

ANNUAL PUBLICATIONS

2020



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

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Graduate School of Medical and Dental Sciences

Medical and Dental Sciences

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Oral Pathology

Professor
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Graduate Students
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Fukawa Hironori

(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. Nguyen CTK, Sawangarun W, Mandasari M, Morita KI, Harada H, Kayamori K, Yamaguchi A, Sakamoto K. AIRE is induced in oral squamous cell carcinoma and promotes cancer gene expression. *PloS one*. 2020; 15(2); e0222689
2. Shibata Eri, Morita Kei-ichi, Kayamori Kou, Maruiwa Mayuko, Michi Yasuyuki, Sato Yukiko, Takeuchi Kengo, Ikeda Tohru, Harada Hiroyuki, Yoda Tetsuya. Report Secretory carcinoma around Stensen's duct misdiagnosed as salivary duct cyst *INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY*. 2020; 13(8); 2211-2217
3. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer science*. 2020.02;
4. Yukimori A, Tsuchiya M, Wada A, Michi Y, Kayamori K, Sakamoto K, Ikeda T. Genetic and histopathological analysis of a case of primary intraosseous carcinoma, NOS with features of both ameloblastic carcinoma and squamous cell carcinoma. *World journal of surgical oncology*. 2020.02; 18(1); 45
5. Ishii Hiroki, Saitoh Masao, Sakamoto Kaname, Sakamoto Kei, Saigusa Daisuke, Kasai Hirotake, Ashizawa Kei, Miyazawa Keiji, Takeda Sen, Masuyama Keisuke, Yoshimura Kentaro. Lipidome-based rapid diagnosis with machine learning for detection of TGF-beta signalling activated area in head and neck cancer *BRITISH JOURNAL OF CANCER*. 2020.02; 122(7); 995-1004
6. Yamamoto Daisuke, Kayamori Kou, Sakamoto Kei, Tsuchiya Maiko, Ikeda Tohru, Harada Hiroyuki, Yoda Tetsuya, Watabe Tetsuro, Hara-Yokoyama Miki. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis(和訳中) *Cancer Science*. 2020.02; 111(2); 700-712
7. Yokokawa M, Morita KI, Oikawa Y, Kayamori K, Sakamoto K, Ikeda T, Harada H. Co-expression of EGFR and MET has a synergistic effect on the prognosis of patients with oral squamous cell carcinoma *J Oral Pathol Med*. 2020.03; 49(3); 235-242
8. ゲエン・ファン・テー・フィ , 坂本 啓, 池田 通. 舌の前癌病変を示唆する組織学的特徴を同定するためのディープラーニングの応用 (Deep-learning application for identifying histological features suggestive of precancer in tongue) *日本病理学会会誌*. 2020.03; 109(1); 398
9. Hirai H, Ohsako T, Kugimoto T, Tomioka H, Michi Y, Kayamori K, Yoda T, Miura M, Yoshimura R, Harada H. Comparison of 50- and 66-Gy total irradiation doses for postoperative cervical treatment of patients with oral squamous cell carcinoma. *Oral oncology*. 2020.04; 107; 104708
10. Shimamoto H, Hirota Y, Kashima Y, Kinoshita N, Yokokawa M, Ikeda T, Harada H. Granulocyte colony-stimulating factor-producing squamous cell carcinoma of the tongue exhibiting characteristic fluorine-18 deoxyglucose accumulation on positron emission tomography-computed tomography: A case report. *World Journal Clinical Cases*. 2020.05; 8(9); 1666-1673
11. Keiko Miura, Takumi Akashi, Takeshi Namiki, Tsunekazu Hishima, Yuan Bae, Urara Sakurai, Keimei Murano, Junichi Shiraishi, Masahiro Warabi, Toru Tanizawa, Michio Tanaka, Ekapot Bhunchet, Jiro Kumagai, Shinya Ayabe, Takahiro Sekiya, Noboru Ando, Hiroshi Shintaku, Yuko Kinowaki, Shohei Tomii, Susumu Kirimura, Kou Kayamori, Kurara Yamamoto, Takashi Ito, Yoshinobu Eishi. Engrailed Homeobox 1 and Cytokeratin 19 Are Independent Diagnostic Markers of Eccrine Porocarcinoma and Distinguish It From Squamous Cell Carcinoma. *Am. J. Clin. Pathol.*. 2020.06;
12. Shibata E, Morita KI, Kayamori K, Maruiwa M, Michi Y, Sato Y, Takeuchi K, Ikeda T, Harada H, Yoda T.. Secretory carcinoma around Stensen's duct misdiagnosed as salivary duct cyst. *Int J Clin Exp Pathol*. . 2020.08; 13(8); 2211-2217
13. Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis. *Pathology international*. 2020.10;

