeutic modalities based on findings from the fundamental researches. We have largely focused on three major research directions to understand the molecular mechanisms of breast cancer development: 1) Uncovering DNA damage repair function and genome stabilization mechanism, 2) Uncovering hormone-dependent cellular proliferation, and 3) Determining how the tumor microenvironment contributes to cancer development and progression. Utilizing a wide variety of approaches in genomics, molecular biology, biochemistry and informatics, we are addressing an integrative understanding of multidisciplinary analyses.

(2) Research

1. Molecular Mechanisms of Breast Cancer Progression
 - ◆ Understanding Molecular Mechanisms of Metastasis, Invasion, Recurrence in Cancer
 - ◆ Uncovering Molecular functions of hereditary breast cancer genes, BRCA1 and BRCA2
2. Cancer Genomics Research
 - ◆ Cancer Genomics Research with Next-Generation Sequencing
 - ◆ Identification of Genes Involved in Human Cancer Using Genome-Wide Association Studies
3. Cell Death Signaling in Cancer
4. DNA Damage Repair and Genome Instability in Cancer
5. Hormone-Dependent Breast Cancer Cell Growth
6. Cancer Microenvironment

(3) Education

Our research is directed at understanding the molecular mechanism of carcinogenesis, based on basic molecular cell biology and molecular genetics. We have applied new findings and information obtained by basic research to develop the new diagnosis, treatment, and prevention of cancer. Our objective in the graduate course is to provide students opportunity to study basic science and applied genome science for cancer research.

(4) Publications

[Original Articles]

1. Nguyen CT, Okamura T, Morita K, Yamaguchi S, Harada H, Miki Y, Izumo T, Kayamori K, Yamaguchi A, Sakamoto K. LAMC2 is a predictive marker for the malignant progression of leukoplakia *Journal of Oral Pathology and Medicine*. 2017.03; 46(3); 223-231
2. Takaoka M, Ito S, Miki Y, Nakanishi A.. FKBP51 regulates cell motility and invasion via RhoA signaling. *Cancer Science*. 2017.03; 108(3); 380-389
3. Hirata Makoto, Nagai Akiko, Kamatani Yoichiro, Ninomiya Toshiharu, Tamakoshi Akiko, Yamagata Zentaro, Kubo Michiaki, Muto Kaori, Kiyohara Yutaka, Mushiroda Taisei, Murakami Yoshinori, Yuji Koichiro, Furukawa Yoichi, Zembutsu Hitoshi, Tanaka Toshihiro, Ohnishi Yozo, Nakamura Yusuke, Matsuda Koichi, BioBank Japan Cooperative Hospital Group. Overview of BioBank Japan follow-up data in 32 diseases. *J Epidemiol*. 2017.03; 27(3S); S22-S28
4. Hirata Makoto, Kamatani Yoichiro, Nagai Akiko, Kiyohara Yutaka, Ninomiya Toshiharu, Tamakoshi Akiko, Yamagata Zentaro, Kubo Michiaki, Muto Kaori, Mushiroda Taisei, Murakami Yoshinori, Yuji Koichiro, Furukawa Yoichi, Zembutsu Hitoshi, Tanaka Toshihiro, Ohnishi Yozo, Nakamura Yusuke, Matsuda Koichi, BioBank Japan Cooperative Hospital Group. Cross-sectional analysis of BioBank Japan clinical data: A large cohort of 200,000 patients with 47 common diseases. *J Epidemiol*. 2017.03; 27(3S); S9-S21
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6. Koshi Nakamura, Emiko Okada, Shigekazu Ukawa, Makoto Hirata, Akiko Nagai, Zentaro Yamagata, Yutaka Kiyohara, Kaori Muto, Yoichiro Kamatani, Toshiharu Ninomiya, Koichi Matsuda, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Rai Shimoyama, Koichi Maekawa, Kiyoshi Kaneko, Hiromasa Harada, Shiro Minami, Hiroyuki Takei, Mitsue Saito, Yasuhisa Terao, Satoru Takeda, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Hajime Abe, Tomoharu Shimizu, Yukihiro Koretsune, Norikazu Masuda, Yasutaka Takeda), Akiko Tamakoshi. Characteristics and prognosis of Japanese female breast cancer patients: The BioBank Japan project. *J Epidemiol*. 2017.03; 27(3S); S58-S64
7. Shigekazu Ukawa, Koshi Nakamura, Emiko Okada, Makoto Hirata, Akiko Nagai, Zentaro Yamagata, Kaori Muto, Koichi Matsuda, Toshiharu Ninomiya, Yutaka Kiyohara, Yoichiro Kamatani, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Ichiro Miura, Katsuhiko Takatama, Yoshiyuki Nabeshima, Kazuo Misumi, Shiro Minami, Yukihiro Kondo, Go Kimura, Shigeo Horie, Shinichi Ohba, Shigaku Ikeda, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Keisei Okamoto, Susumu Kageyama, Yukihiro Koretsune, Yuko Nishigaki, Tsutomu Yoshida), Akiko Tamakoshi. Clinical and histopathological characteristics of patients with prostate cancer in the BioBank Japan project. *J Epidemiol*. 2017.03; 27(3S); S65-S70
8. Tamakoshi A, Nakamura K, Ukawa S, Okada E, Hirata M, Nagai A, Matsuda K, Kamatani Y, Muto K, Kiyohara Y, Yamagata Z, Ninomiya T, Kubo M, Nakamura Y, BioBank Japan Cooperative Hospital Group (Wataru Ono, Hiromasa Harada, Shunji Kawamoto, Nobuaki Shinozaki, Shiro Minami, Takeshi Yamada, Hideyuki Suzuki, Kazuhiro Sakamoto, Kazuo Kaneko, Shinichi Ohba, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Tomoharu Shimizu, Shigeyuki Naka, Yukihiro Koretsune, Mitsugu Sekimoto, Hiroyuki Kokuto). Characteristics and prognosis of Japanese colorectal cancer patients: The BioBank Japan Project. *J Epidemiol*. 2017.03; 27(3S); S36-S42
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10. Hiroshi Yokomichi, Akiko Nagai, Makoto Hirata, Yutaka Kiyohara, Kaori Muto, Toshiharu Ninomiya, Koichi Matsuda, Yoichiro Kamatani, Akiko Tamakoshi, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Hiromasa Harada, Sunao Matsubayashi, Rieko Komi, Kazuo Misumi, Shiro Minami, Hitoshi Sugihara, Eitaro Kodani, Akio Kanazawa, Hiromasa Gotoh, Hidenori Haruna, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Satoshi Ugi, Shinichi Araki, Yukihiro Koretsune, Hideki Taki, Takayuki Nakagawa), Zentaro Yamagata. Survival of macrovascular disease, chronic kidney disease, chronic respiratory disease, cancer and smoking in patients with type 2 diabetes: BioBank Japan cohort. *J Epidemiol.* 2017.03; 27(3S); S98-S106
 11. Koshi Nakamura, Shigekazu Ukawa, Emiko Okada, Makoto Hirata, Akiko Nagai, Zentaro Yamagata, Toshiharu Ninomiya, Kaori Muto, Yutaka Kiyohara, Koichi Matsuda, Yoichiro Kamatani, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Hiromasa Harada, Makoto Hibino, Atsushi Okuyama, Nobuyasu Kano, Shiro Minami, Akihiko Genma, Jitsuo Usuda, Kenji Suzuki, Mitsuaki Sekiya, Satoru Takeda, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Noriaki Tezuka, Yasutaka Nakano, Yukihiro Koretsune, Mitsumasa Ogawara, Kazunari Yamana), Akiko Tamakoshi. Characteristics and prognosis of Japanese male and female lung cancer patients: The BioBank Japan Project. *J Epidemiol.* 2017.03; 27(3S); S49-S57
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 13. Hiroshi Yokomichi, Akiko Nagai, Makoto Hirata, Akiko Tamakoshi, Yutaka Kiyohara, Yoichiro Kamatani, Kaori Muto, Toshiharu Ninomiya, Koichi Matsuda, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Kazuo Misumi, Nobuyoshi Higa, Sunao Matsubayashi, Kei Matsuura, Shiro Minami, Hitoshi Sugihara, Naoya Emoto, Hirotohi Ohmura, Akihiro Inui, Michihiro Ogasawara, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seiji Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Satoshi Ugi, Hiroshi Maegawa, Yukihiro Koretsune, Hideo Kusuoka, Masako Ueyama), Zentaro Yamagata. Statin use and all-cause and cancer mortality: BioBank Japan cohort. *J Epidemiol.* 2017.03; 27(3S); S84-S91
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 15. Hiroshi Yokomichi, Akiko Nagai, Makoto Hirata, Yutaka Kiyohara, Kaori Muto, Toshiharu Ninomiya, Koichi Matsuda, Yoichiro Kamatani, Akiko Tamakoshi, Michiaki Kubo, Yusuke Nakamura, BioBank

- Japan Cooperative Hospital Group (Sunao Matsubayashi, Hiromasa Harada, Kazuo Misumi, Rieko Komi, Shiro Minami, Hitoshi Sugihara, Naoya Emoto, Akio Kanazawa, Yusuke Suzuki, Yoshimune Hiratsuka, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seijiro Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Satoshi Ugi, Hiroshi Maegawa, Yukihiko Koretsune, Hideki Taki, Takeshi Osawa), Zentaro Yamagata. Serum glucose, cholesterol and blood pressure levels in Japanese type 1 and 2 diabetic patients: BioBank Japan. *J Epidemiol.* 2017.03; 27(3S); S92-S97
16. Jun Hata, Akiko Nagai, Makoto Hirata, Yoichiro Kamatani, Akiko Tamakoshi, Zentaro Yamagata, Kaori Muto, Koichi Matsuda, Michiaki Kubo, Yusuke Nakamura, BioBank Japan Cooperative Hospital Group (Shigeru Saito, Hideki Shimomura, Sinichi Higashiue, Kazuo Misumi, Shiro Minami, Masahiro Yasutake, Hitoshi Takano, Kazunori Shimada, Hakuoh Konishi, Nobukazu Miyamoto, Satoshi Asai, Mitsuhiko Moriyama, Yasuo Takahashi, Tomoaki Fujioka, Wataru Obara, Seijiro Mori, Hideki Ito, Satoshi Nagayama, Yoshio Miki, Akihide Masumoto, Akira Yamada, Yasuko Nishizawa, Ken Kodama, Yoshihisa Sugimoto, Takashi Ashihara, Yukihiko Koretsune, Sachiko Ikeda, Ryoza Yano), Yutaka Kiyohara, Toshiharu Ninomiya. Risk prediction models for mortality in patients with cardiovascular disease: The BioBank Japan project. *J Epidemiol.* 2017.03; 27(3S); S71-S76
 17. Miho Takaoka, Shun Ito, Yoshio Miki, Akira Nakanishi. FKBP51 regulates cell motility and invasion via RhoA signaling. *Cancer Sci.* 2017.03; 108(3); 380-389
 18. Kazuhisa Hosoya, Satoshi Matsusaka, Tomomi Kashiwada, Koichi Suzuki, Norio Ureshino, Akemi Sato, Yoshio Miki, Kazuki Kitera, Mitsuharu Hirai, Kiyohiko Hatake, Shinya Kimura, Naoko Sueoka-Aragane. Detection of KRAS Mutations in Plasma DNA Using a fully Automated Rapid Detection System in Colorectal Cancer Patients. *Pathol. Oncol. Res.* 2017.10; 23(4); 737-744
 19. Katsutoshi Sato, Mio Koyasu, Sachio Nomura, Yuri Sato, Mizuho Kita, Yuumi Ashihara, Yasue Adachi, Shinji Ohno, Takuji Iwase, Dai Kitagawa, Eri Nakashima, Reiko Yoshida, Yoshio Miki, Masami Arai. Mutation status of RAD51C, PALB2 and BRIP1 in 100 Japanese familial breast cancer cases without BRCA1 and BRCA2 mutations. *Cancer Sci.* 2017.11; 108(11); 2287-2294
 20. Sato Katsutoshi, Koyasu Mio, Nomura Sachio, Sato Yuri, Kita Mizuho, Ashihara Yuumi, Adachi Yasue, Ohno Shinji, Iwase Takuji, Kitagawa Dai, Nakashima Eri, Yoshida Reiko, Miki Yoshio, Arai Masami. Mutation status of RAD51C, PALB2 and BRIP1 in 100 Japanese familial breast cancer cases without BRCA1 and BRCA2 mutations *Cancer Science.* 2017.11; 108(11); 2287-2294

[Conference Activities & Talks]

1. Takaoka Miho, Ito Shun, Miki Yoshio, Nakanishi Akira. FKBP51 regulates cell motility and invasion via RhoA signaling. *Cancer Science* 2017.03.01
2. Ami Sato. BRCA2 and estrogen receptor are translocated to nucleus via KPNA7. 2017.12.06
3. Syota Yamada et al. Analysis of synthetic lethality with paclitaxel in BRCA2-deficient cells. *ConBio2017* 2017.12.08
4. Syota Yamada. Analysis of synthetic lethality with paclitaxel in BRCA2-deficient cells. *ConBio2017* 2017.12.08
5. Deng Yu et al. The effects of estrogen in MCF-10A mammary epithelial acini grown in three-dimensional basement membrane cultures.. *ConBio2017* 2017.12.08
6. Yo Tojo et al. The physiological roles of the interaction of BRCA2 with estrogen receptor. 2017.12.08
7. Deng Yu et al. The effects of estrogen in MCF-10A mammary epithelial acini grown in three-dimensional basement membrane cultures.. 2017.12.09
8. Yo Tojo et al. The physiological roles of the interaction of BRCA2 with estrogen receptor. *ConBio2017* 2017.12.09

Molecular Cytogenetics

Professor Johji Inazawa M.D., Ph.D.
Lecturer Jun Inoue Ph.D.
Assistant Professor Tomoki Muramatsu Ph.D.
Assistant Professor Yasuyuki Gen M.D., Ph.D.

(1) Research

1. Identification of genes responsible for intractable diseases including cancer and genomic disorders through integrative genomics and epigenomics.
2. Discovery of molecular mechanisms of cancer-related genes, including microRNAs, in the multistep processes of carcinogenesis and cancer progression, such as cancer stem cell, epithelial-mesenchymal transition (EMT), invasion and metastasis using systems biology.
3. Establishment of autophagy-based diagnosis and therapy in human cancers by understanding cellular context-dependent role of autophagy.
4. Multiple genomic analyses of genetic disorders of unknown etiology, e.g. mental retardation or epilepsy, to detect causative genes and clarify the etiology. Also, an array chip for diagnosis of known congenital disorders, 'Genome Disorder Array', was developed and released for a practical use at 2009.
5. Development of innovative techniques for genomics and epigenomics in medical science.
6. Development of practically useful tools for molecular diagnosis of intractable diseases.

(2) Lectures & Courses

The principal aim of the Department of Molecular Cytogenetics(MCG) is to understand the molecular mechanism underlying intractable diseases, such as cancer and uncharacterized genetic diseases. Main objective of MCG in the graduate course is to provide students opportunity to study molecular cytogenetic approach for intractable diseases, identify genes responsible for those diseases, and develop innovative techniques/ practically useful tools for detection of genomic and epigenomic aberrations in those diseases. It is our goal to bridge the gap between basic and clinical research for the benefit of each of the patients.

(3) Publications

[Original Articles]

1. Yu Oikawa, Kei-Ichi Morita, Kou Kayamori, Kousuke Tanimoto, Kei Sakamoto, Hiroto Katoh, Shumpei Ishikawa, Johji Inazawa, Hiroyuki Harada. Receptor tyrosine kinase amplification is predictive of distant metastasis in patients with oral squamous cell carcinoma. *Cancer Sci.* 2017.02; 108(2); 256-266
2. Masafumi Okuda, Jun Inoue, Naoto Fujiwara, Tatsuyuki Kawano, Johji Inazawa. Subcloning and characterization of highly metastatic cells derived from human esophageal squamous cell carcinoma KYSE150 cells by in vivo selection. *Oncotarget.* 2017.05; 8(21); 34670-34677
3. Hiroaki Nagata, Ken-Ichi Kozaki, Tomoki Muramatsu, Hidekazu Hiramoto, Kousuke Tanimoto, Naoto Fujiwara, Seiya Imoto, Daisuke Ichikawa, Eigo Otsuji, Satoru Miyano, Tatsuyuki Kawano, Johji Inazawa.

Genome-wide screening of DNA methylation associated with lymph node metastasis in esophageal squamous cell carcinoma. *Oncotarget*. 2017.06; 8(23); 37740-37750

4. Hidekazu Hiramoto, Tomoki Muramatsu, Daisuke Ichikawa, Kousuke Tanimoto, Satoru Yasukawa, Eigo Otsuji, Johji Inazawa. miR-509-5p and miR-1243 increase the sensitivity to gemcitabine by inhibiting epithelial-mesenchymal transition in pancreatic cancer. *Sci Rep*. 2017.06; 7(1); 4002
5. H Takahashi, J Inoue, K Sakaguchi, M Takagi, S Mizutani, J Inazawa. Autophagy is required for cell survival under L-asparaginase-induced metabolic stress in acute lymphoblastic leukemia cells. *Oncogene*. 2017.07; 36(30); 4267-4276
6. Shin Hayashi, Daniela Tiaki Uehara, Kousuke Tanimoto, Seiji Mizuno, Yasutsugu Chinen, Shinobu Fukumura, Jun-Ichi Takanashi, Hitoshi Osaka, Nobuhiko Okamoto, Johji Inazawa. Comprehensive investigation of CASK mutations and other genetic etiologies in 41 patients with intellectual disability and microcephaly with pontine and cerebellar hypoplasia (MICPCH). *PLoS ONE*. 2017.08; 12(8); e0181791
7. Burak Akdemir, Yasuaki Nakajima, Johji Inazawa, Jun Inoue. miR-432 Induces NRF2 Stabilization by Directly Targeting KEAP1. *Mol. Cancer Res.* 2017.11; 15(11); 1570-1578

[Conference Activities & Talks]

1. Akdemir B, Inoue J, Kawano T, Inazawa J. High expression of MiR-432-3p is associated with the chemoresistance by NRF2 stabilization via directly targeting KEAP1. 108th annual meeting of American Association for Cancer Research 2017 2017.04.03 Washington D.C., USA.
2. Furusawa A, Inoue J, Tsuda H, Miyasaka N, Inazawa J. Differential requirement of amino acids on cell survival of ovarian cancer cells. 108th annual meeting of American Association for Cancer Research 2017 2017.04.03 Washington D.C. , USA.
3. Inoue J, Takahashi H, Sakaguchi K, Takagi M, Mizutani S, Inazawa J. Autophagy is required for cell survival under L-asparaginase-induced metabolic stress in acute lymphoblastic leukemia cells. 108th annual meeting of American Association for Cancer Research 2017 2017.04.04 Washington D.C., USA.
4. Inazawa J. Exploring novel cancer-related microRNAs and their diagnostic and therapeutic potentials in precision cancer medicine (PCM). 8th International Conference on Nutrition and Physical Activity. 2017.12.10 ChiangMai, Thailand

Hematology

Professor Osamu Miura

Professor(Immunotherapy for Hematopoietic Disorders) Norihiko Kawamata

Junior Associate Professor Tetsuya Fukuda

Assistant Professor Masahide Yamamoto, Toshikage Nagao, Ken Watanabe

Project Assistant Professor Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory) Ayako Nogami

Senior Resident Tatsuya Saito, Hiroki Tsutsumi, Satoru Aoyama, Yoshihiro Umezawa

Graduate Student Hiroki Akiyama, Shinya Ishida, Keigo Okada, Koji Sasaki, Shuhei Fujita
Emi Uchida, Daisuke Watanabe, Sunichiro Yasuda

(1) Outline

The Department of Hematology is responsible for clinical services at our University Hospital with treatment of patients with various hematological disorders including leukemias, lymphomas, anemia, and hemorrhagic diseases by chemotherapies, immunotherapies, molecularly-targeted therapies, and hematopoietic cell transplantation. Our department is also responsible for teaching undergraduate students with the lecture course in hematology as well as the clinical clerkship and for training junior and senior residents. Our department is also actively involved, with doctoral course students, in basic and clinical researches aiming to elucidate the molecular and cellular mechanisms involved in pathogenesis of hematological malignancies as well as in acquisition of therapy resistance to develop novel efficient therapies against these diseases.

(2) Research

The research interests and activities of the Department of Hematology are diverse, and the following projects among others are currently under way. 1. Elucidation of the molecular mechanisms involved in acquisition of resistance against chemotherapies and molecularly-targeted therapies by leukemic cells from chronic myeloid leukemia, acute myeloid leukemia, and various myeloproliferative neoplasms expressing aberrant tyrosine kinases, including BCR/ABL, FLT3-ITD, and Jak2-V617F, aiming to develop novel therapeutic strategies to overcome the resistance. 2. Elucidation of the regulation mechanisms for immune responses to indolent lymphoid neoplasms, including chronic lymphocytic leukemia, for developing novel immunotherapies. 3. Signal transduction mechanisms from cytokine/growth factor receptors regulating proliferation, survival, and adhesion of hematopoietic cells including leukemia and lymphoma cells. The Department is also actively involved in a variety of clinical studies for treatment of various leukemias, lymphomas, and multiple myeloma.

(3) Education

The Department of hematology is responsible for teaching basic and clinical hematology to the 3rd and 4th grade students in the integrated hematology course and the hematology and oncology united block course. The Department is also responsible for teaching the 5th and 6th grade students in clinical clerkship to obtain basic knowledge and problem-solving abilities in hematology as well as general internal medicine. The Department is also actively involved in training about 24 junior residents every year to acquire clinical skills in hematology and internal medicine and about 4 senior residents to practice diagnosis and treatment of various hematological disorders and to obtain the certificate for hematology specialist. As a division in the Graduate School of Medical and Dental Sciences, the Department is actively involved in education of 6 to 8 graduate students, who participate in the research projects listed above, to obtain the Ph. D. degree in medicine.

(4) Lectures & Courses

The major objective of the course is to understand the pathophysiology of blood cells, blood cell-forming organs, and hemostasis to provide a basis for rational diagnosis and treatment of their disorders.

(5) Clinical Services & Other Works

The Department of Hematology provides diagnosis and treatment for hematological diseases, such as leukemia, malignant lymphoma, anemia, and thrombocythemia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, and hematopoietic cell transplantation.

(6) Clinical Performances

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

(7) Publications**[Original Articles]**

1. Erika Onozawa, Haruna Shibayama, Ken-Ichi Imadome, Akiho Tsuzura, Takatoshi Koyama, Osamu Miura, Ayako Arai. Inflammatory cytokine production in chronic active Epstein-Barr virus infection. *Rinsho Ketsueki*. 2017.03; 58(3); 189-196
2. Honami Takada, Ken-Ichi Imadome, Haruna Shibayama, Mayumi Yoshimori, Ludan Wang, Yasunori Saitoh, Shin Uota, Shoji Yamaoka, Takatoshi Koyama, Norio Shimizu, Kouhei Yamamoto, Shigeyoshi Fujiwara, Osamu Miura, Ayako Arai. EBV induces persistent NF- κ B activation and contributes to survival of EBV-positive neoplastic T- or NK-cells. *PLoS ONE*. 2017.03; 12(3); e0174136
3. Ayano Imai, Hiroshi Takase, Ken-Ichi Imadome, Go Matsuda, Iichiro Ohnishi, Kouhei Yamamoto, Takumi Kudo, Yoji Tanaka, Takatoshi Maehara, Osamu Miura, Ayako Arai. Development of Extranodal NK/T-cell Lymphoma Nasal Type in Cerebrum Following Epstein-Barr Virus-positive Uveitis. *Intern. Med.* 2017.05; 56(11); 1409-1414
4. Masahide Yamamoto, Ken Watanabe, Tetsuya Fukuda, Osamu Miura. Prediction of Prognosis for Patients with Diffuse Large B-Cell Lymphoma Refractory to or in First Relapse After Initial R-CHOP Therapy: A Single-Institution Study. *Anticancer Res.* 2017.05; 37(5); 2655-2662
5. Masayuki Shiseki, Chikashi Yoshida, Naoki Takezako, Akira Ohwada, Takashi Kumagai, Kaichi Nishiwaki, Akira Horikoshi, Tetsuya Fukuda, Hina Takano, Yasuji Kouzai, Junji Tanaka, Satoshi Morita, Junichi Sakamoto, Hisashi Sakamaki, Koiti Inokuchi. Dasatinib rapidly induces deep molecular response in chronic-phase chronic myeloid leukemia patients who achieved major molecular response with detectable levels of BCR-ABL1 transcripts by imatinib therapy. *Int. J. Clin. Oncol.* 2017.05; 22(5); 972-979
6. Naoto Tomita, Masahiro Yokoyama, Wataru Yamamoto, Reina Watanabe, Yutaka Shimazu, Yasufumi Masaki, Saburo Tsunoda, Chizuko Hashimoto, Kayoko Murayama, Takahiro Yano, Rumiko Okamoto, Ako Kikuchi, Kazuo Tamura, Kazuya Sato, Kazutaka Sunami, Hirohiko Shibayama, Rishu Takimoto, Rika

- Ohshima, Hiromichi Takahashi, Yuki Yoshi Moriuchi, Tomohiro Kinoshita, Masahide Yamamoto, Ayumi Numata, Hideaki Nakajima, Ikuo Miura, Kengo Takeuchi. The standard international prognostic index for predicting the risk of CNS involvement in DLBCL without specific prophylaxis. *Leuk. Lymphoma*. 2017.06; 1-8
7. Akira Toriihara, Reiko Nakajima, Ayako Arai, Masashi Nakadate, Koichiro Abe, Kazunori Kubota, Ukihide Tateishi. Pathogenesis and FDG-PET/CT findings of Epstein-Barr virus-related lymphoid neoplasms. *Ann Nucl Med*. 2017.07; 31(6); 425-436
 8. Keisuke Tanaka, Gaku Oshikawa, Hiroki Akiyama, Shinya Ishida, Toshikage Nagao, Masahide Yamamoto, Osamu Miura. Acute myeloid leukemia with t(3;21)(q26.2;q22) developing following low-dose methotrexate therapy for rheumatoid arthritis and expressing two AML1/MDS1/EVI1 fusion proteins: A case report. *Oncol Lett*. 2017.07; 14(1); 97-102
 9. Yujin Sekinaka, Noriko Mitsui, Kohsuke Imai, Miharuru Yabe, Hiromasa Yabe, Kanako Mitsui-Sekinaka, Kenichi Honma, Masatoshi Takagi, Ayako Arai, Kenichi Yoshida, Yusuke Okuno, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Satoru Miyano, Hideki Muramatsu, Seiji Kojima, Asuka Hira, Minoru Takata, Osamu Ohara, Seishi Ogawa, Tomohiro Morio, Shigeaki Nonoyama. Common Variable Immunodeficiency Caused by FANCD1 Mutations. *J. Clin. Immunol*. 2017.07; 37(5); 434-444
 10. Masahide Yamamoto, Sayaka Suzuki, Jun-Ichi Mukae, Keisuke Tanaka, Ken Watanabe, Gaku Oshikawa, Tetsuya Fukuda, Naomi Murakami, Osamu Miura. Atypical chronic myeloid leukemia with isochromosome (X)(p10): A case report. *Oncol Lett*. 2017.09; 14(3); 3717-3721
 11. Naoto Takahashi, Tetsuzo Tauchi, Kunio Kitamura, Koichi Miyamura, Yoshio Saburi, Yoshihiro Hatta, Yasuhiko Miyata, Shinichi Kobayashi, Kensuke Usuki, Itaru Matsumura, Yosuke Minami, Noriko Usui, Tetsuya Fukuda, Satoru Takada, Maho Ishikawa, Katsumichi Fujimaki, Hiroshi Gomyo, Osamu Sasaki, Kohshi Ohishi, Takaaki Miyake, Kiyotoshi Imai, Hitoshi Suzushima, Hideki Mitsui, Kazuto Togitani, Toru Kiguchi, Yoshiko Atsuta, Shigeki Ohtake, Kazunori Ohnishi, Yukio Kobayashi, Hitoshi Kiyoi, Yasushi Miyazaki, Tomoki Naoe, . Deeper molecular response is a predictive factor for treatment-free remission after imatinib discontinuation in patients with chronic phase chronic myeloid leukemia: the JALSG-STIM213 study. *Int. J. Hematol.* 2017.09; 107(2); 185-193
 12. S Fujita, D Honma, N Adachi, K Araki, E Takamatsu, T Katsumoto, K Yamagata, K Akashi, K Aoyama, A Iwama, I Kitabayashi. Dual inhibition of EZH1/2 breaks the quiescence of leukemia stem cells in acute myeloid leukemia. *Leukemia*. 2017.09; [Epub ahead of print]
 13. S Tokoro, T Namiki, K Miura, K Watanabe, A Arai, K Imadome, H Yokozeki. Chronic active Epstein-Barr virus infection with cutaneous lymphoproliferation: haemophagocytosis in the skin and haemophagocytic syndrome. *J Eur Acad Dermatol Venereol*. 2017.10; [Epub ahead of print] ;
 14. Akira Toriihara, Ayako Arai, Masashi Nakadate, Kouhei Yamamoto, Ken-Ichi Imadome, Osamu Miura, Ukihide Tateishi. FDG-PET/CT findings of chronic active Epstein-Barr virus infection. *Leuk. Lymphoma*. 2017.10; 1-4
 15. Hirohisa Nakamae, Tetsuya Fukuda, Chiaki Nakaseko, Yoshinobu Kanda, Ken Ohmine, Takaaki Ono, Itaru Matsumura, Akira Matsuda, Makoto Aoki, Kazuo Ito, Hirohiko Shibayama. Nilotinib vs. imatinib in Japanese patients with newly diagnosed chronic myeloid leukemia in chronic phase: long-term follow-up of the Japanese subgroup of the randomized ENESTnd trial. *Int. J. Hematol.* 2017.10; 107(3); 327-336
 16. Yoshihiro Umezawa, Hiroki Akiyama, Keigo Okada, Shinya Ishida, Ayako Nogami, Gaku Oshikawa, Tetsuya Kurosu, Osamu Miura. Molecular mechanisms for enhancement of stromal cell-derived factor 1-induced chemotaxis by platelet endothelial cell adhesion molecule 1 (PECAM-1). *Journal of Biological Chemistry*. 2017.12; 292(48); 19639-19655
 17. Keigo Okada, Ayako Nogami, Shinya Ishida, Hiroki Akiyama, Cheng Chen, Yoshihiro Umezawa and Osamu Miura. FLT3-ITD induces expression of Pim kinases through STAT5 to confer resistance to the PI3K/Akt pathway inhibitors on leukemic cells by enhancing the mTORC1/Mcl-1 pathway Oncotarget. 2017.12; 9; 8870-8886

[Conference Activities & Talks]

1. Tomoko Yamashita, Daisuke Mizuchi, Kouta Yoshifuji, Keisuke Tanaka, Ayako Nogami, Ken Watanabe, Chizuko Sakashita, Tetsuya Fukuda, Ayako Arai, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Busulfan-based conditioning regimen for autologous peripheral blood stem cell transplantation in patients with central nervous system lymphoma. The 39th Annual Meeting of the Japanese Society of Hematopoietic Cell Transplantation 2017.03.03 Matsue
2. Erika Onozawa, Haruna Shibayama, Sho Aoki, Akiho Tuzura, Ken-ich Imadome, Takatoshi Koyama, Osamu Miura, Ayako Arai. STAT3 is constitutively activated and can be a therapeutic target of JAK inhibitors in chronic active Epstein-Barr virus infection. The 22th Congress of European society of Hematology 2017.06.23 Madrid
3. Tetsuya Fukuda. The benefit and optimal patients for Radioimmunotherapy. The 57th annual meeting of Japanese Society for lymphoreticular Tissue Research 2017.07.01 Tokyo
4. Kota Yoshifuji, Tetsuya Saito, Tomoko Yamashita, Ayako Nogami, Ken Watanabe, Tetsuya Fukuda, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Clinical features and treatment outcome of methotrexate-associated Hodgkin lymphoma in our institute. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
5. Tetsuya Saito, Hiroki Tsutsumi, Tomoko Yamashita, Hiroki Akiyama, Yoshihiro Umezawa, Ken Watanabe, Tetsuya Fukuda, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Viral monitoring using multiplex PCR in patients with bone marrow failure treated with rabbit ATG. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
6. Ayako Nogami, Keigo Okada, Cheng Chen, Maho Kawakami, Hiroki Akiyama, Yoshihiro Umezawa, Gaku Oshikawa, Shinya Ishida, Tetsuya Kurosu, Osamu Miura. Modulation of the mTORC1 pathway by ubiquitin-proteasome system via REDD1 in AML with FLT3-ITD. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
7. Ryoto Yoshimoto, Ken Watanabe, Emi Uchida, Shihoko Suwa, Shuji Tohda, Masahiko Hatano, Miura Osamu, Tetsuya Fukuda. IVNSIABP/Nd1 is highly expressed in refractory lymphoma as a novel therapeutic target molecule. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
8. Keigo Okada, Ayako Nogami, Cheng Chen, Maho kawakami, Hiroki Akiyama, Shinya Ishida, Yoshihiro Umezawa, Osamu Miura. FLT3-ITD confers resistance to PI3K/Akt inhibitors by enhancing mTORC1/Mcl-1 pathway via Pim kinase. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
9. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Shinya Ishida, Ayako Nogami, Toshikage Nagao, Osamu Miura. Deubiquitinase inhibitor WP1130 blocks JAK2-V617F to induce apoptosis in leukemic cells. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.21 Tokyo
10. Daisuke Watanabe, Shunichiro Yasuda, Norihiko Kawamata, Ken Watanabe, Masahide Yamamoto, Tetsuya Fukuda, Osamu Miura. Genome editing of the murine Calreticulin gene using the CRISPR-Cas9 system. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.21 Tokyo
11. Takashi Ikeda, Keita Mori, Koji Kawamura, Takehiko Mori, Shotaro Hagiwara, Yasunori Ueda, Kaoru Kahata, Naoyuki Uchida, Nobuhiro Tsukada, Satoshi Murakami, Masahide Yamamoto, Tsutomu Takahashi, Tatsuo Ichinohe, Makoto Onizuka, Yoshiko Atsuta, Yoshinobu Kanda, Shinichiro Okamoto, Kazutaka Sumani. Allogenic SCT for multiple myeloma relapsing or progressing after prior autologous SCT: JSHCT MM-WG. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.22 Tokyo, Japan
12. Tomoko Yamashita, Hiroki Tsutsumi, Kota Yoshifuji, Tetsuya Saito, Yoshihiro Umezawa, Ayako Nogami, Ken Watanabe, Toshikage Nagao, Chizuko Sakashita, Masahide Yamamoto, Ayako Arai, Norihiko Kawamata, Osamu Miura, Tetsuya Fukuda. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma with 11q Deletion. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.22 Tokyo
13. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Shinya Ishida, Ayako Nogami, and Osamu Miura. Deubiquitinase Inhibitor WP1130 Blocks FLT3-ITD to Induce Apoptosis in Leukemic Cells. The 59th American Society of Hematology Annual Meeting & Exposition 2017.12.10 Atlanta

14. Akiho Tsuzura, Mayumi Yoshimori, Kanoko Konno, Ken-Ichi Imadome, Erika Onozawa, Ryunosuke Ohkawa, Minoru Tozuka, Osamu Miura, Ayako Arai. Tumor Cells from EBV-Positive T- or NK-Cell Neoplasms Induce Differentiation and Activation of Macrophages by Secreting Humoral Factors. The 59th American Society of Hematology Annual Meeting 2017.12.11 Atlanta

Molecular Endocrinology and Metabolism

Associate Professor: Takanobu Yoshimoto, Hajime Izumiyama

Assistant Professor: Isao Minami, Kazutaka Tsujimoto, Yasutaka Miyachi, Clinical Fellow: Hideyuki Okuma, Akira Takeuchi, Tomohito Hayashi, Masahiro Ando, Sayo Koseki Resident: Hiroto Yamashita, Aki Saito

Project Assistant Professor: Misa Saijo, Xunmei Yuan¹,

Michiko Shirakawa¹, Ibuki Shirakawa¹

Graduate Students (Doctor's course): Kumiko Shiba,

Kenichi Kawahori, Maki Kawasaki, Toshihiro Goto, Takuya Ohmura, Megumi Hatano, Yujiro Nakano,

Takato Takeuchi, Masahiro Asakawa, Nozomi Hanzawa, Tatsuya Fukuda, Takahiro Fukaishi

Project Associate Professor: Koshi Hashimoto², Kyoko Shirakabe¹

¹Department of Organ Network and Metabolism, ²Department of Preemptive Medicine and Metabolism

(1) Outline

1. Purpose of Education

Our training program enables postdoctoral trainees to prepare for the future academic careers and the clinical practice in the broad discipline of endocrinology and metabolism. The research program provides mentor-based training in experimental design, laboratory and clinical research techniques and methodology, and interpretation and analysis of the results obtained from cellular and molecular biology, physiology, clinical physiology, clinical therapeutics, and health sciences. This training program is designed to educate and establish 'physician-scientist' in the field of endocrinology and metabolism.

2. Research Subjects

- 1) Role of adipose tissue inflammation in the metabolic syndrome
- 2) Molecular mechanisms of saturated fatty acid-induced chronic inflammation
- 3) Molecular mechanism of vascular injury in diabetes, endocrine and metabolic diseases
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors
- 6) Development of novel diagnostic and therapeutic tools in endocrine and metabolic diseases

3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- 1) diseases of the thyroid, pituitary and adrenal glands.
- 2) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

(2) Publications**[Original Articles]**

1. Ohara N, Minami I, Bouchi R, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Loss of skeletal muscle mass and its predictors in type 2 diabetes patients under multifaceted treatment approach. *Diabetol Int.* 2017.01; 8(4); 366-374
2. Fukuda T, Bouchi R, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Association of diabetic retinopathy with both sarcopenia and muscle quality in patients with type 2 diabetes: a cross-sectional study. *BMJ Open Diabetes Res Care.* 2017.01; 5(1); e000404
3. Murakami M, Bouchi R, Ohara N, Fukuda T, Takeuchi T, Minami I, Hashimoto K, Yoshimoto T, Ogawa Y.. Beneficial effect of combination therapy with mitiglinide and voglibose on fasting and postprandial endothelial dysfunction in patients with type2 diabetes: a pilot study. *Integr Obes Diabetes.* 2017.01; 3(1); 2-4
4. Bouchi R, Nakano Y, Fukuda T, Takeuchi T, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Reduction of visceral fat by liraglutide is associated with ameliorations of hepatic steatosis, albuminuria, and micro-inflammation in type 2 diabetic patients with insulin treatment: a randomized control trial. *Endcr J.* 2017.03; 64(3); 269-281
5. Bouchi R, Terashima M, Sasahara Y, Asakawa M, Fukuda T, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y. . luseogliflozin reduces epicardial fat accumulation in patients with type 2 diabetes: a pilot study. *Cardiovasc Diabetol.* 2017.03; 16; 32
6. Miyachi Y, Tsuchiya K, Komiya C, Shiba K, Shimazu N, Yamaguchi S, Deushi M, Osaka M, Inoue K, Sato Y, Matsumoto S, Kikuta J, Wake K, Yoshida M, Ishii M, Ogawa Y.. Roles for Cell-Cell Adhesion and Contact in Obesity-Induced Hepatic Myeloid Cell Accumulation and Glucose Intolerance. *Cell Rep.* 2017.03; 18(11); 2766-2779
7. Komiya C, Tanaka M, Tsuchiya K, Shimazu N, Furuke S, Miyachi Y, Shiba K, Yamaguchi S, Ikeda K, Ochi K, Nakabayashi K, Hata K, Itoh M, Suganami S, Ogawa Y.. Antifibrotic effect of pirfenidone in a mouse model of human nonalcoholic steatohepatitis. *Sci Rep.* 2017.03; 7; 44754
8. Bouchi R, Fukuda T, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Association of Sarcopenia with Both Latent Autoimmune Diabetes in Adults and Type 2 Diabetes: A Cross-Sectional Study. *J Diabetes Complications.* 2017.06; 31(6); 992-996
9. Bouchi R, Fukuda T, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Gender difference in the impact of gynoid and android fat masses on the progression of hepatic steatosis in Japanese patients with type 2 diabetes. *BMC Obes.* 2017.07; 4; 27
10. Bouchi R, Fukuda T, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Insulin Treatment Attenuates Decline of Muscle Mass in Japanese Patients with Type 2 Diabetes. *Calcif Tissue Int.* 2017.07; 101(1); 1-8
11. Fukuda T, Bouchi R, Terashima M, Sasahara Y, Asakawa M, Takeuchi T, Nakano Y, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Ipragliflozin Reduces Epicardial Fat Accumulation in Non-Obese Type 2 Diabetic Patients with Visceral Obesity: A Pilot Study. *Diabetes Ther.* 2017.08; 8(4); 851-861
12. Murakami M, Yoshimoto T, Nakabayashi K, Nakano Y, Fukaishi T, Tsuchiya K, Minami I, Bouchi R, Okamura K, Fujii Y, Hashimoto K, Hata KI, Kihara K, Ogawa Y.. Molecular characteristics of the KCNJ5 mutated aldosterone-producing adenomas. *Endocrine Related Cancer.* 2017.10; 24(10); 531-541
13. Tsuchiya K, Ogawa Y. the biology and pathophysiological roles in diabetes. *J Diabetes Investig.* 2017.11; 8; 726-734
14. Okuma H, Bouchi R, Masuda S, Takeuchi T, Murakami M, Minami I, Izumiyama H, Hashimoto K, Yoshimoto T, Ogawa Y.. Suppression of extrapancreatic glucagon by octreotide may reduce fasting and postprandial glucose levels in a diabetic patient after total pancreatectomy: a case report. *Intern Med.* 2017.11; 56; 3061-3066

15. Okuma H, Hashimoto K, Wang X, Ohkiba N, Murooka N, Akizuki N, Inazawa T, Ogawa Y. . Systemic Sarcoidosis with Thyroid Involvement. *Intern Med.* 2017.11; 56; 2181-2186
16. Bouchi R, Fukuda T, Takeuchi T, Minami I, Yoshimoto T, Ogawa Y.. Sarcopenia is associated with incident albuminuria in patients with type 2 diabetes: A retrospective observational study. *J Diabetes Investig.* 2017.11; 8(6); 783-787

Hepatobiliary and Pancreatic Surgery

Director & Professor

Minoru Tanabe MD, PhD

Lecturer

Atsushi Kudo MD, PhD

Assistant Professor

Takanori Ochiai MD, PhD

Daisuke Ban MD, PhD

Arihiro Aihara MD, PhD

Satoshi Matsumura MD, PhD

Yusuke Mitsunori MD, PhD

Satoshi Matsumura MD, PhD

Hiromitsu Ito MD (Center for Minimally Invasive Surgery) (since April)

Taku Sato MD (Bioresource Reseach Center)(until September)

Graduate School Students

Hiromitsu Ito MD (until March)

Eriko Katsuta MD (until March)

Keisuke Nakao MD (until March)

Takaki Furuyama MD (until March)

Keiichi Akakhoshi MD

Atsushi Ohba MD

Yasuhito Iwao MD (joining April)

Hiroki Ueda MD

Yoshiteru Ohata MD

Taku Sato MD (since October)

Yuki Mizuno MD

Norimichi Chiyonobu MD

Haku Liu MD

Shuichi Watanabe (joining April)

Yoshiya Ishikawa (joining April)

(1) Outline

The department of Hepato-Biliary-Pancreatic Surgery at Tokyo Medical and Dental University focus on the liver, biliary tract and pancreas with benign and malignant disorders. We constantly strive to provide the highest level of complex and innovative surgical care, comprehensive surgical training for tomorrow's leaders as well as groundbreaking basic science and clinical research.

(2) Research

We conduct medical research in both clinical and laboratory settings and develop novel ideas in research which impact patient outcomes, teaching, and clinical care.

Our research programs encompass:

- Biomolecular mechanisms of carcinogenesis, cancer growth, invasion and metastasis
- Molecular target therapy for malignant diseases

- Cancer stem cell
- Extended indication for hepatectomy
- The system of liver microcirculation
- Laparoscopic surgery for hepatobiliary pancreatic diseases
- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary pancreatic diseases

(3) Education

Medical students program:

We conduct the various experiences of hepatobiliary pancreatic diseases, diagnosis and management, through lectures, pre-clinical clerkship and clinical clerkship. Clinical clerkship exposes students to the surgical patients and basic surgical techniques. It also provides opportunities to participate in peri-operative care as well as operative procedures. Students learn interpersonal and communication skills that result in the effective exchange of information and teaming with patients, their families, and professional associates.

Surgical training program:

The aim of our surgical training program cultivates not only training for certified board surgeons, but also the future surgical leaders, through experiences from the academic, the operative, and the outpatient aspects of management in university hospital and affiliated hospitals. Clinically, the trainees receive training and experience in the preoperative, operative, and post-operative care of patients and basic science and clinical research in our training programs strive to help young surgeons develop both technical and cognitive expertise.

(4) Clinical Performances

Our highly experienced surgeons offer state-of-the-art diagnosis and treatment, such as the multidisciplinary treatments (based on radical surgery) for advanced malignant diseases, minimally invasive procedures (including reduced port surgery).

Annually, 255 operations (hepatectomy: 96 cases, pancreatectomy: 73 cases) were performed in 2014, placing one of the top high volume medical centers in the country for hepatobiliary pancreatic surgery.

(5) Publications

[Original Articles]

1. Yuichiro Watanabe, Hideyuki Ishida, Hiroyuki Baba, Takeo Iwama, Atsushi Kudo, Minoru Tanabe, Hideki Ishikawa. Pancreas-sparing total duodenectomy for Spigelman stage IV duodenal polyposis associated with familial adenomatous polyposis: experience of 10 cases at a single institution. *Fam. Cancer.* 2017.01; 16(1); 91-98
2. Fujii T, Obara H, Matsubara K, Fujimura N, Yagi H, Hibi T, Abe Y, Kitago M, Shinoda M, Itano O, Tanabe M, Masugi Y, Sakamoto M, Kitagawa Y.. Oral administration of cilostazol improves survival rate after rat liver ischemia/reperfusion injury *J Surg Res.* 2017.02; 213; 207-214
3. Atsushi Oba, Atsushi Kudo, Keiichi Akahoshi, Mitsuhiro Kishino, Takumi Akashi, Eriko Katsuta, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Yoshinobu Eishi, Ukihide Tateishi, Minoru Tanabe. A simple morphological classification to estimate the malignant potential of pancreatic neuroendocrine tumors. *J. Gastroenterol.* 2017.05; 52(10); 1140-1146
4. Keiichi Akahoshi, Takanori Ochiai, Ayumi Takaoka, Takuya Kitamura, Daisuke Ban, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Emergency Cholecystectomy for Patients on Antiplatelet Therapy. *Am Surg.* 2017.05; 83(5); 486-490
5. Ohata Y, Shimada S, Akiyama Y, Mogushi K, Ito H, Matsumura S, Aihara A, Mitsunori Y, Ban D, Ochiai T, Kudo A, Tanabe M, Tanaka S . Acquired resistance with epigenetic alterations under long-term anti-angiogenic therapy for hepatocellular carcinoma. *Molecular Cancer Therapeutics.* 2017.06; 16(6); 1155-1165

6. Ishikawa Y, Ban D, Matsumura S, Mitsunori Y, Ochiai T, Kudo A, Tanaka S, Tanabe M. Surgical pitfalls of jejunal vein anatomy in pancreaticoduodenectomy. *J Hepatobiliary Pancreat Sci.* 2017.07; 4(7); 394-400
7. Ueda H, Ban D, Kudo A, Ochiai T, Tanaka S, Tanabe M. Refractory Long-Term Cholangitis After Pancreaticoduodenectomy: A Retrospective Study. *World J Surg.* 2017.07; 41(7); 1882-1889
8. Conrad C, Wakabayashi G, Asbun HJ, Dallemagne B, Demartines N, Diana M, Fuks D, Giménez ME, Goumard C, Kaneko H, Memeo R, Resende A, Scatton O, Schneck AS, Soubrane O, Tanabe M, van den Bos J, Weiss H, Yamamoto M, Marescaux J, Pessaux P. IRCAD recommendation on safe laparoscopic cholecystectomy *J Hepatobiliary Pancreat Sci.* 2017.10; 24; 603-615
9. Yasuhito Iwao, Hidenori Ojima, Tatsushi Kobayashi, Yoji Kishi, Satoshi Nara, Minoru Esaki, Kazuaki Shimada, Nobuyoshi Hiraoka, Minoru Tanabe, Yae Kanai. Liver atrophy after percutaneous transhepatic portal embolization occurs in two histological phases: Hepatocellular atrophy followed by apoptosis *World Journal of Hepatology.* 2017.11; 9(32); 1227-1238

[Conference Activities & Talks]

1. Ochiai T, Asano D, Yoshino J, Watanabe S, Ishikawa Y, Chiyonobu N, Mizuno Y, Sato T, Ueda H, Iwao Y, Ono H, Mitsunori Y, Matsumura S, Ban D, Kudo A, Tanaka S, Tanabe M. Surgical Strategy of Hepatic Resection with Inferior Vena Cava Resection for Liver Cancers. 12th Annual Academic Surgical Congress 2017.02.07 Las Vegas, USA
2. Akahoshi K, Ban D, Kuboki R, Matsumura S, Mitsunori Y, Ochiai T, Kudo A, Tanabe M. OPRT as a Predictor of Benefit from S-1 Adjuvant Chemotherapy for Cholangiocarcinoma Patients. 12th Annual Academic Surgical Congress 2017.02.08 Las Vegas
3. Keiichi Akahoshi, Atsushi Kudo, Minoru Tanabe. Ischemic Reperfusion of Selective Hepatic Artery Clamping Induced Temporary Increase of the Sinusoidal Flow in the Rat Model. Proceedings of the Third International Symposium 2017.03.09 Nara
4. Minoru Tanebe. Knack for Whipple operation; a better understanding of Treitz ligament and vascular anatomy. TAIWAN SURGICAL ASSOCIATION 2017.03.19 Taiwan
5. Minoru Tanebe. Pancreatic neuroendocrine tumor (PNET): current status and future perspectives . TAIWAN SURGICAL ASSOCIATION 2017.03.19 Taiwan
6. Tanaka S, Shimada S, Akiyama Y, Muramatsu S, Mitumori Y, Aihara A, Ochiai T, Ban D, Kudo A, Arii S, Tanabe M. Significance of molecular subtypes and therapeutic resistance mechanisms in hepato-biliary-pancreatic malignancies for precision cancer medicine . The 117th Annual Congress of Japan Surgical Society 2017.04.27 Yokohama
7. Daisuke Ban, Minoru Tanabe. How to set up difficulty scoring system in laparoscopic liver resection . 6th A-PHPBA & 29th JSHBPS 2017.06.07 yokohama
8. Shuichi Watanabe, Daisuke Ban, Yasuhito Iwao, Keiichi Akahoshi, Akihiro Ono, Yusuke Mitsunori, Satoshi Matsumura, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Study of the prognosis of recurrent pancreatic cancer: The significance of the solitary recurrence. 2017.06.08
9. Atsushi Kudo, Daisuke Ban, Keiichi Akahoshi, Yusuke Mitsunori, Shinji Tanaka, Minoru Tanabe. Systemic therapy may decide surgical indication for patients with Unresectable of Metastatic Pancreatic Neuroendocrine Tumor. 6th A-PHPBA & 29th JSHBPS 2017.06.08
10. Yusuke Mitsunori, Daisuke Ban, Hiroaki Ono, Keiichi Akahoshi, Yasuhito Iwao, Satoshi Matsumura, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Can we predict postoperative diabetes mellitus in patient with distal pancreatectomy?. 6th A-PHPBA 29th JSHBPS 2017.06.08 yokohama
11. Hiroaki Ono, Keiichi Akahoshi, Yasuhito Iwao, Satoshi Matsumura, Yuusuke Mitsunori, Daisuke Ban, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical evaluation of lymph node metastasis after surgery of IPMN. 6th A-PHPBA 29th JSHBPS 2017.06.08 yokohama

12. Atsushi Kudo, Daisuke Ban, Keiichi Akahoshi, Satoshi Matsumura, Yusuke Mitsunori, Yasuhito Iwao, Shinji Tanaka, Minoru Tanabe. How to manage liver metastases of pancreatic NET?. 6th A-PHPBA & 29th JSHBPS 2017.06.08 yokohama
13. Takehiro Okabayashi, Daisuke Asano, Keiichi Akahoshi, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The optimal management depending on the features of CT imaging of borderline resectable pancreatic cancer. 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
14. Kenichi Okada, Daisuke Ban, Keiichi Akahoshi, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Satoshi Matsumura, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. The optimal pancreatic stump closure method of a laparoscopic distalpancreatectomy: wrapping and fibrin capping technique. 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
15. Daisuke Ban . Meet the Experts 12 / Reduced Accesses Cholecystectomy . 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
16. Hiroki Ueda, Daisuke Ban, Atsushi Kudo, Takanori Ochiai, Shinji Tanaka, Minoru Tanabe . Refractory long-term cholangitis after pancreaticoduodenectomy: a retrospective study . 6th A-PHPBA & 29th JSHBPS 2017.06.09 yokohama
17. Yuki Mizuno, Atsushi Kudo, Yoshiya Ishikawa, Shuichi Watanabe, Norimichi Chiyonobu, Hiroaki Ono, Satoshi Masumura, Yusuke Mitsunori, Daisuke Ban, Takanori Ochiai, Minoru Tanabe. Analysis of the relationship between PD-L1 expression and clinicopathological factors in GEP-NETs. 6th A-PHPBA & 29th JSHBPS 2017.06.10 yokohama
18. Takehisa Yazawa, Hiroaki Ono¹, Yasuhito Iwao, Satoshi Matsumura, Yusuke Mitsunori, Daisuke Ban, Takanori Ochiai, Atsushi Kudo, Shinji Tanaka, Minoru Tanabe. Clinical significance of enhancing nodules in preoperative imaging studies of IPMN. 6th A-PHPBA & 29th JSHBPS 2017.06.10 yokohama
19. Jun Yoshiono, Daisuke Ban, Atsushi Kudo, Minoru Tanabe. The safe resection of liver parenchyma in laparoscopic surgery by CUSA with soft coagulation technique. The 63rd Annual Congress of International College of Surgeons Japan Section 2017.06.17
20. Toshiro Ogura, Daisuke Ban, Jun Yoshino, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Tips for the safe approach in laparoscopic liver resection of segment 7 and 8. The 63rd Annual Congress of International College of Surgeons Japan Section 2017.06.17
21. Daisuke Ban, Jun Yoshino, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Atsushi Kudo, Minoru Tanabe. Safely expanding of the laparoscopic liver resection according to difficulty scoring system. The 63rd Annual Congress of International College of Surgeons Japan Section 2017.06.17 Tokyo
22. Minoru Tanabe. Difficulty score . International Laparoscopic Liver Society 2017 2017.07.06 Paris
23. Tanaka S, Oba A, Ogawa Y, Ono H, Mitunori Y, Ban D, Kudo A, Arie S, Tanabe M. . Personalized medicine to target the cancer stemness of hepato-biliary-pancreatic malignancies (Symposium).. The 72rd General Meeting of the Japanese Society of Gastroenterological Surgery 2017.07.22 Kanazawa
24. Minoru Tanabe . SILS Laparoscopic cholecystectomy . IRCAD TAIWAN 2017.11.27 Taiwan
25. Minoru Tanabe . Prerecorded LIVE case : Single Port laparoscopic cholecystectomy . IRCAD TAIWAN 2017.11.27 Taiwan

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa

Associate Professor: Toshitaka Yoshii

Junior Associate Professor: Hiroyuki Inose,

Assistant Professor: Yuko Segawa, Koji Fujita, Takashi Hirai, Hirotaka Koyanagi, Masato Yuasa

Department of Orthopaedic and Trauma Research

Associate Professor: Shinichi Sotome, Yoshinori Asou

Junior Associate Professor: Yoto Oh

Joint Research Department of Advanced Medical Technology

Specially Appointed Professor: Shigenori Kawabata

(1) Outline

Members of our section and Orthopaedic Joint Surgery section work together in a clinic and OR. Through these practices we train to make the clinical diagnosis and to plan the adequate surgery. We study findings of clinical problem of the locomotorium lesion such as joints, spine and spinal cord, peripheral nerve disorders, aging, injury, tumorigenesis mechanism, and image findings. To solve a lot of clinical question and develop new methodology to treat patients having severe orthopaedic problems, we especially research spinal cord function, bone regeneration, and pain perception mechanism at dorsal root ganglion.

(2) Research

Research themes:

Bone and cartilage metabolism

Development and evaluation of biomaterials for clinical application

Mechanism of spinal ligament ossification

Development of measuring device for spinal cord magnetic signals

Research of bone and spinal metastatic tumors

We collaborate with other sections in our university such as the Clinical Anatomy, the Neurology, and the Physiology and Cell Biology.

(3) Education

Our department has several regular program such as "Bedside Professor Round" at Monday 14:30-16:30, "Clinical Conference" at Monday 7:30-9:00, and "Journal Clubs or Research Progress meeting" at 7:30-8:00 of Tuesday, Thursday, and Friday.

Graduate students in our department can acquire the basic techniques of orthopaedic research and can learn a up-dated knowledge of clinical medicine through regularly-held journal clubs and research meetings.

(4) Lectures & Courses

Japanese orthopaedic research is characterised by the fact that orthopaedic surgeon himself participates experiments while he is working as a clinician. A lot of new knowledge concerning bone, cartilage and nerve were discovered by this so-called "surgeon scientist".

We have already taken a new artificial bone developed in our section to the market and have been preparing a revolutionary measuring device for spinal magnetic signals. We think it very important that research by a surgeon should be based on clinical problems even when methodology of molecular biology is used.

Our graduate students learn basic technique of orthopaedic research and also acquire the ability of life-continuing attitude for clinical studies.

(5) Clinical Services & Other Works

Our orthopaedic department consists of two graduate school sections, the Orthopaedic and Spinal Surgery and the Joint Surgery and Sports Medicine. We deal with all kinds of orthopaedic diseases such as spine, hand, hip, knee, and musculo-skeletal tumor. More than twenty registered orthopaedic surgeons belong to our department.

Our anterior cervical operation for OPLL results in a good clinical outcome. We also organize many spinal surgeons who are members of a nation-wide research organization for spinal ligament ossification supported by the Ministry of Health, Labour and Welfare.

(6) Clinical Performances

We aim to provide safer surgery to the patients with intractable spinal disease using many kinds of modality as navigation, microscopic surgery, spinal cord monitoring, and intraoperative CAT scan. Treatments of adult spinal deformity and osteoporotic vertebral fracture are our other interest. We have also developed an original artificial bone composed of hydroxyapatite and collagen, now promoting to use aggressively to fill large bone defect.

(7) Publications**[Original Articles]**

1. Mitsuhiro Enomoto, Kazuyoshi Yagishita, Kae Okuma, Takuya Oyaizu, Yasushi Kojima, Atsushi Okubo, Takuma Maeda, Satoko Miyamoto, Atsushi Okawa. Hyperbaric oxygen therapy for a refractory skin ulcer after radical mastectomy and radiation therapy: a case report. *J Med Case Rep.* 2017.01; 11(1); 5
2. Kenichiro Sakai, Toshitaka Yoshii, Takashi Hirai, Yoshiyasu Arai, Kenichi Shinomiya, Atsushi Okawa. Impact of the surgical treatment for degenerative cervical myelopathy on the preoperative cervical sagittal balance: a review of prospective comparative cohort between anterior decompression with fusion and laminoplasty. *Eur Spine J.* 2017.01; 26(1); 104-112
3. Yoshii Toshitaka, Hirai Takashi, Yamada Tsuyoshi, Inose Hiroyuki, Kato Tsuyoshi, Sakai Kenichiro, Enomoto Mitsuhiro, Kawabata Shigenori, Arai Yoshiyasu, Okawa Atsushi. Intraoperative evaluation using mobile computed tomography in anterior cervical decompression with floating method for massive ossification of the posterior longitudinal ligament. *J Orthop Surg Res.* 2017.01; 12(1); 12
4. Jinno Tetsuya, Koga Daisuke, Asou Yoshinori, Morita Sadao, Okawa Atsushi, Muneta Takeshi. Intraoperative evaluation of the effects of femoral component offset and head size on joint stability in total hip arthroplasty. *J Orthop Surg (Hong Kong).* 2017.01; 25(1); 2309499016684298
5. Nicholas A Mignemi, Masato Yuasa, Courtney E Baker, Stephanie N Moore, Rivka C Ihejirika, William K Oelsner, Christopher S Wallace, Toshitaka Yoshii, Atsushi Okawa, Alexey S Revenko, A Robert MacLeod, Gourab Bhattacharjee, Joey V Barnett, Herbert S Schwartz, Jay L Degen, Matthew J Flick, Justin M Cates, Jonathan G Schoenecker. Plasmin Prevents Dystrophic Calcification After Muscle Injury. *J. Bone Miner. Res.* 2017.02; 32(2); 294-308
6. Gaku Koyano, Tetsuya Jinno, Daisuke Koga, Yuki Yamauchi, Takeshi Muneta, Atsushi Okawa. Comparison of Bone Remodeling Between an Anatomic Short Stem and a Straight Stem in 1-Stage Bilateral Total Hip Arthroplasty. *J Arthroplasty.* 2017.02; 32(2); 594-600

7. Takuya Oyaizu, Mitsuhiro Enomoto, Toshihide Tsujimoto, Yasushi Kojima, Atsushi Okawa, Kazuyoshi Yagishita. Elimination of CT-detected gas bubbles derived from decompression illness with abdominal symptoms after a short hyperbaric oxygen treatment in a monoplace chamber: a case report. *Undersea Hyperb Med.* 2017.03; 44(2); 167-171
8. Toshitaka Yoshii, Takashi Hirai, Kenichiro Sakai, Shinichi Sotome, Mitsuhiro Enomoto, Tsuyoshi Yamada, Hiroyuki Inose, Tsuyoshi Kato, Shigenori Kawabata, Atsushi Okawa. Anterior Cervical Corpectomy and Fusion Using a Synthetic Hydroxyapatite Graft for Ossification of the Posterior Longitudinal Ligament. *Orthopedics.* 2017.03; 40(2); e334-e339
9. Atsuyuki Kawabata, Hiroyuki Inose, Dai Ukegawa, Shigenori Kawabata, Tsuyoshi Yamada, Atsushi Okawa. A foreign body granuloma after the usage of polyglycolic acid mesh and fibrin glue for dural repair. A case report. *J Orthop Sci.* 2017.03; 22(2); 371-374
10. Atsushi Kimura, Atsushi Seichi, Katsushi Takeshita, Hirokazu Inoue, Tsuyoshi Kato, Toshitaka Yoshii, Takeo Furuya, Masao Koda, Kazuhiro Takeuchi, Shunji Matsunaga, Shoji Seki, Yoshimoto Ishikawa, Shiro Imagama, Masashi Yamazaki, Kanji Mori, Yosuke Kawasaki, Koji Fujita, Kenji Endo, Kimiaki Sato, Atsushi Okawa. Fall-related Deterioration of Subjective Symptoms in Patients with Cervical Myelopathy. *Spine.* 2017.04; 42(7); E398-E403
11. Naofumi Taniguchi, Tetsuya Jinno, Daisuke Koga, Tetsuo Hagino, Atsushi Okawa, Hirotaka Haro. Cementless Hip Stem Anteversion in the Dysplastic Hip: A Comparison of Tapered Wedge vs Metaphyseal Filling. *J Arthroplasty.* 2017.05; 32(5); 1547-1552
12. Sumiya Satoshi, Kawabata Shigenori, Hoshino Yuko, Adachi Yoshiaki, Sekihara Kensuke, Tomizawa Shoji, Tomori Masaki, Ishii Senichi, Sakaki Kyohei, Ukegawa Dai, Ushio Shuta, Watanabe Taishi, Okawa Atsushi. Magnetospinography visualizes electrophysiological activity in the cervical spinal cord. *Sci Rep.* 2017.05; 7(1); 2192
13. R Takada, T Jinno, D Koga, K Miyatake, T Muneta, A Okawa. Comparison of wear rate and osteolysis between second-generation annealed and first-generation remelted highly cross-linked polyethylene in total hip arthroplasty. A case control study at a minimum of five years. *Orthop Traumatol Surg Res.* 2017.06; 103(4); 537-541
14. Ushio Shuta, Kawabata Shigenori, Sumiya Satoshi, Kato Tsuyoshi, Yoshii Toshitaka, Yamada Tsuyoshi, Enomoto Mitsuhiro, Okawa Atsushi. A multi-train electrical stimulation protocol facilitates transcranial electrical motor evoked potentials and increases induction rate and reproducibility even in patients with preoperative neurological deficits. *J Clin Monit Comput.* 2017.07;
15. Hirai Takashi, Yoshii Toshitaka, Arai Yoshiyasu, Sakai Kenichiro, Torigoe Ichiro, Maehara Hidetsugu, Tomori Masaki, Taniyama Takashi, Sato Hirokazu, Okawa Atsushi. A Comparative Study of Anterior Decompression With Fusion and Posterior Decompression With Laminoplasty for the Treatment of Cervical Spondylotic Myelopathy Patients With Large Anterior Compression of the Spinal Cord. *Clin Spine Surg.* 2017.10; 30(8); E1137-E1142
16. Ogawa T, Sasaki T, Masayuki-Kawashima M K, Okawa A, Mahito-Kawashima M K. Internal Fixation of Only the Distal End in a Bipolar Segmental Clavicle Fracture: A Case Report. *Malays Orthop J.* 2017.11; 11(3); 47-49
17. Oh Yoto, Fujita Koji, Wakabayashi Yoshiaki, Kurosa Yoshiro, Okawa Atsushi. Location of atypical femoral fracture can be determined by tensile stress distribution influenced by femoral bowing and neck-shaft angle: a CT-based nonlinear finite element analysis model for the assessment of femoral shaft loading stress. *Injury.* 2017.12; 48(12); 2736-2743
18. Wakasugi Takuma, Shirasaka Ritsuro, Kawauchi Toshiyuki, Fujita Koji, Okawa Atsushi. Carpal Tunnel Syndrome and Trigger Wrist Caused by Localized Amyloidosis: A Case Report. *J Hand Surg Asian Pac Vol.* 2017.12; 22(4); 508-511

[Misc]

1. Y. Adachi, J. Kawai, Y. Haruta, M. Miyamoto, S. Kawabata, K. Sekihara, G. Uehara. Recent advancements in the SQUID magnetospinogram system, *Supercond Sci Tech.* 2017.03; Vol30; 63001

[Conference Activities & Talks]

1. Koji Fujita, Hidetoshi Kaburagi, Akimoto Nimura, Takashi Miyamoto, Atsushi Okawa. Distal radius fracture patients show declined ability of dynamic body balancing.. American Association for Hand Surgery 2017 Annual Meeting 2017.01.09 Hawaii
2. Taishi Watanabe, Shigenori Kawabata, Miho Akaza, Yoshiaki Adachi, Kensuke Sekihara, Atsushi Okawa. Combination of neurophysiological and the morphological information in brachial plexus using SQUID biomagnetometer system. ACNS 2017 2017.02.08 Arizona PHOENIX
3. Shigenori Kawabata, Shuta Ushio; Takumi Yamaga; Yuki Hasegawa; Taishi Watanabe; Kensuke Sekihara; Yoshiaki Adachi; Atsushi Okawa Shuta Ushio; Takumi Yamaga; Yuki Hasegawa; Taishi Watanabe; Kensuke Sekihara; Yoshiaki Adachi; Atsushi Okawa. Diagnosis of Spinal Conduction Block by Magnetospinography. ACNS 2017 2017.02.08 Arizona PHOENIX
4. Satoshi Sumiya, Shigenori Kawabata; Shuta Ushio; Yuko Hoshino; Kensuke Sekihara; Taishi Watanabe; Takumi Yamaga; Yoshiaki Adachi; Hiromichi Komori; kenichi Shinomiya; Atsushi Okawa. Noninvasive evaluation by magnetospinography of electrophysiological activity in the cervical spine after peripheral nerve stimulation. ACNS 2017 2017.02.08 Arizona PHOENIX
5. Shuta Ushio, Shigenori Kawabata, Koji Fujita, Toru Sasaki, Satoshi Sumiya, Taishi Watanabe, Kensuke Sekihara, Yuki Hasegawa, Tomohiko Shibuya, Shuichi Okawa, Yoshiaki Adachi, Atsushi Okawa . Visualization of muscle electrical activity evoked by electrical stimulation of the ulnar nerve using superconducting quantum interference device sensors. ACNS 2017 2017.02.08 Arizona PHOENIX
6. Satoru Egawa, Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Hiroyuki Inose, Shigenori Kawabata, Atsushi Okawa. Prevertebral Soft Tissue Swelling (PSTS) of anterior cervical surgery in Ossification of Posterior Longitudinal Ligament Is Higher Than Other Cervical Degenerative Disorders; A Radiographic Analysis.. CSRS-AP 2017 2017.03.09 koube
7. Takashi Hirai, Toshitaka Yoshii, Kenichiro Sakai, Satoru Egawa, Atsushi Okawa. Long-term results of a prospective study of anterior decompression with fusion and posterior decompression with laminoplasty for the treatment of cervical spondylotic myelopathy. CSRS-AP 2017 2017.03.09 koube
8. Satoru Egawa, Wei Xue Tao, Toshitaka Yoshii, Hiroaki Yasuda, Rempei Matsumoto, Atsushi Okawa, Shinichi Sotome. Repair of Femoral Bone Defects in Rats Using Hydroxyapatite/Collagen (HAp/Col) with BMP-2. ORS 2017.03.19 San Diego, USA
9. Rempei Matsumoto, Wei Xue Tao, Toshitaka Yoshii, Hiroaki Yasuda, Atsushi Okawa, Shinichi Sotome. Transplantation of Paclitaxel Impregnation Hap/Col to Bone Metastasis Model Rat. ORS 2017.03.19 San Diego, USA
10. Toshitaka Yoshii, Takashi Hirai, Tsuyoshi Yamada, Akio Iwanami, Kazuhiro Takeuchi, Kanji Mori, Atsushi Okawa, Yoshiharu Kawaguchi . Co-existence of ossification of the nuchal ligament is associated with spinal hyperostosis in patients with cervical ossification of the posterior longitudinal ligament - A Multicenter CT study-. ORS 2017.03.19 San Diego, USA
11. Yoshii Toshitaka, Hirai Takashi, Inose Hiroyuki, Yamada Tsuyoshi, Kawabata Shigenori, Okawa Atsushi. Intraoperative evaluation using mobile computed tomography in anterior cervical decompression for ossification of the posterior longitudinal ligament. 90th Annual Meeting of JOA 2017.05.18 Sendai
12. Inose Hiroyuki, Yamada Tsuyoshi, Hirai Takashi, Yoshii Toshitaka, Kawabata Shigenori, Okawa Atsushi. Bone turnover markers as a new predicting factor for non-union after spinal fusion surgery. 90th Annual Meeting of JOA 2017.05.18 Sendai
13. Toshifumi Watanabe, Takeshi Muneta, Hideyuki Koga, Masafumi Horie, Koji Otabe, Toshiyuki Ohara, Kaori Nakamura, Mai Katakura, Atsushi Okawa Ichiro Sekiya. Post-cam Design and Contact Stress on Tibial Posts in Total Knee Prostheses: Comparison between a Rounded and a Squared Design. Annual Meeting of JOA 2017.05.19
14. Shigenori Kawabata, Shuta Ushio, Taishi Watanabe, Kensuke Sekihara, Yoshiaki Adachi. Clinical application of magnetospinography. Biomagnetic Sendai 2017 2017.05.22 Sendai

15. Atsuhiko Yagishita, Yasuhiro Shirai, Tomohiko Shibuya, Shuta Ushio, Shuichi Okawa, Shigenori Kawabata. Biomagnetic measurement using relocatable MR sensor array. Biomagnetic Sendai 2017 2017.05.22 Sendai
16. Yasuhiro Shirai, Taishi Watanabe, Yuki Hasegawa, Kensuke Sekihara, Shigenori Kawabata. Noninvasive evaluation of electrical activity in left atrium and pulmonary vein using SQUID system: Comparison between before and after pulmonary vein isolation.. Biomagnetic Sendai 2017 2017.05.22 Sendai
17. Kensuke Sekihara, Tomohiko Shibuya, Shuichi Okawa, Shigenori Kawabata. Environmental noise cancellation for room-temperature magnetoresistive (MR) sensor array. Biomagnetic Sendai 2017 2017.05.22 Sendai
18. Taishi Watanabe, Kensuke Sekihara, Isamu Ozaki, Shigenori Kawabata, Atsushi Okawa. Removal of stimulation artifact noise near the measurement site using CSP. Biomagnetic Sendai 2017 2017.05.22 Sendai
19. Isamu Ozaki, Taishi Watanabe, Miho Akaza, Yoshiaki Adachi, Shigenori Kawabata, Kensuke Sekihara. Magnetic recordings of sensory action currents along the peripheral nerves at hand, forearm or upper arm and the brachial plexus. Biomagnetic Sendai 2017 2017.05.22 Sendai
20. Miho Akaza, Shigenori Kawabata, Isamu Ozaki, Yuki Hasegawa, Taishi watanabe, Yoshiaki Adachi, Yuki Sumi, Takanori Yokota. Magnetic recordings of sensory action currents in the cervical cord.. Biomagnetic Sendai 2017 2017.05.22 Sendai
21. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Takeshi Muneta, Atsushi Okawa. Comparison Of Wear Rate And Osteolysis Between Second-Generation Annealed And First-Generation Remelted Highly Cross-Linked Polyethylene In Total Hip Arthroplasty. 15th EFORT 2017.05.31 Viena
22. Koji Fujita, Hidetoshi Kaburagi, Akimoto Nimura, Takashi Miyamoto, Atsushi Okawa . Distal radius fracture patients over 70 years of age showed declined body balancing ability and osteoporosis. Eurohand 2017 2017.06.21 Budapest, Hungary
23. Takuya Oyaizu, Mitsuhiro Enomoto, Masaki Horie, Kazuyoshi Yagishita. Hyperbaric and high-oxygen environments reduce circulating inflammatory cells, convert infiltrated macrophage phenotype, and activate satellites cell following skeletal muscle contusion in rats. . Undersea and Hyperbaric Medical Society (UHMS) 2017 Annual Scientific Meeting 2017.06.29 frolida, USA
24. Akira Takahashi, Hiroyuki Inose, Atsushi Okawa. Cdk1 is essential for bone formation and fracture repair. ASBMR 2017 Annual Meeting 2017.09.08 Denver, USA
25. Takuro Watanabe, Yuta Sugiura, Natsuki Miyata, Koji Fujita, Akimoto Nimura, and Maki Sugimoto. DanceDanceThumb: Tablet App for Rehabilitation for Carpal Tunnel Syndrome. The 16th International Conference on Entertainment Computing 2017 (ICEC '17) 2017.09.18 Tsukuba
26. Shigenori Kawabata, Shuta Ushio , Takumi Yamaga, Yuki Hasegawa, Taishi Watanabe, Kensuke Sekihara, Yoshiaki Adachi, Atsushi Okawa. Evaluation of spinal conduction block in myelopathy patients by magnetospinography. XXIII World Congress of Neurology 2017 2017.09.19 Kyoto
27. Takahisa Ogawa, Yasuhiro Seki, Shinichi Shirasawa. Arthroscopic ganglionectomy of a toe with color-aided visualization of the ganglion stalk. 6TH Triennial IFFAS meeting 2017.09.29 Lisbon, Portugal
28. Koji Fujita, Hidetoshi Kaburagi, Akimoto Nimura, Takashi Miyamoto, Atsushi Okawa. Distal radius fracture patients showed declined dynamic body balancing ability and Grip strength. 11th APFSSH 2017 2017.11.07 Cebu,Philippines
29. Tatsunobu Ikeda et.al. RADIATION-INDUCED DEDIFFERENTIATED CHONDROSARCOMA OF THE LEFT PUBIS: A CASE REPORT. CTOS 2017 Annual Meeting 2017.11.08 Maui, Hawaii
30. Toshitaka Yoshii, Tsuyoshi Yamada, Takashi Hirai, Kenichiro Sakai, Atsushi Okawa. Tandem Spinal Stenosis in Patients with Symptomatic Cervical Ossificatoin of the Posterior Longitudinal Ligament(OPLL). Cevical Spine Research Society 45th Annual Meeting 2017.11.30 Hollywood, Florida
31. Satoshi Sumiya, Shigenori Kawabata, Toshitaka Yoshii, Atsushi Okawa . Cervical spinal cord impairment associated with neck flexion in posterior cervical decompression. Cevical Spine Research Society 45th Annual Meeting 2017.11.30 Hollywood, Florida

32. Hirotaka Koyanagi, Toshitaka Yoshii, Takashi Hirai, Shingo Sato, Atsushi Okawa. Treatment of Lumbar Giant Cell Tumor. 108 Military Hospital and 24th Annual Meeting of The Spine Society of HCMC 2017.12.14 Ha Noi, Viet Nam

[Awards & Honors]

1. Biomagnetic Sendai 2017:Young Investigator Award(Taishi Watanabe), Biomagnetic, 2017.05
2. President's awards: Best Resident/Trainee Oral Presentation(Oyaizu Takuya), Undersea and Hyperbaric Medical Society, 2017.06
3. ASBMR 2017 Annual Meeting: Young Investigator Award (Akira Takahashi), ASBMR, 2017.09
4. ASBMR 2017 Annual Meeting:Plenary Poster(Akira Takahashi), ASBMR, 2017.09

Diagnostic Radiology and Nuclear Medicine

Professor Ukihide Tateishi
Project Professor Yukihisa Saida
Associate Professors Ichiro Yamada
Lecturers Yoshio Kitazume, Yoshiaki Katada (~ June)
Research Associates Makiko Honda, Tomohiro Yoneyama, Akira Toriihara (~ Mar.),
Tomoyuki Fujioka, Yoshihiro Iwasa, Jun Oyama
Hospital Staff members Yoko Shirakawa (~ Mar.),
Takumi Oshima, Kyoko Sugimoto, Sayumi Tsuyuzaki,
Akane Ozawa (~ Mar.), Nobuhiro Takaya (~ Mar.),
Kenichi Fukui (~ Mar.), Ruonan Li (~ June), Yuka Yashima (Apr. ~),
Resident Kazuma Sasamura, Takahiro Sato, Hyeyel Bae,
Momo Wakui, Hiroshi Watanebe

(1) Outline

While diagnostic radiology and nuclear medicine demand high-level capabilities and therefore extensive training to acquire those capabilities, keeping a watch on developments in medical knowledge and maintaining those skills is also an issue for these disciplines. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment. Contributing to the community is a basic responsibility of diagnostic radiology so it remains the university's mission to unflinchingly fulfill its responsibility to provide high-level, advanced medical care, working toward resolution of community problems through education, research and medical activities, as well as to develop the diagnostic radiology professionals who will bear the responsibility for providing community medical care, and to develop professionals who have a global outlook and can flourish in this age of globalization. More than ever, advancing the fundamental medical concepts of "patient-oriented medical care" and "thorough medical safety management" are core principles in the field of diagnostic radiology and nuclear medicine, so continuing to maintain capabilities from this perspective is essential in daily practice.

Under the new radiologist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiologist examination (sixth year after graduation). After passing that examination, it is then possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

Diagnostic radiology and nuclear medicine was divided off the specialist field responsible for diagnostic radiology in July 2013. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide it without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 15 external affiliated hospitals approved by JRS as

training hospitals. When commencing specialist training, students are allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. In addition, many also obtain certification as a senior (first class) radiation protection supervisor.

In recent times, diagnostic radiology has been experiencing an increasing load in terms of image processing, the number of image readings, and server storage, owing to improvements in instrument performance. As hybrid imaging such as PET/CT, SPECT/CT, PET/MRI become more prevalent, the diversification of diagnostic methods is accelerating. This trend is expected to continue, so there is a need for work on adequate personnel responses, including infrastructure improvement. And because the combined use of functional images to monitor metabolism and blood flow from morphologic images alone will be fundamental, it is essential that the university goes on enhancing education for radiologists so that they acquire the capabilities to extract and analyze clinically useful information from the complex data gathered.

Remote diagnostic imaging is a good example of this. In regard to its responsibility to contribute to the community, there have been changes in the way diagnostic radiology today has been active in society. The community gives special privileges to the diagnosing doctor, including the exclusive or primary responsibility to provide specified medical services. The university must unwaveringly fulfill its mission as such by providing advanced medical care through medical practice, as well as developing the doctors who will provide healthcare to communities. Although it could not be claimed that the environment surrounding diagnostic radiology in community healthcare has fully matured, as specialists, it is necessary to contribute to the development of local communities and to exercise the privileges granted as specialists: we should carry out our responsibilities while firmly holding to this approach.

(2) Research

Diagnostic specialists must keep up with the latest research in their fields, applying medical research findings to clinical practice, and making use of continuing education, continuing professional development programs, medical journals, society activities and the internet to maintain their skills. Along with the importance of maintaining awareness of how to interpret and apply research findings to the patient, it is also necessary to go on formulating broad education programs from a specialist perspective, in order to stay well informed about the fundamentals of research methods and to practice appropriate medicine. By managing the faculty effectively, it will go on clarifying radiological perspectives designed to effect inter-disciplinary research activities, taking a whole-university outlook that crosses over the limits of individual departments or graduate schools. The faculty ensures the education and research activities at graduate schools are reflected in the departments while also energetically tackling strategies to secure external funding and strengthen industry collaborations, with the aim of further improving research results. The faculty continues to actively advance international cooperative networks with the Radiological Society of North America (RSNA), the European Congress of Radiology (ECR), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), etc. from the standpoint of diagnostic radiology and nuclear medicine, and continues to advance research based on a thorough awareness of the impacts emerging in the field and the potentialities developing in related practical application fields.

Diagnostic radiology provides diagnoses by extracting information about the morphology of organs and tissues, three-dimensional structures. It is important in terms of learning to systematically organize that information for comparison of imaging study analyses with the reference pathological tissue. Within that, using CT or MRI for tissue characterization that reflects the macro-pathology is important for identifying diseases.

Diagnostic radiology is a discipline in which it is possible to zero in on understanding of a pathological condition by collecting and analyzing blood flow and metabolic data over time. The faculty is continuing research into a minimally invasive method of extracting in vivo blood flow data to enable the use of in vivo dynamic analysis as a biomarker with formulation of dynamic scan protocols that obtain images over time with bolus contrast injection before high-resolution, multi-slice CT or high magnetic field MRI. Texture analysis and AI imaging are applied to both of anatomic and functional imaging modalities. We investigate from first order (kurtosis) to high order (NGLCM, NGTDM, GLSZM). The faculty is also formulating scan protocols that obtain images over time with 3D PET/CT, as a minimally invasive technique of extracting in vivo metabolic data. Known tracers include 18F-FDG (glucose metabolism), 11C-choline (lipid metabolism), 11C-acetate (lipid metabolism), 18F-FAZA (hypoxia), 18F-FACBC (amino acid metabolism), 62/64Cu-ATSM (redox), 18F-FLT (DNA synthesis), 18F-NaF (bone metabolism), 68Ga-DOTATATE (somatostatin receptor), and 18F-Fluorobetapir (Amyloid), 18F-Flutemetamol (Amyloid). The usefulness of multiple tracers in the discipline of oncology has been observed in numerous carcinomas. 177Lu-DOTATATE PRRT started as the first domestic Phase I study. Given

the need for examination with standardized imaging and assessment techniques, by conducting a multi-center joint study using PET/CT, the faculty is working to realize and to formulate methodologies for standardization to facilitate participation in global clinical trials in Japan.

(3) Education

In order to meet the expectations of both the patient and diagnostic radiologist, it is important to know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care, and to continue to independently demonstrate them. Diagnostic radiology demands high-level capabilities, so extensive training is required to acquire those capabilities, while keeping a watch on developments in medical knowledge and maintaining those capabilities is also an issue for the discipline. Similarly, it is also necessary to maintain knowledge, skills and capabilities in ethics, not only radiology knowledge and skills, in order to respond to changes in medical practices as well as the social and political environment.

Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global viewpoint, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective. An essential aspect of postgraduate school education is the ongoing maintenance of capabilities from that perspective.

Under the new radiology specialist system, it is possible to obtain a qualification by completing two years of post-graduate clinical training, followed by three years of general training at a training facility approved by the Japan Radiological Society, then sitting the radiology specialist examination (sixth year after graduation). After passing that examination, it is possible to obtain a qualification in either radiotherapy or diagnostic radiology by completing a further two years of specialist training and sitting either the radiotherapist or the diagnostic radiologist examination (eighth year after graduation).

In July 2013, radiation oncology was divided into diagnostic radiology and nuclear medicine responsible for diagnostic radiology and radiotherapeutic oncology, in turn responsible for radiotherapy. However, because the radiologist examination covers both treatment and diagnosis, the plan for the three years of general training is to provide the training without dividing students into treatment or diagnosis streams. In compliance with the specialist training curriculum guidelines set out by the Japan Radiological Society, students generally complete about one year of training in the university, then about two years of training in an external affiliated hospital. There are currently 11 external affiliated hospitals (five in Tokyo and six in the Kanto region) approved by the Society as training hospitals. When students commence specialist training, they will be allocated to their specialist fields. After the two years of specialist training, all students decide whether to aim to become a radiotherapist or a diagnostic radiologist. Almost all students then set out to obtain a further degree by enrolling in either a post-graduate school or adult graduate school. From the standpoint of managing sealed and unsealed sources in nuclear medicine, many students also obtain certification as a senior (first class) radiation protection supervisor before engaging in clinical and research work.

(4) Lectures & Courses

The department delivers education based on the university's fundamental policy aimed at realization of its mission: to contribute to the development of society, with a specific mission to bear the responsibility for the basic functions of education, research and medical care. As a department at the core of medical care, it develops professionals who can engage in practice across different fields, taking the approach that the standards of behavior demonstrated by diagnostic radiologists in clinical practice have far more impact than the formal curriculum in ethics.

The department develops professionals who can continue to work to resolve the issues faced by the university hospital, professionals who know the values, especially empathy, capabilities, and autonomy that lie at the core of medical care to meet the expectations of both the patient and student, can independently demonstrate them, and can flourish while maintaining a global outlook. Education in the department aims to develop professionals equipped with the capabilities to resolve a range of problems and the attitude to identify and

research topics themselves, by developing three subject groups, problem presentation, technical skill acquisition, and collaboration with the profession, and by formulating and implementing specialist education based on those groups, from the radiological perspective. Education in the postgraduate school aims to develop professionals who can resolve the problems faced by humanity from a global perspective, implementing research into leading-edge topics within a framework for research guidance under numerous teachers in addition to the acquisition of specialist knowledge, delivering education that develops inventive and practical research capabilities, from the radiological perspective.

(5) Clinical Services & Other Works

Diagnostic Radiology

- CT: A total of three CT scanners are involved in diagnostic radiology: two in the radiology department (64-slice MDCT) and one in the ER center (16-slice MDCT). Not only has the number of examinations using MDCT increased, but it has been possible to obtain improved diagnostic performance by reading MPR (multi-planar reconstruction) images and 1-mm thick images.
- MRI: A total of four MRI scanners are involved in diagnostic radiology: two 1.5-tesla scanners and two 3-tesla scanners. This has allowed for an increase in examinations.
- Ultrasound: The main examinations carried out by diagnostic radiologists are breast and abdominal examinations.
- Angiography and Interventional Radiology (IVR): In the vascular area: TAE for hepatic carcinoma, PTA and stent placement for occlusive arterial disease, intraarterial injection for pelvic tumor, and emergency hemostasis for ER center patients. In the non-vascular area: mainly CT-guided chest biopsy, breast mass biopsy and lymph node biopsy.
- Breast: The department is responsible for breast diagnostic radiology and collaborates with the breast surgery department in team medical care. The department endeavors to diagnose breast cancer at an early stage, provide accurate pre-surgery diagnoses, and formulate treatment plans by providing high-quality diagnostic radiology services combining mammography reading, ultrasound examination, as well as MRI and FDG-PET/CT, in addition to providing image-guided biopsy and surgical marking.
- Conferences: The department holds inter-disciplinary conferences with all departments on a daily basis. The department holds its internal conference every Friday and participates in externally conducted conferences, as appropriate. The department also takes a lead role in organizing conferences aimed at external attendees (Shoheizaka Radiology: twice a year), and the three-university joint conferences (three times a year).

Nuclear Medicine

- Since the department began operating its second PET/CT scanner in November 2006, it has been conducting 15 to 16 PET examinations per day, mainly for malignant tumor, as well as eight to 10 general radioisotope examinations per day, mainly brain and myocardial SPECT. PET/CT for radiation planning and C-11 acetate PET/CT for hematologic malignancies were introduced in 2016.

(6) Clinical Performances

Being a core diagnosis and treatment department, diagnostic radiology and nuclear medicine is a department that engages in inter-disciplinary clinical practice forming strong partnerships to meet the needs of its internal client departments and works to resolve issues faced by the university hospital, bearing its responsibility to unswervingly fulfill its mission from a global perspective. Diagnostic radiology and nuclear medicine is equipped with the capabilities to process large volumes of imaging information, it develops problem presentation, technical skill acquisition, and collaboration with all departments, and possesses the characteristics to go on conscientiously tackling new modalities, probes and contrasts as well as clinical trials.

(7) Publications

[Original Articles]

1. Nagata K, Endo S, Honda T, Yasuda T, Hirayama M, Takahashi S, Kato T, Horita S, Furuya K, Kasai K, Matsumoto H, Kimura Y, Utano K, Sugimoto H, Kato H, Yamada R, Yamamichi J, Shimamoto T, Ryu Y, Matsui O, Kondo H, Doi A, Abe T, Yamano HO, Takeuchi K, Hanai H, Saida Y, Fukuda K, Näppi J, Yoshida H.. Accuracy of CT Colonography for Detection of Polypoid and Nonpolypoid Neoplasia by

Gastroenterologists and Radiologists: A Nationwide Multicenter Study in Japan. *Am J Gastroenterol.* 2017.01; 112(1); 163-171

2. Kishino M, Yoshimoto T, Nakadate M, Katada Y, Kanda E, Nakaminato S, Saida Y, Ogawa Y, Tateishi U.. Optimization of left adrenal vein sampling in primary aldosteronism: Coping with asymmetrical cortisol secretion. *Endocr J.* 2017.03; 64(3); 347-355
3. Kawauchi N.,Tsunoda H.,Saida Y., et.al. Evaluation of reconstructed 2D mammography in asian women *Jpn J Breast Cancer* . 2017.04; 32(4); 311-319
4. Yamada I, Yoshino N, Hikishima K, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal carcinoma: ex vivo evaluation using 3-T high-spatial-resolution quantitative T2 mapping and its correlation with histopathologic findings. *Magn Reson Imaging.* 2017.05; 38(1); 174-181
5. Atsushi Oba, Atsushi Kudo, Keiichi Akahoshi, Mitsuhiro Kishino, Takumi Akashi, Eriko Katsuta, Yasuhito Iwao, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Shinji Tanaka, Yoshinobu Eishi, Ukihide Tateishi, Minoru Tanabe. A simple morphological classification to estimate the malignant potential of pancreatic neuroendocrine tumors. *J. Gastroenterol.* 2017.05;
6. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Toshimitsu Fujii, Masakazu Nagahori, Maiko Kimura, Tomoyuki Fujioka, Akihiro Araki, Mamoru Watanabe. Magnetic resonance evaluation for small bowel strictures in Crohn's disease: comparison with balloon enteroscopy. *J. Gastroenterol.* 2017.08; 52(8); 879-888
7. Yojiro Umezaki, Anna Miura, Motoko Watanabe, Miho Takenoshita, Akihito Uezato, Akira Toriihara, Toru Nishikawa, Akira Toyofuku. Oral cenesthopathy *Biopsychosoc Med.* 10; 20
8. Masashi Nakadate, Norikazu Miyamoto, Jay Starkey, Akira Toriihara, Ukihide Tateishi. Anterograde degeneration of the nigrostriatal pathway visualized by 123I-FP-CIT SPECT in patient with artery of Percheron infarction. *Clin Nucl Med.* 41; 483-484

[Books etc]

1. Saida Yukihisa. *Cancer-Radiooncology 2017.* 2017.06

[Conference Activities & Talks]

1. Kitazume Y, Takenaka K, Hayashi A, Matsuoka K, Fujii T, Kimura M, Nagahori M, Ohtsuka K, Tateishi U. Computed High b-value Diffusion-Weighted Imaging for Improving Conspicuity of the Bowel Inflammation in Crohn's Disease. *European Congress of Radiology 2017.03.01 Vienna*
2. Kitazume Y, Fujioka T, Takenaka K, Oyama J, Matsuoka K, Fujii T, Nagahori M, Ohtsuka K, Tateishi U. Magnetic Resonance Enterocolonography Scoring System for Crohn's disease: derivation and validation study. *European Congress of Radiology 2017.03.01*
3. Kazunori Kubota, Tomoyuki Fujioka, Akira Toriihara, Ukihide Tateishi, Yukihisa Saida. FDG-PET/CT Pitfalls in Breast Cancer. *ECR 2017 2017.03.03*
4. Kazunori Kubota, Tomoyuki Fujioka, Akira Toriihara, Yukihisa Saida, Ukihide Tateishi. Utility of 18F-FDG PET/CT and MRI imaging findings for predicting the clinicopathologic subtypes of triple negative breast cancer. *ECR 2017 2017.03.04*
5. Kazunori Kubota, Tomoyuki Fujioka, Yukihisa Saida, Ukihide Tateishi. The Role of Abbreviated Breast DWI. *The 76th Annual Meeting of the Japan Radiological Society 2017.04.13 Yokohama*
6. Kitazume Y, Takenaka K, Fujioka T, Ohtsuka K, Watanabe M, Saida Y, Tateishi U. Development and Validation of Magnetic Resonance Enterocolonography scoring system for Crohn's disease using Decision Tree Analysis. *The 76th Annual Meeting of the Japan Radiological Society 2017.04.15*
7. Ukihide Tateishi. Special project for QIBA RSNA/QIBA: Nuclear Medicine. *76th Annual Meeting of JRS 2017.04.16 Yokohama*

8. Ukihide Tateishi. Diagnostic Imaging Guideline 2016 Revised Point of Nuclear Medicine Field. 76th Annual Meeting of JRS 2017.04.18 Yokohama
9. Yoshio Kitazume. Recent and emerging imaging techniques to evaluate IBD. The 6th asian congress of abdominal radiology 2017.04.21 Busan
10. Ukihide Tateishi. regulations and ethics. Japanese Society of Nuclear Medicine 2017.04.22 Tokyo, Akihabara UDX
11. Ukihide Tateishi. PET-CT reading seminar. PET-CT reading seminar 2017.05.20 Tokyo, Station Conference
12. Kazuma Toda, Akira Toriihara, Keiko Nakagawa, Mio Kojima, Takuya Nagano, Ukihide Tateishi, Ryoichi Yoshimura. Time Dependency of Volume-Based Metabolic Parameters Obtained by Dual-Time-Point TOF-PET/CT for Head and Neck Squamous Cell Cancer. ASTRO 59th annual meeting 2017.09.26 San Diego
13. Yamada I, Hikishima K, Yoshino N, Sakamoto J, Miyasaka N, Yamauchi S, Uetake H, Yasuno M, Saida Y, Tateishi U, Kobayashi D, Eishi Y. Colorectal Carcinoma: Ex Vivo Evaluation using q-Space Imaging and its Correlation with Histopathologic Findings (Yamada I, et al.). The 103rd Scientific Assembly and Annual Meeting of the Radiological Society of North America 2017.11.27 Chicago, USA
14. Yamada I, Yoshino N, Hikishima K, Sakamoto J, Oikawa Y, Harada H, Kurabayashi T, Saida Y, Tateishi U, Izumo T, Asahina S. Oral Carcinoma: Clinical Evaluation using Diffusion Kurtosis Imaging and its Correlation with Histopathologic Findings (Yamada I, et al.). The 103rd Scientific Assembly and Annual Meeting of the Radiological Society of North America 2017.12.01 Chicago, USA

Disease Genomics

Shumpei Ishikawa: Professor
Hiroto Katoh: Assistant Professor
Daisuke Komura: Assistant Professor
Hirofumi Nakanishi: Collaborative Researcher
Reiko Sato: Technical Assistant
Asami Yamamoto: Technical Assistant
Ryouhei Suzuki: Technical Assistant
Hiroki Konishi: Technical Assistant
Ken Tominaga: Technical Assistant
Keisuke Fukuta: Technical Assistant
Chihiro Tonegawa: Technical Assistant
Miharu Tamukai: Secretary

(1) Outline

Tumor tissue is a complex system composed of tumor cells and multiple types of stromal cells. Our purpose is to understand the dynamic multicellular interactions in such a complexed biological system by measuring a large amount of data at the genomic level, which leads the identifications of therapeutic targets and biomarkers. Another objective in the graduate course is to learn the applications, methods and interpretations of the disease genomics and to understand how to apply disease genomics to clinical fields through analyzing clinical human samples.

Laboratory Web site: <http://www.tmd.ac.jp/english/gpat/>

(2) Research

- ① Genomic approach for cancer - stromal interaction
- ② Cancer immunogenomics
- ③ Genomic analysis of clinical cancer samples
- ④ Functional genomic screening in cancer
- ⑤ Image analysis and machine learning in digital pathology

(3) Publications

[Original Articles]

1. Shikata Y, Yoshimaru T, Komatsu M, Katoh H, Sato R, Kanagaki S, Okazaki Y, Toyokuni S, Tashiro E, Ishikawa S, Katagiri T, Imoto M. Protein kinase A inhibition facilitates the antitumor activity of xanthohumol, a valosin-containing protein inhibitor. *Cancer Science*. 2017.01;
2. Yukinobu Ito, Daichi Maeda, Makoto Yoshida, Akihiko Yoshida, Yukitsugu Kudo-Asabe, Hiroshi Nanjyo, Chikako Izumi, Fumio Yamamoto, Masahiro Inoue, Hiroyuki Shibata, Hiroto Katoh, Shumpei Ishikawa, Hiromi Nakamura, Yasushi Totoki, Tatsuhiro Shibata, Shinichi Yachida, Akiteru Goto. Cardiac intimal sarcoma with PDGFR β mutation and co-amplification of PDGFR α and MDM2: an autopsy case analyzed by whole-exome sequencing. *Virchows Archiv*. 2017.05;

3. Shunsuke Kon, Kojiro Ishibashi, Hiroto Katoh, Sho Kitamoto, Takanobu Shirai, Shinya Tanaka, Mihoko Kajita, Susumu Ishikawa, Hajime Yamauchi, Yuta Yako, Tomoko Kamasaki, Tomohiro Matsumoto, Hiro-taka Watanabe, Riku Egami, Ayana Sasaki, Atsuko Nishikawa, Ikumi Kameda, Takeshi Maruyama, Rika Narumi, Tomoko Morita, Yoshiteru Sasaki, Ryosuke Enoki, Sato Honma, Hiromi Imamura, Masanobu Oshima, Tomoyoshi Soga, Jun-Ichi Miyazaki, Michael R Duchon, Jin-Min Nam, Yasuhito Onodera, Shingo Yoshioka, Junichi Kikuta, Masaru Ishii, Masamichi Imajo, Eisuke Nishida, Yoichiro Fujioka, Yusuke Ohba, Toshiro Sato, Yasuyuki Fujita. Cell competition with normal epithelial cells promotes apical extrusion of transformed cells through metabolic changes. *Nature Cell Biology*. 2017.05; 19(5); 530-541
4. Katoh H, Komura D, Konishi H, Suzuki R, Yamamoto A, Kakiuchi M, Sato R, Ushiku T, Yamamoto S, Tatsuno K, Oshima T, Nomura S, Seto Y, Fukayama M, Aburatani H, Ishikawa S. Immunogenetic Profiling for Gastric Cancers Identifies Sulfated Glycosaminoglycans as Major and Functional B Cell Antigens in Human Maligancies *Cell Reports*. 2017.08; 20(5); 1073-1087
5. Hiroki Konishi, Daisuke Komura, Hiroto Katoh, Shinichiro Atsumi, Hirotomo Koda, Asami Yamamoto, Yasuyuki Seto, Masashi Fukayama, Rui Yamaguchi, Seiya Imoto, Shumpei Ishikawa. Capturing the Difference in Humoral Immunity between Normal and Tumor Environments from RNA Sequences of B-Cell Receptors Using Supervised Machine Learning. *bioRxiv*. 2017.09; 187120;

[Misc]

1. Shumpei Ishikawa. Hereditary gastroesophageal cancer *The Journal of Adult Diseases*. 2017.07; 47(7); 831-836
2. Hiroto Katoh, Shumpei Ishikawa. Genomic and Immunological Profiles of Gastric Carcinoma *BIO Clinica*. 2017.08; 6(3); 41-46
3. Daisuke Komura, Shumpei Ishikawa. Machine learning methods for histopathological image analysis *arXiv*. 2017.09;
4. Florian Rubelt, Christian E Busse, et.al.. Adaptive Immune Receptor Repertoire Community recommendations for sharing immune-repertoire sequencing data *Nature Immunology*. 2017.12;

[Conference Activities & Talks]

1. Tsuyoshi Chijiwa, Mizuha Haraguchi, Daisuke Komura, Akira Noguchi, Manabu Shiozawa, Makoto Katayama, Naoki Miyao, Naruaki Matsui, Yuichi Tateishi, Hiroshi Suemizu, Yoshiyasu Nakamura, Takayuki Isagawa, Hiroto Katoh, Shumpei Ishikawa, Masato Nakamura, Yohei Miyagi. Comprehensive and serial analyses of tumor-stroma interactions in individual PDX/NOG models contribute to personalized chemotherapy. AACR International Conference on New Frontiers in Cancer Research 2017.01.18
2. Daisuke Komura, Takayuki Isagawa, Ryohei Suzuki, Kazuki Kishi, Reiko Sato, Hiroto Katoh, Tsuyoshi Ishii, Takahiro Ochiya, Shumpei Ishikawa. Interactome analysis of xenograft models of human cells in mice. The 16th Congress of the Japanese Society for Regenerative Medicine 2017.03.07
3. Shumpei Ishikawa. Genomic Pathology and Therapeutic Targets of Gastric Cancer. 89th Annual Meeting of the Japanese Gastric Cancer Association 2017.03.10 Hiroshima, Japan
4. Shumpei Ishikawa. Global analysis of Cancer-Stromal Interactome by PDX Transcriptome Sequencing. Humanized Mice and Patient Derived Xenografts in Individualized Medicine 2017.03.16 Yokohama, Japan
5. Tsuyoshi Chijiwa, Daisuke Komura, Mizuha Haraguchi, Akira Noguchi, Hidemitsu Sato, Hiroaki Ito, Haruhiko Nakayama, Makoto Katayama, Naoki Miyao, Naruaki Matsui, Yuichi Tateishi, Hiroshi Suemizu, Yoshiyasu Nakamura, Daisuke Furukawa, Takayuki Isagawa, Hiroto Katoh, Shumpei Ishikawa, Masato Nakamura, Yohei Miyagi. An interactome analysis for personalized chemotherapy using PDX/NOG models of non-small cell lung cancer. AACR Annual Meeting 2017 2017.04.01 Walter E. Washington Convention Center Washington, D.C., USA
6. Keisuke Fukuta, Daisuke Komura, Tatsuya Harada, Shumpei Ishikawa. Identifying Metastatic Breast Cancer using Deep Texture Representation. CAMELYON17 in IEEE International Symposium on Biomedical Imaging 2017 2017.04.18 Melbourne, Australia

7. Ryohei Suzuki, Daisuke Komura, Shumpei Ishikawa. Hybrid Prediction Model for Thyroid Cancer Diagnosis. A Grand Challenge for Tissue Microarray Analysis in Thyroid Cancer Diagnosis in IEEE International Symposium on Biomedical Imaging 2017 2017.04.18 Melbourne, Australia
8. Mariko Tanaka, Shumpei Ishikawa, Tetsuo Ushiku, Teppei Morikawa, Hiroto Katoh, Junichi Arita, Yoshihiro Sakamoto, Kiyoshi Hasegawa, Norihiro Kokudo, Masashi Fukayama. EVI1 modulates oncogenic role of GPC1 in pancreatic carcinogenesis. The 106th Annual Meeting of the Japanese Society of Pathology 2017.04.27
9. Daisuke Komura, Ryohei Suzuki, Ken Tominaga, Shumpei Ishikawa. Digital histopathological image analysis using deep learning. The 106th Annual Meeting of the Japanese Society of Pathology 2017.04.27
10. Hiroto Katoh, Daisuke Komura, Hiroki Konishi, Asami Yamamoto, Masashi Fukayama, Shumpei Ishikawa. Immunogenetic profiling of tumor-infiltrating T cells in human gastric carcinoma.. The 106th Annual Meeting of the Japanese Society of Pathology 2017.04.27
11. Daisuke Komura, Takayuki Isagawa, Ryohei Suzuki, Reiko Sato, Hiroto Katoh, Mariko Tanaka, Shogo Yamamoto, Masashi Fukayama, Hiroyuki Aburatani, Shumpei Ishikawa. A system for comprehensive analysis of cancer-stromal interactome for target discovery. The 106th Annual Meeting of the Japanese Society of Pathology 2017.04.28
12. Akihiro Suzuki, Miwako Kakiuchi, Shumpei Ishikawa, Hiroyuki Aburatani. Genomic classification of gastric cancer for treatment selection. The Biology of Genomes 2017.05.09 New York
13. Shumpei Ishikawa, Hiroto Katoh, Daisuke Komura, Hiroyuki Aburatani. Global immunogenetic repertoire profiling of tumor-infiltrating B- and T-cells among gastric carcinoma.. The 13th Scientific Workshop of the ICGC 2017.06.12 the Millennium Seoul Hilton in Seoul, South Korea
14. Daisuke Komura, Takayuki Isagawa, Ryohei Suzuki, Reiko Sato, Mariko Tanaka, Shogo Yamamoto, Masashi Fukayama, Hiroyuki Aburatani, Shumpei Ishikawa. CASTIN: a system for comprehensive analysis of cancer-stromal interactome.. The 12th International Workshop on Advanced Genomics 2017.06.27 National Center of Sciences, Tokyo, Japan
15. Hiroto Katoh, Daisuke Komura, Hiroki Konishi, Ryohei Suzuki, Asami Yamamoto, Masashi Fukayama, Hiroyuki Aburatani, Shumpei Ishikawa. Immunogenomic Repertoire Characterization of Tumor-infiltrating Lymphocytes in Gastric Carcinoma.. The 12th International Workshop on Advanced Genomics 2017.06.27 National Center of Sciences, Tokyo, Japan
16. Shumpei Ishikawa. Global immunogenomic profiling and discovery of functional antigen receptors in gastric cancer. International Conference for Precision Cancer Medicine 2017.06.30 Akio Suzuki Memorial Hall, Medical Research Institute, Tokyo Medical and Dental University
17. Hiroki Konishi, Daisuke Komura, Seiya Imoto, Rui Yamaguchi, Shumpei Ishikawa. Capturing Difference of Humoral Immunity in Normal- and Tumor-Environment from RNA-Sequences of B-Cell Receptors Using Machine Learning.. 17th International Workshop on Bioinformatics and Systems Biology 2017.07.24 Berlin Medical Historical Museum of the Charité, Berlin, Germany
18. Tsuyoshi Chijiwa, Akira Noguchi, Daisuke Komura, Makoto Katayama, Mizuha Haraguchi, Haruo Hashimoto, Hiroshi Suemizu, Yoshiyasu Nakamura, Daisuke Furukawa, Takayuki Isagawa, Hiroto Katoh, Takashi Moriya, Shumpei Ishikawa, Masato Nakamura and Yohei Miyagi. The prevention of lymphoproliferative lesions arising in patient-derived cancer xenografts by anti-graft-versus-host-disease agents. AACR Advances in Modeling Cancer in Mice: Technology, Biology, and Beyond 2017.09.24 Orlando, Florida
19. Hiroto Katoh, Daisuke Komura, Shumpei Ishikawa. Single cell analysis for the human gastric cancer environments. Cold Spring Harbor Laboratory Meeting, Single Cell Analyses 2017.11.08 Cold Spring Harbor, NY, USA

Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka
Project Assistant Professor, Ryo Watanabe

(1) Research

- 1) Elucidation of genetic architecture of human metabolic diseases using genome and meta-genome information
- 2) Identification of biomarkers for personalized medicine
- 3) Pharmacogenomics
- 4) Functional genomics
- 5) Statistical genetics and genome drug discovery

(2) Lectures & Courses

As we say “Every human is different”, human genetic diversity has essential impacts on clinical fields, e.g. disease risk, clinical efficacy, and drug responses. Our laboratory aims to elucidate the diversity of human being through comprehensive research activities including genome and epi-genome analyses of human diseases, methodological development of statistical genetics, and human resources cultivation to achieve personalized medicine.