14. Nishii N, Shimamoto H, Ohsako T, Yokokawa M, Sato Y, Ohata Y, Kayamori K, Ikeda T, Harada H. Renal cell carcinoma metastasis to the maxillary bone successfully treated with surgery after vascular embolization: a case report. *Journal of medical case reports*. 2020.10; 14(1); 193
15. Baba S, Akashi T, Kayamori K, Ohuchi T, Ogawa I, Kubota N, Nakano K, Nagatsuka H, Hasegawa H, Matsuzaka K, Tomii S, Uchida K, Katsuta N, Sekiya T, Ando N, Miura K, Ishibashi H, Ariizumi Y, Asakage T, Michi Y, Harada H, Sakamoto K, Eishi Y, Okubo K, Ikeda T. Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma. *Pathology international*. 2020.12;
16. 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

Bacterial Pathogenesis, Infection and Host Response

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Assistant Professor
SUZUKI Shiho
Research fellow of JSPS
TSUKAZAKI Masayuki
Research fellow
OKANO Tokuju
Graduate Student
ABASS Adiza (Department of Molecular Virology)
Graduate Student
BOONYALEKA Kotchakorn
Graduate Student
IWASAWA Marie
Research Co-investigator
KINOSHITA-DAITOKU Ryo (Osaka University)
Research Co-investigator
TANAKA Mototsugu (PMDA)
Technical Assistant Staff
IIDA Tamako

(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. Toma C, Suzuki T. Evaluation of Intracellular Trafficking in Macrophages. *Methods in molecular biology* (Clifton, N.J.). 2020; 2134; 199-206
2. Prah Isaac, Ayibieke Alafate, 井口 純, Mahazu Samiratu, 佐藤 和佳菜, 鈴木 敏彦, 山岡 昇司, 岩永 史朗, Ablordey Anthony, 齋藤 良一. Virulence Profile of Diarrheagenic *E. coli* from the Western region of Ghana(和訳中) *日本細菌学雑誌*. 2020.01; 75(1); 118
3. 岡野 徳壽, 鈴木 敏彦. *A. actinomycetemcomitans* induces inflammasome activation via lysosomal degradation(和訳中) *日本細菌学雑誌*. 2020.01; 75(1); 90
4. Tanaka M, Kinoshita-Daitoku R, Kiga K, Sanada T, Zhu B, Okano T, Aikawa C, Iida T, Ogura Y, Hayashi T, Okubo K, Kurosawa M, Hirahashi J, Suzuki T, Nakagawa I, Nangaku M, Mimuro H. Group A *Streptococcus* establishes pharynx infection by degrading the deoxyribonucleic acid of neutrophil extracellular traps. *Scientific reports*. 2020.02; 10(1); 3251
5. Kinoshita-Daitoku R, Kiga K, Sanada T, Ogura Y, Bo Z, Iida T, Yokomori R, Kuroda E, Tanaka M, Sood A, Suzuki T, Nakai K, Hayashi T, Mimuro H. Mutational diversity in *mutY* deficient *Helicobacter pylori* and its effect on adaptation to the gastric environment. *Biochemical and biophysical research communications*. 2020.05; 525(3); 806-811
6. Saeki A, Tsuchiya K, Suda T, Into T, Hasebe A, Suzuki T, Shibata KI. Gasdermin D-independent release of interleukin-1b by living macrophages in response to mycoplasmal lipoproteins and lipopeptides. *Immunology*. 2020.06;
7. Ashida H, Sasakawa C, Suzuki T. A unique bacterial tactic to circumvent the cell death crosstalk induced by blockade of caspase-8. *The EMBO journal*. 2020.07; e104469
8. Prah I, Ayibieke A, Huong NTT, Iguchi A, Mahazu S, Sato W, Hayashi T, Yamaoka S, Suzuki T, Iwanaga S, Ablordey A, Saito R. Virulence profile of diarrhoeagenic *Escherichia coli* from the Western region of Ghana. *Japanese journal of infectious diseases*. 2020.08;
9. Alafate Ayibieke, Ayumi Kobayashi, Masato Suzuki, Wakana Sato, Samiratu Mahazu, Isaac Prah, Miyuki Mizoguchi, Kyoji Moriya, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Prevalence and characterization of carbapenem-hydrolyzing class D β -lactamase-producing *Acinetobacter* isolates from Ghana. *Front Microbiol*. 2020.11; 11; 587398