(3) Publications

[Original Articles]

1. Sato H, Suzuki J, Aoyama N, Watanabe R, Kaneko M, Shiheido Y, Yoshida A, Wakayama K, Kumagai H, Ikeda Y, Akazawa H, Komuro I, Isobe M, Izumi Y. A Periodontal pathogen *Porphyromonas gingivalis* deteriorates Isoproterenol-Induced myocardial remodeling in mice. *Hypertens. Res.* 2017; 40(1); 35-40
2. Kaneko M, Suzuki J, Aoyama N, Watanabe R, Yoshida A, Shiheido Y, Izumi Y, Isobe M. Corrigendum: Toll-like receptor-2 has a critical role in periodontal pathogen-induced myocardial fibrosis in the pressure-overloaded murine hearts. *Hypertens. Res.* 2017.02; 40(2); 212
3. Kouji Wakayama, Munehisa Shimamura, Jun-Ichi Suzuki, Ryo Watanabe, Hiroshi Koriyama, Hiroshi Akazawa, Hironori Nakagami, Hideki Mochizuki, Mitsuaki Isobe, Ryuichi Morishita. Angiotensin II Peptide Vaccine Protects Ischemic Brain Through Reducing Oxidative Stress. *Stroke*. 2017.03;
4. Ryo Watanabe, Jun-Ichi Suzuki, Kouji Wakayama, Yasuhiro Maejima, Munehisa Shimamura, Hiroshi Koriyama, Hironori Nakagami, Hidetoshi Kumagai, Yuichi Ikeda, Hiroshi Akazawa, Ryuichi Morishita, Issei Komuro, Mitsuaki Isobe. A peptide vaccine targeting angiotensin II attenuates the cardiac dysfunction induced by myocardial infarction. *Sci Rep*. 2017.03; 7; 43920
5. Nagai Akiko, Hirata Makoto, Kamatani Yoichiro, Muto Kaori, Matsuda Koichi, Kiyohara Yutaka, Nomiya Toshiharu, Tamakoshi Akiko, Yamagata Zentaro, Mushiroda Taisei, Murakami Yoshinori, Yuji Koichiro, Furukawa Yoichi, Zembutsu Hitoshi, Tanaka Toshihiro, Ohnishi Yozo, Nakamura Yusuke, Kubo Michiaki, BioBank Japan Cooperative Hospital Group. Overview of the BioBank Japan Project: Study design and profile. *J Epidemiol*. 2017.03; 27(3S); S2-S8

6. Hirata Makoto, Kamatani Yoichiro, Nagai Akiko, Kiyohara Yutaka, Ninomiya Toshiharu, Tamakoshi Akiko, Yamagata Zentaro, Kubo Michiaki, Muto Kaori, Mushiroda Taisei, Murakami Yoshinori, Yuji Koichiro, Furukawa Yoichi, Zembutsu Hitoshi, Tanaka Toshihiro, Ohnishi Yozo, Nakamura Yusuke, Matsuda Koichi, BioBank Japan Cooperative Hospital Group. Cross-sectional analysis of BioBank Japan clinical data: A large cohort of 200,000 patients with 47 common diseases. *J Epidemiol.* 2017.03; 27(3S); S9-S21
7. Hirata Makoto, Nagai Akiko, Kamatani Yoichiro, Ninomiya Toshiharu, Tamakoshi Akiko, Yamagata Zentaro, Kubo Michiaki, Muto Kaori, Kiyohara Yutaka, Mushiroda Taisei, Murakami Yoshinori, Yuji Koichiro, Furukawa Yoichi, Zembutsu Hitoshi, Tanaka Toshihiro, Ohnishi Yozo, Nakamura Yusuke, Matsuda Koichi, BioBank Japan Cooperative Hospital Group. Overview of BioBank Japan follow-up data in 32 diseases. *J Epidemiol.* 2017.03; 27(3S); S22-S28
8. Yamagata Kenichiro, Horie Minoru, Aiba Takeshi, Ogawa Satoshi, Aizawa Yoshifusa, Ohe Toru, Yamagishi Masakazu, Makita Naomasa, Sakurada Harumizu, Tanaka Toshihiro, Shimizu Akihiko, Hagiwara Nobuhisa, Kishi Ryoji, Nakano Yukiko, Takagi Masahiko, Makiyama Takeru, Ohno Seiko, Fukuda Keiichi, Watanabe Hiroshi, Morita Hiroshi, Hayashi Kenshi, Kusano Kengo, Kamakura Shiro, Yasuda Satoshi, Ogawa Hisao, Miyamoto Yoshihiro, Kapplinger Jamie D, Ackerman Michael J, Shimizu Wataru. Genotype-Phenotype Correlation of SCN5A Mutation for the Clinical and Electrocardiographic Characteristics of Proband with Brugada Syndrome: A Japanese Multicenter Registry. *Circulation.* 2017.03;
9. Christophersen Ingrid E, Rienstra Michiel, Roselli Carolina, Yin Xiaoyan, Geelhoed Bastiaan, Barnard John, Lin Honghuang, Arking Dan E, Smith Albert V, Albert Christine M, Chaffin Mark, Tucker Nathan R, Li Molong, Klarin Derek, Bihlmeyer Nathan A, Low Siew-Kee, Weeke Peter E, Muller-Nurasyid Martina, Smith J Gustav, Brody Jennifer A, Niemeijer Maartje N, Dorr Marcus, Trompet Stella, Huffman Jennifer, Gustafsson Stefan, Schurmann Claudia, Kleber Marcus E, Lyytikainen Leo-Pekka, Seppala Ilkka, Malik Rainer, Horimoto Andrea R V R, Perez Marco, Sinisalo Juha, Aeschbacher Stefanie, Theriault Sebastien, Yao Jie, Radmanesh Farid, Weiss Stefan, Teumer Alexander, Choi Seung Hoan, Weng Lu-Chen, Clauss Sebastian, Deo Rajat, Rader Daniel J, Shah Svati H, Sun Albert, Hopewell Jemma C, DeBette Stephanie, Chauhan Ganesh, Yang Qiong, Worrall Bradford B, Pare Guillaume, Kamatani Yoichiro, Hagemeyer Yanick P, Verweij Niek, Siland Joylene E, Kubo Michiaki, Smith Jonathan D, Van Wagener David R, Bis Joshua C, Perz Siegfried, Psaty Bruce M, Ridker Paul M, Magnani Jared W, Harris Tamara B, Launer Lenore J, Shoemaker M Benjamin, Padmanabhan Sandosh, Haessler Jeffrey, Bartz Traci M, Waldenberger Melanie, Lichtner Peter, Arendt Marina, Krieger Jose E, Kahonen Mika, Risch Lorenz, Mansur Alfredo J, Peters Annette, Smith Blair H, Lind Lars, Scott Stuart A, Lu Yingchang, Bottinger Erwin B, Hernesniemi Jussi, Lindgren Cecilia M, Wong Jorge A, Huang Jie, Eskola Markku, Morris Andrew P, Ford Ian, Reiner Alex P, Delgado Graciela, Chen Lin Y, Chen Yii-Der Ida, Sandhu Roopinder K, Li Man, Boerwinkle Eric, Eisele Lewin, Lannfelt Lars, Rost Natalia, Anderson Christopher D, Taylor Kent D, Campbell Archie, Magnusson Patrik K, Porteous David, Hocking Lynne J, Vlachopoulou Efthymia, Pedersen Nancy L, Nikus Kjell, Orho-Melander Marju, Hamsten Anders, Heeringa Jan, Denny Joshua C, Kriebel Jennifer, Darbar Dawood, Newton-Cheh Christopher, Shaffer Christian, Macfarlane Peter W, Heilmann-Heimbach Stefanie, Almgren Peter, Huang Paul L, Sotoodehnia Nona, Soliman Elsayed Z, Uitterlinden Andre G, Hofman Albert, Franco Oscar H, Volker Uwe, Jockel Karl-Heinz, Sinner Moritz F, Lin Henry J, Guo Xiuqing, Dichgans Martin, Ingelsson Erik, Kooperberg Charles, Melander Olle, Loos Ruth J F, Laurikka Jari, Conen David, Rosand Jonathan, van der Harst Pim, Lokki Marja-Liisa, Kathiresan Sekar, Pereira Alexandre, Jukema J Wouter, Hayward Caroline, Rotter Jerome I, Marz Winfried, Lehtimäki Terho, Stricker Bruno H, Chung Mina K, Felix Stephan B, Gudnason Vilmundur, Alonso Alvaro, Roden Dan M, Kaab Stefan, Chasman Daniel I, Heckbert Susan R, Benjamin Emelia J, Tanaka Toshihiro, Lunetta Kathryn L, Lubitz Steven A, Ellinor Patrick T, METASTROKE Consortium of the ISGC. Large-scale analyses of common and rare variants identify 12 new loci associated with atrial fibrillation. *Nat Genet.* 2017.04;
10. Cassandra N Spracklen, Peng Chen, Young Jin Kim, Xu Wang, Hui Cai, Shengxu Li, Jirong Long, Ying Wu, Ya Xing Wang, Fumihiko Takeuchi, Jer-Yuarn Wu, Keum-Ji Jung, Cheng Hu, Koichi Akiyama, Yonghong Zhang, Sanghoon Moon, Todd A Johnson, Huaixing Li, Rajkumar Dorajoo, Meian He, Maren E Cannon, Tamara S Roman, Elias Salfati, Keng-Hung Lin, Xiuqing Guo, Wayne H H Sheu, Devin Absher, Linda S Adair, Themistocles L Assimes, Tin Aung, Qiuyin Cai, Li-Ching Chang, Chien-Hsiun Chen, Li-Hsin Chien, Lee-Ming Chuang, Shu-Chun Chuang, Shufa Du, Qiao Fan, Cathy S J Fann, Alan B Feranil, Yechiel Friedlander, Penny Gordon-Larsen, Dongfeng Gu, Lixuan Gui, Zhirong Guo, Chew-Kiat Heng, James Hixson, Xuhong Hou, Chao Agnes Hsiung, Yao Hu, Mi Yeong Hwang, Chii-Min Hwu, Masato Isono,

Jyh-Ming Jimmy Juang, Chiea-Chuen Khor, Yun Kyoung Kim, Woon-Puay Koh, Michiaki Kubo, I-Te Lee, Sun-Ju Lee, Wen-Jane Lee, Kae-Woei Liang, Blanche Lim, Sing-Hui Lim, Jianjun Liu, Toru Nabika, Wen-Harn Pan, Hao Peng, Thomas Quertermous, Charumathi Sabanayagam, Kevin Sandow, Jinxiu Shi, Liang Sun, Pok Chien Tan, Shu-Pei Tan, Kent D Taylor, Yik-Ying Teo, Sue-Anne Toh, Tatsuhiko Tsunoda, Rob M van Dam, Aili Wang, Feijie Wang, Jie Wang, Wen Bin Wei, Yong-Bing Xiang, Jie Yao, Jian-Min Yuan, Rong Zhang, Wanting Zhao, Yii-Der Ida Chen, Stephen S Rich, Jerome I Rotter, Tzung-Dau Wang, Tangchun Wu, Xu Lin, Bok-Ghee Han, Toshihiro Tanaka, Yoon Shin Cho, Tomohiro Katsuya, Weiping Jia, Sun-Ha Jee, Yuan-Tsong Chen, Norihiro Kato, Jost B Jonas, Ching-Yu Cheng, Xiao-Ou Shu, Jiang He, Wei Zheng, Tien-Yin Wong, Wei Huang, Bong-Jo Kim, E-Shyong Tai, Karen L Mohlke, Xueling Sim. Association analyses of East Asian individuals and trans-ancestry analyses with European individuals reveal new loci associated with cholesterol and triglyceride levels. *Hum. Mol. Genet.* 2017.05; 26(9); 1770-1784

11. Siew-Kee Low, Atsushi Takahashi, Yusuke Ebana, Kouichi Ozaki, Ingrid E Christophersen, Patrick T Ellinor, , Soichi Ogishima, Masayuki Yamamoto, Mamoru Satoh, Makoto Sasaki, Taiki Yamaji, Motoki Iwasaki, Shoichiro Tsugane, Keitaro Tanaka, Mariko Naito, Kenji Wakai, Hideo Tanaka, Tetsushi Furukawa, Michiaki Kubo, Kaoru Ito, Yoichiro Kamatani, Toshihiro Tanaka. Identification of six new genetic loci associated with atrial fibrillation in the Japanese population. *Nat. Genet.* 2017.06; 49(6); 953-958
12. T Sudo, Y Okada, K Ozaki, K Urayama, M Kanai, H Kobayashi, M Gokyu, Y Izumi, T Tanaka. Association of NOD2 Mutations with Aggressive Periodontitis. *J. Dent. Res.* 2017.06; 22034517715432
13. Yusuke Ebana, Kouichi Ozaki, Lian Liu, Hitoshi Hachiya, Kenzo Hirao, Mitsuaki Isobe, Michiaki Kubo, Toshihiro Tanaka, Tetsushi Furukawa. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25. *J Cardiol.* 2017.10; 70(4); 366-373

[Conference Activities & Talks]

1. R. Watanabe et al. Identification of novel long QT syndrome-associated mutations by targeted sequencing analyses. European Human Genetics Conference 2017.05.27 Copenhagen, Denmark
2. Toshihiro Tanaka. Genomic Medicine and Cardiovascular Diseases. 2017.06.28
3. R. Watanabe 他. Targeted deep sequencing reveals novel mutations in Japanese long QT syndrome patients.. The 62nd Annual Meeting of the Japan Society of Human Genetics 2017.11.17 Kobe.

Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Assistant Professor: Masafumi HORIE, Koji OTABE, Hisako KATANO

Project Assistant Professor: Nobutake OZEKI, Yusuke NAKAGAWA,
Mitsuru MIZUNO, Keiichiro KOMORI

Graduate Student: Kenta KATAGIRI, Yuji KONO, Naoto WATANABE,
Yoshihisa KUSHIDA, So SUZUKI, Akinobu HYODO,
Hayato AOKI, Mana NARITOMI

Technical Staff : Shizuka FUJII, Emi KODA, Atsuko TAKEBE,
Mika WATANABE

Assistant Clerk: Kimiko TAKANASHI

(1) Outline

Our purpose is to support and advance stem cell research and regenerative medicine for the discovery and development of cures, therapies, diagnostics and research technologies to relieve human suffering from chronic disease and injury.

(2) Research

- 1) Development of regenerative medicine with stem cells.
- 2) Realization and industrialization of cell and regenerative therapy.
- 3) Establishment of safety test for regenerative medicine.
- 4) Translational research.
- 5) Development of software for 3D analysis of knee MRI.

(3) Clinical Services & Other Works

Investigator initiated clinical trial “treatment for degenerative meniscus injury by autologous synovial stem cells” was started and cell transplantation was completed for 10 patients.

(4) Publications

[Original Articles]

1. Saito R, Muneta T, Ozeki N, Nakagawa Y, Udo M, Yanagisawa K, Tsuji K, Tomita M, Koga H, Sekiya I. Strenuous running exacerbates knee cartilage erosion induced by low amount of mono-iodoacetate in rats. *BMC Musculoskelet Disord.* 2017.01; 18(1); 36
2. Akihisa Hatakeyama, Soshi Uchida, Hajime Utsunomiya, Manabu Tsukamoto, Hirotaka Nakashima, Ei-ichiro Nakamura, Cecilia Pascual-Garrido, Ichiro Sekiya, Akinori Sakai. Isolation and Characterization of Synovial Mesenchymal Stem Cell Derived from Hip Joints: A Comparative Analysis with a Matched Control Knee Group. *Stem Cells Int.* 2017.01;

3. Matsumura E, Tsuji K, Komori K, Koga H, Sekiya I, Muneta T.. Pretreatment of IL-1 β enhances proliferation and chondrogenic potential of synovium-derived mesenchymal stem cells. *Cytotherapy*. 2017.02; 19(2); 181-193
4. Yuuki A, Muneta T, Ohara T, Sekiya I, Koga H.. Associated lateral/medial knee instability and its relevant factors in anterior cruciate ligament-injured knees. *J Orthop Sci*. 2017.03; 22(2); 300-305
5. Jae-Sung An, Takeshi Muneta, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Hideyuki Koga. Osteochondral lesion of lateral tibial plateau with extrusion of lateral meniscus treated with retrograde osteochondral autograft transplantation and arthroscopic centralisation. *AP-SMART*. 2017.04; 8; 18-23
6. Mai Katakura, Hideyuki Koga, Kaori Nakamura, Ichiro Sekiya, Takeshi Muneta. Effects of different femoral tunnel positions on tension changes in anterolateral ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2017.04; 25(4); 1272-1278
7. Katagiri Kenta, Yu Matsukura, Takeshi Muneta, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Ichiro Sekiya.. Fibrous synovium releases higher numbers of mesenchymal stem cells than adipose synovium in a suspended synovium culture model. *Arthroscopy*. 2017.04; 33(4); 800-810
8. Mikio Shioda, Takeshi Muneta, Kunikazu Tsuji, Mitsuru Mizuno, Keiichiro Komori, Hideyuki Koga, Ichiro Sekiya. TNF α promotes proliferation of human synovial MSCs while maintaining chondrogenic potential. *PLoS ONE*. 2017.05; 12(5); e0177771
9. Takao Minami, Takeshi Muneta, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Hideyuki Koga. Lateral meniscus posterior root tear contributes to anterolateral rotational instability and meniscus extrusion in anterior cruciate ligament-injured patients. *Knee Surg Sports Traumatol Arthrosc*. 2017.05; 26(4); 1174-1181
10. Nobutake Ozeki, Takeshi Muneta, Kenichi Kawabata, Hideyuki Koga, Yusuke Nakagawa, Ryusuke Saito, Mio Udo, Katsuaki Yanagisawa, Toshiyuki Ohara, Tomoyuki Mochizuki, Kunikazu Tsuji, Tomoyuki Saito, Ichiro Sekiya. Centralization of extruded medial meniscus delays cartilage degeneration in rats. *J Orthop Sci*. 2017.05; 22(3); 542-548
11. Yuji Kohno, Mitsuru Mizuno, Nobutake Ozeki, Hisako Katano, Keiichiro Komori, Shizuka Fujii, Koji Otabe, Masafumi Horie, Hideyuki Koga, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaneko, Yuji Takazawa, Takeshi Muneta, Ichiro Sekiya. Yields and chondrogenic potential of primary synovial mesenchymal stem cells are comparable between rheumatoid arthritis and osteoarthritis patients. *Stem Cell Res Ther*. 2017.05; 8(1); 115
12. Kunikazu Tsuji, Miyoko Ojima, Koji Otabe, Masafumi Horie, Hideyuki Koga, Ichiro Sekiya, Takeshi Muneta. Effects of Different Cell-Detaching Methods on the Viability and Cell Surface Antigen Expression of Synovial Mesenchymal Stem Cells. *Cell Transplant*. 2017.06; 26(6); 1089-1102
13. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yuji Kohno, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Hideyuki Koga, Takeshi Muneta, Ichiro Sekiya. Complete human serum maintains viability and chondrogenic potential of human synovial stem cells: suitable conditions for transplantation. *Stem Cell Res Ther*. 2017.06; 8(1); 144
14. Carballo CB, Nakagawa Y, Sekiya I, Rodeo SA.. Basic Science of Articular Cartilage. *Clin Sports Med*.. 2017.07; 36(3); 413-425
15. Eriko Grace Suto, Yo Mabuchi, Nobuharu Suzuki, Koji Suzuki, Yusuke Ogata, Miyu Taguchi, Takeshi Muneta, Ichiro Sekiya, Chihiro Akazawa. Prospectively isolated mesenchymal stem/stromal cells are enriched in the CD73(+) population and exhibit efficacy after transplantation. *Sci Rep*. 2017.07; 7(1); 4838
16. Kei Inomata, Ichiro Sekiya, Koji Otabe, Tomomasa Nakamura, Masafumi Horie, Hideyuki Koga, Toshifumi Watanabe, Takeshi Muneta. Acute arterial occlusion after total knee arthroplasty: a case report. *Clin Case Rep*. 2017.08; 5(8); 1376-1380
17. Hideyuki Koga, Toshifumi Watanabe, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Toshiyuki Ohara, Mai Katakura, Ichiro Sekiya, Takeshi Muneta. Augmentation of the pullout repair of a medialmeniscus posterior root tear by arthroscopic centralization 2017.08; 6(4); 1335-1339

18. Kaori Nakamura, Hideyuki Koga, Ichiro Sekiya, Toshifumi Watanabe, Tomoyuki Mochizuki, Masafumi Horie, Tomomasa Nakamura, Koji Otabe, Takeshi Muneta. Evaluation of pivot shift phenomenon while awake and under anaesthesia by different manoeuvres using triaxial accelerometer. *Knee Surg Sports Traumatol Arthrosc.* 2017.08; 25(8); 2377-2383
19. Ichiro Sekiya, Darwin J.Prockop.. Beginning of an Unresolved Debate:Should Mesenchymal Stem Cells Be Expanded at Low Density to Preserve Early Progenitors? *STEM CELLS 35Anniversary.* 2017.09; 1; 36-37
20. Toshifumi Watanabe, Hideyuki Koga, Masafumi Horie, Hiroki Katagiri, Ichiro Sekiya, Takeshi Muneta. Post-Cam Design and Contact Stress on Tibial Posts in Posterior-Stabilized Total Knee Prostheses: Comparison Between a Rounded and a Squared Design. *J Arthroplasty.* 2017.12; 32(12); 3757-3762

[Conference Activities & Talks]

1. Ichiro Sekiya. Preclinical and Clinical Studies of Meniscus Regeneration by Synovial Stem Cells. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 SanDiego, USA
2. Naoto Watanabe, Mitsuru Mizuno, Jumpei Matsuda, Hisako Katano, Nobutake Ozeki, Koji Otabe, Keiichiro Komori, Yuji Kono, Kenta Katagiri, Takeshi Muneta, Ichiro Sekiya.. Decellularization of the meniscus by high hydrostatic pressure: temperature condition for removal of cell debris.. Orthopaedic Research Society 2017 Annual Meeting 2017.03.20 SanDiego, USA
3. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya.. Recombinant peptide petaloid pieces enhance in vitro cartilage formation of mesenchymal stem cells. Orthopaedic Research Society 2017 Annual Meeting 2017.03.20 SanDiego, USA
4. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yuji Kohno, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya.. Complete Human Serum Maintains Viability and Chondrogenic Potential of Human Synovial Stem Cells: Suitable Condition for Transplantation. Orthopaedic Research Society 2017 Annual Meeting 2017.03.21 SanDiego, USA
5. Koji Otabe, Mai Katakura, Toshiyuki Ohara, Kaori Nakamura, Masafumi Horie, Hideyuki Koga, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta.. Automatic Knee X Ray Analysis System Reveals that Meniscus Repair during Anterior Cruciate Ligament Reconstruction Surgery cannot prevent the Development of Osteoarthritis. Orthopaedic Research Society 2017 Annual Meeting 2017.03.21 SanDiego, USA
6. Kenta Katagiri, Mitsuru Mizuno, Hideyuki Koga, Nobutake Ozeki, Yusuke Nakagawa, Yuji Kono, Koji Otabe, Masafumi Horie, Hisako Katano, Kunikazu Tsuji, Hideo Ono, Takeshi Muneta, Ichiro Sekiya.. Transplantation of Synovial Mesenchymal Stem Cells Enhances the Effect of Cetralization with Suture Anchor and Promotes Meniscus Regeneration for Extruded Meniscus After Partial Meniscectomy in Mice. Orthopaedic Research Society 2017 Annual Meeting 2017.03.22 SanDiego, USA
7. Yuji Kono, Mitsuru Mizuno, Kenta Katagiri, Koji Otabe, Nobutake Ozeki, Hisako Katao, Keiichiro Komori, Masafumi Horie, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaeko, Yuji Takazawa, Takeshi Muneta, Ichiro Sekiya.. Harvested cell number varies greater in RA than in OA after a suspended synovium culture. Orthopaedic Research Society 2017 Annual Meeting 2017.03.22 SanDiego, USA

[Awards & Honors]

1. Yusuke Nakagawa, Best Poster Presentation Award, Japanese Medical Society of America, Japan Society for the Promotion of Science, 2017.04

Minimally Invasive Medical Treatment

Professor KOJIMA Kazuyuki

(1) Outline

1. Investigation and research for the social needs identification of minimally invasive medical treatment in the next generation of the medical and the dental areas.
2. Medical equipment and development of treatment to meet the needs of minimally invasive medical treatment in the next generation of the medical and the dental fields.
3. Research and development of the education curriculum and evaluation methods of minimally invasive treatment in the medical and the dental fields.
4. Development and operation of minimally invasive treatment of industry-academia cooperation in the medical and the dental fields.
5. Development and operation of technology certification strategy of minimally invasive treatment in the medical and the dental areas.

(2) Publications

[Original Articles]

1. Hiki N, Katai H, Mizusawa J, Nakamura K, Nakamori M, Yoshikawa T, Kojima K, Imamoto H, Ninomiya M, Kitano S, Terashima M. Stomach Cancer Study Group of Japan Clinical Oncology Group. Long-term outcomes of laparoscopy-assisted distal gastrectomy with suprapancreatic nodal dissection for clinical stage I gastric cancer: a multicenter phase II trial (JCOG0703) *Gastric Cancer*. 2017.01; published online;
2. Inokuchi M, Murase H, Otsuki S, Kawano T, Kojima K. Different clinical significance of FGFR1-4 expression between diffuse-type and intestinal-type gastric cancer *World J Surg Oncol*. 2017.01; 15(1);
3. Tomii C, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. TPX2 expression is associated with poor survival in gastric cancer *World J Surg Oncol*. 2017.01; 15(1);
4. Higuchi K, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. Cadherin 5 expression correlates with poor survival in human gastric cancer *J Clin Pathol*. 2017.03; 70; 217-221
5. Keisuke Okuno, Kentaro Gokita, Toshiro Tanioka, Norihito Ogawa, Sho Otsuki, Mikito Inokuchi, Toshio Takayama, Kazuyuki Kojima. Esophagojejunostomy Using the Purse-String Suturing Device After Laparoscopic Total or Proximal Gastrectomy for Gastric Cancer *World J Surg*. 2017.04; published online;
6. Tomoki Aburatani, Kazuyuki Kojima, Sho Otsuki, Hideaki Murase, Keisuke Okuno, Kentaro Gokita, Chi-haru Tomi, Toshiro Tanioka, Mikito Inokuchi. Double-tract reconstruction after laparoscopic proximal gastrectomy using detachable ENDO-PSD *Surg Endosc*. 2017.04; published online;
7. Baongoc Nasri, Mikito Inokuchi, Toshiaki Ishikawa, Hiroyuki Uetake, Yoko Takagi, Sho Otsuki, Kazuyuki Kojima, Tatsuyuki Kawano. High expression of EphA3 (erythropoietin-producing hepatocellular A3) in gastric cancer is associated with metastasis and poor survival *BMC Clin Pathol*. 2017.04; 17;

8. Mikito Inokuchi, Masatoshi Nakagawa, Toshiro Tanioka, Keisuke Okuno¹, Kentaro Gokita, Kazuyuki Kojima. Long- and short-term outcomes of laparoscopic gastrectomy versus open gastrectomy in patients with clinically and pathological locally advanced gastric cancer: a propensityscore matching analysis *Surgical Endoscopy*. 2017.07; published online;
9. Tomoki Aburatani, Mikito Inokuchi, Yoko Takagi, Toshiaki Ishikawa, Keisuke Okuno, Kentaro Gokita, Chiharu Tomii, Toshiro Tanioka, Hideaki Murase, Sho Otsuki, Hiroyuki Uetake, Kazuyuki Kojima, Tatsuyuki Kawano. High expression of P21-activated kinase 5 protein is associated with poor survival in gastric cancer. *Oncol Lett*. 2017.07; 14(1); 404-410
10. Mikito Inokuchi, Toshiro Tanioka, Masatoshi Nakagawa, Keisuke Okuno, Kentaro Gokita, Kazuyuki Kojima. Laparoscopic Distal Gastrectomy is Feasible in Very Elderly Patients as Compared with Open Distal Gastrectomy. *JOURNAL OF INVESTIGATIVE SURGERY*. 2017.08; 1-7
11. Mikito Inokuchi, Toshiro Tanioka, Masatoshi Nakagawa, Kazuyuki Kojima. Intracorporeal esophagojejunostomy with Roux-en-Y reconstruction after laparoscopic total gastrectomy *Annals of Laparoscopic and Endoscopic Surgery*. 2017.10; 2(153);
12. M. Nakagawa, C. Tomii¹, M. Inokuchi, S. Otsuki¹, K. Kojima. Feasibility Of A Clinical Pathway With Early Oral Intake And Discharge For Laparoscopic Gastrectomy *Scandinavian journal of surgery*. 2017.12; Published online ;
13. Inokuchi M, Otsuki S, Ogawa N, Tanioka T, Okuno K, Gokita K, Kawano T, Kojima K. Postoperative Complications of Laparoscopic Total Gastrectomy versus Open Total Gastrectomy for Gastric Cancer in a Meta-Analysis of High-Quality Case-Control Studies. *Gastroenterology Res Pract*.
14. Yamada I, Hikishima K, Miyasaka N, Kato K, Ito E, Kojima K, Kawano T, Kobayashi D, Eishi Y, Okano H. q-Space MR Imaging of Gastric Carcinoma Ex Vivo: Correlation with Histopathologic Findings. *Magn Reson Med*.
15. Inokuchi M, Otsuki S, Murase H, Kojima K, Kawano T. Feasibility of laparoscopy-assisted gastrectomy for patients with poor physical status: A propensity-score matching study. *Int J Surg*.
16. Akiyama Y, Koda Y, Byeon SJ, Shimada S, Nishikawaji T, Sakamoto A, Chen Y, Kojima K, Kawano T, Eishi Y, Deng D, Kim WH, Zhu WG, Yuasa Y, Tanaka S. Reduced expression of SET7/9, a histone mono-methyltransferase, is associated with gastric cancer progression. *Oncotarget*.
17. Kobayashi k, Inokuchi M, Takagi Y, Otsuki S, Fujimori Y, Sato Y, Yanaka Y, Higuchi K, Aburatani T, Tomii C, Uetake H, Kojima K, Kawano T. Prognostic significance of PAK4 expression in gastric cancer. *J Clin Pathol*.
18. Yamada I, Hikishima K, Miyasaka N, Kato K, Kojima K, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H. Gastric carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. *Magnetic Resonance Imaging*.

[Conference Activities & Talks]

1. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Norihito Ogawa, Mikito Inokuchi, Kazuyuki Kojima.. Roux-en-Y reconstruction after LDG - surgical technique and functional advantages . China-Japan-Korea Laparoscopic gastrectomy 2017.02.11
2. Kazuyuki Kojima. Esophagojejunostomy using a circular stapler with a purse-string suturing device. Korea International Gastric Cancer Week 2017 2017.03.25
3. Keisuke Okuno, Kentaro Gokita, Toshiro Tanioka, Norihito Ogawa, Sho Otsuki, Mikito Inokuchi, Kazuyuki Kojima. A study on gastroesophageal reflux disease after laparoscopic distal gastrectomy. 12th International Gastric Cancer Congress 2017.04.21
4. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Mikito Inokuchi, Kazuyuki Kojima. Effect of postoperative complications on the long-term survival of patients with gastric cancer. 12th International Gastric Cancer Congress 2017.04.21

5. Masatoshi Nakagawai, Mikito Inokuchi, Sho Otuki, Norihito Ogawa, Toshiro Tanioka, Kazuyuki Kojima. Is laparoscopic approach an effective tool for total gastrectomy to obese patients. 12th International Gastric Cancer Congress 2017.04.22
6. Kazuyuki Kojima. Endoscopic Surgical Skill Qualification System – Laparoscopic gastrectomy. The Korean Society of Endoscopic and Laparoscopic Surgeons 2017.05.16
7. Kazuyuki Kojima. “JSES’ accreditation system. Seoul National University Bundang Hospital 2017.05.17
8. Kazuyuki Kojima. Standardization of laparoscopic surgery for upper gastric cancer in our department. The third session of Changchun International Gastrointestinal Surgery Summit Forum and Sino-Japanese Korean Gastrointestinal Seminar 2017.07.07
9. K.Kojima, T.Tanioka, M.Inokuchi. Reconstruction after laparoscopic gastrectomy-Our procedure and clinical results-. Japan Digestive Disease Week 2017 2017.10.13 Fukuoka
10. Toshiro Tanioka, Keisuke Okuno, Kentaro Gokita, Masatoshi Nakagawa, Mikito Inokuchi, Kazuyuki Kojima. An Intraoperative Educational Annotation System for Endoscopic Surger. 103th Annual Clinical Congress of the American College of Surgeons(ACS2017) 2017.10.25 San Diego(USA)

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi
Junior Associate Professor: Takahiro Arakawa
Assistant Professor: Koji Toma
Lecturer (part-time): Kazuyoshi Yano

(1) Outline

Our research is based on a broad range of areas such as electrochemistry, mechanical engineering, electrical engineering, material science and biochemistry. The group aims to pursue interdisciplinary research in bio-MEMS, bio-optics, bio-electronics or bioinformatics by combining biotechnology and information technology.

(2) Research

1. Detachable “Cavitas sensors” as bioinformation monitoring systems in body cavities

“Cavitas sensors” such as a soft contact-lens biosensor and a mouth guard biosensor have been developed for novel biomonitoring methods by using advanced polymer microelectromechanical systems (MEMS) techniques.

2. Biochemical gas sensor “Bio-sniffers” and spatiotemporal gas visualization system “Sniff-camera” for volatile organic compounds from human body

Highly selective gas sensors “Bio-sniffers” and gas visualization systems “Sniff-camera” for acquiring spatiotemporal information of distribution of volatile chemicals have been developed by exploiting metabolizing enzymes in human liver. Potential applications of these gas sensors include halitosis analysis, breath alcohol and aldehyde measurement, medical screening or dental health, etc.

3. Immunosensors for medical treatment and environmental medicine

Development of optical or surface acoustic wave immunosensors have been pursued for semi-continuous (rapid and repeated) measurement of antigens in body and airborne allergens in living environment.

4. “Organic engine” based on chemo-mechanical energy conversion

A novel chemo-mechanical energy conversion system (organic engine) that utilizes enzyme reactions and active transport of chemicals have been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

(3) Education

In advanced medicine, technologies enabling to accurately measure biological information are highly demanded. The development of “human-friendly” non-invasive measurement methods could release patients from the pain and the risks of sampling. The students will learn the basic knowledge and skills of biological information measurement through the lectures (e.g., “Biomedical Device Science and Engineering”, “Practice in Global Linkage between University and Industry” and “Nanobiotechnology”), seminars and practical training. Especially research including biochemical measurement, the development of biosensing devices and their applications to medicine will be carried out based on “sensor and biomedical engineering.”

(4) Lectures & Courses

The students will learn the basic technology related to advanced medicine and biological information measurement. Through practical training, they will also engage in research activities for biochemical measurement, the development of biosensing devices and their applications to medicine based on “sensor and biomedical engineering”. The objective of this course is to help the students be able to think about and conduct a research by themselves throughout the activities with academic researches.

(5) Publications**[Original Articles]**

1. Takahiro Arakawa, Toshiyuki Sato, Kenta Iitani, Koji Toma, Kohji Mitsubayashi. Fluorometric biosniffer camera “Sniff-cam” for direct imaging of gaseous ethanol in breath and transdermal vapor *Analytical Chemistry*. 2017.04; 89(8); 4495-4501
2. Po-Jen Chien, Takuma Suzuki, Masato Tsujii, Ming Ye, Koji Toma, Takahiro Arakawa, Yasuhiko Iwasaki, Kohji Mitsubayashi. Bio-sniffer (gas-phase biosensor) with secondary alcohol dehydrogenase (S-ADH) for determination of isopropanol in exhaled air as a potential volatile biomarker. *Biosensors and Bioelectronics*. 2017.05; 91; 341-346
3. Daisuke Mori, Koji Kurihara, Munkhjargal Munkhbayar, Koji Toma, Takahiro Arakawa, Kazuyoshi Yano, Kohji Mitsubayashi. Glucose driven drug release system using improved decompression unit *IEEE Transactions on Sensors and Micromachines*. 2017.06; 137(6); 174-178
4. Kohji Mitsubayashi. Body cavity sensors offer monitoring solutions in daily medicine *TMDU Research Activities*. 2017.06; 13
5. Kenta Iitani, Toshiyuki Sato, Munire Naisierding, Yuuki Hayakawa, Koji Toma, Takahiro Arakawa, Kohji Mitsubayashi. Fluorometric gas-imaging system (sniff-cam), using the extinction of NADH with an ADH reverse reaction, for acetaldehyde in the gas phase. *Analyst*. 2017.07;
6. Kenta Iitani, Po-Jen Chien, Takuma Suzuki, Koji Toma, Takahiro Arakawa, Yasuhiko Iwasaki, Kohji Mitsubayashi. Improved sensitivity of acetaldehyde biosensor by detecting ADH reverse reaction-mediated NADH fluoro-quenching for wine evaluation *ACS Sensors*. 2017.07; 2(7); 940-946
7. Koji Toma, Mai Horibe, Chisato Kishikawa, Naoyuki Yoshimura, Takahiro Arakawa, Hiromi Yatsuda, Hiroji Shimomura, Kohji Mitsubayashi. Rapid and repetitive immunoassay with a surface acoustic wave device for monitoring of dust mite allergens *Sensors and Actuators B: Chemical*. 2017.09; 248; 924-929
8. Midori Taniguchi, Hirokazu Saito, Kohji Mitsubayashi K. Repetitive Immunosensor with a Fiber-Optic Device and Antibody-Coated Magnetic Beads for Semi-Continuous Monitoring of *Escherichia coli* O157:H7 *Sensors*. 2017.09; 17(9); 2145
9. Ming Ye, Takahiro Arakawa, Po-Jen Chien, Takuma Suzuki, Koji Toma, Kohji Mitsubayashi. Acetone biosensor based on fluorometry of reduced nicotinamide adenine dinucleotide consumption in reversible reaction by secondary alcohol dehydrogenase *IEEE Sensors Journal*. 2017.10;
10. Koji Toma, Daisuke Miki, Naoyuki Yoshimura, Takahiro Arakawa, Hiromi Yatsuda, Kohji Mitsubayashi. A gold nanoparticle-assisted sensitive SAW (surface acoustic wave) immunosensor with a regeneratable surface for monitoring of dust mite allergens *Sensors and Actuators B: Chemical*. 2017.10; 249; 685-690
11. Koji Toma, Yume Harashima, Naoyuki Yoshimura, Takahiro Arakawa, Hiromi Yatsuda, Kiyoko Kanamori, Kohji Mitsubayashi. Semicontinuous measurement of mite allergen (Der f 2) using a surface acoustic wave immunosensor under moderate pH for long sensor lifetime *Sensors and Materials*. 2017.12; 29(12); 1679-1687

[Books etc]

1. Koji Toma, Mana Toma, Martin Bauch, Simone Hageneder, and Jakub Dostalek. *Fluorescence Biosensors Utilizing Grating-Assisted Plasmonic Amplification, Surface Plasmon Enhanced, Coupled, and Controlled Fluorescence*. WILEY, 2017.03 (ISBN : 978-1-118-02793-6)

[Conference Activities & Talks]

1. Mitsubayashi K. Cavitax sensors and sniff-imaging system for daily medicine. International Workshop on Nanodevice Technologies 2017 2017.03.02 Higashi-Hiroshima, Japan
2. Toma K, Arakawa T, Mitsubayashi K. Cavitax sensors into human cavities: soft-contact lens and mouth-guard sensors. 19th International Conference on Biomedical Device and Instrumentation Development (ICBDID 2017) 2017.03.26 Madrid, Spain
3. Arakawa T, Tomoto K, Zhang Z, Nitta H, Toma K, Takeuchi S, Sekita T, Minakuchi S, Mitsubayashi K. Mouthguard biosensor integrated with wireless module for monitoring human oral information. 2017 International Conference on Electronics Packaging 2017.04.19 Yamagata, Japan
4. Arakawa T, Tomoto K, Zhang Z, Nitta H, Toma K, Takeuchi S, Sekita T, Minakuchi S, Mitsubayashi K. Mouthguard Biosensor Integrated with Wireless Module for Monitoring Human Oral Information. 2017.04.21 Tendo, Yamagata
5. Mitsubayashi K. Cavitax biosensors using biocompatible polymer and MEMS techniques. MEMS Engineer Forum 2017 2017.04.26 Ryogoku, Tokyo
6. Chien PJ, Suzuki T, Tsujii M, Ming Y, Toma K, Arakawa T, Iwasaki Y, Mitsubayashi K. Gas phase biosensor (bio-sniffer) using S-ADH (secondary alcohol dehydrogenase) for exhaled isopropanol as a potential volatile biomarker. 5th International Conference on Bio-Sensing Technology 2017.05.07 Riva del Garda, Italy
7. Xie R, Seshima F, Toma K, Arakawa T, Mitsubayashi K. Air bio-battery with a gas/liquid diaphragm cell for medical and health care devices. 5th International Conference on Bio-Sensing Technology 2017.05.07 Riva del Garda, Italy
8. Toma K, Kishikawa C, Arakawa T, Mitsubayashi K. Regenerable and antibody-immobilized surface architecture on surface plasmon biosensor for continuous immunosensing. 5th International Conference on Bio-Sensing Technology 2017.05.07 Riva del Garda, Italy
9. Chien PJ, Ming Y, Tsujii M, Suzuki T, Toma K, Arakawa T, Mitsubayashi K. An optical bio-sniffer for exhaled acetone as a potential biomarker of lipid metabolism. 2017 E-MRS Spring Meeting and Exhibit 2017.05.22 Strasbourg, France
10. Mitsubayashi K. Non-Invasive Biosensing for Dairy Medicine- Cavitax Sensors for Tear & Saliva and Biosniffer Devices for Volatiles. Matrafured2017, International Conference on Electrochemical Sensors 2017.06.13 Visegrád, Hungary
11. Toma K, Kishikawa C, Arakawa T, Mitsubayashi K. Regeneratable surface plasmon resonance immunosensor for monitoring in medical care and environmental medicine. 9th International Conference on Molecular Electronics and Bioelectronics 2017.06.26 Kanazawa, Japan
12. Sato T, Iitani K, Toma K, Arakawa T, Mitsubayashi K. Sniff-cam (fluorometric gas-imaging system) with enzyme mesh for gaseous ethanol from human body (breath, skin). EuroAnalysis 2017 2017.08.28 Stockholm, Sweden
13. Mitsubayashi K. Non-Invasive Biosensing for Dairy Medicine -Cavitax Sensors for Tear & Saliva and Bio-sniffer Devices for Volatile Chemicals-. SISPAD2017 Workshop2 2017.09.06 Kamakura, Kanagawa
14. Toma K, Tomoto K, Zhang Z, Nitta H, Arakawa T, Takeuchi S, Sekita T, Minakuchi S, Mitsubayashi K. Mouthguard biosensor integrated with BLE telemetry system for monitoring human oral information. The 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya, Japan
15. Toma K, Arakawa T, Mitsubayashi K. UV curable MPC polymer for stable enzyme immobilization on a mouthguard biosensor in saliva glucose monitoring. 3rd International Conference on Bioinspired and Zwitterionic Materials (ICBZM 2017) 2017.10.18 Kanagawa, Japan
16. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Gas-imaging system "Sniff-cam" based on pH-dependent redox reaction of alcohol dehydrogenase for ethanol and acetaldehyde after drinking. Irigo 2017 2017.11.01 Tokyo, Japan

17. Oishi K, Suzuki Y, Toma K, Arakawa T, Kanamori K, Mitsubayashi K. A chemifluorometric fiber-optic immunosensor for sensitive detection of influenza virus. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo, Japan
18. Sugiyama T, Munkhjargal M, Arakawa T, Yano K, Mitsubayashi K. A co-immobilized enzyme membrane for advancing chemo-mechanical drug-release system for diabetes. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo, Japan
19. Toma K, Yoshimura N, Arakawa T, Yatsuda H, Mitsubayashi K. Reusable immunosensors allowing semi-continuous measurement for clinical and environmental medicine. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo, Japan
20. Iitani K, Naisierding M, Hayakawa Y, Toma K, Arakawa T, Mitsubayashi K. Volatile imaging system “Sniff-cam” using alcohol dehydrogenase for ethanol and acetaldehyde after drinking. The 12th Asian Conference on Chemical Sensors (ACCS2017) 2017.11.12 Hanoi, Vietnam
21. Toma K, Yoshimura N, Arakawa T, Yatsuda H, Mitsubayashi K. Semi-continuous immunosensing for monitoring in clinical and environmental medicine. International Workshop "Frontiers in materials, sensors, and devices for humanophilic innovation" 2017.11.20 Nara, Japan
22. Mitsubayashi K. Sniff-cam (biochemical gas-imaging system) with enzyme mesh as artificial olfactory receptor for ethanol vapor from human body (breath, skin). EMN Mauritius Meeting 2017 2017.11.26 Port Louis, Mauritius
23. Toma K, Oishi K, Yoshimura N, Yatsuda H, Arakawa T, Mitsubayashi K. Regeneratable surface acoustic wave (saw) immunosensor for monitoring of physiological information. 2017 Eleventh International Conference on Sensing Technology (ICST) 2017.12.04 Sydney, Australia
24. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Bio-chemical gas sensor (bio-sniffer) for breath acetaldehyde after drink. Bio4Apps2017 2017.12.11 Tokyo, Japan
25. Yokota K, Toma K, Arakawa T, Iwasaki Y, Mitsubayashi K. A mouthguard biosensor with GOD membrane immobilized by UV curable MPC polymer for saliva glucose monitoring. Bio4Apps2017 2017.12.11 Tokyo, Japan
26. Yasuda N, Tomoto K, Yokota K, Toma K, Arakawa T, Mitsubayashi K. Mouthguard type controller with BLE wireless transmission for external equipment. Bio4Apps2017 2017.12.11 Tokyo, Japan
27. Fujimaki H, Iitani K, Sato T, Toma K, Arakawa T, Mitsubayashi K. Bio-fluorometric imaging system “Sniff-cam” for gaseous ethanol. Bio4Apps2017 2017.12.11 Tokyo, Japan
28. Sugiyama T, Kurihara K, Toma K, Arakawa T, Mitsubayashi K. Glucose-driven decompression device assembled by dissimilar polymer joining for autonomous artificial pancreas. Bio4Apps2017 2017.12.11 Tokyo, Japan
29. Oishi K, Toma K, Yoshimura N, Yatsuda H, Arakawa T, Mitsubayashi K. Surface acoustic wave (SAW) immunosensor for semi-continuous measurement of anti-mouse IgG. Bio4Apps2017 2017.12.11 Tokyo, Japan
30. Iwasaki K, Chien PJ, Toma K, Arakawa T, Mitsubayashi K. Biochemical gas sensor (bio-sniffer) for measurement of isopropanol in human breath. Bio4Apps2017 2017.12.11 Tokyo, Japan
31. Ishikawa T, Kuroki Y, Toma K, Arakawa T, Mitsubayashi K. Wireless mouthguard biosensor for measurement of saliva glucose. Bio4Apps2017 2017.12.11 Tokyo, Japan
32. Aota T, Ye M, Toma K, Arakawa T, Mitsubayashi K. Acetone biosensor based on secondary alcohol dehydrogenase (S-ADH). Bio4Apps2017 2017.12.11 Tokyo, Japan
33. Mitsubayashi K. Non-Invasive biosensing for healthcare and future medicine. International conference on BioSensors, BioElectronics, BioMedical Devices 2017.12.12 Tokyo, Japan

[Awards & Honors]

1. BEST PRESENTATION AWARD, WASET, World Academy of Science, Engineering and Technology, 2017.03

[Others]

1. Implanted Flexible Neural Prostheses and MEMS by Dr. Chengkuo Lee, 190th IBB Seminar, 2017.05
Implanted flexible neural interfaces and MEMS devices currently become popular because they are considered as the viable solution to realize implanted prostheses for novel applications such as human-machine interface and electroceuticals.
2. "Mulling over the aromas of wine", American Chemical Society NEWS, 2017.07
Acetaldehyde is frequently found in a lot of places and foods, such as fruits, vegetables and human saliva. When present in high amounts in wine, it produces an unpleasant odor and affects the fermentation process. Therefore, it is important for winemakers to monitor the acetaldehyde levels, which can vary with temperature, pH and oxygen concentrations. Current methods involve trained experts, long processing times and complex equipment. Kohji Mitsubayashi and colleagues propose a sensitive, versatile detector that is more selective than its predecessors.

Biomedical Information

Professor Yoshikazu NAGAJIMA
 Research Assistant Teruyo MORI
 Graduate Student Yoshihiro SUGIO

(1) Research

1. Surgical Scene Recognition with Artificial Intelligence
2. Deep-Learning Segmentation and Annotation of Brain MRI volumes
3. Probabilistic Approach of Error-distribution Estimation in 2D Projection Measurement
4. Pneumatic Stiffness-Tunable Mechanism and its Application for Laparoscopic Surgeries

(2) Publications

[Original Articles]

1. Kim J, Nakajima Y, Kobayashi K. A Suction-Fixing Stiffness-Tunable Liver Manipulator for Laparoscopic Surgeries *IEEE Trans. on Mechatronics*. 2017.11; 23(1); 262-273

[Conference Activities & Talks]

1. Kim J, Nakajima Y, Kobayashi K. Suction-fixing and stiffness-turning manipulator for laparoscopic liver resection. *Computer Assisted Radiology and Surgery (CARS) 2017* 2017.06.22
2. Gabin H, Nakajima Y. Recognizing of hand pose in basic surgical tasks using depth images. *Computer Assisted Radiology and Surgery (CARS) 2017* 2017.06.23 Barcelona
3. Kaneko T, Shimada J, Nomura F. Measurement of extracellular potential in single cardiomyocytes arranged on multi-electrode array with agarose microchambers. 9th international conference on Molecular Electronics and Bioelectronics (M&BE9) 2017.06.26 Kanazawa, Japan
4. Fujii K, Nomura F, Kaneko T. Response of single-cell-level-arranged cardiomyocyte networks on agarose microchamber by electrical stimulation. 9th international conference on Molecular Electronics and Bioelectronics (M&BE9) 2017.06.26 Kanazawa, Japan
5. Fujii K, Nomura F, Kaneko T. Analysis of response to external electric stimulations by cardiomyocytes-network arranged at single-cell-level. The 55th Annual Meeting of the Biophysical Society of Japan 2017.09.18 Kumamoto, Japan
6. Nakajima Y. Integration of sensing, Simulation and AI Analysis in Medicine. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
7. Nakajima Y. Artificial Intelligence and IoT in Medicine. 1st International Symposium on Frontier of Science, Technology and Engineering(FOSTE) 2017.11.20 Bangkok

Bioelectronics

Staff

Yuji Miyahara (Professor)
Akira Matsumoto (Associate Professor)
Tatsuro goda (Assistant Professor)
Miyuki Tabata (tenure track Assistant Professor)
Yukichi Horiguchi (Assistant Professor)
Toshihiro Yoshizumi (Specially Appointed Assistant Professor)
Taiki Miyazawa (Project Assistant Professor)
Siyuan Chen (Collaborative Researcher)
Hiroko Matsumoto (Technical Assistant)
Yuki Morooka (Technical Assistant)
Chiharu Mizoi (Technical Assistant)
Sayo Kotaki (Technical Assistant)
Kayoko Nakagawa (Staff Assistant)
Ulala Minamibata (Staff Assistant)

Graduate student

Chindanai RATANAPORNCHAROEN, Hideki Fujisaki, Dilinaer AINIWAER, Hiroaki Hatano,
Chattarika KHAMHANGLIT, Maki Shikatani, Ayumu Tsuchiya

(1) Outline

Bioelectronics group is engaged in developing methodologies to determine and analyze functions of biomolecules and their relationships to diseases based on solid-state biosensor technology. Our interests include design & understanding of physicochemical properties of the interface between biomolecules and the device materials, signal-transduction mechanism as well as the pursuit of improved sensitivity and selectivity. These technologies involve many different disciplines of science and engineering, through which we propose new solutions to future medicine.

(2) Research

1. Bioelectronics for Next-generation DNA Sequencing

Our research is focused on the development of nano-interfaces between biomolecules and semiconducting materials for label-free and highly sensitive electrical monitoring of nucleotide base sequences and their amplification processes. The goal of the project is to provide a smaller and cheaper alternative next-generation DNA sequencer to the traditional techniques that involve optical sensing using fluorescence and bioluminescence.

2. Devices for Early Cancer Diagnosis

For applications to early-stage diagnostics of cancers, we aim to establish the device technology enabling detection of small amount of cancer markers out of blood samples with remarkable quickness and sensitivity. The focus is on the design of nano-interfaces that involves chemical modification of biomolecular targets as well as solid/ liquid interfaces in order to achieve efficient biomolecular recognitions on the electrode surfaces. We also pursue optimized materials and the surface property of the electrode in order to obtain remarkably target-specific signals out of complicated electrical signals obtained from raw biological samples.

3. Discovering Intra/Extracellular Molecular Dynamics on Inflammatory Response

Molecular dynamics at inflammation and bacterial infection is investigated using biomimetic surfaces. The term

“biomimetics” in this context represents mimicking the interplay between biomolecules and local changes of microenvironment that has evolved as a mechanism for inauguration of immune responses. Our new nano-bio-technology will reveal unidentified active molecular dynamics in pathophysiology.

4. “Artificial Pancreas” to Treat Diabetes

Development of self-regulated insulin delivery systems to treat diabetes is a long-standing challenge of biomedical engineering. We propose a synthetic gel based solution, which could offer a remarkably simple, “electronics-free” and thus significantly low-cost alternative to the ongoing efforts of artificial pancreas.

(3) Education

1. Engagement: we are engaged in teaching a part of Biomedical Engineering course and mentoring master & doctor students.

2. Course objective: Serum components play crucial roles in metabolic cycles and their concentration homeostasis reflects dynamic equilibrium of life. On occasion of abnormal metabolic pathway, it is manifested as a fluctuation of each specific serum component. Our lecture provides an overview of advanced materials and engineering aimed at determination of body fluids including serum components and mechanisms for their concentration homeostasis.

3. Deepen knowledge of theory, mechanisms, methodologies, application, and limitation of detection technology for biomolecules in various clinical samples. Learn integrative technology of advanced materials/devices and biology/medicine, present problems and future perspective in bioelectronics. Familiarize each student with other related techniques, lab skills including planning of experiments, presenting research results and preparing reports.

(4) Publications

[Original Articles]

1. Tatsuro Goda, Yuji Miyahara. Calcium-independent binding of human C-reactive protein to lysophosphatidylcholine in supported planar phospholipid monolayers *Acta Biomaterialia*. 2017.01; 48; 206-214
2. Miyuki Tabata, Yurika Katayama, Fahmida Mannan, Ayaka Seichi, Koji Suzuki, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Label-free and electrochemical detection of nucleic acids based on isothermal amplification in combination with solid-state pH sensor *Procedia Engineering*. 2017.01; 168; 419-422
3. Miyuki Tabata, Yurika Katayama, Fahmida Mannan, Ayaka Seichi, Koji Suzuki, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Label-free and Electrochemical Detection of Nucleic Acids Based on Isothermal Amplification in Combination with Solid-state pH Sensor 2017.01; 168; 419-422
4. Miyuki Tabata, Chindanai Ratanaporncharoen, Aoi Asano, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami, Yuji Miyahara. Miniaturized Ir/IrOx pH Sensor for Quantitative Diagnosis of Dental Caries *Procedia Eng.* 2017.01; 168; 598-601
5. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Direct and label-free influenza virus detection based on multisite binding to sialic acid receptors. *Biosensors and Bioelectronics*. 2017.02; 92; 234-240
6. Yuki Imaizumi, Tatsuro Goda, Daniel F. Schaffhauser, Jun-ichi Okada, Akira Matsumoto, Yuji Miyahara. Proton-Sensing Transistor Systems for Detecting Ion Leakage from Plasma Membranes under Chemical Stimuli *Acta Biomater.* 2017.03; 50; 502-509
7. Wenfeng Hai, Tatsuro Goda, Hiroaki Takeuchi, Shoji Yamaoka, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Specific Recognition of Human Influenza Virus with PEDOT Bearing Sialic Acid-Terminated Trisaccharides. *ACS Appl Mater Interfaces*. 2017.04; 9; 14162-14170
8. Wenfeng Hai, Tatsuro Goda, Hiroaki Takeuchi, Shoji Yamaoka, Yukichi Horiguchi, Akira Matsumoto, Yuji Miyahara. Specific Recognition of Human Influenza Virus with PEDOT Bearing Sialic Acid-Terminated Trisaccharides *ACS Appl. Mater. Interfaces*. 2017.04; 9; 14162-14170

9. Akira Matsumoto, Shohei Sato, Tomoko Sakamaki, Mai Sanjo, Miyuki Tabata, Tatsuro Goda, Taka-aki Asoh, Akihiko Kikuchi, Yuji Miyahara. Demonstration of Thermo-Sensitive Tetra-Gel with Implication for Facile and Versatile Platform for a New Class of Smart Gels *J. Biomater. Sci. Polym. Ed.*. 2017.04; 28; 1000-1009
10. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Application of surface enhanced Raman spectroscopy as a diagnostic system for hypersialylated metastatic cancers. *Bio-materials*. 2017.07; 134; 143-153
11. A Matsumoto, A J Stephenson-Brown, T Khan, T Miyazawa, H Cabral, K Kataoka, Y Miyahara. Heterocyclic boronic acids display sialic acid selective binding in a hypoxic tumor relevant acidic environment. *Chem Sci*. 2017.09; 8(9); 6165-6170
12. Yuki Imaizumi, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Identification of types of membrane injuries and cell death using whole cell-based proton-sensitive field-effect transistor systems *Analyst*. 2017.09; 142(18); 3451-3458
13. Akira Matsumoto, Shohei Sato, Tomoko Sakamaki, Mai Sanjo, Miyuki Tabata, Tatsuro Goda, Taka-aki Asoh, Akihiko Kikuchi, Yuji Miyahara. Demonstration of thermo-sensitive tetra-gel with implication for facile and versatile platform for a new class of smart gels *Journal of Biomaterials Science, Polymer Edition*. 2017.10; 28(10-12); 1000-1009
14. Akira Matsumoto, Miyako Tanaka, Hiroko Matsumoto, Kozue Ochi, Yuki Moro-Oka, Hirohito Kuwata, Hironori Yamada, Ibuki Shirakawa, Taiki Miyazawa, Hitoshi Ishii, Kazunori Kataoka, Yoshihiro Ogawa, Yuji Miyahara, Takayoshi Suganami. Synthetic "smart gel" provides glucose-responsive insulin delivery in diabetic mice. *Sci Adv*. 2017.11; 3(11); eaaq0723

[Books etc]

1. T. Yoshizumi, Y. Miyahara. Different Types of Field-Effect Transistors - Theory and Applications. InTech, 2017.06 (ISBN : 978-953-51-3176-2)

[Misc]

1. Tatsuro Goda. Mimicking and Passing Plasma Membranes Membrane. 2017.03; 42(3); 90-96

[Conference Activities & Talks]

1. Akira Matsumoto. Synthetic boronate gel-driven "closed-loop" insulin delivery system with feasible safety and efficacy in mic. 11th International Gel Symposium 2017.03.09
2. Tatsuro Goda, Yuji Miyahara. Chemical induction of cell membrane leakage measured under ammonia superfusion conditions using whole cell-based pH sensing transistors. 5th International Conference on Bio-Sensing Technology 2017.05.07 Riva Del Garda, Italy
3. Yuji Miyahara. Exploring Fusion between Life Science and Electronics. 1st International Symposium on Precision Medicine and Biomedical Technologies 2017.06.03 Carp City Hotel, Quanzhou, China
4. Yuji Miyahara, Akira Matsumoto, Tatsuro Goda, Miyuki Tabata. Functional gate-field effect transistors for electrically neutral molecules. Matrafured 2017 2017.06.11 Thermal Hotel Visegrad Superior
5. Yuji Miyahara, Akira Matsumoto, Tatsuro Goda, Miyuki Tabata. Functional gate-field effect transistors for electrically neutral molecules. Matrafured 2017 2017.06.11

6. Yuji Miyahara. Functional gate-field effect transistors for electrically neutral molecules. Matrafured 2017 2017.06.13 Thermal Hotel Visegrad Superior, Budapest, Hungary
7. Tatsuro Goda. Biomimetic engineering for biosensing and bioscience. The 9th International Conference on Molecular Electronics and Bioelectronics (M&BE9) 2017.06.26 Ishikawa Conert Hall
8. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Diagnosis of Hypersialylated Metastatic Cancers by Phenylboronic Acid-installed PEGylated Gold Nanoparticle. The 17th Society of Free Radical Research JAPAN 2017.06.28 International Congress Center, Ibaraki
9. Yuji Miyahara, Miyuki Tabata, Chindanai Ratanaporncharoen, Aoi Asano, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami. Fabrication of needle type pH sensor for quantitative caries detection. European Advanced Materials Congress 2017 2017.08.22 Stockholm, Sweden
10. Yuji Miyahara, Miyuki Tabata, Chindanai Ratanaporncharoen, Aoi Asano, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami. Fabrication of needle type pH sensor for quantitative caries detection. European Advanced Materials Congress 2017 2017.08.22 Stockholm, Sweden
11. Miyuki Tabata, Enrico Tenaglia, Tatsuro Goda, Akira Matsumoto, Carlotta Guiducci, Yuji Miyahara. Label-free nucleic acid amplification detection using micro pH devices. European Advanced Materials Congress 2017 2017.08.22 Stockholm, Sweden
12. Yuji Miyahara, Miyuki Tabata, Chindanai Ratanaporncharoen, Aoi Asano, Yuichi Kitasako, Masaomi Ikeda, Tatsuro Goda, Akira Matsumoto, Junji Tagami. Fabrication of needle type pH sensor for quantitative caries detection. European Advanced Materials Congress 2017 2017.08.22
13. Miyuki Tabata, Enrico Tenaglia, Tatsuro Goda, Akira Matsumoto, Carlotta Guiducci, Yuji Miyahara. Label-free nucleic acid amplification detection using micro pH devices. European Advanced Materials Congress 2017 2017.08.22
14. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Label-free selective detection of influenza A virus subtype H1N1 using multisite binding of sialic acid receptors. The 15th International Conference on Advanced Materials (IUMRS-ICAM 2017) 2017.08.27 Kyoto University
15. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Label-free selective detection of influenza A virus subtype H1N1 using multisite binding of sialic acid receptors. The 15th International Conference on Advanced Materials (IUMRS-ICAM 2017) 2017.08.27
16. Babita Shashni, Yukichi Horiguchi, Kosuke Kurosu, Hitoshi Furusho, Yukio Nagasaki. Application of Surface-Enhanced Raman Spectroscopy for Detection of Hypersialylated Metastatic Cancers. The 76th Annual Meeting of the Japanese Cancer Association 2017.09.28
17. Tatsuro Goda. Phospholipid-mimicked materials: Applications to biosensing and cell penetration. The 3rd International Conference on Bioinspired and Zwitterionic Materials (ICBZM 2017) 2017.10.18 Tokyo University
18. Chindanai Ratanaporncharoen, Miyuki Tabata, Noboru Ishihara, Kazuya Masu, Mana Sriyudthsak, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Miniaturized Ir/IrOx wireless pH sensing system for biosensor application. The 2nd International Symposium on Biomedical Engineering 2017.11.09 東京大学
19. Miyuki Tabata, Yusuke Yoshioka, Tatsuro Goda, Akira Matsumoto, Takahiro Ochiya, Yuji Miyahara. Label-free microRNA detecting sensors for liquid biopsy. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo University
20. Miyuki Tabata, Enrico Tenaglia, Tatsuro Goda, Akira Matsumoto, Carlotta Guiducci, Yuji Miyahara. pH detecting devices for label-free electrochemical monitoring of isothermal nucleic acid amplification. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo University
21. Chindanai Ratanaporncharoen, Miyuki Tabata, Noboru Ishihara, Kazuya Masu, Mana Sriyudthsak, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Miniaturized Ir/IrOx wireless pH sensing system for biosensor application. The 2nd International Symposium on Biomedical Engineering 2017.11.09

22. Miyuki Tabata, Yusuke Yoshioka, Tatsuro Goda, Akira Matsumoto, Takahiro Ochiya, Yuji Miyahara. Label-free microRNA detecting sensors for liquid biopsy. The 2nd International Symposium on Biomedical Engineering 2017.11.09
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26. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Investigation of the Influenza Virus Detection System Using Sialic Acid Receptor. The 19th Takayanagi Kenjiro Memorial Symposium 2017.11.21 Research Institute of Electronics Shizuoka University
27. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Investigation of the Influenza Virus Detection System Using Sialic Acid Receptor. The 19th Takayanagi Kenjiro Memorial Symposium, Research Institute of Electronics 2017.11.21
28. Yukichi Horiguchi, Tatsuro Goda, Akira Matsumoto, Hiroaki Takeuchi, Shoji Yamaoka, Yuji Miyahara. Human Influenza A Virus Detection Using Resistive Pulse Sensing with Nanoparticle-based Molecular Recognition. The 27th Japan MRS Annual Meeting 2017.12.05 Yokohama
29. Miyuki Tabata, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Label-free electrochemical monitoring of isothermal nucleic acid amplification using micro pH sensors. 4th COINS symposium 2017.12.08 iCONN, Kawasaki
30. Miyuki Tabata, Tatsuro Goda, Akira Matsumoto, Yuji Miyahara. Label-free electrochemical monitoring of isothermal nucleic acid amplification using micro pH sensors. 4th COINS symposium 2017.12.08

Material-Based Medical Engineering

Prof. Akio KISHIDA
Assoc. Prof. Tsuyoshi KIMURA
Assist. Prof. Yoshihide HASHIMOTO
Research Associate Naoko NAKAMURA

Division of Acellular Tissue and Regenerative Medical Material
Assoc. Prof. Seiichi FUNAMOTO
Lecturer Akitatsu YAMASHITA
Assist. Prof. Yongwei ZHANG

Secretary Naomi HIWATARI

Doctor Course Student Masaki WATANABE

(1) Outline

In our laboratory, we deal with many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices.

The key words of our policy are "contribution to medical care" and "exploration of basic scientific principles".

(2) Research

In order to develop technologies that contribute to the medical and dental care, there is a need for a system to build up the design concepts at the molecular level and to realize it. Based on polymer chemistry, organic chemistry, and physical chemistry, we proceed a research aimed at specific clinical applications using cell engineering, genetic engineering techniques. Target area are new medical material development, regenerative medicine, gene therapy, and the treatment engineering.

(1) Regenerative medicine using decellularized biological tissue

In order to remove the xenogeneic cells, the living tissue is decellularized using a new processing method, high-hydrostatic pressure (HHP) method has been developed. Using this process, complete removal of infectious bacteria, viruses, and cells was accomplished.

(2) Molecular aggregates formed by the high-hydrostatic pressure process. Hydrogen bond assembles molecular assembly under high pressure. Using the HHP processing of more than 6,000 atmospheres, we prepare the nucleic acid assembly and apply them as gene delivery system.

(3) Extracellular matrix remodeling

We are conducting research on tissue remodeling using artificially reconstructed extracellular matrix structure. Specifically, we are researching the application of as artificial skin and artificial cornea of precision design artificial extracellular matrix structure.

(4) Immune control system: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulates immune reactions, to be able to enhance the anti-tumor immune responses have been revealed. We are developing technologies to capture and recover Treg using interfacial science.

(3) **Education**

In the Graduate School of Medical and Dental Sciences, we provide the lectures entitled “biological functional materials science”, “applied biomaterials”, and “medical, dental and pharmaceutical industrial engineering”.

(4) **Publications**

[Original Articles]

1. Jun Negishi, Yoshihide Hashimoto, Akitatsu Yamashita, Tsuyoshi Kimura, Akio Kishida, Seiichi Funamoto. Histological structure affects recellularization of decellularized arteries. *Mater Sci Eng C Mater Biol Appl.* 2017.01; 70(Pt 1); 450-455
2. G.E. Cinay, P. Erkok, M. Alipour, Y. Hashimoto, Y. Sasaki, K. Akiyoshi, S. Kizilel. Nanogel-integrated pH responsive composite hydrogels for controlled drug delivery. *ACS Biomaterials Science and Engineering.* 2017.01; 3(3); 370-380
3. Ryo Harada, Seiichi Funamoto, Jun Negishi, Yusuke Kasahara, Tsuyoshi Kimura, Kwangwoo Nam, Toru Masuzawa, Akio Kishida, Tetsuya Higami. Novel Adhesion device for living tissue *The Sapporo Medical Journal.* 2017.03; (85); 57-65
4. Hiroki Maeda, Hiroshi Kobayashi, Takayuki Miyahara, Yoshihide Hashimoto, Kazunari Akiyoshi, Shohei Kasugai. Effects of a polysaccharide nanogel-crosslinked membrane on wound healing. *J. Biomed. Mater. Res. Part B Appl. Biomater..* 2017.04; 105(3); 544-550
5. Jun Negishi, Yoshihide Hashimoto, Akitatsu Yamashita, Yongwei Zhang, Tsuyoshi Kimura, Akio Kishida, Seiichi Funamoto. Evaluation of small-diameter vascular grafts reconstructed from decellularized aorta sheets. *J Biomed Mater Res A.* 2017.05; 105(5); 1293-1298
6. Tsuyoshi Kimura, Naoko Nakamura, Kanji Umeda, Yoshihide Hashimoto, Akio Kishida. Capture and release of cells using a temperature-responsive surface that immobilizes an antibody through DNA duplex formation. *J Biomater Sci Polym Ed.* 2017.07; 28(10-12); 1172-1182

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1. Frontier of artificial corneas 2017.02; 54(1); 10-13
2. Biomaterials including tissues, organs and extracellular matrix obtained from animals 2017.02; 54(1); 6-9
3. Y. Sawa, G. Matsumiya, K. Matsuda, E. Tatsumi, T. Abe, K. Fukunaga, S. Ichiba, A. Kishida, 他. *Journal of Artificial Organs* 2016:the year in review *J. Artif Organs.* 2017.03; 20(1); 1-7
4. K. Akazawa, K. Iwasaki, M. Nagata, N. Yokoyama, H. Ayame, K. Yamaki, Y. Tanaka, I. Honda, C. Morioka, T. Kimura, M. Komaki, A. Kishida, Y. Izumi, I. Morita. Cell transfer technology for tissue engineering *Inflammation and Regeneration.* 2017.10; 37(21); 1-6

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1. T. Kimura, N. Nakamura, Y. Hashimoto, A. Odawara, I. Suzuki, A. Kishida. Neural network reconstruction on sliced acellular brains for brain organoids. *SFB2017 Annual Meeting and Exposition 2017.04.05 Minneapolis,USA*
2. T. Kimura, N. Nakamura, Y. Hashimoto, S. Sakaguchi, S. Kimura, A. Kishida. Selective capture of regulatory T cells for cancer immunotherapy. *SFB2017 Annual Meeting and Exposition 2017.04.05 Minneapolis,USA*

3. Akio Kishida. Biomedical application of decellularized tissues. ASAIO 63rd Annual Conference 2017.06.21 Chicago,USA
4. Naruki Kimura, Yoshihide Hashimoto, Seiichi Funamoto, Akio Kishida, Yongwei Zhang, Akitatsu Yamashita, Kei Oya, Takeo Nakano. Fabrication of visible marker on decellularized tissue for ultrasonography via reactive sputtering. 2017 TERMIS-EU Conference 2017.06.26 Davos, Switzerland
5. Tsuyoshi Kimura, Takaaki Kubota, Naoko Nakamura, Yoshihide Hashimoto, Akio Kishida. Preparation of ICD induced cancer cells and activation of immune system. iLIM-2 2017.09.29 Nagoya, Japan
6. Akio Kishida. Preparation, characterization and in vivo performance of decellularized cornea. The 6th Asian Biomaterials Congress 2017.10.25 India
7. Masahiro Okada, Takuya Matsumoto, Akio kishida, Tsuyoshi Kimura. Brush-like hydroxyapatite coating on biodegradable polymer substrate at low temperature. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
8. Hironobu Takahashi, Tsuyoshi Kimura, Akio kishida, Tatsuya Shimizu. 3D construction of anisotropic cell sheets combined with membranous structures. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
9. Masaya Yamamoto, Tsuyoshi Kimura, Akio kishida. Raman spectroscopic imaging analysis of decellularized joint tissue. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
10. Ikuro Suzuki, Aoi Odawara, Naoko Nakamura, Akio Kishida, Tsuyoshi Kimura. Reconstruction of brain circuit on decellularized brain tissue. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
11. Naruki Kimura, Kei Oya, Yoshihide Hashimoto, Yuki Suzuki, Yuichiro Nawa, Seiichi Funamoto, Akio Kishida, Takeo Nakano. Sputter-deposition of distinguishable marker on decellularized tissue for non-invasive imaging techniques. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
12. Naoko Nakamura, Tsuyoshi Kimura, Masahiro Yamada, Toshiya Fujisato, Takashi Tsuji, Akio Kishida. Periodontal tissue reconstruction using artificial tooth and decellularized PDL matrix. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
13. Naoko Nakamura, Tsuyoshi Kimura, Yoshihide Hashimoto, Shimon Sakaguchi, Shunsaku Kimura, Akio Kishida. Label-free capture and collection of target cells using a surface immobilizing antibody via desthiobiotin-avidin interaction. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
14. Jun Negishi, Seiichi Funamoto, Yoshihide Hashimoto, Akitatsu Yamashita, Yongwei Zhang, Akio Kishida. Evaluation of adult and fetal porcine decellularized tissues. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
15. Akio Kishida. Control of biological response of polymers by surface modification. APA2017 2017.11.23 India
16. T. Kimura, N. Nakamura, Y. Hashimoto, A. Kishida. Development of an antibody immobilizing device for label-free selective capture and collection of stem cells. TERMIS-AM 2017 2017.12.03

Organic and Medicinal Chemistry

Professor Hiroyuki KAGECHIKA
Assistant Professor Syuichi MORI
Assistant Professor Mari YUASA
Eng Official Emiko KAWACHI
Secretary Mayumi SHIKAMA

Graduate Student
Dilihumaer AINIWAER
Yusuke Okazaki
Nozomi Tsuemoto
Sayuri Goryoda
Hidekazu Yokoo
Hiroto Inuma
Kazuhiro Imaida
Ryohei Iwashita
Tsuyoshi Oikawa
Yuki Noji
Mititake Hirano
Takahiro Miura
Daiki Kato
Chihiro Komatsu
Rie Tsukamoto

(1) Outline

1) Medicinal Chemistry of Retinoids

Retinoids regulates various significant biological phenomena, such as cell differentiation, proliferation, morphogenesis, metabolism and homeostasis. We have developed novel synthetic retinoid, Am80 (tamibarotene) as drug for acute promyelocytic leukemia. Novel synthetic retinoids have been developed for clinical use in the field of autoimmune diseases, neurodegenerative diseases, metabolic syndromes.

2) Medicinal Chemistry of Nuclear Receptors

Small hydrophobic molecules such as steroid hormones and activated vitamins A/D control various biological phenomena, including growth, development, metabolism, and homeostasis, by binding to and activating specific nuclear receptors. Nuclear receptors have become one of the most significant molecular targets for drug discovery in the fields of cancer, metabolic syndrome, autoimmune diseases, and so on. In this project, novel ligands of various nuclear receptors have been developed.

3) Development of Novel Functional Fluorescent Molecules for Elucidation of Intracellular Signal Transduction Pathways

Functional fluorescent molecules useful in many fields of scientific research, including analytical chemistry or cell biology have been developed.

4) Aromatic Architecture Based on the Steric Properties of N-Methylated Amides

The amide bond structure of amide derivatives often plays a key role in functions such as molecular recognition events or biological activities. In contrast to the extended trans structures of most secondary amides, the corresponding N-methylated compounds exist in cis form in the crystals and predominantly in cis form in various solvents. The cis conformational preference is useful as a building block to construct aromatic molecules with

unique crystal or solution structures.

(2) Lectures & Courses

Organic and Medicinal Chemistry covers several aspects of organic chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand the fundamental knowledge, recent topics, and experimental techniques related to these fields.

(3) Publications

[Original Articles]

- Oya, Y.; Mondal, A.; Rawangkan, A.; Umsumarng, S.; Iida, K.; Watanabe, T.; Kanno, M.; Suzuki, K.; Li, Z.; Kagechika, H.; Shudo, K.; Fujiki, H.; Suganuma, M.. Down-regulation of histone deacetylase 4, - 5 and - 6 as a mechanism of synergistic enhancement of apoptosis in human lung cancer cells treated with the combination of a synthetic retinoid, Am80 and green tea catechin *Journal of Nutritional Biochemistry*. 2017.01; 42; 7-16
- Tsuji, M.; Shudo, K.; Kagechika, H.. The receptor subtype selectivity of retinoid X and retinoic acid receptors via quantum mechanics *FEBS Open Bio*. 2017.03; 7; 391-396
- Suzuki Yukina, Akima Ryunosuke, Murayama Takashi, Kurebayashi Nagomi, Ishigami-Yuasa Mari, Mori Syuichi, Kagechika Hiroyuki, Suzuki Junji, Kanemaru Kazunori, Iino Masamitsu, Oyamada Hideto, Oguchi Katsuji, Ogawa Haruo, Toyoshima Chikashi, Sakurai Takashi. A novel screening method for drugs inhibiting type 1 ryanodine receptor (RyR1) by ER Ca²⁺ monitoring *JOURNAL OF PHARMACOLOGICAL SCIENCES*. 2017.03; 133(3); S195
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- Hoang, H. N.; Nagashima, Y.; Mori, S.; Kagechika, H.; Matsuda, T.. CO₂-expanded bio-based liquids as novel solvents for enantioselective biocatalysis *Tetrahedron* . 2017.05; 73(20); 2984-2989
- Nguyen, B. N.; Okuno, Y.; Ajiro, M.; Iida, K.; Denawa, M.; Yamamoto, M.; Sakamoto, N.; Kagechika, H.; Hagiwara, M.. Retinoid derivative Tp80 exhibits anti-hepatitis C virus activity through restoration of GI-GPx expression *Journal of Medical Virology*. 2017.05; 89(7); 1224-1234
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- Yuki Yoshizaki, Takayasu Mori, Mari Ishigami-Yuasa, Eriko Kikuchi, Daiei Takahashi, Moko Zeniya, Naohiro Nomura, Yutaro Mori, Yuya Araki, Fumiaki Ando, Shintaro Mandai, Yuri Kasagi, Yohei Arai, Emi Sasaki, Sayaka Yoshida, Hiroyuki Kagechika, Tatemitsu Rai, Shinichi Uchida, Eisei Sohara. Drug-Repositioning Screening for Keap1-Nrf2 Binding Inhibitors using Fluorescence Correlation Spectroscopy. *Sci Rep*. 2017.06; 7(1); 3945
- Ishigami-Yuasa, M.; Watanabe, Y.; Mori, T.; Masuno, H.; Fujii, S.; Kikuchi, E.; Uchida, S.; Kagechika, H.. Development of WNK signaling inhibitors as a new class of antihypertensive drugs *Bioorganic and Medicinal Chemistry*. 2017.06; 25(14); 3845-3852
- Mari Ishigami-Yuasa, Yuko Watanabe, Takayasu Mori, Hiroyuki Masuno, Shinya Fujii, Eriko Kikuchi, Shinichi Uchida, Hiroyuki Kagechika. Development of WNK signaling inhibitors as a new class of antihypertensive drugs. *Bioorg. Med. Chem.* 2017.07; 25(14); 3845-3852
- Yoshioka, H.; Yamada, A.; Nishiyama, Y.; Kagechika, H.; Hashimoto, Y.; Fujii, S.. Development of non-steroidal glucocorticoid receptor modulators based on N-benzyl-N-(4-phenoxyphenyl)benzenesulfonamide scaffold *Bioorganic and Medicinal Chemistry*. 2017.07; 25(13); 3461-3470

12. Yoshizaki, Y.; Mori, T.; Ishigami-Yuasa, M.; Kikuchi, E.; Takahashi, D.; Zeniya, M.; Nomura, N.; Mori, Y.; Araki, Y.; Ando, F.; Mandai, S.; Kasagi, Y.; Arai, Y.; Sasaki, E.; Yoshida, S.; Kagechika, H.; Rai, T.; Uchida, S.; Sohara, E.. Drug-Repositioning Screening for Keap1-Nrf2 Binding Inhibitors using Fluorescence Correlation Spectroscopy *Science Reports*. 2017.07; 7; 3945
13. Mori, S.; Hirano T.; Takaguchi, A.; Fujiwara, T.; Okazaki, Y.; Kagechika, H.. Selective Reagent for Detection of N- ϵ -Monomethylation of a Peptide Lysine Residue through SNAr Reaction *European Journal of Organic Chemistry*. 2017.07; 3606-3611
14. Shuichi Mori, Tomoya Hirano, Asuka Takaguchi, Takashi Fujiwara, Yusuke Okazaki, and Hiroyuki Kagechika. Selective reagent for detection of N-epsilon-monomethylation of peptide lysine residue via SNAr reaction *Eur. J. Org. Chem.*. 2017.07; 3603-3611
15. Hoang Hai N., Granero-Fernandez Emanuel, Yamada Shinjiro, Mori Shuichi, Kagechika Hiroyuki, Medina-Gonzalez Yaocihuatl, Matsuda Tomoko. Modulating Biocatalytic Activity toward Sterically Bulky Substrates in CO₂-Expanded Biobased Liquids by Tuning the Physicochemical Properties *ACS SUSTAINABLE CHEMISTRY & ENGINEERING*. 2017.11; 5(11); 11051-11059
16. Mori Shuichi, Takagaki Ryohei, Fujii Shinya, Urushibara Ko, Tanatani Aya, Kagechika Hiroyuki. Novel Non-steroidal Progesterone Receptor Ligands Based on m-Carborane Containing a Secondary Alcohol: Effect of Chirality on Ligand Activity *Chemical & Pharmaceutical Bulletin*. 2017.11; 65(11); 1051-1057
17. Yuta Endo, Taku Kasahara, Kenicni Harada, Miwa Kubo, Tadahiro Etoh, Masami Ishibashi, Aki Ishiyama, Masato Iwatsuki, Kazuhiko Otoguro, Satoshi O Mura, Gokithi Akisue, Tomoya Hirano, Hiroyuki Kagechika, Yoshiyasu Fukuyama, Ayumi Ohsaki. Sucupiranins A-L, Furanocassane Diterpenoids from the Seeds of *Bowdichia virgilioides*. *J. Nat. Prod.*. 2017.12; 80(12); 3120-3127

[Books etc]

1. Yoshihiro Takemoto. Research Coaching. YODOSHA, 2017.01 (ISBN : 978-4-7581-0160-8)
2. Yoshihiro Takemoto. Research Coaching. YODOSHA, 2017.02 (ISBN : 978-4-7581-0161-5)

[Misc]

1. Tomoya Hirano, Shuichi Mori, Hiroyuki Kagechika. Development of therapeutic strategies based on chemical biological studies of histone methyltransferase 2017.11; 27(4); 208-212

[Conference Activities & Talks]

1. Mari Ishigami-Yuasa, Hisao Ekimoto, Hiroyuki Kagechika. Synergistic effect of synthetic retinoid Am80 with epigenetic modulators on human leukemic cell proliferation. The 35th Medicinal Chemistry Symposium Scientific Program 2017.10.25
2. Ishigami-Yuasa, M., Ekimoto, H., Kagechika, H.. Synergistic inhibition of several human cancer cell proliferations by a synthetic retinoid tamibarotene (Am80) in combination with the epigenetic modulators. FASEB meeting on retinoid Florida, USA
3. Tsuemoto, N., Mori, S., Kawachi, E., Kagechika, H.. Design and synthesis of novel RAR ligands containing pentafluorosulfanyl group. FASEB meeting on retinoid Florida, USA

[Patents]

1. Lck binding protein, Patent Number : United States Patent 5891673
2. IKK3 kinase, Patent Number : United States Patent 6576439
3. A protein kinase (IKK4) involved in the phosphorylation of IKB, Patent Number : WO/2001/044444

[Works]

1. Expression Vectors <http://dna.brc.riken.jp/search/dep3357.html>, Other, RIKEN

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Yoshitake NISHIYAMA
Research Assistant	Takamoto MORITA
Technical Assistant	Yoshihiro MISAWA, Yuki HAZAMA, Tomoko KURIBARA
Graduate Students	Kazuya KANEMOTO, Keisuke UCHIDA, Tomohiro MEGURO, Yu NAKAMURA, Harumi ITO, Kotaro MUTSUURA, Youngchan KIM, Yuya TAMURA, Shonan CHIN, Saki FUJII, Tsubasa MATSUZAWA, Keisuke ADACHI, Saki OZAWA, Shuhei KAMADA, Keita SHIMIZU, Norikazu TERASHIMA Naoya TOKUNAGA, Yoshihiro MIYATA

(1) Outline

Development of new organic synthetic methods, new chemical methodologies, and new chemical tools, those are useful for biological and drug discovery researches.

(2) Research

- 1) Development of novel generation methods for benzyne species and their synthetic applications.
- 2) Development of new bioconjugation methods using strained alkynes.
- 3) Target identification of drugs or drug candidates by photoaffinity labeling based on diazido probe method..
- 4) Development of new molecular ligation methods based on new azido chemistry.
- 5) Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
- 6) Design and synthesis of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

[Original Articles]

1. Morita T, Nishiyama Y, Yoshida S, Hosoya T. Facile Synthesis of Multisubstituted Benzo[*b*] furans via 2,3-Disubstituted 6,7-Furanobenzynes Generated from *ortho*-Iodoaryl Triflate-type Precursors. *Chem Lett.* 2017.01; 46(1); 118-121
2. Morita T, Yoshida S, Kondo M, Matsushita T, Hosoya T. Facile Diversification of Simple Benzo[*b*] thiophenes via Thienobenzynes Intermediates. *Chem Lett.* 2017.01; 46(1); 81-84
3. Yoshida S, Nakajima H, Uchida K, Yano T, Kondo M, Matsushita T, Hosoya T. Reactions of Arynes with Sulfoximines: Formal Sulfinylation vs. *N*-Arylation. *Chem Lett.* 2017.01; 46(1); 77-80

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- Meguro T, Yoshida S, Hosoya T. Sequential Molecular Conjugation using Thiophene *S,S*-Dioxides Bearing a Clickable Functional Group. *Chem Lett.* 2017.08; 46(8); 1137-1140
- Niwa T, Ochiai H, Hosoya T. Facile Transformation of α , β -Unsaturated Carboxylic Acids to Alkenylboronic Esters via Rhodium-Catalyzed Decarbonylative Borylation of α , β -Unsaturated Thioesters. *Chem Lett.* 2017.09; 46(9); 1315-1318
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- Nakano-Kobayashi A, Awaya T, Kii I, Sumida Y, Okuno Y, Yoshida S, Sumida T, Inoue H, Hosoya T, Hagiwara M. Prenatal neurogenesis induction therapy normalizes brain structure and function in Down syndrome mice. *Proc Natl Acad Sci USA.* 2017.09; 114(38); 10268-10273
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21. Yoshida S, Shimizu K, Uchida K, Hazama Y, Igawa K, Tomooka K, Hosoya T. Construction of Condensed Polycyclic Aromatic Frameworks through Intramolecular Cycloaddition Reactions Involving Arynes Bearing an Internal Alkyne Moiety. *Chem Eur J.* 2017.11; 23(61); 15332-15335
22. Kusuhara H, Takashima T, Fujii H, Takashima T, Tanaka M, Ishii A, Tazawa S, Takahashi K, Takahashi K, Tokai H, Yano T, Kataoka M, Inano A, Yoshida S, Hosoya T, Sugiyama Y, Yamashita S, Hojo T, Watanabe Y. Comparison of pharmacokinetics of newly discovered aromatase inhibitors by a cassette microdosing approach in healthy Japanese subjects. *Drug Metab Pharmacokinet.* 2017.12; 32(6); 293-300

[Conference Activities & Talks]

1. Yoshida S, Nakamura Y, Yano T, Uchida K, Hazama Y, Misawa Y, Sugimura Y, Igawa K, Shimizu S, Tomooka K, Hosoya T. Synthesis of Aniline Derivatives via Aryne Intermediates Enabling Facile Preparation of Nitrogen-Containing Heterocyclic Compounds. 26th International Society of Heterocyclic Chemistry (ISHC 2017) 2017.09.05 Regensburg, Germany
2. Uchida K, Yoshida S, Hosoya T. Generation of Arynes Triggered by Carbon-Carbon Bond Cleavage Reaction. 26th International Society of Heterocyclic Chemistry (ISHC 2017) 2017.09.06 Regensburg, Germany
3. Nishiyama Y, Kamada S, Yoshida S, Hosoya T. Generation of Arynes Triggered by Cleavage of a Carbon-Phosphorus Bond. Otsu Conference 2017 2017.09.11 Otsu
4. Ito H, Yoshida S, Hosoya T, Kii I. Fluorescence pulse-chase trace analysis on assembly of extracellular matrix. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo
5. Yoshida S. Single C-F Bond Cleavage of Trifluoromethylarenes with an *ortho*-Silyl Group. Tateshina Conference on Organic Chemistry 2017 2017.11.10
6. Nishiyama Y, Fujii S, Hazama Y, Yoshida S, Hosoya T. Multi-Click Chemistry for Rapid Functionalization of Middle Molecules. 11th International Symposium on Integrated Synthesis (ISONIS-11) & 3rd International Symposium on Middle Molecular Strategy (ISMMS-3) 2017.11.16 Kobe

[Patents]

1. Coelenterazine analogues and coelenteramide analogues , Patent Number : GB2479441
2. Coelenterazine analogues and coelenteramide analogues , Patent Number : GB2540896
3. Coelenterazine analogues and coelenteramide analogues , Patent Number : GB2540897
4. Coelenterazine analogues and coelenteramide analogues , Patent Number : GB2543965
5. COMPOUND AND PHARMACEUTICAL COMPOSITION FOR NEUROPSYCHOLOGICAL DISORDER OR MALIGNANT TUMOR, Patent Number : ZL201380040385.8
6. COMPOUND AND PHARMACEUTICAL COMPOSITION FOR NEUROPSYCHOLOGICAL DISORDER OR MALIGNANT TUMOR, Patent Number : 9745323

Biomechanics

Kenji Kawashima
Takahiro Kanno
Tetsuro Miyazaki
Toshihiro Kawase

(1) Outline

Kawashima Lab. mainly working on the development of medical devices and systems based on control engineering, robotics and fluid dynamics.

Key word is system integration such as hardware and software, electrical and pneumatics, human and machine.

(2) Research

- 1)Surgical robot system
- 2)Power assist devices using pneumatic actuators
- 3)Forceps manipulator for minimally invasive surgery
- 4)Development of soft robots
- 5)Haptic device using biological and visual information

(3) Education

Learn about mechanical design and control engineering for medical devices based on biomechanics. Master a basic skill to develop the devices from the researchers and engineers working on the medical devices and systems. Learn the basic control method of a surgical robot using a personal computer.

(4) Lectures & Courses

The object is to provide the ability to design and develop medical devices based on biomechanics, which studies the structure and function of biological systems, with mechanical dynamics, robotics and control engineering.

(5) Publications**[Original Articles]**

1. Sato Y, Kawase T, Takano K, Spence C, Kansaku K. Incorporation of prosthetic limbs into the body representation of amputees: Evidence from the crossed hands temporal order illusion. *Progress in brain research*. 2017; 236; 225-241
2. Toshihiro Kawase, Natsue Yoshimura, Hiroyuki Kambara, Yasuharu Koike. Controlling an electromyography-based power-assist device for the wrist using electroencephalography cortical currents *Advanced Robotics*. 2017.01; 31(1-2); 88-96
3. Toshihiro Kawase, Takeshi Sakurada, Yasuharu Koike, Kenji Kansaku. A hybrid BMI-based exoskeleton for paresis: EMG control for assisting arm movements *Journal of Neural Engineering*. 2017.02; 14(1); 016015
4. Tetsuro MIYAZAKI, Takuya IIJIMA, Yuuichi HIRAHARA and Kazushi SANADA. Development and performance evaluation of supporting arm worn by factory worker for reducing body load *Transactions of the JSME (in Japanese)*. 2017.05; 83(849); 16-00544
5. Hitoshi Yoshiki, Kotaro Tadano, Kenji Kawashima. Surgical Aspirator with Steam-jet Coagulator for Hepatic Surgery 3rd World Congress on Electrical Engineering and Computer Systems and Science. 2017.06;
6. Hitoshi Yoshiki, Kotaro Tadano, Kenji Kawashima. Cauterization Device with Double-Layered Nozzle using Steam and Suction 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. 2017.07;
7. Takahiro Kanno, Norihiki Ito, Kenji Kawashima. A cornea holding device for transplantation surgery *IEEE Conference on Control Technology and Applications*. 2017.08; 720-725
8. Masahiki Minamoto, Yutaro Suzuki, Takahiro Kanno, Kenji Kawashima. Effect of Robot Operation by a Camera with the Eye Tracking Control *IEEE International Conference on Mechatronics and Automation*. 2017.08; 1983-1988
9. Akinari Onishi, Kouji Takano, Toshihiro Kawase, Hiroki Ora, Kenji Kansaku. Affective stimuli for an auditory P300 brain-computer interface *Frontiers in Neuroscience*. 2017.09; 11(522);
10. Natsue Yoshimura, Hayato Tsuda, Toshihiro Kawase, Hiroyuki Kambara, Yasuharu Koike. Decoding finger movement in humans using synergy of EEG cortical current signals *Scientific Reports*. 2017.09; 7; 11382
11. Tetsuro MIYAZAKI, Takuya IIJIMA, Yuuichi HIRAHARA and Kazushi SANADA. Performance Evaluation of Supporting Arm for Reducing Body Load Using Surface Electromyography *The 10th JFPS International Symposium on Fluid Power FUKUOKA 2017*. 2017.10; (2B12); 1-8
12. Tetsuro MIYAZAKI, Kazushi SANADA. Experimental Validation of an Optimum Design Method for a Ball Throwing Robot Considering Degrees of Freedom, Link Parameters, and Motion Pattern *Mechanical Engineering Journal*. 2017.10; 4(5); 17-00147
13. In Kim, Kotaro Tadano, Takahiro Kanno, Kenji Kawashima. Implementing Pseudo Haptic Feedback in a Semi-Isometric Master Interface for Robotic Surgery *International Journal of Advanced Robotic Systems*. 2017.10; 14(5); 1-9
14. Daisuke Morisaki, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Development of a Pinch-type Servo Valve Embedded in a Pneumatic Artificial Rubber Muscle *Proceedings of the 2017 IEEE/SICE International Symposium on System Integration*. 2017.12; TuC4.4
15. Keisuke Naito, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Development of Minimally Invasive Lifting Device Using Extension and Flexion of Pneumatic Soft Actuator for Laparoscopic Surgery *Proceedings of the 2017 IEEE/SICE International Symposium on System Integration*. 2017.12; WeB4.4
16. Kengo Watanabe, Takahiro Kanno, Kazuhisa Ito, Kenji Kawashima. Single Master Dual Slave Surgical Robot with Automated Relay of Suture Needle *IEEE Transactions on Industrial Electronics*. 2017.12;
17. Hongbing Li, Kenji Kawashima. Achieving Stable Tracking in Wave-Variable-Based Teleoperation. (AC-CEPT) *IEEE/ASME Transactions on Mechatronics (TMECH)*.

[Books etc]

1. Robot Control Handbook. 2017.12

[Misc]

1. Toshihiro Kawase, Yasuharu Koike, Kenji Kansaku. Hybrid Control of BMI-based Exoskeletons for Upper Extremities using EEG and EMG Signals Proceedings of LIFE 2017. 2017.09; 78-79

[Conference Activities & Talks]

1. Tetsuro MIYAZAKI, Kazushi SANADA. Joint Gear Ratio and Motion Design of Ball Throwing Robot Maximizing Ball Throwing Performance. The Robotics and Mechatronics Conference 2017 (ROBOMECH 2017) 2017.05.10
2. Masahiko Minamoto, Yutaro Suzuki, Takahiro Kanno, Kenji Kawashima. Effect of robot operation by a camera with the eye tracking control. 2017 IEEE International Conference on Mechatronics and Automation 2017.08.08
3. Takahiro Kanno, Norihiko Ito, Kenji Kawashima. A Cornea Holding Device for Transplantation Surgery Using Negative Pressure. 2017 IEEE Conference on Control Technology and Applications 2017.08.28
4. Yuichi HIRAHARA, Takuya IJIMA, Tetsuro MIYAZAKI, and Kazushi SANADA. A Study of Pneumatic Assist Arm for Physical Load Reduction of Worker. MoViC 2017 2017.08.29
5. Takashi Hasegawa, Takahiro Kanno, Kenji Kawashima. Development of poppet-type servo valve. The 10th JFPS International Symposium on Fluid Power 2017.10.25
6. Ryoken Miyazaki, Takahiro Kanno, Kenji Kawashima. Master-slave integrated surgical robot for laparoscopic surgery with semi-automation control using hand rotation. The 10th JFPS International Symposium on Fluid Power 2017.10.26
7. Takuya Iwai, Richi Fujita, Takahiro Kanno, Kenji Kawashima. Development of a master slave integrated robotic forceps with pneumatic actuators. 2017.10.26
8. Takahiro Kanno, Kenji Kawashima. Pneumatically-driven 4-DOF surgical manipulator with a separation mechanism using cranks. The 10th JFPS International Symposium on Fluid Power 2017.10.26
9. Tetsuro Miyazaki, Takahiro Kanno, Kenji Kawashima. Development of micro actuator using mutual induction for minimally invasive surgical instruments. Annual Meeting of the Japanese Society for Biomaterials 2017.11.20
10. Toshihiro TAGAMI, Tetsuro MIYAZAKI, Takahiro KANNO, Shinichiro YAMAMOTO, Kenji KAWASHIMA. Development of master-slave type gait teaching system. SICE 2017 Industrial Application Division Conference 2017.11.20
11. Tadatoshi SATO, Takahiro KANNO, Tetsuro MIYAZAKI, Toshinori Fujita, Kenji KAWASHIMA. Development of forceps holder with remote center of motion using flexible actuator. SICE 2017 Industrial Application Division Conference 2017.11.20
12. Daisuke Morisaki, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Development of a Pinch-Type Servo Valve Embedded in a Pneumatic Artificial Rubber Muscle. 2017.12.12
13. Keisuke Naito, Takahiro Kanno, Tetsuro Miyazaki, Kenji Kawashima. Development of Minimally Invasive Lifting Device Using Extension and Flexion of Pneumatic Soft Actuator for Laparoscopic Surgery. 2017 IEEE/SICE International Symposium on System Integration 2017.12.13

[Awards & Honors]

1. JSME Award 2016 (Paper), JSME, 2017.04
2. 2017 IEEE/SICE International Symposium on System Integration Award Finalists, SICE, 2017.12

Molecular Cell Biology

Professor Hiroshi Shibuya
Associate Professor Toshiyasu Goto
Assistant Professor Atsushi Sato

(1) Education

Various signaling molecules inducing the cell-growth and differentiation regulate morphogenesis and organogenesis of the vertebrate. The failure of these signal molecules has also been caused with induction of the diseases. Therefore, the elucidation of signal transduction network regulating generation and differentiation is important upon clarifying the mechanism of morphogenesis, organogenesis and diseases. Our research aim is to clarify the signal transduction network regulating the mechanisms of morphogenesis and organogenesis in developmental process. We serve these research and following education to provide graduate students who will become senior scientists in life sciences.

(2) Publications

[Original Articles]

1. Michiue T, Yamamoto T, Yasuoka Y, Goto T, Ikeda T, Nagura K, Nakayama T, Taira M, Kinoshita T.. High variability of expression profiles of homeologous genes for Wnt, Hh, Notch, and Hippo signaling pathways in *Xenopus laevis*. *Dev Biol.* 2017.06; 426(2); 270-290

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.
Associate Professor Jun Hirayama, Ph.D.
Assistant Professor Norio Miyamura, Ph.D.
Assistant Professor Erika Ishihara, Ph.D.
Assistant Professor Ruoxing YU, Ph.D.
Secretary Kazuko Tanaka

(1) Outline

Our goal is to define the molecular basis for the mechanism of organ formation and regeneration using knockout mice and mutant fishes. To accomplish this goal, we have focused on defining signaling molecules and pathways that regulate liver formation and stress responses. Moreover, we are trying to establish a cell therapy for intractable diseases such as liver failures using self-bone marrow cells. Our study will provide new insights into understanding the precise molecular mechanisms that underlie organ failures found in human disease and will lead to the development of new rational therapy for the diseases.

(2) Research

1. Studies on vertebrate early embryogenesis and developmental toxicity
2. Studies on vertebrate organogenesis
3. Studies on organ homeostasis
4. Studies on behavioral rhythm and locomotor activity

(3) Publications

[Original Articles]

1. Yoichi Asaoka, Hiroshi Nishina, Makoto Furutani-Seiki. YAP is essential for 3D organogenesis withstanding gravity. *Dev. Growth Differ.* 2017.01; 59(1); 52-58
2. Seiichiro Mori, Takamasa Takeuchi, Yoshiyuki Ishii, Takashi Yugawa, Tohru Kiyono, Hiroshi Nishina, Iwao Kukimoto. Human Papillomavirus 16 E6 Upregulates APOBEC3B via the TEAD Transcription Factor. *J. Virol.* 2017.03; 91(6);
3. K Otsubo, H Goto, M Nishio, K Kawamura, S Yanagi, W Nishie, T Sasaki, T Maehama, H Nishina, K Mimori, T Nakano, H Shimizu, T W Mak, K Nakao, Y Nakanishi, A Suzuki. MOB1-YAP1/TAZ-NKX2.1 axis controls bronchioalveolar cell differentiation, adhesion and tumour formation. *Oncogene*. 2017.07; 36(29); 4201-4211

4. Norio Miyamura, Shoji Hata, Tohru Itoh, Minoru Tanaka, Miki Nishio, Michiko Itoh, Yoshihiro Ogawa, Shuji Terai, Isao Sakaida, Akira Suzuki, Atsushi Miyajima, Hiroshi Nishina. YAP determines the cell fate of injured mouse hepatocytes in vivo. *Nat Commun.* 2017.07; 8; 16017
5. Negishi J, Omori Y, Shindo M, Takanashi H, Musha S, Nagayama S, Hirayama J, Nishina H, Nakakura T, Mogi C, Sato K, Okajima F, Mochimaru Y, Tomura H. Manganese and cobalt activate zebrafish ovarian cancer G-protein coupled receptor 1 but not GPR4 *J Recept Signal Transduct Res.* 2017.08; (137); 401-408
6. Yamasaki T, Deki-Arima N, Kaneko A, Miyamura N, Iwatsuki M, Matsuoka M, Fujimori-Tonou N, Okamoto-Uchida Y, Hirayama J, Marth J, Yamanashi Y, Kawasaki H, Yamanaka K, Penninger J, Shibata S, Nishina H. Age-dependent motor dysfunction due to neuron-specific disruption of stress-activated protein kinase MKK7 *Sci. Rep.* 2017.08; (7); 7348
7. Tokiwa Yamasaki, Norie Deki-Arima, Asahito Kaneko, Norio Miyamura, Mamiko Iwatsuki, Masato Matsuoka, Noriko Fujimori-Tonou, Yoshimi Okamoto-Uchida, Jun Hirayama, Jamey D Marth, Yuji Yamanashi, Hiroshi Kawasaki, Koji Yamanaka, Josef M Penninger, Shigenobu Shibata, Hiroshi Nishina. Age-dependent motor dysfunction due to neuron-specific disruption of stress-activated protein kinase MKK7. *Sci Rep.* 2017.08; 7(1); 7348
8. Jun Negishi, Yuka Omori, Mami Shindo, Hayate Takanashi, Shiori Musha, Suminori Nagayama, Jun Hirayama, Hiroshi Nishina, Takashi Nakakura, Chihiro Mogi, Koichi Sato, Fumikazu Okajima, Yuta Mochimaru, Hideaki Tomura. Manganese and cobalt activate zebrafish ovarian cancer G-protein-coupled receptor 1 but not GPR4. *J. Recept. Signal Transduct. Res.* 2017.08; 37(4); 401-408
9. Tatsuyuki Matsudaira, Kojiro Mukai, Taishin Noguchi, Junya Hasegawa, Tomohisa Hatta, Shun-Ichiro Iemura, Tohru Natsume, Norio Miyamura, Hiroshi Nishina, Jun Nakayama, Kentaro Semba, Takuya Tomita, Shigeo Murata, Hiroyuki Arai, Tomohiko Taguchi. Endosomal phosphatidylserine is critical for the YAP signalling pathway in proliferating cells. *Nat Commun.* 2017.11; 8(1); 1246

Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D.
Associate Professor: Takahiro ADACHI, Ph.D.
Assistant Professors: Naoko Matsubara, Ph.D.
Assistant Professors: Chizuru AKATSU, Ph.D.
Lecturer: Ji-Yang WANG, Ph.D.
Researcher: Mohammad Aslam, Ph.D.
Researcher: Medzhidov Nazim, Ph.D.
Technicians: Shigeko NAKANO, Yukie KURUSU
Technicians: Takato YODOZAWA, Shukun HOTTA
Secretary: Chikako SAWADA

Graduate Students: Yang-Yang Feng
Graduate Students: Amin ALBORZIAN DESHEIKH
Graduate Students: Sundararaman RENGARAJAN
Graduate Students: Tatsuya YONEMIZU, Ayaka ENDO
Graduate Students: Kyoko NISHIDA
Graduate Students: Yang Hongrui, Li Xuexin
Graduate Students: Moe ENDO, Huang Yuming
Graduate International Research Student: Long Wang

(1) Research

The nature of immune responses depends on whether they respond to protein or non-protein antigens because T lymphocytes recognize only protein antigens. Normal immune system removes pathogens and cancer cells but does not respond to non-microbial foreign substances or self-antigens. Immune responses to non-microbial foreign substances and self-antigens cause allergy and autoimmune diseases, respectively. How the immune system distinguishes pathogens from non-microbial antigens and self-antigens is already clarified for protein antigens. However, little is known about such distinction for non-protein antigens. Immune responses to non-protein antigens play crucial roles in host defense against pathogens such as tuberculosis bacilli and meningococci, and autoimmune diseases such as lupus and immuno-neurological disorders. Thus, immune responses to non-protein antigens constitute a remaining frontier in immunology research. Followings are our research subjects.

1. Recognition of endogenous non-protein antigens by inhibitory B cell co-receptors such as CD22, CD72 and Siglec-10 and its role in the regulation of immune responses and prevention of autoimmune diseases.
2. Mechanisms for B cell response to polysaccharide antigens, and the role of endosomal signaling in these mechanisms
3. Development of drugs that mimic glycan signals to regulate regulatory B cells.
4. Development of therapeutic vaccines for antibody-mediated therapy.

(2) Education

Lecture course on immunology at the master course aims at giving the students the basic ideas how immune system recognize and respond to the antigens, and how immune system efficiently remove pathogens without responding to self-antigens and environmental antigens. In the lecture course in biomedical Science at the doctor course, lectures on immune responses are given so that the students are introduced with the current topics in the field of humoral immune responses. Research projects in both master and doctor courses aims at training the students to acquire basic research techniques on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

(3) Publications**[Original Articles]**

1. Shigeru Hishinuma, Kiyoe Kosaka, Chizuru Akatsu, Yoshihiro Uesawa, Hiroyuki Fukui, and Masaru Shoji. Asp73-dependent and -independent regulation of the affinity of ligands for human histamine H1 receptors by Na⁺ Biochemical Pharmacology. 2017.03; 128; 46-54-54
2. Tsubata, T. B cell tolerance and autoimmunity F1000Research. 2017.03; 6; 391
3. Alborzian Deh Sheikh, A., Akatsu, C., Imamura, A., Abdu-Allah, H. H. M., Takematsu, H., Ando, H., Ishida, H. and Tsubata, T.. Proximity labeling of cis-ligands of CD22/Siglec-2 reveals stepwise α 2,6 sialic acid-dependent and -independent interactions. Biochem. Biophys. Res. Comm. (Epub). 2017.11; 495; 854-859
4. Liu, J., Xiong, E., Zhu, H., Mori, H., Yasuda, S., Kinoshita, K., Tsubata, T. and Wang, J.-Y. . Efficient induction of Ig gene hypermutation in ex vivo-activated primary B cells J. Immunol. 2017.11; 199(9); 3023-3030

[Conference Activities & Talks]

1. Mohammad Aslam, Martin Weigert and Takeshi Tsubata. Regulation of self-reactive B cells by CD72 and Fas . 11th International Symposium of The Institute Network "Frontiers in Biomedical Sciences" 2017.01.26 Tokushima
2. Taro Watabe, Takashi Nagaishi, Akinori Hosoya, Nisha Jose, Arisa Tokai, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. The lack of secreted IgA spontaneously induces the mucosal inflammation specifically in the ileum. DDW (AGA) 2017.05.09 Chicago
3. Takashi Nagaishi, Taro Watabe, Nisha Jose, Akinori Hosoya, Yudai Kojima, Naoya Tsugawa, Takahiro Adachi, Mamoru Watanabe. IgA Deficiency Induces Spontaneous Inflammation in the Ileum. FOCIS 2017 2017.06.14 Chicago
4. Feng Yangyang, Rengarajan Sundararaman, Tang Miao, Tsubata Takeshi. Role of prolonged ROS in B cell receptor signaling. The Regular Meeting of the Japanese Biochemical Society, Kanto Branch 2017 2017.06.17 Tokyo
5. Amin Alborzian-Deh-Sheikh, Chizuru Akatsu, Hideharu Ishida², and Takeshi Tsubata. Cis-ligand dependent and independent interaction of receptor type protein tyrosine phosphatase CD45 with B cell inhibitory receptor CD22. The Regular Meeting of the Japanese Biochemical Society, Kanto Branch 2017 2017.06.17 Tokyo
6. MEDZHIDOV Nazim, TAKATA Toshitaro, SUZUKI Mitsuhiro, ICHINOSE Shizuko, TSUBATA Takeshi. Distinct ubiquitination level and sorting of the B cell receptor. The Regular Meeting of the Japanese Biochemical Society, Kanto Branch 2017 2017.06.17 Tokyo
7. Akinori Hosoya, Takashi Nagaishi, Taro Watabe, Naoya Tsugawa, Nisha Jose, Yudai Kojima, Takahiro Adachi, Mamoru Watanabe. Verification of immunoglobulin A protection of intestinal mucosa from microflora. The 5th Annual Meeting of AOCC 2017.06.17 Seoul
8. Takashi Nagaishi, Taro Watabe, Nisha Jose, Akinori Hosoya, Yudai Kojima, Naoya Tsugawa, Takahiro Adachi, Mamoru Watanabe.. Deficiency of IgA Induces Microflora Alteration and Ileal Inflammation.. ICMI 2017 2017.07.21 Washington DC

9. Nobutaka Numoto, Chizuru Akatsu, Kenro Shinagawa, Takeshi Tsubata, Nobutoshi Ito. Charge distribution regulates the ligand-binding affinity of B cell inhibitory receptor CD72. The 55th Annual Meeting of the Biophysical Society of Japan 2017.09.20 Kumamoto
10. Takeshi Tsubata. Inhibitory B cell co-receptor CD72 regulates self-tolerance through SHP-1 activation. University of Freiburg 2017.10.11 Freiburg, Germany
11. Naoya Tsugawa, Takashi Nagaishi, Taro Watabe, Nisha Jose, Akinori Hosoya, Yudai Kojima, Takahiro Adachi, Richard S. Blumberg, Mamoru Watanabe. Verification of Immunoglobulin A regulation of microflora and protection of intestinal mucosa.. UEGW 2017 2017.10.31 Barcelona
12. Takeshi Tsubata. Inhibitory B cell co-receptor and autoimmunity. Seoul National University School of Dentistry 2017.11.08 Seoul
13. Chizuru Akatsu, Hongrui Yang and Takeshi Tsubata,. The Inhibitory B Cell Co-Receptor CD72 Regulates B Cell Response to Self Nucleic Acids Crucial for Development of SLE. Korean Association of Immunologists (KAI) International Meeting 2017 2017.11.10 Seoul
14. Chizuru Akatsu, Amin Alborzian Deh Sheikh, Takeshi Tsubata. Role of CD45 (PTPRC) in the regulation of SHP-1 (PTPN6)-activating receptor CD22. The 3rd Japan-Taiwan Bilateral Conference on Protein Phosphatase 2017.11.19 Sendai
15. Takeshi Tsubata, Hongrui Yang, Chizuru Akatsu. CD72 recognizes RNA-related self-antigens and prevents autoimmunity. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai
16. Kyoko Nishida, Akihiro Kimura, Takeshi Tsubata, Harumi Suzuki. NQO1 play a pathogenic role in autoimmune diseases through the suppression of IL-10 production in Th17 cells. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.12 Sendai
17. Takahiro Adachi, Soichiro Yoshikawa, Hajime Karasuyama. Intravital imaging of Ca²⁺ signals in lymphocytes of the Ca²⁺ biosensor YC3.60 transgenic mice. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai
18. Feng Yangyang, Rengarajan Sundararaman, Tang Miao, Tsubata Takeshi. Role of NADPH oxidases in BCR ligation-induced ROS production and activation. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai
19. MEDZHIDOV Nazim, TAKATA Toshitaro, SUZUKI Mitsuhiko, ICHINOSE Shizuko, YAMAGUCHI Hirofumi, ARAKAWA Satoko, SHIMIZU Shigeomi, TSUBATA Takeshi.. Role of poor B cell receptor ubiquitination in efficient antigen presentation. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai
20. Naoya Tsugawa, Takashi Nagaishi, Taro Watabe, Akinori Hosoya, Nisha Jose, Yudai Kojima, Soichiro Yoshikawa, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. Verification of immunoglobulin A regulation of mucosal microflora and homeostasis. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai
21. Taro Watabe, Takashi Nagaishi, Akinori Hosoya, Nisha Jose, Naoya Tsugawa, Yudai Kojima, Soichiro Yoshikawa, Hajime Karasuyama, Takahiro Adachi, Mamoru Watanabe. Analysis of ileocecal immune response in an experimental colitis model using intra-vital imaging. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Sendai

[Awards & Honors]

1. Eugen-und-Ilse-Seibold-Preis, Eugen and Ilse Seibold Prize, Deutsche Forschungsgemeinschaft, 2017.10

Epigenetics

Professor Fumitoshi Ishino
 Associate Professor Takashi Kohda
 Assistant Professor Hirosuke Shiura
 Assistant Professor Yuki Kawasaki
 Project Lecturere Jiyoung Lee
 Adjanct Lecturere Shin Kobayashi

(1) Outline

Epigenetics and Genetics are basics of biology that enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of the organisms including our human beings. Genomic imprinting is a mammalian-specific epigenetic mechanism that gives rise to functional differences between paternally- and maternally-derived genomes in development, behavior and growth. Somatic cloned animals give us unique chances to examine ‘genetically identical but epigenetically diverged animals’. Mammalian-specific LTR retrotransposon-derived genes are essential for mammalian development, such as placenta and brain functions. These studies show us how Epigenetics and Genetics are important in mammalian biology. We focus on these mammalian-specific genomic functions to elucidate how these genomic functions work and have been evolved as new genomic functions during evolution. Our final goal is to contribute to the human biology as well as medicine in the 21st century by novel understanding of genomic functions.

(2) Research

- 1) Genomic imprinting in human and mammalian development.
- 2) Placenta function and its evolution in mammals.
- 3) Somatic cloning: its epigenetic effects and application to regenerative medicine.
- 4) Assisted reproductive technology: its epigenetic effects and safer application.
- 5) Role of retrotransposon-derived genes in mammalian specific genomic functions.