[Misc]

1. Ashida H, Suzuki T, Sasakawa C. *Shigella* infection and host cell death: A double-edged sword for the host and pathogen survival *Current Opinion in Microbiology*. 2020.08; 59; 1-7

Molecular Immunology

Professor	Miyuki Azuma
Associate Professor	Shigenori Nagai
Assistant Professor	Yohei Kawano (~ Mar.) Chenyang Zhang (Jun. ~)
Adjunct instructor	Hiroshi Kiyono Emi Nishii Yohei Kawano (Jun. ~)
Graduate Students (Doctor)	Yue Yang (~ Mar.) Yoshihisa Kashima (Oral and Maxillofacial Surgery) (~ Mar.) Xiang Ao (Pulp Biology and Endodontics) Keeratika Wongtim Amrita Widyagarini Subagyo Droonpan Pissacha
Research Students	Farzana Sultana (Oct. ~)
Short-term exchange students	Yuto Nagatomo (Kitasato Uni.) (Oct. ~)

(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. Fujii M, Kawashima N, Tazawa K, Hashimoto K, Nara K, Noda S, Nagai S, Okiji T.. Hypoxia-inducible factor 1 α promotes interleukin 1 β and tumour necrosis factor α expression in lipopolysaccharide-stimulated human dental pulp cells. *International Endodontic Journal*. 2020.01;
2. Nakagawa D, Nakamura M, Nagai S, Aizawa M. Fabrications of boron-containing apatite ceramics via ultrasonic spray-pyrolysis route and their responses to immunocytes *J Mater Sci Mater Med..* 2020.01; 31(2); 20
3. Fujii M, Kawashima N, Tazawa K, Hashimoto K, Nara K, Noda S, Kuramoto M, Orikasa S, Nagai S, Okiji T . HIF1 α inhibits LPS-mediated induction of IL-6 synthesis via SOCS3-dependent CEBP β suppression in human dental pulp cells *Biochemical and Biophysical Research Communications .* 2020.02; 522(2); 308-314
4. Ikeda E, Shiba T, Ikeda Y, Suda W, Nakasato A, Takeuchi Y, Azuma M, Hattori M, Izumi Y. Japanese subgingival microbiota in health vs disease and their roles in predicted functions associated with periodontitis. *Odontology*. 2020.04; 108(2); 280-291
5. Kashima Y, Nishii N, Tachinami H, Furusawa E, Nagai S, Harada H, Azuma M. Orthotopic tongue squamous cell carcinoma (SCC) model exhibiting a different tumor-infiltrating T-cell status with margin-restricted CD8⁺ T cells and regulatory T cell-dominance, compared to skin SCC. *Biochem. Biophys. Res. Commun..* 2020.05; 526(1); 218-224
6. J Rodriguez-Barbosa, Azuma M, Zelinsky G, J Perez-Simon, M Del Rio. Critical role of PD-L1 expression on non-tumor cells rather than on tumor cells for effective anti-PD-L1 immunotherapy in a transplantable mouse hematopoietic tumor model. *Cancer Immunol Immunother.* 2020.06; 69(6); 1001-1014
7. Yang Y, Nagai S, Kang S, Xia Y, Kawano Y, Miyake K, Karasuyama H, Azuma M. Tolerogenic properties of CD206⁺ macrophages appeared in the sublingual mucosa after repeated antigen-painting. *International Immunology .* 2020.07; 32(8); 509-518
8. Azuma T, Sato Y, Ohno T, Azuma M, Kume H. Serum soluble B7-H3 is a prognostic marker for patients with non-muscle-invasive bladder cancer. *PloS one.* 2020.12; 15(12); e0243379