(3) Education

Graduate School of Medical and Dental Science
 Life Science and Technology Track
 Bioscience I
 Medical and Dental Science and Technology Track
 Molecular and Cellular Biology
 Deveelopmenta and Regenerative Bioscience
 Molecular Cell Biology
 Introduction to Human Molecular Genetics

Faculty of Medicine
 Molecular Genetics

(4) Lectures & Courses

Obtain basic and applicative knowledges and techniques by challenging cutting-edge themes.

(5) Clinical Services & Other Works

Research Center for Science Systems, Senior Researcher
Japan Society for Biological Sciences, Board member
Japan Society for Epigenetics, Secretary

(6) Publications

[Original Articles]

1. Tamio Furuse, Kunio Miyake, Takashi Kohda, Hideki Kaneda, Takae Hirasawa, Ikuko Yamada, Tomoko Kushida, Misho Kashimura, Kimio Kobayashi, Fumitoshi Ishino, Takeo Kubota, Shigeharu Wakana. Protein-restricted diet during pregnancy after insemination alters behavioral phenotypes of the progeny. *Genes Nutr.* 2017; 12; 1
2. Moe Kitazawa, Masaru Tamura, Tomoko Kaneko-Ishino, Fumitoshi Ishino. Severe damage to the placental fetal capillary network causes mid- to late fetal lethality and reduction in placental size in Peg11/Rtl1 KO mice. *Genes Cells.* 2017.02; 22(2); 174-188

Medical Science Mathematics

Professor: Tatsuhiko Tsunoda, Junior Associate Professor: Daichi Shigemizu, Assistant Professor: Fuyuki Miya

(1) Outline

Medical application of rapidly progressing omic profiling technologies and, in particular, the promotion of personalized/precision/preventive medicine have been keenly desired. Our department overcomes such medical science issues by using a combination of mathematics and computational sciences: (1) Integrative analysis of clinical and omic data for exploring etiologies of intractable diseases, (2) Molecular classification of and systems approach to understanding disease based on omic profiling, and (3) Prediction for personalized/precision/preventive medicine - we apply mathematical methods, e.g, machine learning techniques, to optimum therapy prediction for each patient when she/he visits to a hospital/medical institute, and we can also apply these methods to disease prevention based on an individual's health check records.

(2) Publications

[Original Articles]

1. Yutaka Negishi, Fuyuki Miya, Ayako Hattori, Yoshikazu Johmura, Motoo Nakagawa, Naoki Ando, Ikumi Hori, Takao Togawa, Kohei Aoyama, Kei Ohashi, Shinobu Fukumura, Seiji Mizuno, Ayako Umemura, Yoko Kishimoto, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Makoto Nakanishi, Shinji Saitoh. A combination of genetic and biochemical analyses for the diagnosis of PI3K-AKT-mTOR pathway-associated megalencephaly. *BMC Med. Genet.* 2017.01; 18(1); 4
2. Nanako Hamada, Yutaka Negishi, Makoto Mizuno, Fuyuki Miya, Ayako Hattori, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Hidenori Tabata, Shinji Saitoh, Koh-Ichi Nagata. Role of a heterotrimeric G-protein, Gi2, in the corticogenesis: possible involvement in periventricular nodular heterotopia and intellectual disability. *J. Neurochem.* 2017.01; 140(1); 82-95
3. Alok Sharma, Keith A Boroevich, Daichi Shigemizu, Yoichiro Kamatani, Michiaki Kubo, Tatsuhiko Tsunoda. Hierarchical Maximum Likelihood Clustering Approach. *IEEE Trans Biomed Eng.* 2017.01; 64(1); 112-122
4. Negishi Y, Miya F, Hattori A, Johmura Y, Nakagawa M, Ando N, Hori I, Togawa T, Aoyama K, Ohashi K, Fukumura S, Mizuno S, Umemura A, Kishimoto Y, Okamoto N, Kato M, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Nakanishi M, Saitoh S.. A combination of genetic and biochemical analyses for the diagnosis of PI3K-AKT-mTOR pathway-associated megalencephaly. *BMC Med. Genet.* 2017.01; (18); 4
5. Hamada N, Negishi Y, Mizuno M, Miya F, Hattori A, Okamoto N, Kato M, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Tabata H, Saitoh S, Nagata K.. Role of a heterotrimeric G-protein, Gi2, in the corticogenesis: Possible involvement in periventricular nodular heterotopia and intellectual disability. *J. Neurochem.* 2017.01; (140); 82-95

6. Mayuko Furuta, Masaki Ueno, Akihiro Fujimoto, Shinya Hayami, Satoru Yasukawa, Fumiyoshi Kojima, Koji Arihiro, Yoshiiku Kawakami, Christopher P Wardell, Yuichi Shiraishi, Hiroko Tanaka, Kaoru Nakano, Kazuhiro Maejima, Aya Sasaki-Oku, Naoki Tokunaga, Keith A Boroevich, Tetsuo Abe, Hiroshi Aikata, Hideki Ohdan, Kunihito Gotoh, Michiaki Kubo, Tatsuhiko Tsunoda, Satoru Miyano, Kazuaki Chayama, Hiroki Yamaue, Hidewaki Nakagawa. Whole genome sequencing discriminates hepatocellular carcinoma with intrahepatic metastasis from multi-centric tumors. *J. Hepatol.* 2017.02; 66(2); 363-373
7. Cassandra N Spracklen, Peng Chen, Young Jin Kim, Xu Wang, Hui Cai, Shengxu Li, Jirong Long, Ying Wu, Ya Xing Wang, Fumihiko Takeuchi, Jer-Yuarn Wu, Keum-Ji Jung, Cheng Hu, Koichi Akiyama, Yonghong Zhang, Sanghoon Moon, Todd A Johnson, Huaixing Li, Rajkumar Dorajoo, Meian He, Maren E Cannon, Tamara S Roman, Elias Salfati, Keng-Hung Lin, Xiuqing Guo, Wayne H H Sheu, Devin Absher, Linda S Adair, Themistocles L Assimes, Tin Aung, Qiuyin Cai, Li-Ching Chang, Chien-Hsiun Chen, Li-Hsin Chien, Lee-Ming Chuang, Shu-Chun Chuang, Shufa Du, Qiao Fan, Cathy S J Fann, Alan B Feranil, Yechiel Friedlander, Penny Gordon-Larsen, Dongfeng Gu, Lixuan Gui, Zhirong Guo, Chew-Kiat Heng, James Hixson, Xuhong Hou, Chao Agnes Hsiung, Yao Hu, Mi Yeong Hwang, Chii-Min Hwu, Masato Isono, Jyh-Ming Jimmy Juang, Chiea-Chuen Khor, Yun Kyoung Kim, Woon-Puay Koh, Michiaki Kubo, I-Te Lee, Sun-Ju Lee, Wen-Jane Lee, Kae-Woei Liang, Blanche Lim, Sing-Hui Lim, Jianjun Liu, Toru Nabika, Wen-Harn Pan, Hao Peng, Thomas Quertermous, Charumathi Sabanayagam, Kevin Sandow, Jinxiu Shi, Liang Sun, Pok Chien Tan, Shu-Pei Tan, Kent D Taylor, Yik-Ying Teo, Sue-Anne Toh, Tatsuhiko Tsunoda, Rob M van Dam, Aili Wang, Feijie Wang, Jie Wang, Wen Bin Wei, Yong-Bing Xiang, Jie Yao, Jian-Min Yuan, Rong Zhang, Wanting Zhao, Yii-Der Ida Chen, Stephen S Rich, Jerome I Rotter, Tzung-Dau Wang, Tangchun Wu, Xu Lin, Bok-Ghee Han, Toshihiro Tanaka, Yoon Shin Cho, Tomohiro Katsuya, Weiping Jia, Sun-Ha Jee, Yuan-Tsong Chen, Norihiro Kato, Jost B Jonas, Ching-Yu Cheng, Xiao-Ou Shu, Jiang He, Wei Zheng, Tien-Yin Wong, Wei Huang, Bong-Jo Kim, E-Shyong Tai, Karen L Mohlke, Xueling Sim. Association analyses of East Asian individuals and trans-ancestry analyses with European individuals reveal new loci associated with cholesterol and triglyceride levels. *Hum. Mol. Genet.* 2017.05; 26(9); 1770-1784
8. Abdollah Dehzangi, Yosvany López, Sunil Pranit Lal, Ghazaleh Taherzadeh, Jacob Michaelson, Abdul Sattar, Tatsuhiko Tsunoda, Alok Sharma. PSSM-Suc: Accurately predicting succinylation using position specific scoring matrix into bigram for feature extraction. *J. Theor. Biol.* 2017.05; 425; 97-102
9. Shunsuke Kawamura, Nobuyuki Onai, Fuyuki Miya, Taku Sato, Tatsuhiko Tsunoda, Kazutaka Kurabayashi, Satoshi Yotsumoto, Shoko Kuroda, Katsuto Takenaka, Koichi Akashi, Toshiaki Ohteki. Identification of a Human Clonogenic Progenitor with Strict Monocyte Differentiation Potential: A Counterpart of Mouse cMoPs. *Immunity.* 2017.05; 46(5); 835-848.e4
10. Kato K, Miya F* (*equal contribution), Hori I, Ieda D, Ohashi K, Negishi Y, Hattori A, Okamoto N, Kato M, Tsunoda T, Yamasaki M, Kanemura Y, Kosaki K, Saitoh S.. A novel missense mutation in the HECT domain of NEDD4L identified in a girl with periventricular nodular heterotopia, polymicrogyria, and cleft palate. *J. Hum. Genet.* 2017.05; (in press);
11. Kawamura S, Onai N, Miya F, Sato T, Tsunoda T, Kurabayashi K, Yotsumoto S, Kuroda S, Takenaka K, Akashi K, Ohteki T.. Identification of a Human Clonogenic Progenitor with Strict Monocyte Differentiation Potential: A Counterpart of Mouse cMoPs. *Immunity.* 2017.05; (46); 835-848
12. Yosvany López, Abdollah Dehzangi, Sunil Pranit Lal, Ghazaleh Taherzadeh, Jacob Michaelson, Abdul Sattar, Tatsuhiko Tsunoda, Alok Sharma. SucStruct: Prediction of succinylated lysine residues by using structural properties of amino acids. *Anal. Biochem.* 2017.06; 527; 24-32
13. Nobuhiko Okamoto, Fuyuki Miya, Tatsuhiko Tsunoda, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki. Novel MCA/ID syndrome with ASH1L mutation. *Am. J. Med. Genet. A.* 2017.06; 173(6); 1644-1648
14. Ikumi Hori, Takanobu Otomo, Mitsuko Nakashima, Fuyuki Miya, Yutaka Negishi, Hideaki Shiraishi, Yutaka Nonoda, Shinichi Magara, Jun Tohyama, Nobuhiko Okamoto, Takeshi Kumagai, Konomi Shimoda, Yoshiya Yukitake, Daigo Kajikawa, Tomohiro Morio, Ayako Hattori, Motoo Nakagawa, Naoki Ando, Ichizo Nishino, Mitsuhiro Kato, Tatsuhiko Tsunoda, Hirotomo Saito, Yonehiro Kanemura, Mami Yamasaki, Kenjiro Kosaki, Naomichi Matsumoto, Tamotsu Yoshimori, Shinji Saitoh. Defects in autophagosome-lysosome fusion underlie Vici syndrome, a neurodevelopmental disorder with multisystem involvement. *Sci Rep.* 2017.06; 7(1); 3552

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16. Okamoto N, Miya F, Tsunoda T, Kato M, Saitoh S, Yamasaki M, Kanemura Y, Kosaki K. . Novel MCA/ID syndrome with ASH1L mutation. *Am. J. Med. Genet. A.* 2017.06; (in press);
17. Okamoto N, Miya F, Hatuskawa Y, Suzuki Y, Kawato K, Yamamoto Y, Tsunoda T, Kato M, Saitoh S, Yamasaki M, Kanemura Y, Kosaki K.. Siblings with Optic Neuropathy and RTN4IP1 Mutation. *J. Hum. Genet.* 2017.06; (in press);
18. Kazuyoshi Ishigaki, Yuta Kochi, Akari Suzuki, Yumi Tsuchida, Haruka Tsuchiya, Shuji Sumitomo, Kensuke Yamaguchi, Yasuo Nagafuchi, Shinichiro Nakachi, Rika Kato, Keiichi Sakurai, Hirofumi Shoda, Katsunori Ikari, Atsuo Taniguchi, Hisashi Yamanaka, Fuyuki Miya, Tatsuhiko Tsunoda, Yukinori Okada, Yukihide Momozawa, Yoichiro Kamatani, Ryo Yamada, Michiaki Kubo, Keishi Fujio, Kazuhiko Yamamoto. Polygenic burdens on cell-specific pathways underlie the risk of rheumatoid arthritis. *Nat. Genet.* 2017.07; 49(7); 1120-1125
19. Daichi Shigemizu, Takuji Iwase, Masataka Yoshimoto, Yasuyo Suzuki, Fuyuki Miya, Keith A Boroevich, Toyomasa Katagiri, Hitoshi Zembutsu, Tatsuhiko Tsunoda. The prediction models for postoperative overall survival and disease-free survival in patients with breast cancer. *Cancer Med.* 2017.07; 6(7); 1627-1638
20. Artem Lysenko, Keith Anthony Boroevich, Tatsuhiko Tsunoda. Arete - candidate gene prioritization using biological network topology with additional evidence types. *BioData Min.* 2017.07; 10; 22
21. Ishigaki K, Kochi Y, Suzuki A, Tsuchida Y, Tsuchiya H, Sumitomo S, Yamaguchi K, Nagafuchi Y, Nakachi S, Kato R, Sakurai K, Shoda H, Ikari K, Taniguchi A, Yamanaka H, Miya F, Tsunoda T, Okada Y, Momozawa Y, Kamatani Y, Yamada R, Kubo M, Fujio K, Yamamoto K.. Polygenic burdens on cell-specific pathways underlie the risk of rheumatoid arthritis. *Nat. Genet.* 2017.07; (49); 1120-1125
22. Shigemizu D, Iwase T, Yoshimoto M, Suzuki Y, Miya F, Boroevich KA, Katagiri T, Zembutsu H, Tsunoda T.. The prediction models for postoperative overall survival and disease-free survival in patients with breast cancer. *Cancer Med.* 2017.07; (6); 1627-1638
23. Hosoe J*, Kadowaki H*, Miya F*, Aizu K, Kawamura T, Miyata I, Satomura K, Ito T, Hara K, Tanaka M, Ishiura H, Tsuji S, Suzuki K, Takakura M, Boroevich KA, Tsunoda T, Yamauchi T, Shojima N, Kadowaki T.. Structural Basis and Genotype-phenotype Correlations of INSR Mutations Causing Severe Insulin Resistance. *Diabetes.* 2017.08; (in press);
24. Okamoto N*, Tsuchiya Y*, Miya F*, Tsunoda T, Yamashita K, Boroevich KA, Kato M, Saitoh S, Yamasaki M, Kanemura Y, Kosaki K, Kitagawa D.. A Novel Genetic Syndrome with STARD9 Mutation and Abnormal Spindle Morphology. *Am. J. Med. Genet. A.* 2017.08; (in press);
25. Koji Kato, Fuyuki Miya, Ikumi Hori, Daisuke Ieda, Kei Ohashi, Yutaka Negishi, Ayako Hattori, Nobuhiko Okamoto, Mitsuhiro Kato, Tatsuhiko Tsunoda, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Shinji Saitoh. A novel missense mutation in the HECT domain of NEDD4L identified in a girl with periventricular nodular heterotopia, polymicrogyria and cleft palate. *J. Hum. Genet.* 2017.09; 62(9); 861-863
26. Jun Hosoe, Hiroko Kadowaki, Fuyuki Miya, Katsuya Aizu, Tomoyuki Kawamura, Ichiro Miyata, Kenichi Satomura, Takeru Ito, Kazuo Hara, Masaki Tanaka, Hiroyuki Ishiura, Shoji Tsuji, Ken Suzuki, Minaka Takakura, Keith A Boroevich, Tatsuhiko Tsunoda, Toshimasa Yamauchi, Nobuhiro Shojima, Takashi Kadowaki. Structural Basis and Genotype-Phenotype Correlations of INSR Mutations Causing Severe Insulin Resistance. *Diabetes.* 2017.10; 66(10); 2713-2723
27. Nobuhiko Okamoto, Yuki Tsuchiya, Fuyuki Miya, Tatsuhiko Tsunoda, Kumiko Yamashita, Keith A Boroevich, Mitsuhiro Kato, Shinji Saitoh, Mami Yamasaki, Yonehiro Kanemura, Kenjiro Kosaki, Daiju Kitagawa. A novel genetic syndrome with STARD9 mutation and abnormal spindle morphology. *Am. J. Med. Genet. A.* 2017.10; 173(10); 2690-2696

28. Ronesh Sharma, Maitsetseg Bayarjargal, Tatsuhiko Tsunoda, Ashwini Patil, Alok Sharma. MoRFPred-plus: Computational Identification of MoRFs in Protein Sequences using Physicochemical Properties and HMM profiles. *J. Theor. Biol.*. 2017.10; 437; 9-16
29. Jae-Jung Kim, Sin Weon Yun, Jeong Jin Yu, Kyung Lim Yoon, Kyung-Yil Lee, Hong-Ryang Kil, Gi Beom Kim, Myung-Ki Han, Min Seob Song, Hyoung Doo Lee, Kee Soo Ha, Sejung Sohn, Todd A Johnson, Atsushi Takahashi, Michiaki Kubo, Tatsuhiko Tsunoda, Kaoru Ito, Yoshihiro Onouchi, Young Mi Hong, Gi Young Jang, Jong-Keuk Lee, . A genome-wide association analysis identifies NMNAT2 and HCP5 as susceptibility loci for Kawasaki disease. *J. Hum. Genet.*. 2017.12; 62(12); 1023-1029
30. Shiu Kumar, Alok Sharma, Tatsuhiko Tsunoda. An improved discriminative filter bank selection approach for motor imagery EEG signal classification using mutual information. *BMC Bioinformatics*. 2017.12; 18(Suppl 16); 545
31. Alok Sharma, Yosvany López, Tatsuhiko Tsunoda. Divisive hierarchical maximum likelihood clustering. *BMC Bioinformatics*. 2017.12; 18(Suppl 16); 546
32. Alok Sharma, Piotr J Kamola, Tatsuhiko Tsunoda. 2D-EM clustering approach for high-dimensional data through folding feature vectors. *BMC Bioinformatics*. 2017.12; 18(Suppl 16); 547
33. Ueki M, Maeda M, Sugiyama T, Kohmoto R, Kojima S, Ikeda T, Harada A, Kanemura Y, Miya F, Tsunoda T, Yamasaki M. A Case of Dandy-Walker Malformation Complicated by Axenfeld-Rieger Syndrome *International Journal of Ophthalmology & Eye Science*. 2017.12; S1:02:001; 1-3

[Conference Activities & Talks]

1. Tatsuhiko Tsunoda. Multiomics and clinical analysis of cancer. CREST International Symposium on Big Data Application 2017.01.12 Tokyo, Japan
2. Tatsuhiko Tsunoda. Future medicine based on genomic big data and artificial intelligence. Citizen public lecture 2017.02.17
3. Tatsuhiko Tsunoda. New development of genomic medicine based on omic analysis. The 8th Symposium on Biological Statistics Network 2017.03.27
4. Shinji Saitoh, Ikumi Hori, Takanobu Otomo, Mitsuko Nakashima, Fuyuki Miya, Yutaka Negishi, Ayako Hattori, Tatsuhiko Tsunoda, Naomichi Matsumoto, Tamotsu Yoshimori. Clinical heterogeneity of genetically confirmed nine patients with Vici syndrome. 14th Asian and Oceanian Congress of Child Neurology (AOCCN) 2017.05.11
5. Tatsuhiko Tsunoda. Omic analysis drives precision medicine. International Conference for Precision Cancer Medicine 2017.06.30 Tokyo, Japan
6. Tatsuhiko Tsunoda. Multi-omic Analysis based on Medical Big Data. Workshop for collaboration between TMDU and Waseda University 2017.07.12 Tokyo, Japan
7. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Big Data Fields Joint Meeting 2017.09.16 Tokyo, Japan
8. Tatsuhiko Tsunoda. Multi-omic analysis for precision cancer medicine. DNA sequencing technologies and their application in practice 2017.10.12 Yerevan, Armenia
9. Tatsuhiko Tsunoda. Trans-omic analysis drives precision medicine. The 1st International Symposium for Trans-Omics 2017.11.21 Tokyo
10. Tatsuhiko Tsunoda. Exploring etiologies, sub-classification, and risk prediction of diseases based on big-data analysis of clinical and whole omics data in medicine. CREST Big Data Fields Joint Meeting 2017.12.18 Tokyo, Japan

[Patents]

1. METHOD FOR SELECTING IPS CELL CLONE, AND METHOD FOR SELECTING GENE USED IN METHOD FOR SELECTING SAME, Announcement Number : WO 2012/115270

[Works]

1. Arete - an analysis toolkit for network-based gene prioritisation, Software, 2017.04
2. 2D-EM: Matlab package of 2D-EM clustering approach, Software, 2017.08
3. DRAGON: Matlab package of DRAGON clustering approach, Software, 2017.09

[Others]

1. Discovery of new gene regions related to asthma, 2017.12
Appeared in newspaper Kagaku-Kougyou-Nippou

Structural Biology

Professor Nobutoshi ITO
Associate Professor Teikichi IKURA
Assistant Professor Nobutaka NUMOTO

(1) Outline

The advance of genome science and proteomic analysis has produced a large amount of information about the primary structure of proteins and their spatial and temporal distributions. On the other hand, most of the proteins only function when they take certain three dimensional structures. As obviously seen in so-called prion diseases, proteins which are chemically correct but structurally incorrect not only fail to function properly but also can harm cells. Our laboratory aims to understand the function of biological macromolecules at atomic level through structure analysis and other methods of physical chemistry, in the hope that accumulation of such knowledge will eventually lead to development of drugs. We are also involved in providing database of such structural data to scientists through the activities of Protein Data Bank Japan.

(2) Research

Collaborating with groups within and outside of the university, we are engaged in various research projects including;

- 1) Structural analyses of B-cell coreceptors
- 2) Physicochemical analysis on the mechanism of the signal transduction for activation of T cells
- 3) Structural analyses of potential drug targets of nuclear receptors
- 4) Analysis of interactions between tau protein and Pin1
- 5) Molecular mechanism of the sero-specificity of dengue virus
- 6) Structural basis of giant hemoglobins
- 7) Molecular basis of suppression of HIV-1
- 8) Structure based drug design for protein kinases
- 9) Improvement in Protein Data Bank

(3) Lectures & Courses

The students learn theoretical basis of structure determination, mainly X-ray crystallography, of proteins and other biological macromolecules. Recent advance in structural biology is also discussed in seminar. Students learn lab techniques related to large-scale production, purification and crystallization of protein samples. They also learn computational methods to determine and refine crystal structures.

(4) Publications**[Original Articles]**

1. Satomi Inaba, Nobutaka Numoto, Shuhei Ogawa, Hisayuki Morii, Teikichi Ikura, Ryo Abe, Nobutoshi Ito, Masayuki Oda. Crystal Structures and Thermodynamic Analysis Reveal Distinct Mechanisms of CD28 Phosphopeptide Binding to the Src Homology 2 (SH2) Domains of Three Adaptor Proteins. *J. Biol. Chem.* 2017.01; 292(3); 1052-1060
2. Yurina Miyashita, Eiji Ohmae, Teikichi Ikura, Kaoru Nakasone, Katsuo Katayanagi. Halophilic mechanism of the enzymatic function of a moderately halophilic dihydrofolate reductase from *Haloarcula japonica* strain TR-1. *Extremophiles*. 2017.05; 21(3); 591-602

[Conference Activities & Talks]

1. Nobutoshi Ito. Protein Data Bank and Structure Deposition at PDBj. CCP4 Crystallography School and Workshop 2017.01.27 SPring8, Harima, Japan
2. Teikichi Ikura, Nobutoshi Ito. Catalytic Mechanism of a Protease Derived from Pin1. The 17th Annual Meeting of the Protein Science Society of Japan 2017.06.21 Sendai
3. Nobutaka Numoto, Chizuru Akatsu, Kenro Shinagawa, Takeshi Tsubata, Nobutoshi Ito. Prediction of ligand-binding site of B cell inhibitory receptor CD72 through crystal structure. The 17th Annual Meeting of the Protein Science Society of Japan 2017.06.22 Sendai
4. Teikichi Ikura, Nobutoshi Ito. Functional conversion from peptidyl-prolyl isomerase to protease by a single amino acid substitution. the joint 19th International Union of Pure and Applied Biophysics 2017.07.17 Edinburgh, UK
5. Takeshi Kawabata, Masayuki Oda, Satomi Inaba, Nobutaka Numoto, Fusako Kawai. Structural and mutational analysis of PET-hydrolyzing enzyme, Cut190, based on the 3D docking structure with model compounds of PET. 254th American Chemical Society National Meeting & Exposition 2017.08.20 Washington, DC, USA
6. Nobutaka Numoto, Chizuru Akatsu, Kenro Shinagawa, Takeshi Tsubata, Nobutoshi Ito. Charge distribution regulates the ligand-binding affinity of B cell inhibitory receptor CD72. The 55th Annual Meeting of the Biophysical Society of Japan 2017.09.20 Kumamoto
7. Teikichi Ikura, Nobutoshi Ito. Quantitative evaluation of activity of a protease derived from Pin1 for tau protein. The 56th Annual Meeting of the Biophysical Society of Japan 2017.09.21 Kumamoto, Japan
8. Nobutaka Numoto. Combination of microspectrophotometric and X-ray crystallographic analyses in structural biology. SPring-8 Workshop -New method of protein structural analysis- 2017.11.29 Hyogo

Neuroscience

Professor Kohichi Tanaka
Associate Professor Tomomi Aida
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Zhao Zhuoyang
Kaori Sugiyama
Takehisa Handa

Graduate Student (master course)
Haruka Takigawa
Hiroshi Ogawa
Kurumi Hagiawara
Bi Haining

Technical Staff
Harumi Ishikubo

Secretary
Satomi Ohno

(1) Outline

The final goal of our research is to understand molecular, cellular, and neuronal ensemble mechanisms underlying higher order brain functions including learning and memory. For that purpose, we combine molecular genetics, physiological and behavioral methods. The laboratory also studies the mechanism that underlies neuronal cell death and regeneration.

(2) Research

1. Functions of glutamate transporters in the brain

Glutamate is a major excitatory neurotransmitter and plays an important role in neuronal plasticity and neurotoxicity in the central nervous system. Glutamate transport proteins provide the mechanism by which synaptically released glutamate is inactivated and kept below toxic levels in the extracellular space. By now, five subtypes of high-affinity glutamate transporters have been identified in the mammalian brain. Our lab studies the physiological and pathological roles of glutamate transporter subtypes using subtype-specific knockout mice. Despite glial glutamate transporter dysfunction leading to excitotoxicity has been documented in many neurological diseases, it remains unclear whether its dysfunction is a primary cause or secondary outcome of neuronal death at disease state. Here we show the combined loss of glial glutamate transporters GLT1 and GLAST in spinal cord caused motor neuronal death and hindlimb paralysis. Further, our novel mutant exhibits the nuclear irregularities and calpain-mediated progressive nuclear pore complex degradation. Our study reveals that glial glutamate transporter dysfunction is sufficient to cause motor neuronal death in vivo (Sugiyama et al., 2017).

We show that GLAST, a major glutamate transporter in the cerebellar cortex, is essential for synaptic wrapping by Bergmann glia and synaptic wiring on Purkinje cells (PCs) by parallel fibers (PFs) and climbing fibers (CFs). Without GLAST, monoinnervation of PCs by single strong CFs and segregation of CF and PF territories along PC dendrites cannot develop normally or be maintained. PCs are frequently innervated by additional CF, whereas innervation by main CFs becomes weaker. Ectopic PF synapses appear at proximal dendrites, causing disruption of CF and PF territory segregation along PC dendrites. We conclude that GLAST is indispensable for the establishment of excitatory synaptic wiring to PCs through competition between CFs and between CFs and PFs (Miyazaki et al., 2017).

2. Role of DEPDC5 in the pathogenesis of epilepsy and psychiatric disorder

Epilepsy is one of the most frequent (1%) neurological disorders characterized by spontaneous and recurrent seizures. However, pharmacoresistance occurs in 30% of the patients. Recently, a role for genetic factors in idiopathic epilepsies, with no identified structural lesion or metabolic cause, is becoming clear. DEP (Dishevelled, Egl-10 and Pleckstrin) domain containing protein 5 (DEPDC5) is a newly identified causative gene for epilepsy (Ishida et al., 2013). DEPDC5 has no transmembrane domain and no homology with known epilepsy genes encode ion channel or transmitter receptor subunits. Its role in epileptogenesis likely differs from the mechanisms known so far. In addition, some individuals also have psychiatric disorder, like autistic features and schizophrenia. This suggests that DEPDC5 is a common genetic actor in refractory epilepsy and psychosis. We revealed that *Depdc5* inhibits mTORC1 signaling, and *Depdc5* KO rats are embryonic lethal (Marsan and Ishida et al., 2016). To avoid the lethality and deeply understand the function of DEPDC5, we conditionally delete *Depdc5* in specific brain region or neuronal cells in mice by Cre-loxP system. This year, we have generated *Depdc5* floxed mice using CRISPR-Cas9 system. We strongly promote our research with this mouse. Research of DEPDC5 is likely to give new insight into epilepsy and psychosis research.

(3) Education

Goals/Outline:

Students should generate genetically modified animals to comprehensively understand the cognitive mechanisms at the level of molecule to behavior. Then, students should analyze cognitive deficits of mutant animals and those molecular mechanisms.

Available programs:

Participation in the ongoing research project; as needed

Training for cell biology: five times a year 13:00 – 16:00

Experiment:

1. Gene cloning and generation of targeting vector.
2. Generation of genetically modified mice
3. Behavioral analysis of the mice
4. Morphological analysis of central nervous systems.

(4) Lectures & Courses

The aim of this practice is to learn molecular biological, anatomical, electrophysiological and psychological approaches to elucidate the mechanism of cognition. Moreover, based on previous case reports of cognitive deficits, students should plan and discuss what kinds of the researches are possible and meaningful to elucidate the pathology of these diseases, leading to unveil the mechanism of cognition.

(5) Publications

[Original Articles]

1. Tomoharu Nakamori, Tomomi Kato, Hiroyuki Sakagami, Kohichi Tanaka, Hiroko Ohki-Hamazaki. Regulation of visual Wulst cell responsiveness by imprinting causes stimulus-specific activation of rostral cells.

Sci Rep. 2017.02; 7; 42927

2. Ken-Ichiro Kubo, Kimiko Deguchi, Taku Nagai, Yukiko Ito, Keitaro Yoshida, Toshihiro Endo, Seico Benner, Wei Shan, Ayako Kitazawa, Michihiko Aramaki, Kazuhiro Ishii, Minkyung Shin, Yuki Matsunaga, Kanehiro Hayashi, Masaki Kakeyama, Chiharu Tohyama, Kenji F Tanaka, Kohichi Tanaka, Sachio Takashima, Masahiro Nakayama, Masayuki Itoh, Yukio Hirata, Barbara Antalffy, Dawna D Armstrong, Kiyofumi Yamada, Ken Inoue, Kazunori Nakajima. Association of impaired neuronal migration with cognitive deficits in extremely preterm infants. *JCI Insight*. 2017.05; 2(10);
3. Taisuke Miyazaki, Miwako Yamasaki, Kouichi Hashimoto, Kazuhisa Kohda, Michisuke Yuzaki, Keiko Shimamoto, Kohichi Tanaka, Masanobu Kano, Masahiko Watanabe. Glutamate transporter GLAST controls synaptic wrapping by Bergmann glia and ensures proper wiring of Purkinje cells. *Proc. Natl. Acad. Sci. U.S.A.*. 2017.07; 114(28); 7438-7443
4. Kaori Sugiyama, Tomomi Aida, Masatoshi Nomura, Ryoichi Takayanagi, Hanns U Zeilhofer, Kohichi Tanaka. Calpain-Dependent Degradation of Nucleoporins Contributes to Motor Neuron Death in a Mouse Model of Chronic Excitotoxicity. *J. Neurosci.*. 2017.09; 37(36); 8830-8844

[Patents]

1. Mouse deficient in glutamate transporter GLAST function, Patent Number : U.S. Patent Application No. 10/533, 051

Bio-informational Pharmacology

Professor	Tetsushi Furukawa
Associate professor	Junko Kurokawa
Assistant professor	Yusuke Ebana
Post-doc (RPD)	Masami Kodama
Post-doc	Kensuke Ihara
D4	Yuya Karube
D4	Akiko Koizumi
D4(Dept. Cardiovascular Medicine)	Kentaro Takahashi
D4(Dept. Cardiovascular Medicine)	Kouji Sugiyama
D2	Peng Zhang
D2	Lian Liu
M2	Miki Fujizuka
M1	Saki Ito
M1	Terumi Sato
M1	Erina Hayashi
M1	Xiaoki Yang
Technician	Tomoko Ando
Technician	Ayumi Sakata
Technician	Reiko Kimura
Secretary	Kuniko Yamaguchi

(1) Outline

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

(2) Research

1. Gender-specific medicine (GSM) for cardiovascular diseases

In the past few years, we have shown that non-genomic regulation of cardiac ion channels by sex hormones underlies, at least in part, gender difference in cardiac electrophysiology, and thus susceptibility to arrhythmias. This year, we used FRET imaging and LC/MS technology to show that non-genomic regulation of cardiac ion channels by sex hormones cross-talks with adrenergic receptor signaling specifically in the raft micro-domain.

2. Pathogenesis of atrial fibrillation (AF)

Atrial fibrillation (AF) is the most frequent arrhythmias, reaching more than 1 million patients in Japan. Associated cerebral infarction due to cardiogenic thrombosis (250,000 patients /year in Japan) and higher incidence of cognitive impairment cause reduced QOL and are main causes of bedridden old people. Thus, establishment of therapeutic strategy for AF is an urgent requirement.

(1) GWAS for AF

We had carried out most extensive GWAS (genome-wide association study) in Japan to determine gene polymorphisms associated with AF. Since 2011, we have participated in the international Meta-analysis called as CHARGE study. CHARGE study found 10 SNPs associated with AF: among them, 6 SNPs were associated with both European/American and Japanese, and 4 with European/American but not with Japanese.

(2) Functional analysis of AF associated genes

One of the sales-points of GWAS is the identification of novel pathogenic pathways and therapeutic targets due to its comprehensibility. We carried out functional analysis for 6 genes associated with Japanese AF patients, and found a novel pathway generating abnormal automaticity in the pulmonary vein myocardium, which is the main triggering factor of atrial fibrillation.

(3) Risk stratification

Another sales-point of GWAS is the risk stratification of the diseases and its use for future personalized medicine. Based on GWAS data, we calculated AF risk score and classified them into 4 quartile groups. The highest risk group has 5.5 higher risk of AF development relative to the lowest risk group (left panel in Figure 1). The risk stratification yielded around 60% sensitivity and specificity (right panel in Figure 1), which are not enough for personalized medicine, and further studies to increase odds ratio are needed.

3. Pathogenesis of ventricular fibrillation (VF) and sudden cardiac death

Despite extensive effort by many researchers for years, VF remains the main cause of sudden death, and the biggest challenge in arrhythmia research. Last year, we showed that genetic deletion of the His-Purkinje system-specific transcription factor in mice exhibited exercise-related ventricular tachyarrhythmias. This year, we searched for genetic disturbance of this transcription factor in patients with idiopathic VF, and found that the mutations of this factor are responsible for idiopathic VF, and a common variant is a modifier of causative gene mutations for idiopathic VF.

4. Use of iPS cells for arrhythmia research

In the past few years, we have aimed to use human iPS-derived cardiomyocytes (hiPS-CMs) for drug screening. hiPS-CMs include various types of cardiomyocytes, such as atrial, ventricular, and nodal types of cardiomyocytes, and exhibit relatively immature electrophysiological properties of cardiac cells, hindering high-quality drug screening. In order to generate mature ventricular-like hiPS-CMs, we over-expressed a gene into hiPS-CMs. The genetically-altered hiPS-CMs exhibited mature forms of action potentials and drug sensitivity. Our novel technique would be useful for evaluation of drug-induced alternation of repolarization processes in the human cardiomyocytes.

5. Use of state-of-art technology for cardiovascular research

(1) Use of motion vector technology for in vitro analysis of cardiac contraction

Motion vector technology created by Sony Co. (Dr. Matsui E. et al.) is the in vitro system to assay non-invasively contraction and relaxation speed of cardiac myocytes. We have tried to broaden its application to screening of cardiac toxicity of drugs. This year, we applied to examine cardiac toxicity of anti-cancer drugs.

(2) Use of 3-D cardiac simulator (UT-heart) for screening of cardiac toxicity of drugs

Prof. Hisada T. et al. in the University of Tokyo have developed 3-D cardiac simulator (UT-heart). We have tried to broaden its application to screening of cardiac toxicity of drugs. This year, we examined 10 standard drugs (high risk, intermediate risk, and no risk).

(3) Education

School of Medicine

2nd grade Introduction to Neurophysiology (2 units)

2nd grade Physiology (6 units)

3rd grade Cardiology (1 unit)

4th grade Project semester

School of Health Care Medicine

3rd/4th grade Cardiac physiology (8 units)

(4) Publications

[Original Articles]

1. Kuroda Y, Yuasa S, Watanabe Y, Ito S, Egashira T, Seki T, Hattori T, Ohno S, Kodaira M, Suzuki T, Hashimoto H, Okata S, Tanaka A, Aizawa Y, Murata M, Aiba T, Makita N, Furukawa T, Shimizu W, Kodama I, Ogawa S, Kokubun N, Horigome H, Hoeir M, Kamiya K, Fukuda K. Flecainide ameliorates arrhythmogenicity through NCX flux in Andersen-Tawil syndrome-iPS cell derived cardiomyocytes *Biochemical Biophysical Reports*. 2017.01; 9; 245-256
2. Ihara Kensuke, Sasano Tetsuo, Sugiyama Koji, Takahashi Kentaro, Furukawa Tetsushi. CRISPR/Cas9ベースの in vivo Generating Biological Pacemaker by CRISPR/Cas9 Based in Vivo Genome Editing. Scientific Meeting of the Japanese Circulation Society Absuttract. 2017.03; 81 th; PE-036
3. Takahashi Kentaro, Sasano Tetsuo, Ihara Kensuke, Isobe Mitsuki, Furukawa Tetsushi. Pannexin-1 は「Pannexin-1 Contributes to the Maintenance of Cardiac Function against Acute Pressure-overload as a 'Mechanosensor」 Scientific Meeting of the Japanese Circulation Society Absuttract. 2017.03; 81th; PE-439
4. Furukawa Tetsushi, Liu Lian, Ebana Yusuke, Nitta Jun-ichi, Takahashi Yoshihida, Miyazaki Shinsuke, Komura Masatoshi, Tanaka Toshihiro, Isobe Mitsuki. Genetic Background of Atrial Fibrillation Japanese Circulation Society Scientific Meeting Abstracts. 2017.03; 81; TP2-1
5. Fukuda Shun, Kodama Masami, Nagamori Shushi, Isozumi Noriyoshi, Fujizuka Miki, Kita Satomi, Iwamoto Takahiro, Kanai Yoshikatsu, Furukawa Tetsushi, Kurokawa Junko. Roles of macromolecular complexes in calcium-sensitivity of the cardiac I-Ks channel *JOURNAL OF PHARMACOLOGICAL SCIENCES*. 2017.03; 133(3); S166
6. Fukuda Shun, Kodama Masami, Nagamori Shushi, Isozumi Noriyoshi, Fujizuka Miki, Kita Satomi, Iwamoto Takahiro, Kanai Yoshikatsu, Furukawa Tetsushi, Kurokawa Junko. Roles of macromolecular complexes in calcium-sensitivity of the cardiac IKs channel. *Journal of Pharmacological Sciences*. 2017.03; 133(3Suppl.); S166
7. Kodama Masami, Fukuda Shun, Nagamori Shushi, Isozumi Noriyoshi, Fujizuka Miki, Kanai Yoshikatsu, Furukawa Tetsushi, Kurokawa Junko. Roles of macromolecular complex formation in calcium-sensitivity of the cardiac IKs channel. *The Journal of Physiological Sciences*. 2017.03; 67(Suppl.1); S156
8. Liu L, Ebana Y, Nitta J, Takahashi Y, Miyazaki S, Tanaka T, Komura M, Isobe M, Furukawa T. Genetic variants associated with susceptibility to atrial fibrillation in Japanese population *Canadian Journal of Cardiology*. 2017.04; 33; 443-449
9. Siew-Kee Low, Atsushi Takahashi, Yusuke Ebana, Kouichi Ozaki, Ingrid E Christophersen, Patrick T Ellinor, , Soichi Ogishima, Masayuki Yamamoto, Mamoru Satoh, Makoto Sasaki, Taiki Yamaji, Motoki Iwasaki, Shoichiro Tsugane, Keitaro Tanaka, Mariko Naito, Kenji Wakai, Hideo Tanaka, Tetsushi Furukawa, Michiaki Kubo, Kaoru Ito, Yoichiro Kamatani, Toshihiro Tanaka. Identification of six new genetic loci associated with atrial fibrillation in the Japanese population. *Nat. Genet.*. 2017.06; 49(6); 953-958
10. Min Li, Yasunari Kanda, Takashi Ashihara, Tetsuo Sasano, Yuji Nakai, Masami Kodama, Erina Hayashi, Yuko Sekino, Tetsushi Furukawa, Junko Kurokawa. Overexpression of KCNJ2 in induced pluripotent stem cell-derived cardiomyocytes for the assessment of QT-prolonging drugs. *J. Pharmacol. Sci.*. 2017.06; 134(2); 75-85
11. Low SK, Takahashi A, Ebana Y, Ozaki K, Christophersen IE, Ellinor PT; AFGen Consortium., Ogishima S, Yamamoto M, Satoh M, Sasaki M, Yamaji T, Iwasaki M, Tsugane S, Tanaka K, Naito M, Wakai K, Tanaka H, Furukawa T, Kubo M, Ito K, Kamatani Y, Tanaka . Identification of six new genetic loci associated with atrial fibrillation in the Japanese population *Nature Genetics*. 2017.06; 49(6); 953-958
12. Li M, Kanda Y, Ashihara T, Sasano T, Nakai Y, Kodama M, Hayashi E, Sekino Y, Furukawa T, Kurokawa J. Overexpression of KCNJ2 in induced pluripotent stem cell-derived cardiomyocytes for the assessment of QT-prolonging drugs *Journal of Pharmacological Science*. 2017.06; 134(2); 75-85

13. Li Min, Kanda Yasunari, Ashihara Takashi, Sasano Tetsuo, Nakai Yuji, Kodama Masami, Hayashi Erina, Sekino Yuko, Furukawa Tetsushi, Kurokawa Junko. Overexpression of KCNJ2 in induced pluripotent stem cell-derived cardiomyocytes for the assessment of QT-prolonging drugs. *Journal of Pharmacological Sciences*. 2017.06; 134(2); 75-85
14. Tsuji M, Kawasaki T, Matsuda T, Arai T, Gojo S, Takeuchi JK.. Sexual dimorphisms of mRNA and miRNA in human/murine heart disease. *PLoS One*. 2017.07; 12(7);
15. Koshiba-Takeuchi K., Morita Y., Nakamura R., Takeuchi JK.*. Combinatorial functions of transcription factors and epigenetic factors in heart development and disease. *Etiology and Morphogenesis of Congenital Heart Disease*. 2017.07;
16. Tsuji M., Kawasaki T., Matsuda T., Arai T., Gojo S. and Takeuchi JK*.. Sexual Dimorphisms of mRNA and miRNA in Human/ Murine Heart Disease. 2017.07; 12(7);
17. Zaw KTT, Sato N, Ikeda S, Thu KS, Mieno MN, Arai T, Mori S, Furukawa T, Sasano T, Sawabe M, Tanaka M, Muramatsu M. Association of ZFH3 gene variant with atrial fibrillation, cerebral infarction, and lung thromboembolism:An autopsy study *Journal of Cardiology*. 2017.08; 70(2); 180-184
18. Khin Thet Thet Zaw , Sato Noriko, Ikeda Shinobu, Kaung Si Thu , Naka Mieno Makiko, Arai Tomio, Mori Seiji, Furukawa Tetsushi, Sasano Tetsuo, Sawabe Motoji, Tanaka Masashi, Muramatsu Masaaki. Association of ZFH3 gene variation with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study *Journal of Cardiology*. 2017.08; 70(1-2); 180-184
19. Shinsuke Miyazaki, Yusuke Ebana, Lian Liu, Hiroaki Nakamura, Hitoshi Hachiya, Hiroshi Taniguchi, Takamitsu Takagi, Takatsugu Kajiyama, Tomonori Watanabe, Miyako Igarashi, Shigeki Kusa, Takashi Niida, Yoshito Iesaka, Tetsushi Furukawa. Chromosome 4q25 variants and recurrence after second-generation cryoballoon ablation in patients with paroxysmal atrial fibrillation. *Int. J. Cardiol.*. 2017.10; 244; 151-157
20. Ebana Y, Ozaki K, Liu L, Hachiya H, Hirao K, Isobe M, Kubo M, Tanaka T, Furukawa T. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25 *Journal of Cardiology*. 2017.10; 70(4); 366-373
21. Miyazaki S, Ebana Y, Liu L, Nakamura H, Hachiya H, Taniguchi H, Takagi T, Kajiyama T, Watanabe T, Igarashi M, Kusa S, Niida T, Iesaka Y, Furukawa T. Chromosome 4q25 variants and recurrence after second-generation cryoballoon ablation in patients with paroxysmal atrial fibrillation *International Journal of Cardiology*. 2017.10; 244; 151-157
22. Ebana Yusuke, Ozaki Kouichi, Liu Lian, Hachiya Hitoshi, Hirao Kenzo, Isobe Mitsuaki, Kubo Michiaki, Tanaka Toshihiro, Furukawa Tetsushi. Clinical utility and functional analysis of variants in atrial fibrillation-associated locus 4q25 *Journal of Cardiology*. 2017.10; 70(3-4); 366-373
23. Yusuke Ebana, Junichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Masahito Suzuki, Lian Liu, Kenzo Hirao, Eiichiro Kanda, Mitsuaki Isobe, Tetsushi Furukawa. Association of the Clinical and Genetic Factors With Superior Vena Cava Arrhythmogenicity in Atrial Fibrillation. *Circ. J.*. 2017.12; 82(1); 71-77
24. Kenji Yoshioka, Shunsuke Kuroda, Kentaro Takahashi, Tetsuo Sasano, Tetsushi Furukawa, Akihiko Matsumura. Calcification of joints and arteries with novel NT5E mutations with involvement of upper extremity arteries. *Vasc Med*. 2017.12; 22(6); 541-543
25. Yoshioka K, Kuroda S, Takahashi K, Sasano T, Furukawa T, Matsumura A. Calcification of joints and arteries with novel NT5E mutations with involvement of upper extremity arteries *Vascular Medicine*. 2017.12; 22(6); 541-543
26. Ebana Yusuke, Nitta Junichi, Takahashi Yoshihide, Miyazaki Shinsuke, Suzuki Masahito, Liu Lian, Hirao Kenzo, Kanda Eiichiro, Isobe Mitsuaki, Furukawa Tetsushi. Association of the Clinical and Genetic Factors With Superior Vena Cava Arrhythmogenicity in Atrial Fibrillation *Circulation Journal*. 2017.12; 82(1); 71-77

[Books etc]

1. Tetsushi Furukawa. How to interpret ECG from its basic. 2017.10 (ISBN : 978-4-88378-656-5)

[Misc]

1. Tetsushi Furukawa. Arrhythmias originating from localized areas of the heart SEITAI NO KAGAKU. 2017.12; 68(6); 564-568

[Conference Activities & Talks]

- 1.
2. Ihara K, Sasano T, Sugiyama K, Takahashi K, Furukawa T. . Generating biological pacemaker by CRISPR/Cas9 based in vivo genome editing.. The 81st Annual Scientific Meeting of the Japanese Circulation Society. 2017.03.23 金沢.
3. Takahashi K, Sasano T, Ihara K, Isobe M, Furukawa T. . Pannexin-1 Contributes to the Maintenance of Cardiac Function against Acute Pressure-overload as a ‘Mechanosensor’ . . The 81st Annual Scientific Meeting of the Japanese Circulation Society. 2017.03.23 Kanazawa.
4. Sasano T, Takahashi K, Zhang P, Ihara K, Sugiyama K, Tamura N, Nishimura T, Shirai Y, Tao S, Sasaki T, Kawabata M, Goya M, Hirao K, Isobe M, Furukawa T.. Comprehensive analysis linking microRNA and atrial inflammation in mouse and human.. The 79th Annual Scientific Meeting of the Japanese Circulation Society. 2017.03.23 Osaka.
5. Jun Takeuchi. 2-defined factors are essential for the production of functional cardiomyocytes with the selective innervation. 2017 Keystone Symposia Conference X7: Molecular Mechanisms of Heart Development 2017.03.28
6. Jun Takeuchi. Direct cardiomyocyte specification and differentiation by the defined factors. 2017 Weinstein Cardiovascular Development and Regeneration Meeting 2017.05.04 Hilton Columbus Downtown, Columbus, Ohio
7. Lian Liu, Yusuke Ebana, Jun-ichi Nitta, Yoshihide Takahashi, Shinsuke Miyazaki, Toshihiro Tanaka, Masatoshi Komura, Mitsuaki Isobe, Tetsushi Furukawa. Common genetic variants indicate the risk of atrial fibrillation in Japanese population. Annual Meeting of the Japanese Heart Rhythm Society 2017.07.16 Sapporo.
8. Ihara K, Sasano T, Takahashi K, Furukawa T. . Pacemaker activity generated by in vivo genome editing.. The 10th Asia-pacific Heart Rhythm Society Scientific Session. 2017.09.14 Yokohama. Japan.
9. Yamazoe M, Sasano T, Nakamura W, Takahashi K, Ihara K, Furukawa T. . Cell-Free DNA Released from Atrial Cardiomyocytes Promotes Pro-Inflammatory Cytokine IL-6 Expression in Macrophages. . The 10th Asia-pacific Heart Rhythm Society Scientific Session. 2017.09.14 Yokohama. Japan.
10. Nagata T, Ohyagi M, Ihara K, Kaburagi H, Nishina K, Piao W, Yoshida-Tanaka K, Guo H, Kuwahara H, Yoshioka K, Yokota T. . The effect of DNA/RNA heteroduplex oligonucleotides on muscle. . XXIII World Congress of Neurology. 2017.09.16 Kyoto. Japan.
11. Jun Takeuchi. Heart cell specification and maturation by 2-defined factors. TAKAO International Symposium 2017.10.07 Shimane.
12. Furukawa T, Okata S, Yuasa S, Suzuki T, Makita N, Kurokawa J, Egashira T, Yamakawa H, Seki T, Aizawa T, Hashimoto H, Kuroda Y, Tanaka A, Yae K, Murata M, Aiba T, Shimizu W, Horie M, Kodama I, Ogawa S, Fukuda K. Disease modeling using iPS cells. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo
13. Sato Y, Satoh A, Nitta J, Honda Y, Kuroda S, Sekigawa M, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Impact of SNP on IL6R (rs7514452) for age at onset of atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

14. Sekigawa M, Satoh A, Nitta J, Sato Y, Honda Y, Kuroda S, Kanoh M, Suzuki M, Inaba O, Muramatsu K, Yamato T, Matsumura Y, Asakawa K, Ebana Y, Furukawa T, Hirao K, Isobe M. Effect of SNP on 9q22 (rs6479562) on the progression from paroxysmal atrial fibrillation to persistent atrial fibrillation. The 78th Annual Scientific Meeting of the Japanese Circulation Society Tokyo

Epigenetic Epidemiology

Professor: Masaaki MURAMATSU

Associate Professor : Noriko SATO

Assistant Professor : Chihiro Imai

Adjunct Instructor : Tomio Arai

Graduate Student: Fujitani, Tay Zar Kyaw, Tadaaki Katsuta,

Shilpa Pavethynath, Maidina Abudushataer, Ake Ko Ko Minn

Yuri Tsubota, Zong Yuan, Naomi Hichiwa, Jin Xin

Research Resident: Arisa Nakata

(1) Outline

Many common chronic diseases are multifactorial in that they are caused by multiple genetic and environmental factors. By applying the technology and information of human genome to epidemiological studies, we aim to clarify the role of genetic polymorphisms, epigenetic changes, as well as their interaction with environmental factors, which may contribute to the development of these diseases.

(2) Research

Our research subjects are as follows.

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Responder vs non-responder of prodrugs and polymorphisms of drug metabolizing enzymes.
4. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
5. The role of epigenetic regulation and fetal programming in common diseases.
6. Likelihood ratio based integrated personal risk assessment of type 2 diabetes.

(3) Education

Masaaki Muramatsu: Holistic Study of Disease Prevention I

Masaaki Muramatsu: Environmental/Social Health

Masaaki Muramatsu: Negotiation and Debate in English

Noriko Sato, Masaaki Muramatsu: Bioscience I

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

(4) Lectures & Courses

We focus on common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis which are caused by multiple genetic and environmental factors, and aim to decipher these factors as well as their interactions by applying the technology and information of human genome to epidemiology. Our goal is not only to identify disease genes and polymorphisms but also to elucidate gene-environment interactions that contribute to the onset and progression of the diseases. Epigenetic changes in common diseases are also in our scope. A new project has been started to study methods for educating genome-based health literacy by employing information generated from personal genome sequences

(5) Publications

[Original Articles]

1. [Molecular Epidemiology : SATO Noriko] Sariya Dechamethakun, Noriko Sato, Shinobu Ikeda, Motoji Sawabe, Seiji Mori, Yoshiji Yamada, Masashi Tanaka Masaaki Muramatsu and Tomio Arai. Association of Macrophage Capping Protein (CAPG) Arg335His Polymorphism and Cancer Susceptibility in the Elderly Japanese Journal of Gerontology and Geriatric Research. 2017.04; 6(2); 417
2. [Molecular Epidemiology : IMAI Chihiro] Noriko Sato, Katsuko Sudo, Masayo Mori, Chihiro Imai, Masaaki Muramatsu, Masahiro Sugimoto. Early gestational maternal low-protein diet diminishes hepatic response to fasting in young adult male mice. Sci Rep. 2017.08; 7(1); 9812
3. [Molecular Epidemiology : SATO Noriko] Kumpei Tanisawa, Nobuyoshi Hirose, Yasumichi Arai, Hiroshi Shimokata, Yoshiji Yamada, Hisashi Kawai, Motonaga Kojima, Shuichi Obuchi, Hirohiko Hirano, Hiroyuki Suzuki, Yoshinori Fujiwara, Yu Taniguchi, Shoji Shinkai, Kazushige Ihara, Maki Sugaya, Mitsuru Higuchi, Tomio Arai, Seiji Mori, Motoji Sawabe, Noriko Sato, Masaaki Muramatsu, Masashi Tanaka. Inverse association between height-increasing alleles and extreme longevity in Japanese women. J. Gerontol. A Biol. Sci. Med. Sci.. 2017.08;
4. [Department of Molecular Pathology : SAWABE Motoji] Khin Thet Thet Zaw , Sato Noriko, Ikeda Shinobu, Kaung Si Thu , Naka Mieno Makiko, Arai Tomio, Mori Seiji, Furukawa Tetsushi, Sasano Tetsuo, Sawabe Motoji, Tanaka Masashi, Muramatsu Masaaki. Association of ZFH3 gene variation with atrial fibrillation, cerebral infarction, and lung thromboembolism: An autopsy study. Journal of Cardiology. 2017.08; 70(1-2); 180-184
5. [Comprehensive Reproductive Medicine : MIYASAKA Naoyuki] Rina Komazaki, Sayaka Katagiri, Hirokazu Takahashi, Shogo Maekawa, Takahiko Shiba, Yasuo Takeuchi, Yoichiro Kitajima, Anri Ohtsu, Sayuri Udagawa, Naoki Sasaki, Kazuki Watanabe, Noriko Sato, Naoyuki Miyasaka, Yuichiro Eguchi, Keizo Anzai, Yuichi Izumi. Periodontal pathogenic bacteria, Aggregatibacter actinomycetemcomitans affect non-alcoholic fatty liver disease by altering gut microbiota and glucose metabolism. Sci Rep. 2017.10; 7(1); 13950

[Misc]

1. [Molecular Epidemiology : SATO Noriko] Kazuki Mochizuki, Chihiro Imai, Noriko Sato, Takeo Kubota. The roles of epigenetics in developmental programming/Developmental Origins of Health and Disease theory. OBM Genetics. 2017.10; 1(4);

[Conference Activities & Talks]

1. [Molecular Epidemiology : SATO Noriko] Noriko Sato, Hidemi Takimoto, Motoko Okamitsu, Tay Zar Kyaw, Chihiro Imai, Nay Chi Htun, Satoshi Yago, Tomoko Aoyama, Seiji Yamaguchi and Naoyuki Miyasaka. Study design: the evaluation of interindividual differences in neonatal epigenome - the BC-GENIST project. the 21st World Congress of Epidemiology, International Epidemiological Association 2017.08.21 Saitama, Japan
2. [Molecular Epidemiology : SATO Noriko] Hidemi Takimoto, Motoko Okamitsu, Noriko Sato, Tay Zar Kyaw, Nay Chi Htun, Chihiro Imai, Yui Tsubota, Reiko Tajirika-Shirai, Satoshi Yago, Tomoko Aoyama, Naoyuki Miyasaka. Dietary intakes from 3-day weighed dietary records among pregnant participants in

the Birth Cohort - Gene and ENvironment Interaction Study of TMDU (BC-GENIST). the 21st World Congress of Epidemiology, International Epidemiological Association 2017.08.21 Saitama, Japan

RIKEN Molecular and Chemical Somatology

Visiting Professor	Soichi Kojima
Visiting Professor	Mikiko Sodeoka
Visiting Professor	Nobumoto Watanabe
Visiting Professor	Yoshiki Yamaguchi
Visiting Professor	Ichiro Taniuchi
Visiting Professor	Motomasa Tanaka
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Ambara R. Pradipta
Visiting Lecturer	Takeshi Nakano
Visiting Lecturer	Kosuke Dodo
Visiting Lecturer	Ryo Endo
Visiting Lecturer	Akiko Tane
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Tetsuya Koide
Graduate Students	D3 Sayoko Yamasaki Kruthi Sharamjeet Suvarna
	D2 Mengqian Li
	D1 Chih-Hao Shen

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field to understand basis of Bioorganic Chemistry, Chemical Biology, Structural Biology and Molecular Immunology and Molecular Neuroscience as well as their applications to Medicine and Biology by dealing with variety of molecules that regulate cellular functions including low molecular weight organic compounds, proteins, sugars, and hormones. Students will hear and discuss about outlines and/or latest topics on discovery, structure, synthesis, biology, and management of these key molecules/factors, and deepen their understanding of this new study field.