Advanced Biomaterials

Professor UO Motohiro
Assistant Professor WADA Takahiro
Graduate Student CHAIAMORNSUP Patcharanun
Graduate Student Wang Liwei
Graduate Student KOYAMA Akihiro (Orthodontic Science)
Graduate Student KINJO Rio (Sports Medicine and Dentistry)
Graduate Student Saleh Sherif Adel Abdelfattah (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. Gen Tanabe, Hiroshi Churei, Takahiro Wada, Hidekazu Takahashi, Motohiro Uo, Toshiaki Ueno. The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine *Journal of Oral Science*. 2020.01; 62(1); 23-27
2. Chaiamornsups P, Iwasaki N, Yasue T, Uo M, Takahashi H. Effects of build conditions and angle acuteness on edge reproducibility of casting patterns fabricated using digital light projection. *Dental materials journal*. 2020.01; 39(1); 135-140
3. Kusumasari C, Abdou A, Tichy A, Hatayama T, Hosaka K, Foxton RM, Wada T, Sumi Y, Nakajima M, Tagami J. Effect of smear layer deproteinization with chemo-mechanical caries removal agents on sealing performances of self-etch adhesives. *Journal of dentistry*. 2020.02; 103300
4. Minkhant Koko, Tomohiro Takagaki, Ahmed Abdou, Masanao Inokoshi, Masaomi Ikeda, Takahiro Wada, Motohiro Uo, Toru Nikaido, Junji Tagami. Effects of the ratio of silane to 10-methacryloyloxydecyl

- dihydrogenphosphate (MDP) in primer on bonding performance of silica-based and zirconia ceramics *Journal of the Mechanical Behavior of Biomedical Materials*. 2020.08; 112; 104026
5. Yuki Wakisaka, Bing Hu, Daiki Kido, Takahiro Wada, Bapurao Bharate, Quiyi Yuan, Shingo Mukai, Yasuo Takeichi, Satoru Takakusagi, Kiyotaka Asakura Asakura. Bent Crystal Laue Analyser Combined with Polarisation-Dependent Total Reflection Fluorescence Extended X-ray Absorption Spectroscopy and its Application to Surface Studies *Journal of Synchrotron Radiation*. 2020.11; 27(6); 1618-1625
 6. Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Basic properties of novel S-PRG filler-containing cement. *Dent Mater J*. 2020.12; 39(6); 963-969
 7. Takahiro Wada, Hiroshi Churei, Mako Yokose, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Application of Glass Fiber and Carbon Fiber-Reinforced Thermoplastics in Face Guards. *Polymers (Basel)*. 2020.12; 13(1); 18

[Conference Activities & Talks]

1. Hatano K, Inokoshi M, Tamura M, Shimizubata M, Wada T, Uo M, Takahashi R, Imai K, Minakuchi S. Antimicrobial effect of a novel denture adhesive containing S-PRG filler. 98th General Session & Exhibition of the IADR 2020.03
2. Takahiro Wada, Yasuhito Takashima, Rio Kinjo, Kasei Aoyagi, Hiroshi Churei, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takashi, Fumiyoshi Minami, Motohiro Uo. Strain distribution analysis of face guards made of carbon fiber-reinforced thermoplastics during shock absorption test using high-speed camera and digital image correlation. 4th open forum for "Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development" 2020.03.04 Tokyo, Japan
3. Chaiamornsop Patcharanun, Yumi Tsuchida, Naohiko Iwasaki, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi. Effects of build angle and DLP machine on adaptability of bridge casting pattern. 4th open forum for "Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development" 2020.03.04 Tokyo, Japan
4. Tonprasong W, Inokoshi M, Shimizubata M, Hatano K, Uo M, Wada T, Takahashi R, Minakuchi S. Multi ion release from S-PRG nanofiller containing tissue conditioner. The 75th General Session of the Japanese Society for Dental Materials and Devices 2020.04
5. Wada Takahiro, Kinjo Rio, Uo Motohiro. Ion-Releasing and Shock-Absorbing Properties of Surface Pre-reacted Glass-ionomer Filler in Multilayer Mouth Guards. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)
6. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Uo Motohiro, Ueno Toshiaki. Development of wearable mouth-guard device for monitoring teeth clenching during exercise. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)

Oral Radiation Oncology

Professor	Masahiko MIURA
Assistant Professor	Atsushi KAIDA Yusuke ONOZATO (~March) Hisao HOMMA (April~)
Clinical Fellow	Hitomi NOJIMA (April~)
Graduate Students	Hisao HOMMA (~March) Hitomi NOJIMA (~March) Hiroaki SHIMONO Esther NG FENG YING Kohki TOHYAMA
Adjunct Instructor	Yusuke Onozato (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. Nojima Hitomi, Homma Hisao, Onozato Yusuke, Kaida Atsushi, Harada Hiroyuki, Miura Masahiko. Differential properties of mitosis-associated events following CHK1 and WEE1 inhibitor treatments in human tongue carcinoma cells EXPERIMENTAL CELL RESEARCH. 2020.01; 386(2); 111720
2. Hirai H, Ohsako T, Kugimoto T, Tomioka H, Michi Y, Kayamori K, Yoda T, Miura M, Yoshimura R, Harada H. Comparison of 50- and 66-Gy total irradiation doses for postoperative cervical treatment of patients with oral squamous cell carcinoma. Oral oncology. 2020.04; 107; 104708
3. Hiroaki Shimono, Atsushi Kaida, Hisao Homma, Hitomi Nojima, Yusuke Onozato, Hiroyuki Harada, Masahiko Miura. Fluctuation in radioresponse of HeLa cells during the cell cycle evaluated based on micronucleus frequency. Sci Rep. 2020.11; 10(1); 20873

Oral and Maxillofacial Surgery

Professor Hiroyuki HARADA

Junior Associate Professor Yasuyuki MICHI, Fumihiko TSUSHIMA

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Yuta IKAMI, Junko TAKEI, Phung TRAN XUAN, Rika NOJI, Shiori TOKIZAKI

(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 and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 5) 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, oral mucosal disease, temporomandibular joint 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 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. Nojima H, Homma H, Onozato Y, Kaida A, Harada H, Miura M. Differential properties of mitosis-associated events following CHK1 and WEE1 inhibitor treatments in human tongue carcinoma cells *Exp Cell Res.* 2020.01; 388(2);