(2) Education

- 1) Synthetic Organic Chemistry
 - Design and synthesis of bioactive molecules based on synthetic organic chemistry and chemical biology research.
- 2) Chemical Biology
 - Discovery, target identification and analyses of mechanism of action of bioactive compounds that regulate biological function.
- 3) Molecular Cellular Pathology
 - Clarification of pathogenesis of diseases at molecular and cellular levels utilizing bioprobes.
- 4) Structural Biology
 - Analyses of structure and functions of bioactive glycoproteins and related proteins
- 5) Molecular Immunology
 - Regulatory mechanisms for lymphocyte development
- 6) Molecular Neuropathology
 - Molecular basis of neuropsychiatric diseases

(3) Publications

[Original Articles]

1. Shrestha, R., Shrestha, R., Qin, X-Y., Kou, T.-F., Oshima, Y., Iwatani, S., Teraoka, R., Fujii, K., Hara, M., Li, M., Takahashi-Nakaguchi, A., Chibana, H., Lu, J., Cai, M., Kajiwara, S., and Kojima, S., Fungus-derived hydroxyl radicals kill hepatic cells by enhancing nuclear transglutaminase. *Sci Rep.* 7:4746 (2017) doi: 10.1038/s41598-017-04630-8.
2. Qin, X-Y., et al., Transcriptome analysis uncovers a cell growth-promoting activity of orosomucoid-1 on hepatocytes. *EBioMedicine* 24:257-266 (2017) doi: 10.1016/j.ebiom.2017.09.008.
3. Qin, X-Y., Suzuki, H., Honda, M., Okada, H., Kaneko, S., Inoue, I., Ebisui, E., Hashimoto, K., Carninci, P., Kanki, K., Tatsukawa, H., Ishibashi, N., Masaki, T., Matsuura, T., Kagechika, H., Toriguchi, K., Hatano, E., Shirakami, Y., Shiota, G., Shimizu, M., Moriwaki, H., and Kojima, S., Prevention of hepatocellular carcinoma by targeting MYCN-positive liver cancer stem cells with acyclic retinoid. *Proc. Natl. Acad. Sci. USA* (2018) in press doi/10.1073/pnas.1802279115

4. Dodo, K., Shimizu, T., Sasamori, J., Aihara, K., Terayama, N., Nakao, S., Iuchi, K., Takahashi, M., and Sodeoka, M., Indolylmaleimide Derivative IM-17 Shows Cardioprotective Effects in Ischemia-Reperfusion Injury. *ACS Med. Chem. Lett.* 9, 182-187 (2018) doi: 10.1021/acsmchemlett.7b00454.
5. Suvarna, K., Honda, K., Kondoh, Y., Osada H., and Watanabe, N., Identification of a small molecule ligand of β -arrestin1 as an inhibitor of stromal fibroblast cell migration accelerated by cancer cells. *Cancer Med.* 7, 883-893 (2018) doi: 10.1002/cam4.1339.
6. Seo W, Muroi S, Akiyama K and Taniuchi I, Distinct requirement of Runx complexes for TCR β enhancer activation at distinct developmental stages. *Sci Rep* 7:41351 (2017) doi: 10.1038/srep41351.
7. Kakugawa, K., Kojo, S., Tanaka, H., Seo, W., Endo, T., Kitagawa, Y., Muroi, S., Teno, M., Yasmin, N., Kohwi, Y., Sakaguchi, S., Kowhi-Shigematsu, T., and Taniuchi, I., Essential roles of SATB1 in specifying T lymphocyte subsets. *Cell Rep.* 19:1176-1188, (2017) doi: 10.1016/j.celrep.2017.04.038.
8. Tenno, M., Shiroguchi, K., Muroi, S., Kawakami, E., Koseki, K., Kryukov, K., Imanishi, T., Ginhoux, F., and Taniuchi, I., Cbfb2-deficiency preserves Langerhans cell precursors by lack of selective TGF β receptor signaling. *J. Exp. Med.* 214:2933-2946, (2017) doi: 10.1084/jem.20170729.
9. Nieke, S., Yasmin, N., Muroi, S., Yokomizo, T., Tenno, M., Kakugawa, K., and Taniuchi, I., Unique N-terminal sequences in two Runx1 isoforms are dispensable for Runx1 protein function. *BMC Dev Biol.* 17:14, (2017) doi: 10.1186/s12861-017-0156-y.
10. Kojo, S., Tanaka, H., Endo, T.A., Muroi, S., Liu, Y., Seo, W., Tenno, M., Kakugawa, K., Naoe, Y., Nair, K., Moro, K., Katsuragi, Y., Kanai, A., Inaba, T., Egawa, T., Venkatesh, B., Minoda, A., Kominami, R. and Taniuchi, I., Priming of lineage-specifying genes by Bcl11b is required for lineage choice in post-selection thymocytes. *Nat. Commun.* 8:702, (2017) doi: 10.1038/s41467-017-00768-1.
11. Tanaka, M., Ishizuka, K., Nekooki-Machida, Y., Endo, R., Takashima, N., Sasaki, H., Komi, Y., Gathercole, A., Huston, E., Ishii, K., Hui, K.K., Kurosawa, M., Kim, S.H., Nukina, N., Takimoto, E., Houslay, M.D., and Sawa, A., Aggregation of scaffolding protein DISC1 dysregulates phosphodiesterase 4 in Huntington's disease. *J. Clin. Invest.*, 127, 1438-50 (2017). doi: 10.1172/JCI85594.
12. Tenno, M., Kojo, S., Lawir, D.-F., Hess, I., Shiroguchi, K., Ebihara, T., Endo, T., Muroi, S., Satoh, R., Kawamoto, H., Boehm, T. and Taniuchi, I., Cbfb2 controls differentiation of and confers homing capacity to pre-thymic progenitors. *J. Exp.*

Med. 215:595-610, (2018) doi: 10.1084/jem.20171221

13. Wada, H., Ohno-Oishi, M., Nike, S., Muroi, S. and Taniuchi, I., Requirement for intron structure in activating the Cd8a locus. *Proc. Natl. Acad. Sci. USA.* (2018) in press doi: 10.1073/pnas.1718837115.
14. Ohhashi, Y., Yamaguchi, Y., Kurahashi, H., Kamatari, Y.O., Sugiyama, S., Uluca, B., Piechatzek, T., Komi, Y., Shida, T., Müller, H., Hanashima, S., Heise, H., Kuwata, K, and Tanaka, M., Molecular basis for diversification of yeast prion strain conformation, *Proc. Natl. Acad. Sci. U. S. A.*, 115, 2389-2394 (2018). doi: 10.1073/pnas.1715483115.

[Review Articles]

1. Seo, W. and Taniuchi, I., Regulation of hematopoiesis and immune responses by long noncoding (lnc) RNAs. *Int Immunol.* 29(4):165-172 (2017) doi: 10.1093/intimm/dxx021.
2. Ebihara, T., Seo, W., Taniuchi, I., Roles of RUNX Complexes in Immune Cell Development. *Adv Exp Med Biol.* 962:395-413 (2017) doi: 10.1007/978-981-10-3233-2_24.

[Books]

1. Hirai, G. and Sodeoka, M. Natural Products Analogues for Chemical Biology Research. *CJS Current Review 27: Total Synthesis of Natural Products.* Ed. by Chemical Society of Japan, Chapter 14, 152-159.
2. Watanabe, N.: WEE1. In *Encyclopedia of Signaling Molecules. Second Edition* (Choi, S. ed.) Springer International 5986-5991 (2017)
3. Watanabe, N, Osada H.: Cell proliferation and differentiation. In *Bioprobes. Second edition* (Osada, H. ed.) Springer Japan 11-35 (2017)

[Conference Activities & Talks]

1. Kojima, S. “Control of nuclear TG2 in hepatic disease” Debrecen University Symposium on Transglutaminases in Medicine, Debrecen, Hungary, August, 2017.
2. Kojima, S. “Genomic and Nongenomic Actions of Acyclic Retinoid on Deletion of MYCN+CD133+ Liver Cancer Stem Cells ” Xiamen University AFPS2017-Asian Federation for Pharmaceutical Sciences 2017, Xiamen, China, November, 2017
3. Sodeoka, M. “Turn-on Fluorescent Labeling Using O-NBD Unit.” 6th Official Conference of the International Chemical Biology Society, Shanghai, China, 2017.

4. Suvarna, K., Osada, H., and Watanabe, N. “Identification of a ligand compound of β -arrestin as an inhibitor of metastasis of carcinoma associated fibroblasts” The 76th Annual Meeting of the Japanese Cancer Association, 2017. Sep. Pacifico Yokohama
5. Taniuchi, I. “Regulation of T cell development in the thymus by transcription factors” Symposium in honor of Ellen Rothenberg: The Molecular Developmental Biology of Lymphocytes. Los Angeles, USA, April, 2017.
6. Taniuchi, I. “Unique roles of the C-terminal end sequences in Runx and Cbfb proteins” The 21st International RUNX Conference. Philadelphia, USA, November, 2017.
7. Taniuchi, I. “Roles of Runx Transcription Factors in Immune Cell Development” The 46th Annual Meeting of the Japanese Society for Immunology, Sendai Japan, December 2017.
8. Tanaka, M. “Molecular basis for diversification of yeast prion strain conformations” Asian Pacific Prion Symposium 2017, Melbourne, Australia, October, 2017.

Metallic Biomaterials

Takao HANAWA Prof
 Yusuke TSUTSUMI Senior Assoc Prof
 Maki ASHIDA Assist Prof
 Peng CHEN Assist Prof
 Hisashi DOI Assist Prof
 Akira UMISE Assist Prof
 Shukan OKANO Technical Support Staff
 Noriko NAKAISHI Technical Support Staff
 Tomoko SETOGUCHI Secretary

(1) Outline

1. Bio-functionalization of metals with surface modification

Bio-functionalization of metals is investigated with surface treatment techniques, such as molecule immobilization and anodic oxidation. These surface treatments make it possible to inhibit protein adsorption, platelet adhesion, and biofilm formation, and to enhance wear resistance and hard-tissue compatibility.

2. Development of novel alloys and porous composites for biomedical applications

Novel alloy systems for biomedical applications are designed from the viewpoints of mechanical properties and biocompatibility. Co-Cr-Mo alloys having high strength and ductility for dental applications are developed. The porous alloys having low Young's modulus are obtained with selective laser melting technique.

3. Development of Zr-based alloys for minimizing MRI artifacts

Zr-based alloys with low magnetic susceptibility, high strength and corrosion resistance are investigated for minimizing MRI artifact by controlling their microstructure and constituent phase for aneurysm clips, artificial joints, and dental implants, etc.

4. Effort to minimize metal allergy

Countermeasure techniques for metal ion release from metallic biomaterials which causes metal allergy are investigated. Novel reagents of patch testing for the detection of sensitization to metal ions are developed.

(2) Lectures & Courses

Metallic biomaterials play an important role as medical devices. Our laboratory mainly deals with effects of crystal structure, process, and thermal treatment on mechanical properties (e.g. strength or toughness). We also focus on structure and property of nanometer-scaled surface phenomena: Formation of living tissue on metals, especially, reactions between biomolecules or cells and metals, changes in surface oxide layers in living tissues, and electrochemical property of metallic biomaterials. The aim of the education is perfect understanding of metallic biomaterials, enabling students to select a proper material for medical treatments or researches.

(3) Publications

[Original Articles]

1. Liza S, Hieda J, Akasaka H, Ohtake N, Tsutsumi Y, Nagai A, Hanawa T. Deposition of boron doped DLC films on TiNb and characterization of their mechanical properties and blood compatibility Sci. Technol. Adv. Mater.. 2017.01; 18; 76-87

2. Takada R, Jinno T, Tsutsumi Y, Doi H, Hanawa T, Okawa A. Inhibitory effect of zirconium coating to bone bonding of titanium implants in rat femur Mater. Trans.. 2017.01; 58(1); 113-117
3. Imai H, Tanaka Y, Nomura N, Doi H, Tsutsumi Y, Ono T, Hanawa T. Magnetic susceptibility, artifact volume in MRI, and tensile properties of swaged Zr–Ag composites for biomedical applications J. Mech. Behav. Biomed. Mater.. 2017.02; 66; 152-158
4. Chen P, Aso T, Sasaki R, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Micron/submicron hybrid topography of titanium surfaces influences adhesion and differentiation behaviors of the mesenchymal stem cells J. Biomed. Nanotechnol.. 2017.03; 13(3); 324-336
5. Rajana ST, Nandakumar AK, Hanawa T, Subramanian B. Materials properties of ion beam sputtered Ti-Cu-Pd-Zr thin film metallic glasses J. Non-Cryst. Solids. 2017.04; 461; 104-112
6. Iwata N, Nozaki K, Horiuchi N, Yamashita K, Tsutsumi Y, Miura H, Nagai A. Effects of controlled micro-/nanosurfaces on osteoblast proliferation. J. Biomed. Mater. Res. A. 2017.09; 105(9); 2589-2596
7. Sun X, Zhou W, Kikuchi K, Nomura N, Kawasaki A, Doi H, Tsutsumi Y, Hanawa T. Fabrication and characterization of a low magnetic Zr-1Mo alloy by powder bed fusion using a fiber laser Metals. 2017.11; 7; 501
8. Chen P, Miyake M, Tsukamoto M, Tsutsumi Y, Hanawa T. Response of preosteoblasts to titanium with periodic micro/nanometer scale grooves produced by femtosecond laser irradiation J. Biomed. Mater. Res. A. 2017.12; 105(12); 3456-3464

[Misc]

1. Hanawa T. Focus on endeavor for creation of materials-tissues intelligent interface Sci. Technol. Adv. Mater.. 2017.03; 18(1); 549

[Conference Activities & Talks]

1. Hanawa T. Surface modification of metals with biofunctional molecules to add biofunction. International Workshop: From Amazon Biomolecules to Medical Devices 2017.02.16 Manaus, Brazil
2. Hanawa T. New alloys, process and surface modification techniques for medical implants. EPFL-TMDU Joint Symposium 2017.03.10 Lausanne, Switzerland
3. Chen P, Hanawa T, Aso T, Sasaki R, Tsutsumi Y, Ashida M, Doi H. Micron/nano hierarchical topography of titanium surface influences adhesion and multi-differentiation behaviours of mesenchymal stem cells. Society for Biomaterials 2017 Annual Meeting and Exposition (SFB2017) 2017.04.05 Minneapolis, USA
4. Chen P, Aso T, Sasaki R, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Grid patterns on titanium surface promote adhesion and differentiation of mesenchymal stem cells. Society for Biomaterials 2017 Annual Meeting and Exposition (SFB2017) 2017.04.05 Minneapolis, USA
5. Chen P. Nanotechnology in implant dentistry and bone regeneration. 1st International Symposium on Precision Medicine and Biomedical Technologies 2017.06.04 Quanzhou, China
6. Hanawa T. Next generation implant surface. The 12th International Workshop on Biomaterials in Interface Science 2017.08.04 Sendai, Miyagi, Japan
7. Tsutsumi Y, Koizumi Y, Oishi T, Wei DX, Chiba A, Hanawa T. Evaluation of corrosion resistance of Co-Cr-Mo alloy prepared by electron beam melting process. The 12th International Workshop on Biomaterials in Interface Science 2017.08.04 Sendai, Miyagi, Japan
8. Umise A, Goto K, Chang M, Tahara M, Inamua T, Sone M, Hanawa T, Hosoda H. Deformation of Au-Cu-Al biomedical shape memory alloy micropillars. The 12th International Workshop on Biomaterials in Interface Science 2017.08.04 Sendai, Miyagi, Japan
9. Shimabukuro M, Tsutsumi Y, Yamada R, Nozaki K, Ashida M, Chen P, Doi H, Nagai A, Hanawa T. Electrochemical treatment on titanium surface to realize antibacterial property. Biomaterials International 2017 2017.08.20 Fukuoka, Japan

10. Wang L, Tsutsumi Y, Chen P, Ashida M, Doi H, Ishihara T, Hanawa T. Corrosion evaluation of titanium under thin electrolyte solution layer simulating oral cavity environment. *Biomaterials International* 2017 2017.08.20 Fukuoka, Japan
11. Honma K, Tsutsumi Y, Ashida M, Chen P, Doi H, Shimojo M, Hanawa T. Effect of manufacturing process on microstructure and corrosion behavior of Zr-14Nb-5Ta-1Mo alloy. *Biomaterials International* 2017 2017.08.20 Fukuoka, Japan
12. Hanawa T. Next generation implant materials and surfaces. *Biomaterials International* 2017 2017.08.21 Fukuoka, Japan
13. Ashida M, Chen P, Doi H, Tsutsumi Y, Horita Z, Hanawa T. Strengthening of Ti-6Al-7Nb alloy with bimodal microstructure by high-pressure torsion. *International Workshop on Giant Straining Process for Advanced Materials (GSAM2017)* 2017.09.03 Fukuoka, Japan
14. Hanawa T. Reaction of yttria-stabilized zirconia surface with water and Hanks' solution. *28th Annual Conference of European Society for Biomaterials (ESB 2017)* 2017.09.04 Athens, Greece
15. Hanawa T. Biofunctionalization of metals meeting clinical demand. *20th Roumanian International Conference on Chemistry and Chemical Engineering (RICCCE 2017)* 2017.09.06 Poiana Brasov, Roumania
16. Chen P, Tsukamoto M, Shinonaga T, Tsutsumi Y, Ashida M, Doi H, Hanawa T. Calcification of pre-osteoblasts cultured on titanium with periodic micron/nano-groove topography produced with femtosecond laser irradiation. *2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2)* 2017.09.29 Nagoya, Japan
17. Tsutsumi Y, Ashida M, Chen P, Doi H, Hanawa T. Corrosion behavior of titanium under drying thin electrolyte layer simulating oral cavity environment. *2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2)* 2017.09.29 Nagoya, Japan
18. Arisaka Y, Tamura A, Tsutsumi Y, Hanawa T, Yui N. Immobilization of polyrotaxanes onto Ti for modulating cell function. *2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2)* 2017.09.29 Nagoya, Japan
19. Hanawa T. Surface oxide layer and topography for next generation implants. *TACT2017* 2017.10.15 Hualien, Taiwan
20. Hanawa T. Effect of topography of titanium surface on adhesion and differentiation of mesenchymal stem cells. *The 6th Asian Biomaterials Congress (ABMC6)* 2017.10.25 Kerala, India
21. Umise A, Goto K, Tahara M, Inamua T, Hanawa T, Hosoda H. Microstructure change of Au-27Cu-18Al biomedical superelastic alloys by Fe addition. *The 2nd International Symposium on Biomedical Engineering* 2017.11.09 Tokyo, Japan
22. Homma K, Tsutsumi Y, Nomura N, Doi H, Ashida M, Chen P, Shimojo M, Hanawa T. Effects of heat treatment on mechanical properties and magnetic susceptibility of Zr-14Nb-5Ta-1Mo alloy. *The 2nd International Symposium on Biomedical Engineering* 2017.11.09 Tokyo, Japan
23. Nishijo M, Ebihara A, Tokita D, Doi H, Hanawa T, Okiji T. Evaluation of selected mechanical properties of NiTi rotary glide path files manufactured from controlled memory wires. 2017.11.20 Tokyo

Inorganic Biomaterials

Professor Kimihiro Yamashita
Associate Prof. Miho Nakamura
Assistant Prof. Naohiro Horiuchi
Research Associate Takako Takuma

(1) Outline

(1) Development of Electrovector ceramics

Some ceramics, such as a hydroxyapatite, are able to be ionically polarized by thermoelectrical treatments. Consequently, the polarized ceramics have large and time-durable induced electrostatic charges on their surfaces. The effects of the induced charges profoundly dominate the proximate few millimeter regions. We named the effects “Electrovector effects” and develop “Electrovector ceramics” defined as ceramics emitting the Electrovector Effects.

(2) Control of electrical space on Electrovector ceramic

To translate the Electrovector ceramics into practical applications for medical devices, electrical space on Electrovector ceramics should be suitably controlled under the poling process. We are evaluating the poling mechanisms of some bioceramics, based on the various disciplines. In particular, we are putting emphasis on the relationship between the origin of electrical space and the crystal structure on the surface of the polarized bio-ceramics. The crystal defect, crystal distortion and fine change of ion composition of Electrovector ceramics polarized under various conditions are systematically investigated.

(3) Manipulation of biological responses by Electrovector ceramics

The electrostatic energies of the Electrovector effects aforementioned dominate the limited proximate areas and can control reactions locally. Therefore, the Electrovector ceramics can manipulate biological responses in a target space by both of the surface character and the electrostatic energies of the Electrovector ceramics at ion and tissue levels. We have demonstrated that the Electrovector ceramics enhanced protein adsorption, proliferation, adhesion, and differentiation of cultured cells on the ceramics as well as osteoconductivities in vivo by molecular biological and immunological detections.

(4) Development of applicable devices by ceramic technologies

We apply the Electrovector ceramics aforementioned to implant systems, such as artificial bones, bone joints, tooth roots, and are developing implantable devices with autograft-like osteoconductivities. We are undergoing improvements of sol-gel method for hydroxyapatite thin film coating and materials for vascular regeneration. We are extending our researches based on ceramic technologies farther, such as a control of oral environment, an improvement of oral esthetics, more effective and precise diagnosis systems for clinical laboratory medicine.

(2) Publications

[Original Articles]

1. Norio Wada, Naohiro Horiuchi, Makoto Nishio, Miho Nakamura, Kosuke Nozaki, Akiko Nagai, Kazuaki Hashimoto, Kimihiro Yamashita. Crystallization of calcium phosphate in agar hydrogels in presence of polyacrylic acid under double diffusion conditions *Crystal Growth & Design*. 2017.01; 17(2); 604-611

2. Jun Ito, Yuta Matsushima, Hidero Unuma, Naohiro Horiuchi, Kimihiro Yamashita, and Masahiko Tajika. Preparation and properties of pressureless-sintered dense calcite ceramics *Materials Chemistry and Physics*. 2017.01; 192; 304-310
3. Donghe Shen, Naohiro Horiuchi, Kosuke Nozaki, Michiyo Miyashin, Kimihiro Yamashita, Akiko Nagai. Synthesis and enhanced bone regeneration of carbonate substituted octacalcium phosphate *Bio-Medical Materials and Engineering*. 2017.01; 28(1); 9-21
4. Kazuhiro Kohata, Soichiro Itoh, Naohiro Horiuchi, Taro Yoshioka, Kimihiro Yamashita. Influences of osteoarthritis and osteoporosis on the electrical properties of human bones as in vivo electrets produced due to Wolff's law *Bio-Medical Materials and Engineering*. 2017.01; 28(1); 65-74
5. Naohiro Horiuchi, Yuki Iwasaki, Kosuke Nozaki, Miho Nakamura, Kazuaki Hashimoto, Akiko Nagai, Kimihiro Yamashita. A Critical Phenomenon of Phase Transition in Hydroxyapatite Investigated by Thermally Stimulated Depolarization Currents *Journal of the American Ceramic Society*. 2017.02; 100(2); 501-505
6. K. Igeta, Y. Kuwamura, N. Horiuchi, K. Nozaki, D. Shiraishi, M. Aizawa, K. Hashimoto, K. Yamashita, N. Nagai. Morphological and Functional Changes in RAW264 Macrophage-like Cells in Response to a Hydrated Layer of Carbonate-substituted Hydroxyapatite *Journal of Biomedical Materials Research A*. 2017.04; 105(4); 1063-1070
7. T. Ota, S. Itoh, K. Yamashita. Effectiveness of LIPUS Stimulation in the Treatment of Unstable both Radius and Ulna Fractures in Children *Bio-Medical Materials and Engineering*. 2017.08; 28(5); 545-553
8. Risa Yamada, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Reina Nemoto, Hiroyuki Miura, Akiko Nagai. Ag nanoparticle-coated zirconia for antibacterial prosthesis. *Mater Sci Eng C Mater Biol Appl*. 2017.09; 78; 1054-1060
9. Natsuko Iwata, Kosuke Nozaki, Naohiro Horiuchi, Kimihiro Yamashita, Yusuke Tsutsumi, Hiroyuki Miura, Akiko Nagai. Effects of controlled micro-/nanosurfaces on osteoblast proliferation. *J Biomed Mater Res A*. 2017.09; 105(9); 2589-2596
10. Byung-Nam Kim, Naohiro Horiuchi, Apurv Dash, Young-Wook Kim, Koji Morita, Hidehiro Yoshida, Ji-Guang Li, Yoshio Sakka. Spark Plasma Sintering of Highly Transparent Hydroxyapatite Ceramics. *Journal of the Japan Society of Powder and Powder Metallurgy*. 2017.10; 64(10); 547-551

[Books etc]

1. Akiko Nagai, Naohiro Horiuchi, Miho Nakamura, Norio Wada, Kimihiro Yamashita. Handbook of Solid State Chemistry Volume 6: Functional Materials. 2017.07 (ISBN : 978-3-527-32587-0)

[Misc]

1. Naohiro Horiuchi, Kimihiro Yamashita, Keiichi Katayama. Electric properties of inorganic phosphate 2017.07; 88; 222-229

[Conference Activities & Talks]

1. Naohiro Horiuchi, Kosuke Nozaki, Miho Nakamura, Akiko Nagai, Kimihiro Yamashita. Interfacial polarization caused by proton conduction in hydroxyapatite and its application for electret formation. 20th International Conference on Solid State Ionics (SSI-21) 2017.06.20 Padova, Italy
2. Kosuke Nozaki, Takayuki Endo, Naohiro Horiuchi, Kimihiro Yamashita, Kazuaki Hashimoto, Keiji Itaka, Akiko Nagai. Electrical and structural evaluation of sodium ion doped beta-tricalcium phosphate. The Tenth International Conference on the Science and Technology for Advanced Ceramics (STAC-10) 2017.08.02
3. Naohiro Horiuchi, Kimihiro Yamashita. Dielectric and Ionic properties of hydroxyapatite for biomedical applications. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017) 2017.09.29 Nagoya University, Nagoya, Japan
4. K. Nozaki, K. Fujita, N. Horiuchi, K. Yamashita, H. Miura, A. Nagai, K. Itaka. Regulation of periodontal ligament-derived cell morphology by type III collagen-coated hydroxyapatite. 2nd International Symposium on Creation of Life Innovation Materials 2017.09.30

[Patents]

1. Material for controlling organisms and for selective adsorption of protein, cement and biomaterial, Patent Number : EU 00104225.8-2107
2. METHOD FOR CONTROLLING ORGANISMS AND MATERIAL THEREFORE, METHOD FOR SELECTIVE ADSORPTION OF PROTEINS AND MATERIAL THEREFORE, CEMENT MATERIAL AND BIOMATERIAL, Patent Number : US6777214B1

Organic Biomaterials

Professor: Nobuhiko YUI
 Assistant Professor: Atsushi TAMURA
 Assistant Professor: Yoshinori ARISAKA
 Researcher: Masahiko TERAUCHI
 Secretary: Nanae NISHI

(1) Research

1. Design of Dynamic Biomaterials Surfaces

Biomaterials surfaces with dynamic properties are designed by utilizing a molecularly movable architecture of polyrotaxanes, and examined their effects on a variety of interactions with living body.

2. Modulation of Cellular Functions by Dynamic Ligand-Polymers

Biologically active ligands are introduced into cyclic molecules in polyrotaxanes, and examined the effects of their movability on multivalent interactions with receptor proteins and the subsequent events including intracellular metabolisms.

3. Modulation of Cellular Functions by Complexation of Intracellular Functional Supermolecules with Biomolecules

Cytocleavable polyrotaxanes to form complexes with biomolecules such as nucleic acid and protein are designed and their cellular functions are evaluated.

4. Cytocleavable Polyrotaxanes as Molecular Therapeutics for Congenital Metabolic disorders

Cyclodextrins released from cytocleavable polyrotaxanes specifically at lysosomes are effective to reduce excess cholesterol accumulation in lysosomes as well as ameliorate impaired autophagy in lysosomal disorders.

(2) Publications

[Original Articles]

1. Di He, Yoshinori Arisaka, Kenichi Masuda, Mitsuya Yamamoto, Naoya Takeda. A photoresponsive soft interface reversibly controls wettability and cell adhesion by conformational changes in a spiropyran-conjugated amphiphilic block copolymer. *Acta Biomaterialia*. 2017.03; 51; 101-111
2. Masahiko Terauchi, Takasuke Inada, Tomoki Kanemaru, Go Ikeda, Asato Tonegawa, Kei Nishida, Yoshinori Arisaka, Atsushi Tamura, Satoshi Yamaguchi, Nobuhiko Yui. Potentiating bioactivity of BMP-2 by polyelectrolyte complexation with sulfonated polyrotaxanes to induce rapid bone regeneration in a mouse calvarial defect. *Journal of Biomedical Materials Research Part A*. 2017.03; 105(5); 1355-1363
3. Yoshinori Arisaka, Nobuhiko Yui. Tethered bone morphogenetic protein-2 onto sulfonated-polyrotaxane based surfaces promotes osteogenic differentiation of MC3T3-E1 cells. *Journal of Biomaterials Science, Polymer Edition*. 2017.04; 28(10-12); 974-985
4. Atsushi Tamura, Moe Ohashi, Nobuhiko Yui. Oligo(ethylene glycol)-modified β -cyclodextrin-based polyrotaxanes for simultaneously modulating solubility and cellular internalization efficiency. *Journal of Biomaterials Science, Polymer Edition*. 2017.07; 28(10-12); 1124-1139

5. Atsushi Tamura, Moe Ohashi, Kei Nishida, Nobuhiko Yui. Acid-induced intracellular dissociation of β -cyclodextrin-threaded polyrotaxanes directed towards attenuating phototoxicity of bisretinoids through promoting excretion. *Molecular Pharmaceutics*. 2017.12; 14(12); 4714-4724

[Books etc]

1. Masahiko Terauchi, Atsushi Tamura, Nobuhiko Yui. "Advances in Dental Pharmacology" Regeneration of dental tissue by supramolecular pharmacological agents. Avid Science, 2017.10

[Misc]

1. Ji Hun Seo, Mitsui Hirata, Sachiro Kakinoki, Tetsuji Yamaoka, Nobuhiko Yui. Effect of dynamic polyrotaxane coating on cytoskeletal signaling expression of adhering stem cells and downstream differentiations. *Advances in Science and Technology*. 2017.01; 102; 37-42
2. Atsushi Tamura, Nobuhiko Yui. Rational design of stimuli-cleavable polyrotaxanes for therapeutic applications. *Polymer Journal*. 2017.07; 49(7); 527-534
3. Akihiko Kikuchi, Nobuhiko Yui, Stuart L Cooper, Kazunori Kataoka. In memory of Professor Teiji Tsuruta; great mentor in polymeric biomaterials. *J Biomater Sci Polym Ed*. 2017.08; 28(10-12); 879-880

[Conference Activities & Talks]

1. Nobuhiko Yui. Directing Cell Fate via Supramolecular Characteristics of Polyrotaxanes. EPFL-TMDU joint BiomaterialsI & Bioelectronics Symposium 2017.03.10 Lausanne, Switzerland
2. Atsushi Tamura, Nobuhiko Yui. Acid-labile interlocked cyclodextrin polymers for therapeutic applications to rare diseases. Society for Biomaterials 2017 Annual Meeting & Exposition (SFB2017) 2017.04.06 Minneapolis, Minnesota, USA
3. Kei Nishida, Atsushi Tamura, Nobuhiko Yui. Recruitment of the autophagic machinery by the acid-labile polyrotaxanes exerting intracellular release of methylated β -cyclodextrins. Society for Biomaterials 2017 Annual Meeting & Exposition (SFB2017) 2017.04.07 Minneapolis, Minnesota, USA
4. Arun Kumar Rajendran, Yoshinori Arisaka, Nobuhiko Yui, Sachiko Iseki. Regulation of osteogenic differentiation by utilizing supramolecular mobility of polyrotaxanes for the treatment of craniosynostosis. 2017.07.08
5. N. Yui. Emerging polyrotaxane frameworks for modulating cellular functions.. FBPS'2017 2017.07.13 Seoul, Korea
6. Atsushi Tamura, Nobuhiko Yui. Polyrotaxane-based intracellular delivery of β -cyclodextrins for modulating cholesterol homeostasis in Niemann-Pick type C disease. Controlled Release Society 2017 Annual Meeting & Exposition 2017.07.17 Sheraton Boston Hotel, Massachusetts, USA
7. Yoshinori Arisaka, Atsushi Tamura, Yusuke Tsutsumi, Takao Hanawa, Nobuhiko Yui. Immobilization of polyrotaxanes onto Ti for modulating cell function. 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya, Japan
8. Atsushi Tamura, Nobuhiko Yui. Design of acid-labile polyrotaxanes for the treatment of rare metabolic diseases. 6th Asian Biomaterials Congress 2017 (ABMC2017) 2017.10.25 Apollo DIMORA, Thiruvananthapuram, India
9. Yoshinori Arisaka, Nobuhiko Yui. Surface-tethering of bone morphogenetic proteins onto sulfonated polyrotaxane substrates. 6th Asian Biomaterials Congress (ABMC6) 2017.10.25 Thiruvananthapuram, India
10. Yuma Yamada, Shinnosuke Daikuhara, Atsushi Tamura, Kei Nishida, Nobuhiko Yui, Hideyoshi Harashima. Validation of autophagy induction via the mitochondrial delivery of polyrotaxane by a MITO-Porter. The 2nd International Symposium on Biomedical Engineering 2017.11.09 Tokyo Institute of Technology, Meguro-ku, Tokyo, Japan

11. Atsushi Tamura, Nobuhiko Yui. Design of β -cyclodextrin-threaded acid-labile polyrotaxanes for the treatment of Niemann-Pick type C disease. 9th Asian Cyclodextrin Conference (9ACC) 2017.12.15 National University of Singapore, Singapore
12. Kei Nishida, Atsushi Tamura, Nobuhiko Yui. ER stress-associated autophagy induction by methylated β -cyclodextrin-threaded acid-labile polyrotaxane. 9th Asian Cyclodextrin Conference (9ACC) 2017.12.15 National University of Singapore, Singapore
13. Kentaro Morita, Taishi Higashi, Xia Song, Jing-ling Zhu, Jun Li, Atsushi Tamura, Nobuhiko Yui, Keiichi Motoyama, Hidetoshi Arima. One-pot synthesis of polycatenanes containing cyclodextrins. 9th Asian Cyclodextrin Conference (9ACC) 2017.12.15 National University of Singapore, Singapore
14. Nobuhiko Yui, Ji-Hun Seo, Atsushi Tamura, Yoshinori Arisaka. Modulating cellular functions via supramolecular polyrotaxanes. 9th Asian Cyclodextrin Conference (9ACC) 2017.12.16 National University of Singapore, Singapore

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.
Associate Professor Wataru NOMURA, Ph.D.
Assistant Professor Takuya KOBAYAKAWA, Ph.D.
Support Researcher Ami MASUDA
Technical Assistant Satoko KIKUCHI
Assistant Kayo KANADA, Miho TANABE, Tomoe KAMEI
Adjunct Lecturer Motoyoshi NOMIZU

Graduate students

D3 Shohei TAKETOMI, Kiju KONNO, Kei TOYAMA, Yuzuna HONDA, Maxwell SAKYIYAMA
D2 Daisuke MATSUMOTO, Daisuke MIYAKI
M2 Kento EBIHARA, Tsukasa HASHIMOTO
M1 Tomoki KISHI, Shunsuke SAWAMURA, Kohei TAKAHASHI

External Collaborators

Yuko YAMADA, Takumi KAMIMURA, Masaki KURAKAMI

(1) Outline

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

(2) Research

1. Development of conformational-constrained templates for drug discovery.

Drug-discovery templates for conformational restriction, which enable pharmacophores of bioactive compounds (ex. peptides) to be suitably disposed in three-dimensional space, are being developed. Drug discovery for the chemotherapy of cancer, AIDS, Alzheimer's disease, rheumatoid arthritis, SARS, etc. is being performed based on targeting several receptors, enzymes, etc.

2. Development of bio-probes, bio-sensing, medicinal chemistry towards chemical biology.

Bio-probes that specifically recognize each receptor or enzyme are being developed for research on chemical biology involving imaging and sensing.

3. Structural analysis of the interactions between receptors/enzymes and their ligands.

Using X-ray crystal structural analysis, the mechanism of signal transduction operated by binding of ligands to receptors/enzymes is being analyzed.

4. Development of applications of zinc finger protein for gene therapy and nano technology.

Utilizing DNA sequence-specific recognition of zinc finger protein, technologies for DNA recombination, modifications, and DNA labeling are being developed.

(3) Education

Practice

Goals/Outline:

Presenter reports about the recent topics related to molecular biomedicine from Journals. The report must come with the backgrounds and motivations of research fields. Research designs, experimental methods, data analyses, and perspectives for future development will be discussed about the topics. Students are also encouraged to attend to lectures for the graduate course and discuss about the topics with lecturers.

Available programs:

Lectures for the graduate course: as occasion

Journal Club: Every Thursday from 15:00 to 16:30

Lab

Goals/Outline:

Research in the lab is mainly focused to two topics; 1) development of artificial enzymes for regulation of gene functions and (2) exploration and analyses of cellular functions by methods based on peptide chemistry. Students will learn how to design research, experimental techniques, and analysis methods of research data. Research themes are related to multiple research fields such as molecular biology, chemistry, chemical biology, and synthetic biology.

Available program:

Lab meeting (progress report): every week, about 1 hour per person (will be announced)

(4) Lectures & Courses

Format:

Small group

Venue:

Practice: Third laboratory room (603) at Institute of Biomaterials and Bioengineering

Lab: Laboratory of Medicinal Chemistry (602) at Institute of Biomaterials and Bioengineering

Grading:

Practice: Attendance and report

Lab: Progress of research and report

(5) Publications**[Original Articles]**

1. Mizuguchi T, Ohashi N, Matsumoto D, Hashimoto C, Nomura W, Yamamoto N, Murakami T, Tamamura. Development of Anti-HIV Peptides Based on a Viral Capsid Protein. *Biopolymers: Peptide Science*. 2017.01; 108(1);
2. Tanaka T, Aoki T, Nomura W, Tamamura H. Bivalent 14-mer Peptide Ligands of CXCR4 with Polyproline Linkers with Anti-Chemotactic Activity against Jurkat Cells. *J. Pept. Sci.* 2017.01;
3. Takano T, Narumi T, Nomura W, Tamamura H. Microwave-Assisted Synthesis of Azacoumarin Fluorophores and the Fluorescence Characterization. *J. Org. Chem.* 2017.02; 82(5); 2739-2744
4. Kobayashi K, Mizuguchi T, Hattori Y, Ohara N, Ninomiya R, Iida M, Ooe H, Yamazaki Y, Takata M, Tamamura H, Akaji K. Effects of Replacement and Addition of an Amino Acid Contained in a Cyclic Peptide Corresponding to a β -Hairpin Loop Sequence of Human EGF Receptor. *J. Pept. Sci.* 2017.04;
5. Ohashi N, Kobayashi R, Nomura W, Kobayakawa T, Czikora A, Herold B K, Lewin N E, Blumberg P M, Tamamura H. Synthesis and Evaluation of Dimeric Derivatives of Diacylglycerol-Lactones as Protein Kinase C Ligands. *Bioconjugate Chem.* 2017.07;

6. Kobayakawa T, Tamamura H. Stereoselective Synthesis of Xaa-Yaa Type (Z)-Chloroalkene Dipeptide Isosteres via Efficient Utilization of Organocopper Reagents Mediated Allylic Alkylation. *Tetrahedron*. 2017.07; 73(30); 4464-4471

[Books etc]

1. Ohashi N, Tamamura H. "Peptide-derived mid-sized anti-HIV agents" In "Amino Acids, Peptides and Proteins," ed. by Maxim Ryadnov and Ferenc Hudecz, The Royal Society of Chemistry, Cambridge CB4 0WF, UK, vol. 41. 2017.01

[Conference Activities & Talks]

1. Hashimoto T, Nomura W, Ohura I, Tamamura H. Improved split DNA methylase activity by optimization of assembly on target sites. Keystone Symposia Precision Genome Engineering 2017.01.08 Breckenridge, USA
2. Nomura W, Sugii T, Tamamura H. Chemical-inducible artificial transcription factors based on sequence-specificity of TALE and dCas9. Keystone Symposia Precision Genome Engineering 2017.01.08 Breckenridge, USA
3. Matsumoto D, Nomura W, Tamamura H. Controllable genome editing by chemically inducible split site-specific nucleases. Keystone Symposia Precision Genome Engineering 2017.01.08 Breckenridge, USA
4. Kobayakawa T, Tamamura H. Development of Synthetic Methods for Chloroalkene Dipeptide Isosteres and Their Applications. The 25th American Peptide Symposium and the 9th International Peptide Symposium 2017.06.19 Whistler, Canada
5. Nomura W, Tanaka T, Aoki T, Tamamura H. Bivalent Ligands of the Chemokine Receptor CXCR4 with Polyproline Linkers and Their Anti-chemotactic Activity. The 25th American Peptide Symposium and the 9th International Peptide Symposium 2017.06.21 Whistler, Canada
6. Ebihara K, Honda Y, Nomura W, Murakami T, Tamamura H. Development of HIV-1 fusion inhibitors based on the C34 dimers derived from gp41. The 21st Korean Peptide Protein Society Symposium 2017.06.25 Jeju, Korea
7. Tamamura H. Rigid bivalent ligands of the chemokine receptor CXCR4 and their anti-cancer metastasis activity. KCS Biochemistry Division Summer Workshop 2017.06.27 Jeju, Korea
8. Ohashi N, Harada S, Irahara Y, Ishida Y, Konno K, Kobayakawa T, Nomura W, Matsushita S, Yoshimura K, Tamamura H. CD4 Mimics for Enhancement of Activity of HIV Neutralizing Antibodies. The 11th AFMC International Medicinal Chemistry Symposium 2017.07.24 Melbourne, Australia
9. Nomura W, Matsumoto D, Hashimoto T, Sugii T, Tamamura H. Development of chemical-inducible artificial transcription factors based on sequence-specific DNA binders. the 254th ACS National Meeting and Exposition 2017.08.20 Washington DC, USA
10. Toyama K, Nomura W, Tamamura T. Functional evaluation of intracellular delivery peptides based on the EGF receptor dimerization arm sequences. 12th Australian Peptide Conference 2017 2017.10.16 Noosa, Australia
11. Tamamura H. Synthesis of chloroalkene dipeptide isosteres as peptidomimetics and their biological application. 12th Australian Peptide Conference 2017 2017.10.17 Noosa, Australia
12. Nomura W, Matsumoto D, Sugii T, Kobayakawa T, Tamamura H. Differential regulation of endogenous genes in an orthogonal manner by distinct chemically inducible systems. International Conference on Epigenetics and Bioengineering 2017.12.13 Miami, USA

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Associate Professor	Satoshi FUJII
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Koji OKAMOTO
Visiting Lecturer	Takashi KOHNO
Visiting Lecturer	Michihiro MUTOH
Graduate Students	D3 Kasumi OTSUBO, Yuki YAMAMOTO
	D1 Tomoko WATANABE
	M2 Marina HENMI, Hidenobu SUZUKI, Taichi IJIMA
	M1 Yamato OGIWARA, Maiko TAKAHASHI, Naoki TSUKIMATA, Miyu YOSHIDA

(1) Research

1. Carcinogenesis and molecular mechanism
2. Functions of cancer-associated genes and their alterations
3. Genomic, epigenomic and proteomic analysis of cancer and personalized medicine
4. Tumor microenvironment
5. Cancer stem cells/non-coding RNA/signaling pathway
6. Molecular target/drug delivery/diagnosis and therapy

(2) Education

To learn knowledge and skill for cancer research, students attend lectures and seminars, and attend and/or practice research meeting, journal club, scientific meeting, etc. These practices will enable students to develop an ability to conduct their studies as an

independent cancer researcher in the future. To obtain good skills to carry out experiments that are required for cancer research, students belong to one of our research groups, and conduct their own studies under the guidance of the instructor and/or staff. Students perform various experiments involved in genetics, gene technology, biochemistry, cellular biology, molecular biology, physiology, experimental animal, pathology, genomic/epigenomic/proteomic analysis, imaging, next generation sequencing, etc.

(3) Publications

[Original Articles]

1. Tsuneki M, Kinjo T, Mori T, Yoshida A, Kuyama K, Ohira A, Miyagi T, Takahashi K, Kawai A, Chuman H, Yamazaki N, Masuzawa M, Arakawa H. Survivin: A novel marker and potential therapeutic target for human angiosarcoma. *Cancer Sci.* 108: 2295-2305, 2017.
2. Ishibashi M, Neri S, Hashimoto H, Miyashita T, Yoshida T, Nakamura Y, Udagawa H, Kirita K, Matsumoto S, Umemura S, Yoh K, Niho S, Tsuboi M, Masutomi K, Goto K, Ochiai A, Ishii G. CD200-positive cancer associated fibroblasts augment the sensitivity of Epidermal Growth Factor Receptor mutation-positive lung adenocarcinomas to EGFR Tyrosine kinase inhibitors. *Sci Rep.* 7: 46662, 2017.
3. Deng X, Hamamoto R, Vougiouklakis T, Wang R, Yoshioka Y, Suzuki T, Dohmae N, Matsuo Y, Park JH, Nakamura Y. Critical roles of SMYD2-mediated β -catenin methylation for nuclear translocation and activation of Wnt signaling. *Oncotarget.* 8: 55837-55847, 2017.
4. Yoshioka Y, Suzuki T, Matsuo Y, Tsurita G, Watanabe T, Dohmae N, Nakamura Y, Hamamoto R. Protein lysine methyltransferase SMYD3 is involved in tumorigenesis through regulation of HER2 homodimerization. *Cancer Med.* 6: 1665-1672, 2017.

5. Yasunaga M, Manabe S, Matsumura Y. Immunoregulation by IL-7R-targeting antibody-drug conjugates: overcoming steroid-resistance in cancer and autoimmune disease. *Sci Rep.* 7: 10735, 2017.
6. Hashimoto K, Hayashi R, Mukaigawa T, Yamazaki M, Fujii S. Concomitant expression of ezrin and HER2 predicts distant metastasis and poor prognosis of patients with salivary gland carcinomas. *Hum Pathol.* 63: 110-119, 2017.
7. Higaki E, Yanagi S, Gotohda N, Kinoshita T, Kuwata T, Nagino M, Ochiai A, Fujii S. Intraoperative peritoneal lavage cytology offers prognostic significance for gastric cancer patients with curative resection. *Intraoperative peritoneal lavage cytology offers prognostic significance for gastric cancer patients with curative resection.* *Cancer Sci.* 108: 978-986, 2017.
8. Fujii S, Yamashita S, Yamaguchi T, Takahashi M, Hozumi Y, Ushijima T, Mukai H. Pathological complete response of HER2-positive breast cancer to trastuzumab and chemotherapy can be predicted by HSD17B4 methylation. *Oncotarget.* 8: 19039-19048, 2017.
9. Dendo K, Yugawa T, Nakahara T, Ohno S I, Goshima N, Arakawa H, Kiyono T. Induction of non-apoptotic programmed cell death by oncogenic RAS in human epithelial cells and its suppression by MYC overexpression. *Carcinogenesis.* 39: 202-213, 2018.
10. Yamamoto Y, Nagasato M, Rin Y, Henmi M, Ishikawa Y, Yachida S, Ohki E, Hiraoka N, Tagawa M, Aoki K. Strong antitumor efficacy of a pancreatic tumor-targeting oncolytic adenovirus for neuroendocrine tumors. *Cancer Med.* 6: 2385-2397, 2017.
11. Nagasato M, Rin Y, Yamamoto Y, Henmi M, Hiraoka N, Chiwaki F, Matsusaki

K, Tagawa M, Sasaki H, Aoki K. A tumor-targeting adenovirus with high gene transduction efficiency for primary pancreatic cancer and ascites cells.

Anticancer Res. 37: 3599-3506, 2017.

12. Miyamoto S, Komiya M, Fujii G, Hamoya T, Nakanishi R, Fujimoto K, Tamura S, Kurokawa Y, Takahashi M, Ijichi T, Mutoh M. Preventive effects of heat-killed *Enterococcus faecalis* strain EC-12 on mouse intestinal tumor development. *Int J Mol Sci.* 18: 826, 2017.

[Reviews Articles]

1. Nakamura Y, Arakawa H. Discovery of Mieap-regulated mitochondrial quality control as a new function of tumor suppressor p53. *Cancer Sci.* 108: 809-17, 2017.
2. Yasunaga M, Manabe S, Tsuji A, Furuta M, Ogata K, Koga Y, Saga T, Matsumura Y. Development of antibody–drug conjugates using DDS and molecular imaging. *Bioengineering.* 4: 78, 2017.
3. Yamamoto Y, Nagasato M, Yoshida T, Aoki K. Recent advances in genetic modification of adenovirus vectors for cancer treatment. *Cancer Sci.* 108: 831-837, 2017.

[Conference Activities & Talks]

1. Nakamura Y, Tsuneki M, Yamamoto M, Arakawa H. Mieap, the mitochondria-eating protein induces cell death by eating unhealthy mitochondria. AACR Annual Meeting 2017, (Washington, D.C, USA), April, 2017.
2. Maida Y*, Sakurai M*, Shiromoto Y*, Yasukawa M, Ghilotti M, Ariyoshi K, Nishikura K, Masutomi K. (*Equal contribution) A novel interaction of TERT with RNA editing. Cold Spring Harbor Laboratory Meeting “Telomere and Telomerase” Cold Spring Harbor, (NY, USA) May, 2017.
3. Maida Y*, Sakurai M*, Shiromoto Y*, Yasukawa M, Ghilotti M, Ariyoshi K,

- Masutomi K, Nishikura K. (*Equal contribution) RNA-mediated interaction between ADAR and TERT. 2017 Gordon Research Conference on RNA editing Ventura,(CA, USA), March, 2017.
4. Vassiliki Saloura, Theodore Vougiouklakis, Makda Zewde, Xiaolan Deng, Kazuma Kiyotani, Jae-Hyun Park, Yo Matsuo, Mark Lingen, Naoshi Dohmae, Takehiro Suzuki, Ryuji Hamamoto and Yusuke Nakamura. WHSC1L1-mediated EGFR mono-methylation enhances the cytoplasmic and nuclear oncogenic activity of EGFR in head and neck cancer, AACR Annual Meeting 2017, (Washington, D.C, USA), April, 2017.
 5. Masahiro Yasunaga, Masaru Furuta, Koretsugu Ogata, Yuki Fujiwara, Yoshikazu Koga and Yasuhiro Matsumura. Visualisation of EPR effect and active targeting by using microscopic mass spectrometry. AACR Annual Meeting, (Washington, DC, USA), April, 2017.
 6. Chie Kudo-Saito, Yamato Ogiwara, Kazunori Aoki. Blocking FSTL1 ameliorates immunity against osteosarcoma. AACR Annual Meeting 2017, (Washington, DC, USA), April, 2017.

Cellular and Molecular Medicine

associate professor Yumiko Oishi MD., Ph.D
assistant professor Sumio Hayakawa Ph.D
assistant professor Shinichiro Hayashi Ph.D(-July 2017)

(1) Outline

Cardiovascular disease, as a consequent of the obesity related metabolic syndrome, remains a significant cause of morbidity and mortality in industrialized societies. A major effort of our laboratory has been to investigate the molecular mechanism of an initiation and progression of metabolic syndrome from the viewpoint of transcriptional regulation. Since macrophages contribute to all phases of the pathogenesis of atherosclerosis, we have extensively studied the macrophage diversity that respond to various stress within tissue environment. Additionally, it is recognized that sarcopenia (skeletal muscle loss with) is important for the pathogenesis of metabolic syndrome. The long term goals of our current study are to elucidate: 1) the mechanism of the link between cellular metabolism and immune response of macrophage 2) the mechanism of chronic inflammation that leads to metabolic syndrome, and 3) the mechanism responsible for pathogenesis of sarcopenia and skeletal muscle degeneration.

(2) Research

1. Mechanisms of Coordinated regulation of inflammatory response and lipid homeostasis in macrophage

Chronic low-grade inflammation has been recognized as a key contributing factor in the onset and progression of metabolic syndrome and atherosclerosis. As a multifunctional effector cell, macrophage play pivotal roles in both the enhancement and resolution of this inflammatory process. By utilizing molecular biology technique, lipidomics and bioinformatics, we found that the lipid homeostasis is coordinately regulated with inflammatory response in macrophage. TLR4 activation rapidly, and transiently inhibits Liver X receptor (LXR) signaling, and subsequently activates Sterol regulatory element-binding protein (SREBP). In the late phase of inflammation, LXR and SREBP work together to increase anti-inflammatory fatty acid synthesis, necessary for a resolution of inflammation. Thus, transcriptional/signaling network involving LXR and SREBP play a pivotal role in the regulation of lipid homeostasis and cellular function. By elucidating the crosstalk between cellular function and metabolism, we would be able to accumulate beneficial knowledge to develop novel therapeutic strategy targeting macrophages for the prevention and treatment of metabolic syndrome.

2. Mechanism of skeletal muscle degeneration

Skeletal muscle consume 40% of total energy, playing a key role for the pathogenesis of metabolic syndrome. Sarcopenia is the degenerative loss of skeletal muscle mass, quality and strength associated with aging. Although the causes and mechanisms of sarcopenia still remains unclear, one of the hypotheses is reduction of the number of satellite cells, stem cells in adult muscle, and failure of satellite cell activation. We identified KLF5 as a novel factor that play a pivotal role in skeletal muscle degeneration. KLF5 is a Zinc-finger transcription factor involved in the self-renewal and proliferation of embryonic stem cell and cancer stem cell. KLF5 is transiently induced in the myoblast during differentiation and it plays critical role for muscle degeneration and repair. Although Klf5 is not expressed in the quiescent satellite cells, its expression is dramatically increased in the satellite cells with age. Now we are testing the hypothesis whether the dysregulation of Klf5 causes a malfunction of satellite cells.