2. Kagifuku Y, Tohara H, Wakasugi Y, Susa C, Nakane A, Toyoshima M, Nakakuki K, Kabasawa Y, Harada H, Minakuchi S. What Factors Affect Changes in Body Composition and Swallowing Function in Patients Hospitalized for Oral Cancer Surgery? *Clin Interv Aging*. 2020.01; 15; 1-7
3. Okuyama K, Yanamoto S, Naruse T, Umeda M. Ceftriaxone-induced Epilepticus on a Patient with Renal Dysfunction Who Was Treated for Phlegmon of the Cheek: Report of a Case *Jap J Oral Diag Oral Med*. 2020.02; 33(1); 43-46
4. Furukawa K, Naruse T, Okuyama K, Yanamoto S, Katase N, Umeda M. A Case of Glandular Odontogenic Cyst in the Mandibular Region *Jap J Oral Diag Oral Med*. 2020.02; 33(1); 61-65
5. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis *Cancer Sci*. 2020.02; 111(2); 700-712
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10. Yahara H, Horita S, Yanamoto S, Kitagawa Y, Asaka T, Yoda T, Morita K, Michi Y, Takechi M, Shimasue H, Maruoka Y, Kondo E, Kusukawa J, Tsujiguchi H, Sato T, Kannon T, Nakamura H, Tajima A, Hosomichi K, Yahara K. A Targeted Genetic Association Study of the Rare Type of Osteomyelitis *J Dent Res*. 2020.03; 99(3); 271-276
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13. Takei J, Kaneko MK, Ohishi T, Kawada M, Harada H, Kato Y. A novel anti-EGFR monoclonal antibody (EMab-17) exerts antitumor activity against oral squamous cell carcinomas via antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity *Oncol Lett*. 2020.04; 19(4); 2809-2816
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15. Kato Y, Ito Y, Ohishi T, Kawada M, Nakamura T, Sayama Y, Sano M, Asano T, Yanaka M, Okamoto S, Handa S, Komatsu Y, Takei J, Kaneko MK. Antibody–drug conjugates using mouse–canine chimeric anti-dog podoplanin antibody exerts antitumor activity in a mouse xenograft model *Monoclon Antib Immunodiagn Immunother*. 2020.04; 39(2); 37-44
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39. Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis Pathol Int. 2020.10; 71(1); 80-87
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44. Nishii N, Shimamoto H, Ohsako T, Yokokawa M, Sato Y, Ohata Y, Kayamori K, Ikeda T, Harada H. Renal cell carcinoma metastasis to the maxillary bone successfully treated with surgery after vascular embolization: a case report J Med Case Rep. 2020.12; 14(1); 193
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[Conference Activities & Talks]

1. Yanagisawa S, Iseki S. Gene expression pattern in osteoblasts derived from craniosynostosis and non-craniosynostosis patients. Gordon Research Conference Craniofacial Morphogenesis and Tissue Regeneration 2020.02.23 Renaissance Tuscany Il Ciocco Lucca (Barga), Italy
2. 浅野禎三, 佐山勇輔, 佐野雅人, 武井潤子, 細野秀樹, 金子美華, 加藤幸成. RIEDL tag, a novel peptide tag system is useful for protein purification. 第 93 回日本生化学会大会 2020.09.16 横浜