(3) Education

Lecture: Doctoral Program, Life Science and Technology Track #6110, Bioscience I

Lecture: Master's Program, Medical and Dental Science and Technology Track, Molecular biology

Lecture: School of Dentistry, Second grade, Basic molecular mechanisms of life

Lecture: School of Medicine, Third grade, Public health

(4) Publications**[Original Articles]**

1. Yumiko Oishi, Nathanael J Spann, Verena M Link, Evan D Muse, Tobias Strid, Chantle Edillor, Matthew J Kolar, Takashi Matsuzaka, Sumio Hayakawa, Jenhan Tao, Minna U Kaikkonen, Aaron F Carlin, Michael T Lam, Ichiro Manabe, Hitoshi Shimano, Alan Saghatelian, Christopher K Glass. SREBP1 Contributes to Resolution of Pro-inflammatory TLR4 Signaling by Reprogramming Fatty Acid Metabolism. *Cell Metab.* 2017.02; 25(2); 412-427
2. Yumiko Oishi, Shinichiro Hayashi, Takayuki Isagawa, Motohiko Oshima, Atsushi Iwama, Shigeki Shimba, Hitoshi Okamura, Ichiro Manabe. Bmal1 regulates inflammatory responses in macrophages by modulating enhancer RNA transcription. *Sci Rep.* 2017.08; 7(1); 7086

[Conference Activities & Talks]

1. Yumiko Oishi. SREBP1 contributes to resolution of pro-inflammatory TLR4 signaling by reprogramming fatty acid metabolism.. 11th International Symposium of the Institute Network 2017.01.26 Tokushima, Japan
2. Yumiko Oishi. Coordinated regulation of inflammatory response and fatty acid metabolism in macrophage. Transborder medical research center international symposium, Tsukuba University 2017.06.17 Tsukuba, Japan

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA
Junior Associate Professor Keiko KONDO
Assistant Professor Masayo YASUDA
Specially Appointed Assistant Professor Natsumi NAKAMURA
Graduate Student Anongwee LEEWANANTHAWET, Yuko INOUE
Resident Wataru ONO, Masayuki TOI

(1) Outline

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care. Regarding research, the effects of the functional waters to organism and clinical application of them were investigated.

(2) Research

- 1) Clinical and basic studies on Ozone ultrafine-bubble water (NBW3) :antimicrobials activity and effects to eukaryotic cells (induction of anti-oxidant capacities and wound healing activities etc.)
- 2) Study on virulence factors of periodontopathic bacteria
- 3) Development of education system for dental (oral) hygienists to prevent oral diseases
- 4) Development of assessment program in technical education for dental (oral) hygienists

(3) Education

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care.

(4) Lectures & Courses

Main objective of Lifetime Oral Health Care Sciences is to understand and learn how oral health care contributes to the preservation of general health and healthy life expectancy. Students also learn the newest knowledge on oral pathology and oral health promotion, and are trained to master the modality of oral health care

(5) Clinical Services & Other Works

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(6) Clinical Performances

Oral care clinic provides prevention of oral diseases, such as dental caries or periodontal diseases for maintaining patients' oral and general health in a lifetime.

(7) Publications

[Original Articles]

1. M Doino, M Yokoyama, Y Sasaki, K Kondo, Y Yasuda, S Arakawa. Evaluation of the relationship between salivary concentration of anti-heat shock protein immunoglobulin and clinical manifestations of Behçet's disease. SCANDINAVIAN JOURNAL OF RHEUMATOLOGY. 2017.09; 46(5); 381-387
2. Shinichi Arakawa, Mitsuru Sugisawa, Anongwee Leewanthawet. Application of ozone nanobubble water (ONBW) to peri-implantitis treatment Dentistry. 2017.12; 7(12);

[Misc]

1. Shinichi Arakawa. Ozone antiseptic shows potential for treating severe gum infections Asia Research News 2015.

[Conference Activities & Talks]

1. 荒川真一. Clinical Application of Ozone Nano-Bubble Water (NBW3) to Peri-implantitis Treatment. The 24th International Conference and Exhibition on Dentistry & Oral Care 2017.04.17 Dubai, UAE
2. Shinichi Arakawa. Clinical application of Ozone nano-bubble water -periodontitis & peri-implantitis-. 2017.04.19 Dental College, Gulf Medical University (UAE)
3. The clinical and educational effects of the newly-introduced interprofessional clinical practice. 2017.05.12
4. The clinical and educational effects of the newly-introduced interprofessional clinical practice. 2017.05.13
5. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Naoko SEKI, Yuki OHARA, Masayo YASUDA, Hiromi OTSUKA, Shinichi ARAKAWA, Kouji ARAKI. . Development of a new IPW program for dental students and dental hygiene students in practical clinical training. Working as a dental team. The 36th General and Scientific Meeting of the Japanese Dental Education Association 2017.07.28
6. Development of a new IPW program for Dental students and Dental hygiene students in clinical practice. "Working in a dental team". 2017.07.28

[Awards & Honors]

1. Advanced Education System Development(Kanako Noritake), Japanese Dental Education Association, 2017.07

Oral Care for Systemic Health Support

Professor KABASAWA Yuhji

(1) Outline

(1) Education

We teach the knowledge and skills necessary for oral health activities through classes in charge. Specifically, we will teach about the relationship between oral health and general health such as perioperative oral function management and periodontal disease and diabetes. In addition to teaching health assessment of the oral and maxillofacial area, we will acquire basic knowledge and skills through vital signs measurement practice, emergency life-saving activity practice, which is one of general health evaluation indicators.

Furthermore, we lecture on the pathology, pathophysiology, diagnosis and treatment related to mandibular oral cavity disease, and teach necessary knowledge on oral health education, prevention of oral diseases of people with basic diseases in the medical field.

(2) Research

We will conduct research to support maintenance and promotion of health by oral health. Especially contribute to people's health and well-being through research on perioperative oral cavity function management, research on oral care of people with underlying diseases, research on regeneration of jawbone with FGF-2, etc.

(3) Clinical

In order to maintain and promote general health through oral health, we cooperate with each outpatient at the dentistry hospital and do dental prophylactic treatment of the patient and oral health education at oral care outpatient. In addition to oral care for inpatients at dental and medical hospital while working in cooperation with nurses, nutritionists, pharmacists and others, they practice oral care according to the condition of patients as a member of team medicine.

(2) Research

1. Oral health care of patients with oral cancer, cleft lip and palate and other oral diseases
2. Oral health related QOL of patients with oral cancer, cleft lip and palate, dry mouth
3. Basic research of tooth brush, peeling sponge and tooth paste
4. Morphological, functional research, and oral health of patients with cleft lip and palate
5. Research for safety in supplements in oral functions
6. Basic research for bone regeneration using FGF-2.

(3) Lectures & Courses

From the standpoint of oral health and general health, educate dental hygienists who can contribute to people's health and welfare by teaching the knowledge and skills necessary for oral health care centering on oral medicine education.

(4) Clinical Services & Other Works

Oral care department, in cooperation with each outpatient in the dental school attached hospital, in order to maintain and improve the general health through oral health, do patients' dental preventive measures and oral

health education in oral care outpatient. In addition, we do oral care for hospitalized patients in the dentistry department and medical hospital affiliated hospitals, we receive consultation about patient oral care from ward nurses, and instruct oral care methods according to patient condition.

In oral surgery unit, we are engaged in diagnosis, treatment, oral health guidance etc of various oral disease patients.

(5) Clinical Performances

Based on knowledge of oral medicine through oral care department, we are conducting perioperative oral function management with more specialized expertise.

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA
Assistant Professor Hiromi OTSUKA
Part-time lecturer Atsushi OHYAMA
Graduate Students Master Course
Tomomi ABE,
Makoto KAWANO,
Chie YOSHIZU,
Shin Yujeong,
Liao Shin Ru,

(1) Outline

In order to cultivate students' abilities to prevent and detect oral diseases at an early stage, which are important to maintain and improve the nation's health, we help students acquire deep academic knowledge and high standard skills in preventive oral health care such as skills to check over the condition of oral cavities. Additionally, we help students develop skills to provide oral health counseling and oral health promotion, and nurture human resources who can actively contribute the development of oral health promotion.

(2) Research

- 1) Preventive Oral Health Care Sciences
 - ① Incident factors and preventive methods on dental caries
 - ② Incident factors and preventive methods on periodontal disease
 - ③ Incident factors and preventive methods on oral malodor
 - ④ Incident factors and preventive methods on other oral diseases
- 2) Development of education system for the patients to prevent oral diseases and for dental hygiene students.
- 3) Development of new assessment programs in technical education for dental hygienist students.

(3) Clinical Services & Other Works

In our Oral Health Care Clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases, for the patients to maintain their oral health for the entire lifetime.

(4) Publications

[Original Articles]

1. Chien PJ, Suzuki T, Tsujii M, Ye M, Minami I, Toda K, Otsuka H, Toma K, Arakawa T, Araki K, Iwasaki Y, Shinada K, Ogawa Y, Mitsubayashi K. Biochemical Gas Sensors (Biosniffers) Using Forward and

Reverse Reactions of Secondary Alcohol Dehydrogenase for Breath Isopropanol and Acetone as Potential Volatile Biomarkers of Diabetes Mellitus. *Anal Chem.* 2017.11; 89(22); 12261-12268

[Books etc]

1. Soichirou Asaba, Yuichi Kitasako, Kayoko Shinada et al. . Textbook of patients' education at dental clinic . Quintessence Publishing, 2017.10 (ISBN : 978-4-7812-0581-6)

[Conference Activities & Talks]

1. Naito M, Shinada K, Kunitsuka K, Onishi T, Yamamoto R, Seki N, Morio I, Taniyama K. Intervention survey on oral health at newspaper printing factories . 90th Annual Meeting of the Japan Society for Occupational Health 2017.05.13 Tokyo
2. Kanako NORITAKE, Jun TSURUTA, Koji MIZUTANI, Keiko KONDO, Naoko SEKI, Yuki OHARA, Masayo YASUDA, Hiromi OTSUKA, Shinich ARAKAWA, Kouji ARAKI. . Development of a new IPW program for dental students and dental hygiene students in practical clinical training. Working as a dental team. The 36th General and Scientific Meeting of the Japanese Dental Education Association 2017.07.28

[Awards & Honors]

1. Advanced Education System Development(Kanako Noritake), Japanese Dental Education Association, 2017.07

Oral Health Sciences for Community Welfare

Professor Junichi FURUYA
Junior Associate Professor Keiko ENDO
Graduate Student Michiyo OBANA
Graduate Student Chiaki MATSUBARA
Graduate Research Student Junji TOKUNAGA

(1) Outline

The role of Department of Oral Health Sciences for Community Welfare is to develop education, practice, research for turning out dental profession who can play an important role as profession of oral function and eating in medical care and welfare of super-aging society. All of our research and education is based on daily medical and dental care so that we can produce medical and dental professions who can work globally and locally.

The department is particularly focusing on improving oral health such as mastication, swallowing, dentures and oral hygiene through dysphagia rehabilitation, diet modification support, multi-disciplinary team approach so that the department contributes to prevent and improve aspiration pneumonia, malnutrition, and quality of life. Recently, we're also focusing on oral function of stroke patients and community cooperation, oral function of dementia and MCI patients and dental care, and dentures and swallowing in team approach.

All educational and research activities are based on clinical practice and experiences so that knowledge and skills of oral function will be acquired. Concretely, oral functional rehabilitation and oral hygiene care are performed as oral health management for hospitalized and institutionalized patients, and out patient in clinic. In addition, we supply multi-disciplinary team approach as a member of NST (Nutrition Support Team), PCT (Palliative Care Team), Oral hygiene care team in medical hospital of TMDU, and Visiting Dysphagia Rehabilitation Team.

(2) Research

1. Mastication and swallowing, nutrition, enjoyment of eating in older people
2. Dysphagia rehabilitation and oral health sciences in home-visiting dentistry
3. Oral function and general health, oral health care, and welfare for stroke and dementia patients
4. Dysphagia rehabilitation for older people and disabled people, exercise, nursing-care, and welfare
5. Preoperative oral health and oral hypo-function in Frailty care, Palliative care, Nutrition support care

(3) Education

Gerodontology
Welfare for older people
Nursing-care for older people
Prosthodontics
Home visiting dentistry
Community dental care
Social work
etc

(4) Publications**[Original Articles]**

1. keiko Endo. Elderly dietary education 2017.01;

[Conference Activities & Talks]

1. Koichiro Matsuo, Hiroshige Taniguchi, Kazuharu Nakagawa, Junichi Furuya, Manabu Kanazawa, Shunsuke Minakuchi . The changes in tongue pressure, grip strength and nutritional status during perioperative period in cancer patients. . The 25th annual meeting of Dysphagia Research Society 2017.03.03
2. Onodera S, Furuya S, Yamamoto H, Hara A, Aki S, Tamada Y, Matsuki K, Itsukaichi A, Kondo H. . Impacts of complete dentures on oropharyngeal movements during bolus processing.. 95th general session of international association of dental research 2017.03.25 San Francisco
3. Masayo Sunaga, Hiromi Otsuka, Junichi Furuya, Yumi Hoshino, Atsuhiro Kinoshita. Development and evaluation of computer-assisted learning material regarding oral health care methods for elderly persons requiring long-term care as inter-professional education material for dental hygiene students. . 39th Asia Pacific Dental Congress 2017.03.25 Macau, China
4. Junichi Furuya. Dentures and Swallowing. The IFED 2017 World Congress in Toyama 2017.09.14
5. N Kitoh, K Matsuo, H Taniguchi1, K Nakagawa, M Kanazawa, J Furuya, K Tsuga, K Ikebe, T Ueda, F Tamura, H Nagao, K Yamamoto, K Sakurai, S Minakuchi.. Relationships between oral hypofunction and malnutrition in hospitalized cancer patients in an acute hospital.. 7th European Society for Swallowing Disorders Congress 2017.09.20 Barcelona, Spain
6. Michiyo Obana, Chiaki Matsubara, Keiko Endo, Junji Tokunaga, Junichi Furuya, Tomohisa Ohno, Yasunori Sumi. Oral moisturizing method and oral hygiene care; a simulation study . The 82nd Annual meeting of the Stomatological society 2017.11.19 Tokyo, Japan

Oral Health Care Education

Professor Naomi Yoshida
Junior Associate Professor Yuki Ohara

(1) Research

- 1) Research on oral health behavior
- 2) Research on oral health management
- 3) Research on frailty and oral frailty
- 4) Research and development of education methods in dental hygienists education

(2) Education

Oral health care education is special field of study which deals with establishment of theoretic and skill for health promotion to contribute to the development of the health. Educational objects of Oral health care education in the graduate course is to foster human resources who will be able to implement health promotion program in collaboration with other career or residents in many fields.

(3) Clinical Services & Other Works

In oral health care clinic, dental hygienists support patients' oral health care, and prevent dental caries and periodontal diseases for the patients to maintain the their oral and general health in the entire lifetime.

(4) Publications

[Original Articles]

1. Yutaka Watanabe, Hirohiko Hirano, Hidenori Arai, Shiho Morishita, Yuki Ohara, Ayako Eda, Masaharu Murakami, Hiroyuki Shimada, Takeshi Kikutani, Takao Suzuki. Relationship Between Frailty and Oral Function in Community-Dwelling Elderly Adults. *J Am Geriatr Soc.* 2017.01; 65(1); 66-76
2. Naomi Yoshida, Kumiko Sugimoto, Satoe Suzuki, Hideki Kudo. Change in oral health status associated with menopause in Japanese dental hygienists. *International Journal of Dental Hygiene.* 2017.05;
3. Daisuke Takagi, Yutaka Watanabe, Ayako Eda, Yuki Ohara, Masaharu Murakami, Kohji Murakami, Shouji Hironaka, Yu Taniguchi, Akihiko Kitamura, Shoji Shinkai, Hirohiko Hirano. Factors affecting masticatory function of community-dwelling older people: Investigation of the differences in the relevant factors for subjective and objective assessment. *Gerodontology.* 2017.05; 34(3); 357-364
4. Yuki Ohara, Naomi Yoshida, Hisashi Kawai, Shuichi Obuchi, Hideyo Yoshida, Shiro Mataka, Hirohiko Hirano, Yutaka Watanabe. Development of an oral health-related self-efficacy scale for use with older adults. *Geriatr Gerontol Int.* 2017.10; 17(10); 1406-1411
5. Tomoki Tanaka, Kyo Takahashi, Hirohiko Hirano, Takeshi Kikutani, Yutaka Watanabe, Yuki Ohara, Hiroyasu Furuya, Tetsuo Tsuji, Masahiro Akishita, Katsuya Iijima. Oral frailty as a risk factor for physical frailty and mortality in community-dwelling elderly The *Journals of Gerontology: Series A.* 2017.11;

[Conference Activities & Talks]

1. Ayako Edahiro, Hirohiko Hirano, Yutaka Watanabe, Yuki Ohara, Keiko Motokawa, Maki Shirobe, Jun Yasuda, Shuichi Awata. Eating Dysfunction Accompanying Deterioration of AD on the Basis of Functional Assessment Staging. The 21st IAGG World Congress of Gerontology & Geriatrics 2017.07.23 San Francisco
2. Yutaka Watanabe, Hidenori Arai, Hirohiko Hirano, Yuki Ohara, Ayako Edahiro, Hiroyuki Shimada, Takeshi Kikutani, Takao Suzuki. Identifying Oral Function as an Indexing Parameter for Detection of Mild Cognitive Impairment. The 21st IAGG World Congress of Gerontology & Geriatrics 2017.07.24 San Francisco
3. Maki Shirobe, Rena Nakayama, Yuki Ohara, Keiko Endo, Yutaka Watanabe, Hirohiko Hirano, Chiyoko Hakuta. Effect of Oral Health Care on Hypersensitivity Syndrome Among the Elderly in Long-Term Care. The 21st IAGG World Congress of Gerontology & Geriatrics 2017.07.24 San Francisco
4. Naomi Yoshida, Kumiko Sugimoto, Sato Yamanaka, Hiroyuki Sakamaki, Yoko Yamazaki, Yasunari Miyazaki, Yoshimi Sakurai, Kaori Okayasu. Effectiveness of Oral Health Education Program for Women around Menopause. . CED-IADR/NOF 2017.09.21 Vienna/Austria

[Awards & Honors]

1. Advanced Education System Development(Kanako Noritake), Japanese Dental Education Association, 2017.07

Basic Sciences of Oral Health Care

Junior Associate Professor Yujiro Sakamoto

(1) Outline

Graduate School of Medical and Dental Sciences has been reorganized in April 2012, and the section of Basic Sciences of Oral Health Care was established in Medical and Dental Science and Technology master's program course.

(2) Research

- 1) Basic medical and dental studies for oral health care
- 2) Basic study on clinical application of oral health care
- 3) Gross anatomical study of head and neck region

(3) Education

Purpose of Education

Basic sciences of oral health care is a branch of morphological sciences, developmental biology, pathology and the neurosciences to understand the structure and function of human body and its pathological conditions. Students are taught in more detail about the normal tooth anatomy and occlusal function as well as the anatomy of the head and neck with specific attention to the skull, muscles, nerves, and arteries associated with the mouth and teeth. In addition, students are also taught the oral pathology and dental pharmacology and pharmaceuticals.

Subjects and contents.

- Structure and function of human body I and II: anatomy, histology, physiology, embryology, oral anatomy, oral histology, oral physiology.
- Mechanism of disease and promotion of recovery process: pathology, oral pathology, microbiology, immunology, pharmacology.
- Dental Pharmacology and Pharmaceuticals.
- Graduation thesis:

(4) Publications

[Original Articles]

1. Sakamoto Y. Configuration of the extrinsic muscles of the tongue and their spatial interrelationships. *Surgical and Radiologic Anatomy*. 2017; 39(5); 497-506
2. Sakamoto Y. Morphological features of the branching pattern of the hypoglossal nerve. *Anatomical Record*. 2017; In press;
3. Paglio AE, Bradley AP, Tubbs RS, Loukas M, Kozlowski PB, Dilandro AC, Sakamoto Y, Iwanaga J, Schmidt C, D'Antoni AV. Morphometric analysis of temporomandibular joint elements. *Journal of Cranio-MaxilloFacial Surgery*. 2017.07; In press;

[Conference Activities & Talks]

1. Sakamoto Y. Gross anatomical feature of the lingual branches of the hypoglossal nerve. Joint Summer Meeting of the British & European Associations of Clinical Anatomists 2017.07.04 Coventry, UK
2. Sakamoto Y. Gross anatomical observation of the spatial relations between the branches of the hypoglossal nerve. The 34th annual meeting American Association of Clinical Anatomists 2017.07.20 Minneapolis, USA.

Basic Oral Health Engineering

Professor Kazuhiro Aoki
Associate Professor Meiko Oki
Assistant Professor Shingo Kamijo

(1) Outline

Basic Oral Health Engineering is a department assigned to basic science field of oral health in three master course departments which were reorganized from the departments of Oral Health Engineering Course in 2015. The department is originated in Basic Oral Health Sciences.

The department of Basic Oral Health Engineering aims to create a scientific foundation for the clinical applications based on interdisciplinary research between engineering and biology and/or interface studies between basic and clinical sciences. We believe that these research activities, which are focused on the region of the oral cavity, can contribute to attaining healthy and happy living conditions. We have the responsibility to train our students to be medical personnel who are eager to contribute to people's happiness through a broad range of educational courses from basic level courses to professional level courses, which integrate areas of study such as the structure and function of the human body, stomatognathic region, pharmacology and the research process.

(2) Research

Research Subjects

- 1) The development of surface coating materials for the prevention of plaque growth
- 2) Research related to the connection between oral bacteria and systemic health
- 3) The development of non-invasive methods of bone mass augmentation
- 4) The fabrication of facial prostheses using a three-dimensional rapid manufacturing method
- 5) Clinical studies of treatments for patients with maxillofacial defects
- 6) The development of materials for facial prostheses
- 7) The relationship between "medical care to support life" and the dental technician
- 8) The education of dental technicians using computer simulation training

(3) Lectures & Courses

Basic Oral Health Engineering is a department of oral health engineering which deals with the basic oral health sciences to perform evidence-based oral health care and prosthetic treatments to support people to promote oral health and improve quality of life. Main objective of Basic Oral Health Engineering in the undergraduate course is to provide students opportunity to study the structure and function of the human body, pharmacology, fabrication of dental and maxillofacial prostheses, dental CAD/CAM technology and research process.

(4) Clinical Performances

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects
- Making dental and maxillofacial prostheses

(5) Publications**[Original Articles]**

1. Sasipin Lauvahutanon, Maho Shiozawa, Hidekazu Takahashi, Naohiko Iwasaki, Meiko Oki, Werner J. Finger, Mansuang Arksornnukit. Discoloration of various CAD/CAM blocks after immersion in coffee Restorative Dentistry and Endodontics. 2017.01; 42(1); 9-18
2. Naohiko Iwasaki, Chisato Yamaki, Hidekazu Takahashi, Meiko Oki, Tetsuya Suzuki. Effect of long-time immersion of soft denture liners in water on viscoelastic properties. Dent Mater J. 2017.04;
3. Md Zahirul Haque Bhuyan, Yukihiro Tamura, Eri Sone, Yuki Yoshinari, Chizuko Maeda, Mariko Takahashi, Yasuhiko Tabata, Ramachandran Murali, Yoshihiro Waki, Kazuhiro Aoki. The intra-articular injection of RANKL-binding peptides inhibits cartilage degeneration in a murine model of osteoarthritis. J. Pharmacol. Sci.. 2017.06; 134(2); 124-130
4. Ayako Kubota, Meiko Oki, Yasuko Kawakami, Kiyoko Kanamori, Hiroji Shimomura, Shiro Mataka, Kumiko Sugimoto. Effectiveness of Individual Oral Health Education for Japanese University Students International Journal of Dentistry and Oral Health. 2017.10; 3(5);
5. Boosana KABOOSAYA, Lia Kartika WULANSARI, Trang Nguyen V.N., Kazuhiro AOKI, Shohei KASUGAI. Ligation Period Required to Induce Periodontitis in Mice: Analysis with Micro-computed Tomography Journal of Oral Tissue Engineering. 2017.10; 15(1); 25-34
6. Lin DING, Peng ZHANG, Xin WANG, Jia HAO, Kazuhiro AOKI, Shinji KURODA, Shohei KASUGAI. Effect of doxycycline-treated hydroxyapatite surface on bone apposition: A histomorphometric study in murine maxillae Dental Materials Journal. 2017.11;
7. Mikami R, Mizutani K, Aoki A, Tamura Y, Aoki K, Izumi Y. Low-level ultrahigh-frequency and ultrashort-pulse blue laser irradiation enhances osteoblast extracellular calcification by upregulating proliferation and differentiation via transient receptor potential vanilloid 1. Lasers Surg Med. 2017.12; epub;
8. Toru Takemoto, Yuji Kabasawa, Yusuke Higuchi, Yasuhiko Tabata, Kazuhiro Aoki, Yukihiro Tamura, Hiroyuki Harada. Combination of the RANKL-binding peptide W9 and bFGF induces bone regeneration in the rat calvarial defect model. Dent Oral Craniofac Res. 2017.12; 4(3); 1-7
9. Aierken MULATI, Songtao WU, Kazuhiro AOKI, Shohei KASUGAI. Effects of Osteotomy with Drilling on Osteocytes Journal of Oral Tissue Engineering. 2017.12; 15(2); 95-101

[Conference Activities & Talks]

1. Shingo Kamijo, Kumiko Sugimoto, Meiko Oki, Tetsuya Suzuki . Investigation of the needs for prostheses and dental technicians in home-visit dental care in Japan. 6th International Congress of Dental Technology 2017.05.27 New Taipei City, Taiwan
2. Kazuhiro AOKI. Roland gave me a seed of my research. The 59th Annual Meeting of Japanese Association for Oral Biology 2017.09.16 Matsumoto Dental University

[Others]

1. The Wnt agonist R-spondin 3: an unexpected negative regulator of bone formation, 2017.11
Special lecture for PhD course student
Dr. Kenichi Nagano Department of Oral Medicine, Infection and Innunity, Harvard School of Dental Medicine

Oral Biomaterials Development Engineering

Professor
Junior Associate Professor
Assistant Professor

Hidekazu TAKAHASHI
Tohru YASUE
Naohiko IWASAKI

Graduate student (Master course)
Graduate student (Master course)
Graduate student (Doctor course)

Yuko NAKAJIMA (until March)
Yusuke YAMAMOTO (from April)
Patcharanun CHAIAMORNSUP (Advanced Biomaterials)

(1) Outline

Basic knowledge of dental materials and devices for oral health engineering are provided for student. Basic exercise for dental materials and prosthetic training are also provided. Development and evaluation of new dental materials are performed.

(2) Research

1. Evaluation of various factors on mechanical properties of teeth substance.
2. Evaluation of fatigue properties of dentin and dental materials using miniature testing pieces
3. Measurement of characteristics of dental ceramic materials and establishment of new testing methods for dental ceramics
4. Measurement of precise deformation using non-contact methods
5. Development of new composite resin with similar machinability of dentin
6. Study on dental root fracture mechanism
7. Application of various types of fiberglass for dentistry
8. Evaluation of composite resin mechanical properties and improvement their bonding efficiency to various materials.
9. Evaluation of impact force absorption of mouthguard and face protect materials

(3) Education

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices. The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible.

(4) Lectures & Courses

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices

used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices.

The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible. Presentation not only domestic but also international meeting is strongly encouraged.

(5) Clinical Services & Other Works

Participation in various congresses are strongly recommended. Assistance for standard publication is also cooperated. Especially, Prof. Takahashi, head of Oral Biomaterials Engineering acts as the chairperson of ISO TC106 Dentistry/SC9 Dental CAD/CAM systems for publishing ISO standards.

(6) Publications

[Original Articles]

1. Sasipin Lauvahutanon, Maho Shiozawa, Hidekazu Takahashi, Naohiko Iwasaki, Meiko Oki, Werner J. Finger, Mansuang Arksornnukit. Discoloration of various CAD/CAM blocks after immersion in coffee Restorative Dentistry and Endodontics. 2017.01; 42(1); 9-18
2. Ishihata H, Kanehira M, Finger WJ, Takahashi H, Tomita M, Sasaki K. Effect of two desensitizing agents on dentin permeability in vitro. J Appl Oral Sci. 2017.01; 25(1); 34-41
3. Krid Kamonkhantikul, Mansuang Arksornnukit, Hidekazu Takahashi. Antifungal, optical, and mechanical properties of polymethylmethacrylate material incorporated with silanized zinc oxide nanoparticles. Int J Nanomedicine. 2017.03; 12; 2353-2360
4. Naohiko Iwasaki, Chisato Yamaki, Hidekazu Takahashi, Meiko Oki, Tetsuya Suzuki. Effect of long-time immersion of soft denture liners in water on viscoelastic properties. Dent Mater J. 2017.04;
5. Takahiro Shirako, Hiroshi Churei, Naohiko Iwasaki, Hidekazu Takahashi, Toshiaki Ueno. Evaluation of the flexural properties of a new temporary splint material for use in dental trauma splints Journal of Dental Sciences. 2017.09; 12(3); 308-310
6. Kazuyuki Handa, Natsuko Murakami, Toshiki Yamazaki, Hidekazu Takahashi, Noriyuki Wakabayashi. The ball-on-disk cyclic wear of CAD/CAM machinable dental composite and ceramic materials Journal of Oral Science. 2017.12; 59(4); 589-596

[Books etc]

1. The newest series of textbook for dental hygienist- Dental materials. 2017.03 (ISBN : 978-4-263-42851-1)

[Conference Activities & Talks]

1. Kajima Y, Takaichi A, Takahashi H, Wakabayashi N. Effects of support structure on the fatigue strength of additive fabrication. The 126th annual meeting of the Japan Prosthodontic society 2017.07.02 Yokohama
2. Wada Takahiro, Churei Hiroshi, Yokose Mako, Takayanagi Haruka, Iwasaki Naohiko, Ueno Toshiaki, Takahashi Hidekazu, Uo Motohiro. Evaluation of the Mechanical Properties of a Faceguard Made of Fiber-Reinforced Thermoplastics. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya, Japan
3. Naohiko Iwasaki, Maho Shiozawa, Yusuke Yamamoto, Tetsuya Suzuki and Hidekazu Takahashi. Relationship among Marginal Reproducibility, Machinability and Mechanical Property of Zirconia Blank for CAD/CAM System. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya University, Nagoya
4. Tanabe G, Hata T, Tun PS, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards.. The 2017 ADM Annual Meeting 2017.10.07 Nuremberg

5. Takaichi A, Kajima Y, Nakamoto T, Tsutsumi Y, Nomura N, Takahashi H, Hanawa T, Wakabayashi N. Effect of adding support structures for overhanging part on fatigue strength in selective laser melting. . The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata
6. Kajima Y, Takaichi A, Nakamoto T, Nuttaphon K, Nomura N, Takahashi H, Wakabayashi N, Kawasaki A. Study on the effective condition of heat treatment on the anisotropy control of selective laser melted Co-Cr alloy.. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata
7. Mechanical properties of recent composite resin blocks for CAD/CAM. 2017.10.14
8. Hidekazu TAKAHASHI, Naohiko IWASAKI, Tetsuya SUZUKI. FLEXURAL PROPERTIES OF RECENT COMPOSITE RESIN BLOCKS FOR CAD/CAM. 3rd ANNUAL MEETING of the IADDM 2017.12.09 Berlin, Germany

Oral Prosthetic Engineering

Professor Tetsuya SUZUKI
 Junior Associate Professor Masaomi IKEDA
 Research Associate Maho SHIOZAWA

(1) Outline

Oral Health Information Technology educates deepen understanding of the production of the dental prosthesis using the latest computer science and cultivate basics power to new technology development. This course cultivates the ability to offer high quality medical technology taking advantage of expertise or knowledge. And the purpose of this section is to educate professional dental technologists who has ability to apply newly developed materials and technologies and who is able to contribute in not only clinical situation but also research institution or educational organization at international levels. Presently, the latest technologies such as dental implant and dental CAD/CAM etc became popular by the development of materials and the progress in technologies among dental treatment. Therefore, it is necessary to understand and lean knowledge about newly developed materials and technologies for properly control the dental laboratory works. Furthermore, It is necessary that the communication skill for report information about the materials and technologies to dentists and dental hygienists. Based on these evidences, it is an education in which specialists are raised to not be bound by classification as technologist and have ambition.

(2) Research

- 1) The advanced technology which utilized a CAD/CAM system.
- 2) The education of dental technician which utilized computer simulation training.
- 3) Relation of "medical care to support life" and the dental technician.
- 4) Evaluation of newly developed materials.

(3) Education

Introduction of Oral Health Engineering, Introduction of Clinical Dental Technology, Formative Arts Practice, Basic Technology of Manufacturing, Teeth Morphological Curving, Advanced Teeth Morphological Curving, Conservative Dentistry, Science of Occlusion, Clinical Science of Occlusion, Communication Theory, Dental Technologist and law, Health Promotion, Basic Fixed Prosthodontics, Advanced Fixed Prosthodontics, Complete Denture Prosthodontics, Removable Partial Prosthodontics, Oral Rehabilitation Engineering, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Advanced Technology for Oral Health, Digital Image Processing Practice, Oral Appliances, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research, Graduation Product

(4) Publications

[Original Articles]

1. Sato K, Hosaka K, Takahashi M, Ikeda M, Tian F, Komada W, Nakajima M, Foxton R, Nishitani Y, Pashley DH, Tagami J.. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. *J Adhes Dent.* 2017; 19(1); 31-37

2. Sasipin Lauvahutanon, Maho Shiozawa, Hidekazu Takahashi, Naohiko Iwasaki, Meiko Oki, Werner J. Finger, Mansuang Arksornnukit. Discoloration of various CAD/CAM blocks after immersion in coffee Restorative Dentistry and Endodontics. 2017.01; 42(1); 9-18
3. Kento Sato, Keiichi Hosaka, Masahiro Takahashi, Masaomi Ikeda, Fucong Tian, Wataru Komada, Masatoshi Nakajima, Richard Foxton, Yoshihiro Nishitani, David H Pashley, Junji Tagami. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. J Adhes Dent. 2017.02; 19(1); 31-37
4. Naohiko Iwasaki, Chisato Yamaki, Hidekazu Takahashi, Meiko Oki, Tetsuya Suzuki. Effect of long-time immersion of soft denture liners in water on viscoelastic properties. Dent Mater J. 2017.04;
5. Yukari Noda, Masatoshi Nakajima, Masahiro Takahashi, Teerapong Mamane, Keiichi Hosaka, Tomohiro Takagaki, Masaomi Ikeda, Richard M Foxton, Junji Tagami. The effect of five kinds of surface treatment agents on the bond strength to various ceramics with thermocycle aging. Dent Mater J. 2017.07;
6. Saad A, Inoue G, Nikaido T, Ikeda M, MF Burrow, Tagami J. Microtensile Bond Strength of Resin-Modified Glass Ionomer Cement to Sound and Artificial Caries-Affected Root Dentin With Different Conditioning Operative Dentistry. 2017.11; 42(6); 626-635

[Conference Activities & Talks]

1. Ogata Y, Katsuyama K, Tanaka S, Nagano M, Yumoto Y, Ikeda M.. Characteristics of the Nursing practice environment related to creating healthy work environments for nurses. Creating Healthy Work Environments 2017 2017.03.17
2. Maiko Iwaki, Manabu Kanazawa, Toshio Arakida, Tetzuya Suzuki, Shunsuke Minakuchi. Digital impression and jaw relation record for the fabrication of complete dentures. 2017.04.22
3. Shingo Kamijo, Kumiko Sugimoto, Meiko Oki, Tetsuya Suzuki . Investigation of the needs for prostheses and dental technicians in home-visit dental care in Japan. 6th International Congress of Dental Technology 2017.05.27 New Taipei City, Taiwan
4. Tetsuya Suzuki. Efficient and prospective teeth arrangement for complete dentures . The 6th International Congress of Dental Technology 2017.05.27 Taiwan (New Taipei City)
5. Takahashi H, Sumida K, Iwasaki N, Suzuki T. Effects of porcelain thickness and type of alloys on color appearance of porcelain-fused-to-metal restoration. The 6th International Congress of Dental Technology 2017.05.27 Taiwan (New Taipei City)
6. Dhaifallah Alqarni, Keiichi Hosaka, Teerapong Mamane, Masatoshi Nakajima, Masaomi Ikeda, Junji Tagami. Effect of different surface treatments on repair uTBS of composite bonded to resin matrix after water exposure. The 10th World Congress of International Federation of Esthetic Dentistry 2017.09.14 Toyama
7. Naohiko Iwasaki, Maho Shiozawa, Yusuke Yamamoto, Tetsuya Suzuki and Hidekazu Takahashi. Relationship among Marginal Reproducibility, Machinability and Mechanical Property of Zirconia Blank for CAD/CAM System. International Conference on Materials and Systems for Sustainability 2017 (IC-MaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya University, Nagoya
8. G. Tanabe, T. Hada, PS. Tun, H. Churei, T. Wada, M. Uo, H. Takahashi, T. Ueno. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards. The 2017 Academy of Dental Materials Annual Meeting 2017.10.07 Nuremberg
9. Yusuke Yamamoto, Naohiko Iwasaki, Patcharanun Chaiamornsop, Tetsuya Suzuki. Effects of load on machinability of composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Toki Messe, Niigata city
10. Naohiko Iwasaki, Toru Yasue, Maho Shiozawa, Yusuke Yamamoto, Shinji Tanaka, Tetsuya Suzuki, Hidekazu Takahashi.. Mechanical properties of recent composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices, 2017.10.14 Toki Messe, Niigata city

11. Hidekazu TAKAHASHI, Naohiko IWASAKI, Tetsuya SUZUKI. FLEXURAL PROPERTIES OF RECENT COMPOSITE RESIN BLOCKS FOR CAD/CAM. 3rd ANNUAL MEETING of the IADDM 2017.12.09 Berlin, Germany

- Research for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells
- Analyses of molecular mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and clinical factors for therapeutic resistance against antiviral agents.

(3) Education

Primary goal for education in our section is to train highly educated and experienced clinician-researchers in the field of hepatology. Our goal for education of graduate students is to produce clinical researchers thinking from a wide perspective and to bring up leaders of the next generation in hepatology.

(4) Lectures & Courses

Our lectures and courses are collaboration with the Department of Gastroenterology and Hepatology in School of Medicine, TMDU. We also educate clinical residents in Medical Hospital of TMDU and graduate students of the Department of Gastroenterology and Hepatology, in TMDU in collaboration with such department.

(5) Clinical Services & Other Works

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of diseases of liver, biliary duct, and pancreas. We also operate a lot of multicenter study collaborating with the Department of Gastroenterology and Hepatology in TMDU. We participate in four research projects for treatment and eradication of hepatitis virus funded by Japan Agency for Medical Research and Development (AMED). We published a lot of studies in peer-reviewed international journals and presented the recent works in a lot of international and domestic conferences as described below.

(6) Clinical Performances

For the treatment of patients with diseases of liver, biliary duct, and pancreas in Medical Hospital of TMDU, we collaborate with the Department of Gastroenterology and Hepatology in TMDU. We have recently established the outpatient department specialized for chronic hepatitis, cirrhosis, and HCC. We have operated a lot of multicenter study about efficacy of treatment against viral hepatitis, named as “Ochyanomizu Liver Conference”. More than 2000 patients with viral hepatitis were enrolled in such studies. We have clarified the clinical factors predicting accurately the therapeutic prognosis and risk for development of HCC. We are developing the screening programs for the early detection of HCC in patients with chronic hepatitis after eradication of viruses utilizing non-invasive elastography, novel serum markers, and dynamic contrast-enhanced ultrasonography. For the treatment of HCC, three-dimensional location and structure of tumors and vessels are evaluated by multilateral approaches using dynamic contrast-enhanced ultrasonography, Gd-EOB-DTPA enhanced MRI, and real-time virtual ultrasonography (RVS). We have reported the utility and safety of such therapeutic approaches. We are providing patients the appropriate therapeutic option based on collective multimodal therapeutic strategy in collaboration with departments of surgery and radiology.

(7) Publications

[Original Articles]

1. Yoshimoto Nomura, Taro Yamashita, Naoki Oishi, Kouki Nio, Takehiro Hayashi, Mariko Yoshida, Tomoyuki Hayashi, Tomomi Hashiba, Yasuhiro Asahina, Hikari Okada, Hajime Sunagozaka, Hajime Takatori, Masao Honda, Shuichi Kaneko. De Novo Emergence of Mesenchymal Stem-Like CD105(+) Cancer Cells by Cytotoxic Agents in Human Hepatocellular Carcinoma. *Transl Oncol.* 2017.04; 10(2); 184-189
2. Kentaro Matsuura, Hiromi Sawai, Kazuho Ikeo, Shintaro Ogawa, Etsuko Iio, Masanori Isogawa, Noritomo Shimada, Atsumasa Komori, Hidenori Toyoda, Takashi Kumada, Tadashi Namisaki, Hitoshi Yoshiji,

Naoya Sakamoto, Mina Nakagawa, Yasuhiro Asahina, Masayuki Kurosaki, Namiki Izumi, Nobuyuki Enomoto, Atsunori Kusakabe, Eiji Kajiwara, Yoshito Itoh, Tatsuya Ide, Akihiro Tamori, Misako Matsubara, Norifumi Kawada, Ken Shirabe, Eiichi Tomita, Masao Honda, Shuichi Kaneko, Sohji Nishina, Atsushi Suetsugu, Yoichi Hiasa, Hisayoshi Watanabe, Takuya Genda, Isao Sakaida, Shuhei Nishiguchi, Koichi Takaguchi, Eiji Tanaka, Junichi Sugihara, Mitsuo Shimada, Yasuteru Kondo, Yosuke Kawai, Kaname Kojima, Masao Nagasaki, Katsushi Tokunaga, Yasuhito Tanaka, . Genome-Wide Association Study Identifies TLL1 Variant Associated With Development of Hepatocellular Carcinoma After Eradication of Hepatitis C Virus Infection. *Gastroenterology*. 2017.05; 152(6); 1383-1394

3. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. *J. Med. Virol.* 2017.07; 89(7); 1241-1247
4. Miyako Murakawa, Yasuhiro Asahina, Hiroko Nagata, Mina Nakagawa, Sei Kakinuma, Sayuri Nitta, Fukiko Kawai-Kitahata, Satoshi Otani, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Ayako Sato, Yasuhiro Itsui, Seishin Azuma, Toshihiko Nouchi, Yohei Furumoto, Tooru Asano, Yoshimichi Chuganji, Shuji Tohda, Mamoru Watanabe. ITPA gene variation and ribavirin-induced anemia in patients with genotype 2 chronic hepatitis C treated with sofosbuvir plus ribavirin. *Hepatology*. 2017.07; 29(5); 584-593
5. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatology*. 2017.08; 47(9); 941-952
6. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina, Ayako Sato, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Toshihiko Nouchi, Hideki Sakai, Makoto Tomita, Mamoru Watanabe. Effect of interferon-based and -free therapy on early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C. *J. Hepatology*. 2017.11; 67(5); 933-939

[Conference Activities & Talks]

1. Kawai-Kitahata F, Asahina Y, Kakinuma S, Murakawa M, Niita S, Nagata H, Kaneko S, Otani S, Miyoshi M, Tsunoda T, Sato A, Nakagawa M, Itsui Y, Azuma S, Tanaka S, Tanabe M, Maekawa S, Enomoto N, Watanabe M. Genetic differences in hepatocellular carcinoma among chronic persistent hepatitis B virus infection with or without viral suppression and prior hepatitis B virus infection. *EASL The International Liver Congress 2017* 2017.04.20 Amsterdam (Netherlands)
2. Azuma S, Asahina Y, Kakinuma S, Azuma K, Watanabe M. Diabetic retinopathy as a risk factor associated with development of hepatocellular carcinoma in non-alcoholic fatty liver disease. *APDW2017* 2017.09.25 (Hong Kong)
3. Murakawa M, Asahina Y, Nakagawa M, Nitta S, Kawai-Kitahata F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Sato A, Itsui Y, Kakinuma S, Azuma S, Watanabe M. On-treatment higher levels of alpha-fetoprotein and M2BPGi are associated with development of hepatocellular carcinoma during nucleos(t)ide analog therapy in patients with HBV chronic infection. *AASLD, The Liver Meeting 2017* 2017.10.21 Washington DC (USA)
4. Nitta S, Murakawa M, Kato T, Sato A, Tsunoda T, Miyoshi M, Asano Y, Kaneko S, Nagata H, Kawai-Kitahata F, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The analysis of NS5A Resistance-Associated Substitutions (RAS): In vitro study of NS5A recombinant hepatitis C in infectious cell culture system for various RAS detected after treatment failure in chronic hepatitis C patients. *AASLD The Liver Meeting 2017* 2017.10.21 Washington D.C (USA)
5. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Nitta S, Sato A, Asano Y, Nagata H, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A novel culture model for coinfection of hepatitis B and hepatitis C viruses using human induced pluripotent

stem cell-derived hepatic cells for analyses of changes in host-innate immune responses . AASLD The Liver Meeting 2017 2017.10.22 Washington D.C (USA)

6. Nakagawa M, Asahina Y, Nagata H, Kaneko S, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tanaka Y, Watanabe M. Evaluation of an early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C patients treated with All-Oral DAAs - propensity score-matched analysis of a prospective database -. AASLD, The Liver Meeting 2017 2017.10.22 Washington D.C (USA)

Department of Advanced Therapeutics for GI Diseases

Professor	Tetsuya NAKAMURA
Associate Professor	Katsuyoshi MATSUOKA
Associate Professor	Takashi NAGAISHI
Assistant Professor	Michio ONIZAWA
Graduate Student	
	Yuka MATSUMOTO (-03/2017), Shintaro AKIYAMA (-03/2017)

(1) Outline

The goal of our department is to develop novel therapeutic strategies for inflammatory bowel diseases (IBD) in humans. With multiple layers of support of corporations who wish to contribute to our mission, we have been focusing on IBD research from the clinical and basic science perspectives, providing an exceptional education program for graduate students at TMDU.

(2) Research

Our research activities focus on the key areas listed below. We have a particular emphasis on translational (bench to clinic) research on IBD.

- Research on the intestinal epithelium to develop regenerative medicine approaches for IBD
- The study of mucosal immunology to develop novel approaches for the diagnosis and treatment of IBD

(3) Education

We share our expertise and teaching program in graduate course education with the Department of Gastroenterology and Hepatology at TMDU. We are also involved in many programs designed for undergraduates.

(4) Lectures & Courses

Our goal is to create future leaders who are able to reach the highest level of quality in IBD research through the training of fellows and graduate/undergraduate students.

(5) Clinical Services & Other Works

We focus on developing highly advanced technologies, including novel procedures, for diagnosis and treatment of IBD in collaboration with the Department of Gastroenterology and Hepatology at TMDU. In addition, we have been playing a major role in nation-wide survey and multi-center studies on IBD, which is funded by the Japanese Ministry of Health, Labor and Welfare.

(6) Clinical Performances

- Development of new treatment protocol for IBD patients with stem cell therapy or immunomodulators.
- Development of minimally-invasive diagnostic modalities for inflammatory bowel diseases (i.e. MRE).
- Diagnosis and treatment of small intestinal lesions of inflammatory bowel diseases by double-balloon enteroscopy.

(7) Publications**[Original Articles]**

1. Makoto Naganuma, Shigeo Okuda, Tadakazu Hisamatsu, Katsuyoshi Matsuoka, Kiyoto Mori, Naoki Hosoe, Yoshihiro Nakazato, Haruhiko Ogata, Takanori Kanai. Findings of ulceration and severe stricture on MRE can predict prognosis of Crohn's disease in patients treated with anti-TNF treatment. *Abdom Radiol (NY)*. 2017.01; 42(1); 141-151
2. Shinta Mizuno, Kosaku Nanki, Katsuyoshi Matsuoka, Keiichiro Saigusa, Keiko Ono, Mari Arai, Shinya Sugimoto, Hiroki Kiyohara, Moeko Nakashima, Kozue Takeshita, Makoto Naganuma, Wataru Suda, Masahira Hattori, Takanori Kanai. Single fecal microbiota transplantation failed to change intestinal microbiota and had limited effectiveness against ulcerative colitis in Japanese patients. *Intest Res*. 2017.01; 15(1); 68-74
3. Shinichiro Shinzaki, Katsuyoshi Matsuoka, Hideki Iijima, Shinta Mizuno, Satoshi Serada, Minoru Fujimoto, Norimitsu Arai, Noriyuki Koyama, Eiichi Morii, Mamoru Watanabe, Toshifumi Hibi, Takanori Kanai, Tetsuo Takehara, Tetsuji Naka. Leucine-rich Alpha-2 Glycoprotein is a Serum Biomarker of Mucosal Healing in Ulcerative Colitis. *J Crohns Colitis*. 2017.01; 11(1); 84-91
4. Toru Nakata, Hiromichi Shimizu, Sayaka Nagata, Go Ito, Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Reiko Kuno, Sho Anzai, Tatsuro Murano, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Mamoru Watanabe, Ryuichi Okamoto. Indispensable role of Notch ligand-dependent signaling in the proliferation and stem cell niche maintenance of APC-deficient intestinal tumors. *Biochem. Biophys. Res. Commun*. 2017.01; 482(4); 1296-1303
5. Toru Nakata, Hiromichi Shimizu, Sayaka Nagata, Go Ito, Satoru Fujii, Kohei Suzuki, Ami Kawamoto, Fumiaki Ishibashi, Reiko Kuno, Sho Anzai, Tatsuro Murano, Tomohiro Mizutani, Shigeru Oshima, Kiichiro Tsuchiya, Tetsuya Nakamura, Katsuto Hozumi, Mamoru Watanabe, Ryuichi Okamoto. Data showing proliferation and differentiation of intestinal epithelial cells under targeted depletion of Notch ligands in mouse intestine. *Data Brief*. 2017.02; 10; 551-556
6. Shinya Sugimoto, Makoto Naganuma, Yasushi Iwao, Katsuyoshi Matsuoka, Masayuki Shimoda, Shuji Mikami, Shinta Mizuno, Yoshihiro Nakazato, Kosaku Nanki, Nagamu Inoue, Haruhiko Ogata, Takanori Kanai. Endoscopic morphologic features of ulcerative colitis-associated dysplasia classified according to the SCENIC consensus statement. *Gastrointest. Endosc*. 2017.03; 85(3); 639-646.e2
7. Sayako Chiba, Tadakazu Hisamatsu, Hiroaki Suzuki, Kiyoto Mori, Mina T Kitazume, Katsuyoshi Shimamura, Shinta Mizuno, Nobuhiro Nakamoto, Katsuyoshi Matsuoka, Makoto Naganuma, Takanori Kanai. Glycolysis regulates LPS-induced cytokine production in M2 polarized human macrophages. *Immunol. Lett*. 2017.03; 183; 17-23
8. Chiaki Maeyashiki, Shigeru Oshima, Kana Otsubo, Masanori Kobayashi, Yoichi Nibe, Yu Matsuzawa, Michio Onizawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. HADHA, the alpha subunit of the mitochondrial trifunctional protein, is involved in long-chain fatty acid-induced autophagy in intestinal epithelial cells. *Biochem. Biophys. Res. Commun*. 2017.03; 484(3); 636-641
9. Jorg Mahlich, Katsuyoshi Matsuoka, Rosarin Sruamsiri. Shared Decision Making and Treatment Satisfaction in Japanese Patients with Inflammatory Bowel Disease. *Dig Dis*. 2017.04; 35(5); 454-462
10. Shuji Hibiya, Kiichiro Tsuchiya, Ryohei Hayashi, Keita Fukushima, Nobukatsu Horita, Sho Watanabe, Tomoaki Shirasaki, Ryu Nishimura, Natsuko Kimura, Tatsunori Nishimura, Noriko Gotoh, Shigeru Oshima, Ryuichi Okamoto, Tetsuya Nakamura, Mamoru Watanabe. Long-term Inflammation Transforms Intestinal Epithelial Cells of Colonic Organoids. *J Crohns Colitis*. 2017.05; 11(5); 621-630

11. J Mahlich, K Matsuoka, Y Nakamura, R Sruamsiri. The relationship between socio-demographic factors, health status, treatment type, and employment outcome in patients with inflammatory bowel disease in Japan. *BMC Public Health*. 2017.07; 17(1); 623
12. Kento Takenaka, Kazuo Ohtsuka, Yoshio Kitazume, Katsuyoshi Matsuoka, Toshimitsu Fujii, Masakazu Nagahori, Maiko Kimura, Tomoyuki Fujioka, Akihiro Araki, Mamoru Watanabe. Magnetic resonance evaluation for small bowel strictures in Crohn's disease: comparison with balloon enteroscopy. *J. Gastroenterol*. 2017.08; 52(8); 879-888
13. Yuka Matsumoto, Wakana Mochizuki, Shintaro Akiyama, Taichi Matsumoto, Kengo Nozaki, Mamoru Watanabe, Tetsuya Nakamura. Distinct intestinal adaptation for vitamin B12 and bile acid absorption revealed in a new mouse model of massive ileocecal resection. *Biol Open*. 2017.09; 6(9); 1364-1374
14. Nobuharu Suzuki, Kaori Sekimoto, Chikako Hayashi, Yo Mabuchi, Tetsuya Nakamura, Chihiro Akazawa. Differentiation of Oligodendrocyte Precursor Cells from Sox10-Venus Mice to Oligodendrocytes and Astrocytes. *Sci Rep*. 2017.10; 7(1); 14133
15. Jianbo An, Takashi Nagaishi, Taro Watabe, Taeko K Naruse, Mamoru Watanabe, Akinori Kimura. MKL1 expressed in macrophages contributes to the development of murine colitis. *Sci Rep*. 2017.10; 7(1); 13650
16. Yoichi Nibe, Shigeru Oshima, Masanori Kobayashi, Chiaki Maeyashiki, Yu Matsuzawa, Kana Otsubo, Hiroki Matsuda, Emi Aonuma, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Shinichiro Nakada, Mamoru Watanabe. Novel polyubiquitin imaging system, PolyUb-FC, reveals that K33-linked polyubiquitin is recruited by SQSTM1/p62. *Autophagy*. 2017.11; 1-43
17. Shintaro Akiyama, Wakana Mochizuki, Yoichi Nibe, Yuka Matsumoto, Kei Sakamoto, Shigeru Oshima, Mamoru Watanabe, Tetsuya Nakamura. CCN3 Expression Marks a Sulfomucin-nonproducing Unique Subset of Colonic Goblet Cells in Mice. *Acta Histochem Cytochem*. 2017.12; 50(6); 159-168

[Books etc]

1. Nagaishi T, Watanabe M. *Crohn's Disease and Ulcerative Colitis: from Epidemiology and Immunobiology to a Rational Diagnostic and Therapeutic Approach*. 2017.03 (ISBN : 978-3-319-33701-2)

[Misc]

1. Tetsuya Nakamura, Mamoru Watanabe. Intestinal stem cell transplantation. *J. Gastroenterol*. 2017.02; 52(2); 151-157
2. Tetsuya Nakamura, Toshiro Sato. *Advancing Intestinal Organoid Technology Toward Regenerative Medicine*. *Cell Mol Gastroenterol Hepatol*. 2017.11; 5(1); 51-60

[Conference Activities & Talks]

1. Watabe T, Nagaishi T, Hosoya A, Jose N, Tokai A, Kojima Y, Adachi T, Watanabe M. The lack of secreted IgA spontaneously induces the mucosal inflammation specifically in the ileum. *DDW 2017* 2017.05.09 Chicago (USA)
2. Nibe Y, Oshima S, Aonuma E, Matsuda H, Otsubo K, Maeyashiki C, Kobayashia M, Matsuzawa Y, Nakada S, Watanabe M. Novel polyubiquitin imaging reveals that atypical polyubiquitin contribute to autophagy. *GI research Academy 2017* 2017.06.09 Tokyo (JAPAN)
3. Nagaishi T, Watabe T, Jose N, Hosoya A, Kojima Y, Tsugawa N, Adachi T, Watanabe M. IgA Deficiency Induces Spontaneous Inflammation in the Ileum. *FOCIS 2017* 2017.06.14 Chicago (USA)
4. Takenaka K, Ohtsuka K, Kitazume Y, Matsuoka K, Fujii T, Nagahori M, Kimura M, Watanabe M. Magnetic resonance evaluation for small bowel endoscopic remission in patients with crohn's disease. *AOCC2017* 2017.06.15 Seoul (Korea)
5. Fujii T, Kitazume Y, Takenaka K, Kimura M, Matsuoka K, Nagahori M, Ohtsuka K, Watanabe M. The 5-point MR enterocolonography classification based on endoscopic findings for activity assessment of Crohn's disease. *AOCC2017* 2017.06.16 Seoul (Korea)

6. Matsuoka K, Watanabe M. Recent pivotal studies for IBD in Asians: current status and future directions. AOCC2017 2017.06.16 Seoul (Korea)
7. Kawamoto A, Ito G, Nakata T, Fujii S, Suzuki K, Ishibashi F, Shimizu H, Tsuchiya K, Nakamura T, Okamoto R, Watanabe M. Synergy of Notch signaling and pro-inflammatory cytokines leads to up-regulation of UBD in the inflamed intestinal epithelia of IBD patients. The 5th Annual Meeting of Asian Organization for Crohn's and Colitis 2017.06.16 Seoul (Korea)
8. Hosoya A, Nagaishi T, Watabe T, Tsugawa N, Jose N, Kojima Y, Adachi T, Watanabe M. Verification of immunoglobulin A protection of intestinal mucosa from microflora. AOCC2017 2017.06.16 Seoul (Korea)
9. Motobayashi M, Matsuoka K, Iwamoto F, Takenaka K, Fujii T, Nagahori M, Enomoto N, Ohtsuka K, Watanabe M. Correlation of Fecal Calprotectin Levels with Endoscopic Severity Evaluated with Balloon-assisted Endoscopy in Patients with Crohn's Disease . AOCC2017 2017.06.17 Seoul (Korea)
10. Nagaishi T, Watabe T, Jose N, Hosoya A, Kojima Y, Tsugawa N, Adachi T, Watanabe M. Deficiency of IgA Induces Microflora Alteration and Ileal Inflammation. ICMI 2017 2017.07.21 Washington DC (USA)
11. Takenaka K, Ohtsuka K, Kitazume Y, Matsuoka K, Fujii T, Nagahori M, Kimura M, Watanabe M. Magnetic resonance enterography for small bowel mucosal healing in patients with Crohn's disease. APDW2017 2017.09.23 (Hong Kong)
12. Takenaka K, Ohtsuka K, Kitazume Y, Fujii T, Matsuoka K, Kimura M, Nagahori M, Watanabe M. Utility of Magnetic Resonance Evaluation for Small Bowel Endoscopic Healing in Patients with Crohn's Disease. UEGW2017 2017.10.30 Barcelona(Spain)
13. Tsugawa N, Nagaishi T, Watabe T, Jose N, Hosoya A, Kojima Y, Adachi T, Blumberg R, Watanabe M. Verification of immunoglobulin a regulation of microflora and protection of intestinal mucosa. UEGW2017 2017.10.31 Barcelona(Spain)
14. Fujii T, Kitazume Y, Takenaka K, Kimura M, Saito E, Matsuoka K, Nagahori M, Ohtsuka K, Watanabe M. Simplified MR enterocolonography Classification Based on Endoscopic Findings for Activity Assessment of Crohn's Disease. UEGW2017 2017.11.01 Barcelona(Spain)
15. Ishibashi F, Shimizu H, Kawamoto A, Ito G, Nakata T, Fujii S, Suzuki K, Kuno R, Anzai S, Kuwabara K, Kawai M, Takahashi J, Hama M, Nagata S, Tsuchiya K, Nakamura T, Okamoto R, Watanabe M. Reprogrammed Atoh1+ intestinal epithelial cells contribute to regenerate damaged colonic mucosa in DSS-induced colitis. UEGW2017 2017.11.01 Barcelona(Spain)
16. Watanabe S, Tsuchiya K, Shirasaki T, Hibiya S, Ooshima S, Nakamura T, Nishimura R, Okamoto R, Watanabe M. TP53 mutation acquires higher malignant potential in human colon cancer cells. UEGW2017 2017.11.01 Barcelona(Spain)
17. Kawamoto A, Ito G, Nakata T, Fujii S, Suzuki K, Ishibashi F, Shimizu H, Nagata S, Anzai S, Kuno R, Kuwabara K, Kawai M, Takahashi J, Hama M, Tsuchiya K, Nakamura T, Okamoto R, Watanabe M. The ubiquitin-like protein ubiquitin d is up-regulated by synergy of notch and pro-inflammatory cytokines in the inflamed intestinal epithelia of ibd patients.. UEGW2017 2017.11.01 Barcelona(Spain)
18. Chiba A, Nagaishi T, Miyake S. MAIT cells exacerbate the disease course of oxazolone-induced colitis. CD1-MR1 2017 2017.11.05 California (USA)
19. Watabe T, Nagaishi T, Hosoya A, Jose N, Tsugawa N, Kojima Y, Yoshikawa S, Karasuyama H, Adachi T, Watanabe M . Analysis of ileocecal immune response in an experimental colitis model using intra-vital imaging. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Miyagi (Japan)
20. Tsugawa N, Nagaishi T, Watabe T, Hosoya A, Jose N, Kojima Y, Yoshikawa S, Karasuyama H, Adachi T, Watanabe M. Verification of immunoglobulin A regulation of mucosal microflora and homeostasis. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.14 Miyagi (Japan)

Department of Sleep Modulatory Medicine

Professor: Naohiko Inase
Associate Professor: Meiyo Tamaoka
Lecturer: Toshihide Fujie (Respiratory Medicine)
Technician: Takao Miyoshi, Daito Funaki

(1) Research

1. Open-label trial of hyperbaric oxygen therapy on sleep quality
2. Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
3. Development of Non-contact polysomnograph system.
4. The association between OSA and short term blood-pressure variability.
5. The association between OSA and interstitial pneumonia.
6. 24 hours SpO₂ monitoring for patients with chronic respiratory failure

(2) Education

Education of sleep medicine for students, residents and technicians

(3) Clinical Services & Other Works

Clinical Center for Pleasant Sleep provides a variety of medical service for sleep disorder especially for sleep apnea syndrome.