3. 佐野雅人, 浅野禎三, 佐山勇輔, 武井潤子, 細野秀樹, 金子美華, 加藤幸成. DGKzeta に対する新規抗体作製とそのエピトープ解析. 第 93 回日本生化学会大会 2020.09.16 横浜
4. 奥山紘平, 鈴木啓司, 鳴瀬智史, 柳本惣市, 梅田正博, 三浦雅彦, 原田浩之. Potent reduction of cell motility on HNSCC induced by cetuximab demonstrates delayed anti-tumor effect . 第 79 回日本癌学会学術総会 2020.10.01 広島
5. 榎谷振太郎, 井上カタジナアンナ, 高橋和樹, 原田浩之, 渡部徹郎. β 2-アドレナリン受容体シグナルを標的とした口腔扁平上皮癌の進行の阻害. 第 79 回日本癌学会学術総会 2020.10.01 広島
6. 武井潤子, 金子美華, 大石智一, 佐山勇輔, 川田 学, 原田浩之, 加藤幸成. Development of a monoclonal antibody against human epidermal growth factor receptor 2 (HER2). 第 79 回日本癌学会学術総会 2020.10.01 広島
7. 佐山勇輔, 武井潤子, 大石智一, 金子美華, 川田 学, 加藤幸成. Antitumor activity against breast cancer using a novel anti-TROP2 monoclonal antibody. 第 79 回日本癌学会学術総会 2020.10.01 広島
8. Sakakitani S, Podyma-Inoue KA, Takahashi K, Harada H, Watabe T. Inhibition of oral squamous cell carcinoma progression by targeting β 2-adrenergic receptor signals. 2020.12.04 Tokyo
9. Sato H, Chen P, Ashida M, Tsutsumi Y, Harada H, Hanawa T. Cytocompatibility of new designed Zr-14Nb-5Ta-1Mo alloy with mouse osteoblastic cells. 第 3 回日本金属学会 2020.12.12 Web 開催

Oral and Maxillofacial Radiology

Professor: Tohru KURABAYASHI
Associate Professor: Hiroshi WATANABE
Junior Associate Professor: Naoto OHBAYASHI
Assistant Professor: Shin NAKAMURA, Ami KURIBAYASHI, Junichiro SAKAMOTO
Hospital Staff: Yoshikazu NOMURA, Mamiko FUJIKURA
Graduate Student: Sakurako ASAI, Miharuru TAGUCHI, Natnisha PEERAPONG
Secretary:

(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. Ohsako T, Shimamoto H, Tomioka H, Hirai H, Kuroshima T, Mochizuki Y, Kugimoto T, Tsushima F, Nakamura S, Kurabayashi T, Harada H. Detection of extraoral primary cancers by positron emission tomography/computed tomography in patients with oral squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2020; 129(3); 272-276
2. Awuti S, Sumita YI, Hattori M, Yoshi S, Kelimu S, Ohbayashi N, Kurabayashi T, Taniguchi H. Morphological comparison of artificial teeth position utilising denture space in glossectomy patients. *Gerodontology.* 2020; 37(1); 72-77

3. Sakaguchi-Kuma T, Ishida Y, Oishi S, Kurabayashi T, Ono T. Cone-beam computed tomography-based quantitative analysis of the thickness of mandibular alveolar bone in adult females with different vertical facial patterns. *APOS Trends in Orthodontics*. 2020; 10(1); 25-31
4. Teramoto A, Suzuki S, Higashihori N, Ohbayashi N, Kurabayashi T, Moriyama K. 3D evaluation of the morphological and volumetric changes of the tongue and oral cavity before and after orthognathic surgery for mandibular prognathism: a preliminary study *Prog Orthod*.. 2020; 21(1); 30
5. Kawasaki K, Sugawara S, Watanabe K, Hong C, Tu TTH, Watanabe T, Sakamoto J, Yoshino N, Suga T, Mikuzuki L, Takenoshita M, Takada S, Kurabayashi T, Toyofuku A. Differences in the Clinical Characteristics of Persistent Idiopathic Facial Pain (Atypical Odontalgia) Patients with or Without Neurovascular Compression of the Trigeminal Nerve. *Pain medicine (Malden, Mass.)*. 2020.02;
6. Taguchi M, Wamasing P, Watanabe H, Sakamoto J, Kurabayashi T. Applying the paralleling technique in periapical radiographs for Japanese patients by analyzing CT images. *Oral Radiology*. 2020.06;
7. Yamada I, Oshima N, Wakana K, Miyasaka N, Wakabayashi A, Sakamoto J, Saida Y, Tateishi U, Kobayashi D. Uterine Cervical Carcinoma: Evaluation Using Non-Gaussian Diffusion Kurtosis Imaging and Its Correlation With Histopathological Findings. *Journal of computer assisted tomography*. 2020.06;
8. Asai S, Nakamura S, Toriihara A, Tateishi U, Kurabayashi T. Quantitative evaluation of bone single-photon emission computed tomography using Z score analysis in patients with mandibular osteomyelitis *Oral Radiology*. 2020.07; 36(3); 267-274
9. Nomura Y, Watanabe H, Manila NG, Asai S, Kurabayashi T. Evaluation of streak metal artifacts in cone beam computed tomography by using the Gumbel distribution: a phantom study *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2020.08;
10. Kurabayashi T, Ohbayashi N, Sakamoto J, Nakamura S. Usefulness of MR imaging for odontogenic tumors. *Odontology*. 2020.10;
11. Kayamori K, Tsuchiya M, Michi Y, Kuribayashi A, Mikami T, Sakamoto K, Yoda T, Ikeda T. Primordial odontogenic tumor occurred in the maxilla with unique calcifications and its crucial points for differential diagnosis. *Pathology international*. 2020.10;