· Out-patient Clinic

Monday: AM Dr. Terada (Pulmonary Medicine)

PM Dr. Fujie (Pulmonary Medicine)

Tuesday: AM Dr. Hirai (Psychiatry)

Wednesday: AM Dr. Miyazaki (Health Service Center)

Thursday: AM Dr. Tamaoka (Sleep Modulatory Medicine)

PM Dr. Tamaoka (Sleep Modulatory Medicine)

Friday: AM Dr. Uezato (Psychiatry)

AM Dr. Tateishi (Pulmonary Medicine)

PM Dr. Tateishi (Pulmonary Medicine)

· Outpatient visits: 5,712 (New:323) for FY 2017

· Examination: polysomnography: 129 patients for FY 2017

(4) Clinical Performances

We aim to establish personalized medicine for OSA in collaboration with the Dental Clinic for Sleep Disorders.

(5) Publications**[Original Articles]**

1. Chiba S, Okayasu K, Tsuchiya K, Tamaoka M, Miyazaki Y, Inase N, Sumi Y. The C-jun N-terminal kinase signaling pathway regulates cyclin D1 and cell cycle profressin in airway sooth muscle cell proliferation. *Int J Clin Exp Med* . 2017; 10(2); 2252-2262
2. Akihito Uezato, Mitsuhiro Enomoto, Meiyo Tamaoka, Mizue Hobo, Shusuke Inukai, Masayuki Hideshima, Yasunari Miyazaki, Toru Nishikawa and Kazuyoshi Yagishit. Shorter sleep onset latency in patients undergoing hyperbaric oxygen treatment *Psychiatry and Clinical Neurosciences*. 2017.01; 71(1); 73-74
3. Hiroyuki Ishiyama, Shusuke Inukai, Akira Nishiyama, Masayuki Hideshima, Shuhei Nakamura, Meiyo Tamaoka, Yasunari Miyazaki, Kenji Fueki, Noriyuki Wakabayashi. Effect of jaw-opening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial *J Prosthodont Res.*. 2017.07; 61(3); 259-267

[Conference Activities & Talks]

1. Shota Hayashi, Masayuki Hideshima, Naoki Ishihara, Tomohiro Kurashima, Shusuke Inukai, Yuuko Mitsuma, Shuhei Nakamura, Toshihide Fujie, Yasunari Miyazaki, Meiyo Tamaoka. Conversion from continuous positive airway pressure therapy to oral appliance therapy for obstructive sleep apnea in Tokyo Medical and Dental University Hospitals. 16th the Japanese Academy of Dental Sleep Medicine 2017.11.04 Yamaguchi, Japan

Department of Translational Oncology

< Department of Translational Oncology >
Associate Professor: Megumi ISHIGURO
Associate Professor: Toshiaki ISHIKAWA (concurrent)

(1) Outline

Department of Translational Oncology aims to establish the “personalized therapy” in chemotherapy for gastrointestinal cancers through identification of the predictive factors for chemo-responsiveness and prognosis.

(2) Research

Main themes of our research activities is identification of the predictive factors for chemo-responsiveness and prognosis by using our well-organized clinical database, fresh frozen and paraffin-embedded samples, and molecular biological technique, i.e. gene expression micro array analysis, and DNA copy number analysis.

(3) Publications

[Original Articles]

1. Tomii C, Inokuchi M, Takagi Y, Ishikawa T, Otsuki S, Uetake H, Kojima K, Kawano T. TPX2 expression is associated with poor survival in gastric cancer *World J Surg Oncol.* 2017.01; 15(1);
2. Iwata N, Ishikawa T, Okazaki S, Mogushi K, Baba H, Ishiguro M, Kobayashi H, Tanaka H, Kawano T, Sugihara K, Uetake H. Clinical Significance of Methylation and Reduced Expression of the Quaking Gene in Colorectal Cancer. *Anticancer Res.* 2017.02; 37(2); 489-498
3. Suto T, Ishiguro M, Hamada C, Kunieda K, Masuko H, Kondo K, Ishida H, Nishimura G, Sasaki K, Morita T, Hazama S, Maeda K, Mishima H, Ike H, Sadahiro S, Sugihara K, Okajima M, Saji S, Sakamoto J, Tomita N. Preplanned safety analysis of the JFMC37-0801 trial: a randomized phase III study of six months versus twelve months of capecitabine as adjuvant chemotherapy for stage III colon cancer. *Int. J. Clin. Oncol.* 2017.06; 22(3); 494-504
4. Hanaoka M, Yasuno M, Ishiguro M, Yamauchi S, Kikuchi A, Tokura M, Ishikawa T, Nakatani E, Uetake H. Morphologic change of the psoas muscle as a surrogate marker of sarcopenia and predictor of complications after colorectal cancer surgery. *Int J Colorectal Dis.* 2017.06; 32(6); 847-856
5. Ozawa T, Matsuyama T, Toiyama Y, Takahashi N, Ishikawa T, Uetake H, Yamada Y, Kusunoki M, Calin G, Goel A.. CCAT1 and CCAT2 long noncoding RNAs, located within the 8q.24.21 'gene desert', serve as important prognostic biomarkers in colorectal cancer. *Ann Oncol.* 2017.08; 28(8); 1882-1888
6. Hanaoka M, Ishikawa T, Ishiguro M, Tokura M, Yamauchi S, Kikuchi A, Uetake H, Yasuno M, Kawano T. Expression of ATF6 as a marker of pre-cancerous atypical change in ulcerative colitis-associated colorectal cancer: a potential role in the management of dysplasia. *J. Gastroenterol.* 2017.09; [Epub ahead of print]

7. Kusumoto T, Sunami E, Ota M, Yoshida K, Sakamoto Y, Tomita N, Maeda A, Mochizuki I, Okabe M, Kunieda K, Yamauchi J, Itabashi M, Kotake K, Takahashi K, Baba H, Boku N, Aiba K, Ishiguro M, Morita S, Sugihara K. Planned Safety Analysis of the ACTS-CC 02 Trial: A Randomized Phase III Trial of S-1 With Oxaliplatin Versus Tegafur and Uracil With Leucovorin as Adjuvant Chemotherapy for High-Risk Stage III Colon Cancer. *Clin Colorectal Cancer*. 2017.11; [Epub ahead of print]
8. Ueno H, Kanemitsu Y, Sekine S, Ishiguro M, Ito E, Hashiguchi Y, Kondo F, Shimazaki H, Mochizuki S, Kajiwara Y, Shinto E, Yamamoto J. Desmoplastic Pattern at the Tumor Front Defines Poor-prognosis Subtypes of Colorectal Cancer. *Am. J. Surg. Pathol.*. 2017.11; 41(11); 1506-1512

[Conference Activities & Talks]

1. Shinozaki E, Ishiguro M, Nakatani E, Yamaguchi T, Nakamura M, Miyamoto Y, Ojima H, Honma Y, Gotoh M, Ishikawa T, Takahashi K, Shimada Y, Yoshida K, Mizunuma N, Muro K, Komatsu Y, Yamaguchi K, Nakano H, Koike J, Sugihara K.. A phase II study of panitumumab with FOLFOX or FOLFIRI as 1st line chemotherapy for KRAS-wild type metastatic colorectal cancer;the PaFF-J study.. American Society of Clinical Oncology 2018 Gastrointestinal Cancers Symposium (ASCO-GI) 2017.01.21 San Francisco (USA)
2. Yamauchi S, Okazaki S, Kikuchi A, Ishiguro M, Ishikawa T, Uetake H, Yasuno M, Sugihara K.. Prognostic factor of lower rectal cancer with lateral pelvic lymph node metastasis treated with lateral lymph node dissection.. Society of Surgical Oncology (SSO) 2017 Annual Meeting 2017.03.16 Seattle (USA)
3. Hanaoka M, Ishikawa T, Ishiguro M, Tokura M, Yamauchi S, Kikuchi A, Yasuno M, Uetake H, Kawano T. ATF6, a UPR related gene, expression in malignant conversion and progression of Ulcerative colitis (UC)-associated and non-UC-associated colorectal cancer. Society of Surgical Oncology (SSO) 2017 Annual Meeting 2017.03.16 Seattle (USA)
4. Ishikawa T, Ishiguro M, Nakatani E, Uetake H, Ueno H, Murotani K, Matsui S, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Teramukai S, Sugihara K.. Prognostic impact of MSI in stage II colon cancers: An additional translational study of the SACURA trial.. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
5. Ishiguro M, Nakatani E, Ueno H, Ishikawa T, Uetake H, Shimada Y, Takahashi K, Kotake K, Watanabe M, Tomita N, Mochizuki H, Teramukai S, Sugihara K.. Recurrence risk factors and outcome stratification stage II colon cancer patients: A subanalysis of the SACURA trial.. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
6. Ueno H, Ishiguro M, Nakatani E, Ishikawa T, Uetake H, Murotani K, Matsui S, Tomita N, Shimada Y, Takahashi K, Kotake K, Watanabe M, Mochizuki H, Teramukai S, Sugihara K.. Prognostic impact of tumor budding in Stage II colon cancer: A Prospective study(SACURA trial).. American Society of Clinical Oncology (ASCO) 2017 Annual Meeting 2017.06.02 Chicago (USA)
7. Ishiguro M, Nakatani E, Yamaguchi Y, Takahashi K, Shimada Y, Yoshida K, Mizunuma N, Muro K, Komatsu Y, Sugihara K . Impact of early tumor shrinkage (ETS) and depth of response (DoR) on survival: A phase II study of the 1st line therapy with panitumumab for KRAS-wild type metastatic colorectal cancer (the PaFF-J study). The 55th Annual Meeting of Japan Society of Clinical Oncology 2017.10.22 Yokohama
8. Yamauchi S, Yasuno M, Takaoka A, Matsumiya Y, Seki R, Orita F, Sasaki M, Miura T, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Sugihara K.. Clinical significance of extended lateral lymph node dissection for lower rectal cancer.. Asian Surgical Association 21st Asian Congress of Surgery 2017.11.12 Tokyo
9. Miura T, Yamauchi S, Takaoka A, Seki R, Matsumiya Y, Orita F, Sasaki M, Tokura M, Kikuchi A, Matsuyama T, Ishiguro M, Ishikawa T, Uetake H, Yasuno M.. Negative pressure wound therapy for closure of ileostomy and colostomy.. The 1st International Conference of Surgical Infection Society Asia-Pacific 2017.11.29 Tokyo

Clinical Laboratory

General Manager
-Professor : Shuji Tohda

Associate Manager
-Junior Associate Professor : Tadashi Kanouchi

Assistant Professor : Miyako Murakawa
Assistant Professor : Ayako Nogami
Assistant Professor : Hideki Arima
Medical Staff : Shintaro Iida

(1) Outline

The Clinical Laboratory is a central clinical department that conducts laboratory tests in order to obtain information about the diagnosis, treatment, and prevention of diseases. Physiological tests such as electrocardiogram, echocardiography, pulmonary function tests, and electroencephalogram are also performed at our facility.

(2) Research

Our research subjects are

- 1) New genetic tests for hematological disorders,
- 2) Development of tests for molecular pathology and drug sensitivity of hematological malignancies,
- 3) Genotypic analysis of bacteria for monitoring those transmission in the hospital,
- 4) Development of electrophysiological diagnostic tests for peripheral neuropathies,
- 5) Clinical and electrophysiological study for amyotrophic lateral sclerosis,
- 6) Quality control of nerve conduction study,
- 7) Molecular mechanisms of treatment for hepatitis C.
- 8) Novel methods to analyze cardiac function using echocardiography.

(3) Education

We lecture on clinical laboratory medicine and give technical training on clinical laboratory tests and physiological function tests to not only the medical students and medical technologist students in the faculty of medicine of the university but also those in the other vocational school for medical technologists. We give a labo tour and practice to master course graduate students, too. We gave a general training for clinical laboratory medicine to nine junior residents of university hospital in 2017. We also held hands-on seminars of Gram staining, urinary sediment, cardiac and abdominal ultrasonography for the residents.

(4) Clinical Services & Other Works

Clinical laboratory bears an important responsibility for advanced and high quality medical care. Our clinical laboratory is based on the principle of providing the speedy and high quality tests. The highest level of advanced tests, such as qualitative and quantitative analysis of various viral DNA by the PCR method, are also introduced here. In the night time and holidays, the clinical laboratory provides blood products for transfusion in cooperation with the blood transfusion service of the hospital. The updated information on antibiotic sensitivity of the pathogens in each ward is also provided online regularly. Together with the division of infection control and prevention, we monitor the nosocomial transmission of bacteria such as MRSA by genotypic analysis of those. Our clinical laboratory and blood transfusion service have received accreditation of ISO15189 (Medical laboratories - Particular requirements for quality and competence) in June 2014, and renewed it with the latest version in December 2016. It means that the clinical laboratory is an international standard on quality and that our hospital is allowed to conduct the international clinical trials. We give a lecture on laboratory tests at meetings of laboratory medicine-related societies.

(5) Clinical Performances

We are developing new diagnostic methods collaborating with various clinical departments. We are also supporting them in their diagnostic procedure.

(6) Publications**[Original Articles]**

1. S Nogami, N Kawaguchi-Ihara, E Shiratori, M Ohtaka, M Itoh, S Tohda. Detection of the MYD88 mutation by the combination of the allele-specific PCR and quenching probe methods. *Int J Lab Hematol.* 2017.04; 39(2); 163-168
2. Yuki Okuhashi, Mai Itoh, Shuji Tohda. Hedgehog Stimulation Suppresses Clonogenicity and Activates NOTCH Signalling in T-lymphoblastic Leukaemia Jurkat Cells. *Anticancer Res.* 2017.05; 37(9); 5005-5009
3. Miyako Murakawa, Yasuhiro Asahina, Fukiko Kawai-Kitahata, Mina Nakagawa, Sayuri Nitta, Satoshi Otani, Hiroko Nagata, Shun Kaneko, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Yasuhito Tanaka, Sayuki Iijima, Kaoru Tsuchiya, Namiki Izumi, Shuji Tohda, Mamoru Watanabe. Hepatic IFNL4 expression is associated with non-response to interferon-based therapy through the regulation of basal interferon-stimulated gene expression in chronic hepatitis C patients. *J. Med. Virol.* 2017.07; 89(7); 1241-1247
4. Miyako Murakawa, Yasuhiro Asahina, Hiroko Nagata, Mina Nakagawa, Sei Kakinuma, Sayuri Nitta, Fukiko Kawai-Kitahata, Satoshi Otani, Shun Kaneko, Masato Miyoshi, Tomoyuki Tsunoda, Yu Asano, Ayako Sato, Yasuhiro Itsui, Seishin Azuma, Toshihiko Nouchi, Yohei Furumoto, Tooru Asano, Yoshimichi Chuganji, Shuji Tohda, Mamoru Watanabe. ITPA gene variation and ribavirin-induced anemia in patients with genotype 2 chronic hepatitis C treated with sofosbuvir plus ribavirin. *Hepatol. Res.* 2017.07; 29(5); 584-593
5. Fumio Goto, Sei Kakinuma, Masato Miyoshi, Tomoyuki Tsunoda, Shun Kaneko, Ayako Sato, Yu Asano, Satoshi Otani, Seishin Azuma, Hiroko Nagata, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Mina Nakagawa, Yasuhiro Asahina, Mamoru Watanabe. Bone morphogenetic protein-4 modulates proliferation and terminal differentiation of fetal hepatic stem/progenitor cells. *Hepatol. Res.* 2017.08; 47(9); 941-952
6. Hiroko Nagata, Mina Nakagawa, Yasuhiro Asahina, Ayako Sato, Yu Asano, Tomoyuki Tsunoda, Masato Miyoshi, Shun Kaneko, Satoshi Otani, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Toshihiko Nouchi, Hideki Sakai, Makoto Tomita, Mamoru Watanabe. Effect of interferon-based and -free therapy on early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C. *J. Hepatol.* 2017.11; 67(5); 933-939
7. Erika Shiratori, Mai Itoh, Shuji Tohda. MYD88 Inhibitor ST2825 Suppresses the Growth of Lymphoma and Leukaemia Cells. *Anticancer Res.* 2017.11; 37(11); 6203-6209

8. Mika Ohtaka, Mai Itoh, Shuji Tohda. BMI1 Inhibitors Down-regulate NOTCH Signaling and Suppress Proliferation of Acute Leukemia Cells. *Anticancer Res.* 2017.11; 37(11); 6047-6053
9. Yoshihiro Umezawa, Hiroki Akiyama, Keigo Okada, Shinya Ishida, Ayako Nogami, Gaku Oshikawa, Tetsuya Kurosu, Osamu Miura. Molecular mechanisms for enhancement of stromal cell-derived factor 1-induced chemotaxis by platelet endothelial cell adhesion molecule 1 (PECAM-1). *Journal of Biological Chemistry.* 2017.12; 292(48); 19639-19655
10. Keigo Okada, Ayako Nogami, Shinya Ishida, Hiroki Akiyama, Cheng Chen, Yoshihiro Umezawa and Osamu Miura. FLT3-ITD induces expression of Pim kinases through STAT5 to confer resistance to the PI3K/Akt pathway inhibitors on leukemic cells by enhancing the mTORC1/Mcl-1 pathway *Oncotarget.* 2017.12; 9; 8870-8886

[Books etc]

1. Tadashi Kanouchi. Textbook of physiological function tests. Ishiyaku publishers, Inc., 2017.01 (ISBN : 978-4-263-22368-0)

[Conference Activities & Talks]

1. Tomoko Yamashita, Daisuke Mizuchi, Kouta Yoshifuji, Keisuke Tanaka, Ayako Nogami, Ken Watanabe, Chizuko Sakashita, Tetsuya Fukuda, Ayako Arai, Norihiko Kawamata, Osamu Miura, Masahide Yamamoto. Busulfan-based conditioning regimen for autologous peripheral blood stem cell transplantation in patients with central nervous system lymphoma. The 39th Annual Meeting of the Japanese Society of Hematopoietic Cell Transplantation 2017.03.03 Matsue
2. Chihiro Tani. Gene transfer by natural genetic transformation in *Moraxella catarrhalis*. The 90th Annual Meeting of Japanese Society for Bacteriology 2017.03.18
3. Mika Ohtaka, Mai Itoh, and Shuji Tohda. BMI1 inhibitors suppress cell growth and NOTCH signalling of acute leukemia cells. 46th Annual Scientific Meeting of the International Society for Experimental Hematology 2017.08.26 Frankfurt, Germany
4. Ayako Nogami, Keigo Okada, Cheng Chen, Maho Kawakami, Hiroki Akiyama, Yoshihiro Umezawa, Gaku Oshikawa, Shinya Ishida, Tetsuya Kurosu, Osamu Miura. Modulation of the mTORC1 pathway by ubiquitin-proteasome system via REDD1 in AML with FLT3-ITD. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
5. Keigo Okada, Ayako Nogami, Cheng Chen, Maho kawakami, Hiroki Akiyama, Shinya Ishida, Yoshihiro Umezawa, Osamu Miura. FLT3-ITD confers resistance to PI3K/Akt inhibitors by enhancing mTORC1/Mcl-1 pathway via Pim kinase. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
6. Murakawa M, Asahina Y, Nakagawa M, Nitta S, Kawai-Kitahata F, Nagata H, Kaneko S, Asano Y, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Sato A, Itsui Y, Kakinuma S, Azuma S, Watanabe M. On-treatment higher levels of alpha-fetoprotein and M2BPGi are associated with development of hepatocellular carcinoma during nucleos(t)ide analog therapy in patients with HBV chronic infection. AASLD, The Liver Meeting 2017 2017.10.21 Washington DC (USA)
7. Nitta S, Murakawa M, Kato T, Sato A, Tsunoda T, Miyoshi M, Asano Y, Kaneko S, Nagata H, Kawai-Kitahata F, Itsui Y, Nakagawa M, Azuma S, Kakinuma S, Asahina Y. The analysis of NS5A Resistance-Associated Substitutions (RAS): In vitro study of NS5A recombinant hepatitis C in infectious cell culture system for various RAS detected after treatment failure in chronic hepatitis C patients. AASLD The Liver Meeting 2017 2017.10.21 Washington D.C (USA)
8. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Shinya Ishida, Ayako Nogami, Toshikage Nagao, Osamu Miura. Deubiquitinase inhibitor WP1130 blocks JAK2-V617F to induce apoptosis in leukemic cells. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.21 Tokyo
9. Kaneko S, Kakinuma S, Asahina Y, Kamiya A, Miyoshi M, Tsunoda T, Inoue-Shinomiya E, Nitta S, Sato A, Asano Y, Nagata H, Kawai-Kitahata F, Murakawa M, Itsui Y, Nakagawa M, Azuma S, Watanabe M. A novel culture model for coinfection of hepatitis B and hepatitis C viruses using human induced pluripotent stem cell-derived hepatic cells for analyses of changes in host-innate immune responses . AASLD The Liver Meeting 2017 2017.10.22 Washington D.C (USA)

10. Nakagawa M, Asahina Y, Nagata H, Kaneko S, Kawai-Kitahata F, Murakawa M, Nitta S, Itsui Y, Azuma S, Kakinuma S, Tanaka Y, Watanabe M. Evaluation of an early occurrence and recurrence of hepatocellular carcinoma in chronic hepatitis C patients treated with All-Oral DAAs - propensity score-matched analysis of a prospective database -. AASLD, The Liver Meeting 2017 2017.10.22 Washington D.C (USA)
11. Tomoko Yamashita, Hiroki Tsutsumi, Kota Yoshifuji, Tatsuya Saito, Yoshihiro Umezawa, Ayako Nogami, Ken Watanabe, Toshikage Nagao, Chizduko Sakashita, Masahide Yamamoto, Ayako Arai, Norihiko Kawamata, Osamu Miura, Tetsuya Fukuda. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma with 11q Deletion. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.22 Tokyo
12. Hiroki Akiyama, Yoshihiro Umezawa, Keigo Okada, Shinya Ishida, Ayako Nogami, and Osamu Miura. Deubiquitinase Inhibitor WP1130 Blocks FLT3-ITD to Induce Apoptosis in Leukemic Cells. The 59th American Society of Hematology Annual Meeting & Exposition 2017.12.10 Atlanta

Transfusion Medicine

Director(Lecturer) Michiko KAJIWARA
Assistant Director(Medical Technologist) Naoki OHTOMO
Section Chief Medical Technologist Keiko BABA
Assisitant Section Chief Medical Technologist Yukiko OHISHI
Clinical Fellow Shihoko SUWA
Medical Technologist Yukari USUI
Medical Technologist Kaoru OKUYAMA
Medical Technologist Shiho KOBAYASHI (-May,2017)
Medical Technologist Chihiro TOYAMA
Medical Technologist Eriko FURUYA
Medical Technologist Miho Yamasaki (Aug 2017 -)

(1) Research

- 1) Practice of safe and appropriate transfusion therapy (including prevention of medical accident related transfusion)
- 2) Basic and clinical research of hematopoietic stem cell transplantation

(2) Lectures & Courses

Transfusion therapy is a supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of medical treatment. From this point of view, we educate the students of school of medicine, school of allied health sciences, graduate school of medical and dental sciences, medical doctors, and co-medicals.

(3) Clinical Services & Other Works

Clinical Services (The result of 2017)

- 1) The amount of blood products used
Red cell component products 13,035 Units (6,596 bags)
Platelet concentration 28,396 Units (2,538 bags)
Fresh frozen plasma 9,349 Units (4,275 bags)
- 2) Autologous blood collection and transfusion
Autologous blood collection 292 cases (390times, 766Units)
Autologous blood transfusion 265 cases (665 Units)
- 3) The number of clinical tests of transfusion
Blood typing 10,810
Anti red blood cell antibody test 5,393
Cross match 10,258
- 4) Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest 13 cases 13 times
 Allogenic peripheral blood stem cell harvest 2 cases 3 times
 Allogenic bone marrow harvest 14cases 14 times
 (Including Japan Marrow Donor Program donors)
 5) Hematopoietic stem cell transplantation
 (The evaluation and preservation of the stem cells were done in our department)
 Autologous peripheral blood stem cell transplantation 8 cases 8 times
 Allogenic peripheral blood stem cell transplantation 2 cases 2 times
 Allogenic bone marrow transplantation 18 cases 18 times
 Allogenic umbilical cord blood transplantation 2 cases 2 times

(4) Publications

[Original Articles]

1. Masatoshi Takagi, Yasuyoshi Ishiwata, Yuki Aoki, Satoshi Miyamoto, Akihiro Hoshino, Kazuaki Matsumoto, Akira Nishimura, Mari Tanaka, Masakatsu Yanagimachi, Noriko Mitsui, Kohsuke Imai, Hirokazu Kanegane, Michiko Kajiwara, Kanako Takikawa, Tsukasa Mae, Osamu Tomita, Junya Fujimura, Masato Yasuhara, Daisuke Tomizawa, Shuki Mizutani, Tomohiro Morio. HLA haploidentical hematopoietic cell transplantation using clofarabine and busulfan for refractory pediatric hematological malignancy. *Int J Hematol.* 2017.05; 105(5); 686-691
2. Masatoshi Takagi, Shohei Ogata, Hiroo Ueno, Kenichi Yoshida, Tzuwen Yeh, Akihiro Hoshino, Jinhua Piao, Motoy Yamashita, Mai Nanya, Tsubasa Okano, Michiko Kajiwara, Hirokazu Kanegane, Hideki Muramatsu, Yusuke Okuno, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Yuki Bando, Motohiro Kato, Yasuhide Hayashi, Satoru Miyano, Kohsuke Imai, Seishi Ogawa, Seiji Kojima, Tomohiro Morio. Haploinsufficiency of TNFAIP3 (A20) by germline mutation is involved in autoimmune lymphoproliferative syndrome. *J. Allergy Clin. Immunol.* 2017.06; 139(6); 1914-1922
3. Marie Scully, Paul Knöbl, Karim Kentouche, Lawrence Rice, Jerzy Windyga, Reinhard Schneppenheim, Johanna A Kremer Hovinga, Michiko Kajiwara, Yoshihiro Fujimura, Caterina Maggiore, Jennifer Doralt, Christopher Hibbard, Leah Martell, Bruce Ewenstein. Recombinant ADAMTS-13: first-in-human pharmacokinetics and safety in congenital thrombotic thrombocytopenic purpura. *Blood.* 2017.11; 130(19); 2055-2063
4. Masayuki Nagasawa, Noriko Mitsui, Yuki Aoki, Toshiaki Ono, Takeshi Isoda, Kohsuke Imai, Masatoshi Takagi, Michiko Kajiwara, Hirokazu Kanegane, Tomohiro Morio. Effect of reduced-intensity conditioning and the risk of late-onset non-infectious pulmonary complications in pediatric patients *Eur. J. Haematol.* 2017.12; 99(6); 525-531

[Conference Activities & Talks]

1. Ryoto Yoshimoto, Ken Watanabe, Emi Uchida, Shihoko Suwa, Shuji Tohda, Masahiko Hatano, Miura Osamu, Tetsuya Fukuda. IVNSIABP/Nd1 is highly expressed in refractory lymphoma as a novel therapeutic target molecule. The 79th Annual Meeting of the Japanese Society of Hematology 2017.10.20 Tokyo
2. Central venous catheter-related cylindrical thrombosis in right atrium after bone marrow transplantation for X-linked anhidrotic ectodermal dysplasia with immunodeficiency (XL-EDA-ID). 2017.11.09
3. A 7-year-old girl who maintains complete remission after multiple hematopoietic cell transplantation for frequent relapse. 2017.11.11

Center for Cell Therapy

Director: Tomohiro Morio (Dpt. of Pediatrics and Developmental Biology)

Vise Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine)

Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine)

Product manager: Michiko Kajiwara (Department of Blood Transfusion Medicine)

Technicians: Ayako Tsuji, Minhua Sun (to January 2017), Yuri Kohno

Technicians (From Collaborative Research): Takafumi Kato, Megumi Muraoka, Hiroaki Mori, Hiroshi Terakawa

Clerical Assistant: Akiko Hoshikawa, Jun Kusano

(1) Research

1. Development of innovative techniques for quality assurance of cell products
2. Development of a novel measure for rapid and sensitive detection of multiple pathogens
3. Development of multi-virus specific T lymphocytes for adoptive immunotherapy
(Department of Pediatrics and Developmental Biology)
4. Research on a regeneration system of the cartilage bone from the synovial membrane
(Department of Orthopedic Surgery)
5. Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia
(Department of Immunotherapeutics / Department of Hematology)

We are planning to start multi-virus specific T cell therapy for opportunistic viral infection post hematopoietic cell transplantation and expanded colon epithelium for various bowel disorders following approval from the certified committee for regenerative medicine and from MHLW.

(2) Education

We provide assistance to prepare standard operation procedure (SOP) and offer on-the-job training for cell processing/ manipulating procedures and that for quality assurance at the center. Facility for the education and training was recently installed at the CPC annex.

(3) Clinical Services & Other Works

The cell products currently prepared in our center include

#1 Synovium-derived mesenchymal stem cells

#2 Processed peripheral blood stem cells

(4) Clinical Performances

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five independent cell processing rooms (class 10,000 clean rooms). All the rooms are equipped with a bio-safety

cabinet. The hardware as well as software used in our center fulfills all the guidelines that are required for the preparation of cell products of clinical grade.

(5) Publications

[Original Articles]

1. Atsumi Tsuji-Hosokawa, Nozomi Matsuda, Kenji Kurosawa, Kenichi Kashimada, Tomohiro Morio. A Case of MECP2 Duplication Syndrome with Gonadotropin-Dependent Precocious Puberty. *Horm Res Paediatr.* 2017.01; 87(4); 217-216
2. Shintaro Ono, Tsubasa Okano, Akihiro Hoshino, Masakatsu Yanagimachi, Kazuko Hamamoto, Yozo Nakazawa, Toshihiko Imamura, Masaei Onuma, Hidetaka Niizuma, Yoji Sasahara, Hiroshi Tsujimoto, Taizo Wada, Reiko Kunisaki, Masatoshi Takagi, Kohsuke Imai, Tomohiro Morio, Hirokazu Kanegane. Hematopoietic Stem Cell Transplantation for XIAP Deficiency in Japan. *J. Clin. Immunol.* 2017.01; 37(1); 85-91
3. Chikako Morioka, Motohiro Komaki, Atsuko Taki, Izumi Honda, Naoki Yokoyama, Kengo Iwasaki, Sachiko Iseki, Tomohiro Morio, Ikuo Morita. Neuroprotective effects of human umbilical cord-derived mesenchymal stem cells on periventricular leukomalacia-like brain injury in neonatal rats. *Inflamm Regen.* 2017.01; 37; 1
4. Saito R, Muneta T, Ozeki N, Nakagawa Y, Udo M, Yanagisawa K, Tsuji K, Tomita M, Koga H, Sekiya I. Strenuous running exacerbates knee cartilage erosion induced by low amount of mono-iodoacetate in rats. *BMC Musculoskelet Disord.* 2017.01; 18(1); 36
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[Misc]

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[Conference Activities & Talks]

1. Ichiro Sekiya. Preclinical and Clinical Studies of Meniscus Regeneration by Synovial Stem Cells. Orthopaedic Research Society 2017 Annual Meeting 2017.03.19 SanDiego, USA
2. Naoto Watanabe, Mitsuru Mizuno, Jumpei Matsuda, Hisako Katano, Nobutake Ozeki, Koji Otabe, Keiichiro Komori, Yuji Kono, Kenta Katagiri, Takeshi Muneta, Ichiro Sekiya.. Decellularization of the meniscus by high hydrostatic pressure: temperature condition for removal of cell debris.. Orthopaedic Research Society 2017 Annual Meeting 2017.03.20 SanDiego, USA
3. Mana Naritomi, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya.. Recombinant peptide petaloid pieces enhance in vitro cartilage formation of mesenchymal stem cells. Orthopaedic Research Society 2017 Annual Meeting 2017.03.20 SanDiego, USA
4. Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Yuji Kohno, Shizuka Fujii, Nobutake Ozeki, Masafumi Horie, Kunikazu Tsuji, Takeshi Muneta, Ichiro Sekiya.. Complete Human Serum Maintains Viability and Chondrogenic Potential of Human Synovial Stem Cells: Suitable Condition for Transplantation. Orthopaedic Research Society 2017 Annual Meeting 2017.03.21 SanDiego, USA
5. Koji Otabe, Mai Katakura, Toshiyuki Ohara, Kaori Nakamura, Masafumi Horie, Hideyuki Koga, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta.. Automatic Knee X Ray Analysis System Reveals that Meniscus Repair during Anterior Cruciate Ligament Reconstruction Surgery cannot prevent the Development of Osteoarthritis. Orthopaedic Research Society 2017 Annual Meeting 2017.03.21 SanDiego, USA
6. Kenta Katagiri, Mitsuru Mizuno, Hideyuki Koga, Nobutake Ozeki, Yusuke Nakagawa, Yuji Kono, Koji Otabe, Masafumi Horie, Hisako Katano, Kunikazu Tsuji, Hideo Ono, Takeshi Muneta, Ichiro Sekiya.. Transplantation of Synovial Mesenchymal Stem Cells Enhances the Effect of Centralization with Suture Anchor and Promotes Meniscus Regeneration for Extruded Meniscus After Partial Meniscectomy in Mice. Orthopaedic Research Society 2017 Annual Meeting 2017.03.22 SanDiego, USA
7. Yuji Kono, Mitsuru Mizuno, Kenta Katagiri, Koji Otabe, Nobutake Ozeki, Hisako Katao, Keiichiro Komori, Masafumi Horie, Kunikazu Tsuji, Mikio Matsumoto, Haruka Kaeko, Yuji Takazawa, Takeshi Muneta, Ichiro Sekiya.. Harvested cell number varies greater in RA than in OA after a suspended synovium culture. Orthopaedic Research Society 2017 Annual Meeting 2017.03.22 SanDiego, USA
8. Cell and Gene Therapy for Hematological Disorders. The 8th JSH International Symposium 2017 2017.05.01 Miyazaki, Japan
9. Okamoto K, Okano T, Kumaki E, Tanaka E, Ono S, Wada T, Ohnishi H, Kato Z, Nunoi N, Imai K, Kanegane H, Mori M, Morio T. A Case of Non-Pulmonary Sarcoidosis Due to Novel Hypomorphic Missense Mutation of NCF2. *ESID 2017* 2017.09.11 Edinburgh, UK

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11. Okano T, Imai K, Mitui-Sekinaka K, Yeh T.W, Takashima T, Kanegane H, Nonoyama S, Morio T. Combined Immunodeficiency and Progressive Lymphoproliferative Diseases of Activated P13K γ Syndrome Rescued by Hematopoietic. ESID 2017 2017.09.12 Edinburgh, UK
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13. Kumaki E, Ono S, Shiota M, Saito N, Kanazawa N, Ida H, Oda H, Nishikomori R, Saito M, Lin H.T, Otsu M, Morio T. Neutrophil Function in PSTPIP1 Mutations.. ESID 2017 2017.09.13 Edinburg,UK
14. Yamashita M, Mitsui N, Inoue Y, Okada S, Padhi A.K, Zhang K.Y, Ohara O, Taniuchi I, Morio T. Heterozygous IKZF3 Mutation in Patients with B cell Deficiency. ESID 2017 2017.09.14 Edinburgh,UK
15. Morio T. Investigational Gene Analysis for Primary Immunodeficiency Diseases. Asia Pacific Society for Immunodeficiencies(APSID) 2017.10.10 Hong Kong
16. Morio T. Hematopoietic Cell Transplantation for Primary Immunodeficiency Diseases.: Current Situation and Future Direction. Asia Pacific Society for Immunodeficiencies(APSID) 2017.10.10 Hong Kong
17. Matsumoto K, Takagi M, Ishiwata Y, Aoki Y, Miyamoto S, Hoshino A, Nishimura A, Tanaka M, Yanagimachi M, Mitsui N, Imai K, Kanegane H, Kajiwara M, Takikawa K, Mae T, Tomiota O, Fujimura J, Yasuhara M, Tomizawa D, Mizutani S, Morio T. HLA haploidentical HCT using clofarabine and busulfan for refractory pediatric leukemia. JSH 2017 2017.10.20 Tokyo
18. Central venous catheter-related cylindrical thrombosis in right atrium after bone marrow transplantation for X-linked anhidrotic ectodermal dysplasia with immunodeficiency (XL-EDA-ID). 2017.11.09
19. Central venous catheter-related cylindrical thrombosis in right atrium after bone marrow transplantation for X-linked anhidrotic ectodermal dysplasia with immunodeficiency(XL-EDA-ID). 2017.11.09
20. A case of T-cell lymphoblastic lymphoma/leukemia complicated by gait inability during combination chemotherapy with nelarabine. 2017.11.10
21. A 7-year-old girl who maintains complete remission after multiple hematopoietic cell transplantation for frequent relapse. 2017.11.11
22. A 7-year-old girl who maintain complete remission after multiple hematopoietic cell transplantation for frequent relapse of infant leukemia. 2017.11.11
23. Tomohiro Morio. Molecular and cellular basis of systemic immune disease.. The 46th Annual Meeting of The Japanese Society for Immunology 2017.12.13 Miyagi

[Patents]

1. METHOD FOR DETECTING MYCOPLASMA, Announcement Number : 3192878

[Awards & Honors]

1. Yusuke Nakagawa, Best Poster Presentation Award, Japanese Medical Society of America, Japan Society for the Promotion of Science, 2017.04

Cleanroom

Associate Professor SUNAKAWA Mitsuhiro
Assistant Professor MATSUMOTO Hiroyuki

(1) Research

- 1) The development of disposable hygienic materials for dental use.
- 2) The survey for the oral diseases in patients with HIV.
- 3) The survey for the relationship between the consciousness of the staff and students and the needle stick accident in the hospital.

(2) Education

The improvement of the nosocomial infection control system in the University Hospital, Faculty of Dentistry, Tokyo Medical and Dental University and the education of the actual infection control method to all staff and clinical course students.

(3) Publications

Center for Development of Devices and Drugs in Dentistry

Director Junji TAGAMI
Co-Director Hidekazu TAKAHASHI
Hideki HARASAWA
Naoko HARADA
Member Miwako WAGAI (CRC)
Kazuko KOJIMA (CRC)

(1) Outline

Center for development of devices and drugs in dentistry was established in April, 2004 and is committed to a wide range of activities, such as education, consultation for new devices and drugs application, and support for clinical trials in University Hospital of Dentistry.

(2) Education

We provide a program for the 3rd year students of the School of Dentistry, also for the 2nd year students of the School of Oral Health Care Sciences majoring in Oral Health Engineering to help them to gain fundamental knowledge of Pharmaceutical Affairs Act which is required for development and application of dental devices. Collaborating with the Institute of Biomaterials and Bioengineering, we lecture the 1st year students in Master's Program at Graduate School of Medical and Dental Sciences on issues and systems related to the mission that many outcomes from studies about innovative dental devices and materials will be put into use without "device-lag" .

(3) Clinical Services & Other Works

1. Clinical trial supporting Services

In order to accomplish clinical trials successfully, we manage and support from planning, paper work to patient care as a main office of clinical trials in University Hospital of Dentistry.

2. Consultation Services

We provide consultation services about various issues concerning the Pharmaceutical Affairs Act, not only for pharmaceutical and dental companies but also for dentists and researchers in our University.

By the supporting services of clinical trials, we hope that applicant will be able to form a protocol adequately and effectively, and to start the clinical trial swiftly.

(4) Clinical Performances

· Consultation achievements

We managed and supported one clinical trial for dental device in 2017.

The 37 consultation services concerning dental devices were performed in 2017.

(5) Publications

[Original Articles]

1. Sasipin Lauvahutanon, Maho Shiozawa, Hidekazu Takahashi, Naohiko Iwasaki, Meiko Oki, Werner J. Finger, Mansuang Arksornnukit. Discoloration of various CAD/CAM blocks after immersion in coffee Restorative Dentistry and Endodontics. 2017.01; 42(1); 9-18
2. Ishihata H, Kanehira M, Finger WJ, Takahashi H, Tomita M, Sasaki K. Effect of two desensitizing agents on dentin permeability in vitro. J Appl Oral Sci. 2017.01; 25(1); 34-41
3. Kento Sato, Keiichi Hosaka, Masahiro Takahashi, Masaomi Ikeda, Fucong Tian, Wataru Komada, Masatoshi Nakajima, Richard Foxton, Yoshihiro Nishitani, David H Pashley, Junji Tagami. Dentin Bonding Durability of Two-step Self-etch Adhesives with Improved of Degree of Conversion of Adhesive Resins. J Adhes Dent. 2017.02; 19(1); 31-37
4. Krid Kamonkhantikul, Mansuang Arksornnukit, Hidekazu Takahashi. Antifungal, optical, and mechanical properties of polymethylmethacrylate material incorporated with silanized zinc oxide nanoparticles. Int J Nanomedicine. 2017.03; 12; 2353-2360
5. Naohiko Iwasaki, Chisato Yamaki, Hidekazu Takahashi, Meiko Oki, Tetsuya Suzuki. Effect of long-time immersion of soft denture liners in water on viscoelastic properties. Dent Mater J. 2017.04;
6. Yuichi Kitasako, Yoshiyuk Sasaki, Tomohiro Takagaki, Alireza Sadr, Junji Tagami. Erosive Tooth Wear Among Different Tooth Types and Surfaces in Japanese Adults 15 to 89 Years Old. Oral Health and Preventive Dentistry. 2017.07; 15(4); 357-364
7. Yukari Noda, Masatoshi Nakajima, Masahiro Takahashi, Teerapong Mamanee, Keiichi Hosaka, Tomohiro Takagaki, Masaomi Ikeda, Richard M Foxton, Junji Tagami. The effect of five kinds of surface treatment agents on the bond strength to various ceramics with thermocycle aging. Dent Mater J. 2017.07;
8. Mashiko R, Inoue G, Nikaido T, Tagami J. Morphological evaluation of artificial caries-affected dentin after applying FCP-COMPLEX Journal of Oral Science. 2017.09; 59(3); 343-350
9. Araoka D, Hosaka K, Nakajima M, Foxton R, Thanatvarakorn O, Prasansuttiorn T, Yoshimine A, Sato K, Takahashi M, Otsuki M, Tagami J.. The strategies used for curing universal adhesives affect the micro-bond strength of resin cement used to lute indirect resin composites to human dentin Dental Materials Journal. 2017.09;
10. Takahiro Shirako , Hiroshi Churei, Naohiko Iwasaki, Hidekazu Takahashi, Toshiaki Ueno. Evaluation of the flexural properties of a new temporary splint material for use in dental trauma splints Journal of Dental Sciences. 2017.09; 12(3); 308-310
11. Saad A, Inoue G, Nikaido T, Ikeda M, MF Burrow, Tagami J. Microtensile Bond Strength of Resin-Modified Glass Ionomer Cement to Sound and Artificial Caries-Affected Root Dentin With Different Conditioning Operative Dentistry. 2017.11; 42(6); 626-635
12. Survey on the actual situation of oral antibiotics prescription for extraction and treatment other than extraction 2017.12; 36(3); 95-100
13. Kazuyuki Handa, Natsuko Murakami, Toshiki Yamazaki, Hidekazu Takahashi, Noriyuki Wakabayashi. The ball-on-disk cyclic wear of CAD/CAM machinable dental composite and ceramic materials Journal of Oral Science. 2017.12; 59(4); 589-596

[Books etc]

1. The newest series of textbook for dental hygienist- Dental materials. 2017.03 (ISBN : 978-4-263-42851-1)

[Conference Activities & Talks]

1. Ken-ichi Tonami, Shizuko Ichinose, Kazunobu Sano, Naohiko Iwasaki, Hidekazu Takahashi, Shiro Mataka, Kouji Araki. Analysis of the dentin surface after Xe excimer lamp irradiation. The 95th General Session & Exhibition of the IADR 2017.03.22 San Francisco
2. Alireza Sadr, Juri Hayashi, Yasushi Shimada, Junji Tagami. Effects of Fiber Reinforcement on Composite Adaptation in Deep Cavities. 95th General Session & Exhibition of the IADR 2017.03.22
3. Juri Hayashi, Alireza Sadr, Tomohiro Takagaki, Tomoko Numata, Yasushi Shimada, Junji Tagami, Yasunori Sumi. 3D assessment of Bulk-fill Composites Gap Formation and Polymerization Shrinkage. 95th General Session & Exhibition of the IADR 2017.03.22
4. Amr SAAD, Go Inoue, Junji Atomura, Toru Nikaido, Junji Tagami. μ TBS of RM-GIC on demineralized root dentin with several conditioners. 95th General session & exhibition of the IADR 2017.03.22
5. Noda S, Kawashima N, Hashimoto K, Yamamoto M, Aramaki O, Tagami J, Okiji T. Effects of culture density on stem cell properties of human dental pulp stem cells. 2017.06.08
6. Junji Tagami. Keys for the Best Bonding Performance in Various Clinical Situations. IAAD 2017 Meeting, International Academy for Adhesive Dentistry 2017.06.16 The University of Pennsylvania School of Dental Medicine
7. Junji Tagami. About composite resin restoration. 2017.06.21 Showa University
8. Kajima Y, Takaichi A, Takahashi H, Wakabayashi N. Effects of support structure on the fatigue strength of additive fabrication. The 126th annual meeting of the Japan Prosthodontic society 2017.07.02 Yokohama
9. Junji Tagami. Pathophysiology and treatment guidelines of Tooth Wear. 2017.08.20
10. Junji Tagami. Direct bonding strategies in various clinical situations. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.30
11. Meet-the-Expert(Dental materials):Dental materials. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.31
12. Junji Tagami. Is bulkfill composite reliable?. IFEMA, Feria de Madrid, FDI Annual World Dental Congress 2017.08.31
13. Dhaifallah Alqarni, Keiichi Hosaka, Teerapong Mamane, Masatoshi Nakajima, Masaomi Ikeda, Junji Tagami. Effect of different surface treatments on repair μ TBS of composite bonded to resin matrix after water exposure. The 10th World Congress of International Federation of Esthetic Dentistry 2017.09.14 Toyama
14. Kazuo Hirota, Rena Takahashi, Go Inoue, Junji Tagami. No Marginal Gap Around Composite Resin Restoration with Pre-Polymerized HEMA Filler. CED-IADR/NOF Oral Health Research Congress 2017.09.23 Vienna, Austria
15. Wada Takahiro, Churei Hiroshi, Yokose Mako, Takayanagi Haruka, Iwasaki Naohiko, Ueno Toshiaki, Takahashi Hidekazu, Uo Motohiro. Evaluation of the Mechanical Properties of a Faceguard Made of Fiber-Reinforced Thermoplastics. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya, Japan
16. Naohiko Iwasaki, Maho Shiozawa, Yusuke Yamamoto, Tetsuya Suzuki and Hidekazu Takahashi. Relationship among Marginal Reproducibility, Machinability and Mechanical Property of Zirconia Blank for CAD/CAM System. International Conference on Materials and Systems for Sustainability 2017 (ICMaSS2017), 2nd International Symposium on Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development (iLIM-2) 2017.09.30 Nagoya University, Nagoya
17. Tanabe G, Hata T, Tun PS, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Effect of Molding Temperature on Peeling Energy of Laminated Mouthguards.. The 2017 ADM Annual Meeting 2017.10.07 Nuremberg

18. Takaichi A, Kajima Y, Nakamoto T, Tsutsumi Y, Nomura N, Takahashi H, Hanawa T, Wakabayashi N. Effect of adding support structures for overhanging part on fatigue strength in selective laser melting. . The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata
19. Kajima Y, Takaichi A, Nakamoto T, Nuttaphon K, Nomura N, Takahashi H, Wakabayashi N, Kawasaki A. Study on the effective condition of heat treatment on the anisotropy control of selective laser melted Co-Cr alloy.. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Niigata
20. Yusuke Yamamoto, Naohiko Iwasaki, Patcharanun Chaiamornsop, Tetsuya Suzuki. Effects of load on machinability of composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices 2017.10.14 Toki Messe, Niigata city
21. Naohiko Iwasaki, Toru Yasue, Maho Shiozawa, Yusuke Yamamoto, Shinji Tanaka, Tetsuya Suzuki, Hidekazu Takahashi.. Mechanical properties of recent composite resin blocks for CAD/CAM. The 70th General Session of the Japanese Society for Dental Materials and Devices, 2017.10.14 Toki Messe, Niigata city
22. Shin Rozan, Rena Takahashi, Toru Nikaido, Junji Tagami. The effect of resin coating technique on dentin bond strength and internal adaptation of CAD/CAM-fabricated inlays. The 147th Meeting of the Japanese Society of Conservative Dentistry 2017.10.27 Iwate, Japan
23. Ali Alqahtani, Go Inoue, Toru Nikaido, Junji Tagami. Effect of concentrations of potassium and sodium fluoride on micro-shear bond strength and inhibition of demineralization . 147st Hozon Gakkai 2017.10.27
24. Mahmoud Sayed, Naoko Matsui, Noriko Hiraishi, Go Inoue, Toru Nikaido, Junji Tagami. Evaluation of Discoloration of Demineralized Dentin with Silver Diamine Fluoride. 147st Hozon Gakkai 2017.10.27
25. Rena Takahashi, Atsuko Tagami, Toru Nikaido, Junji Tagami. The dentin bond strength of dual-cure resin cements. Brazil-Japan Joint Research Workshop on Adhesive Dentistry 2017.11.01 Campinas, Brazil
26. Takaaki Sato, Tomohiro Takagaki, Rui Guan, Nikaido Toru, Junji Tagami. Evaluation of the enamel/bond interfaces of Multimode One-bottle Self-etching Adhesives. Brazil-Japan Joint Research Workshop on ADHESIVE DENTISTRY 2017.11.01 Brazil, Piracicaba
27. Hidekazu TAKAHASHI, Naohiko IWASAKI, Tetsuya SUZUKI. FLEXURAL PROPERTIES OF RECENT COMPOSITE RESIN BLOCKS FOR CAD/CAM. 3rd ANNUAL MEETING of the IADDM 2017.12.09 Berlin, Germany
28. The evaluation of bond strength of calcium containing adhesive system to artificial demineralized dentin.
29. Toothbrushing timing after acidic drinks affects enamel loss in-situ. Boston, USA

[Awards & Honors]

1. Wilmer Souder Award, The International Association for Dental Research, 2017.03