[Conference Activities & Talks]

1. 道 泰之, 加地博一, 土谷麻衣子, 栢森 高, 坂本潤一郎, 依田哲也, 原田浩之. 下顎に発生した Mixed phenotype acute leukemia/lymphoma の 1 例. 第 65 回日本口腔外科学会総会・学術大会 2020.11.13

Department of Dental Anesthesiology and Orofacial Pain Management

Associate Professor

Ryo WAKITA

Junior Associate Professor

Akira NISHIYAMA , Tomoka MATSUMURA

Assistant Professors

Yukiko Baba, Takuya FUNAYAMA, Yoko YAMAZAKI

Specially Appointed Assistant Professor

Hiroyuki ISHIYAMA, Hiroko IMURA, Atsushi NAKAJIMA

Hospital Staffs

Yushi ABE, Nanako IKEDA, Takaya ITO, Kotomi UCHINUMA,
Hiroko KIMURA, Yu SATO, Maya SAKAMOTO, Shouko TOBE,
Miho HANAOKA, Yuusuke HARADA, Keisuke MIYAZONO

Graduate Students

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Ken TAKAHASHI, KAY THWE YE MIN SOE, Masako TOBE,
Akitoshi HOSODA, Keisuke MIYAZONO

Research Students

Hidemasa KUSUNOKI, Chihiro KUTSUMIZU,
THUNSHUDA SUMPHAO-NGERN, Satoshi YAMADA, Li Xinyue

(1) Outline

Our department is responsible for both dental anesthesiology and orofacial pain control. In addition, orofacial pain control consists of orofacial pain clinic and TMD clinic (former TMJ clinic). In the field of dental anesthesiology, the aim is to provide safe and painless dental treatment. The education includes lectures and practical training on local anesthesia, general anesthesia, sedation, and monitoring. In addition, basic and clinical research is conducted to achieve the above objectives. The number of cases of general anesthesia and sedation is about 1,000 and 2,000, respectively, per year, which is the largest number of anesthesia management among public universities in Japan. In the field of oral and maxillofacial anesthesiology, the orofacial pain clinic and TMJ outpatient clinic are staffed by dedicated specialists.

(2) Research

- 1) Development of a non-invasive drug delivery system
- 2) Development of a new local anesthesia method for dentistry
- 3) Elucidation of the etiology of neuropathic pain in the maxillofacial region and its treatment
- 4) Clinical research on psychosedation and systemic management in dentistry
- 5) Elucidation of the pathogenesis of temporomandibular joint disorder and the relationship between social,

psychological and dental factors

(3) Education

The purpose of our department is to provide knowledge and basic skills in local anesthesia for daily dental practice, sedation and general anesthesia for specialized anesthesia management, systemic management of patients with complications, and maxillofacial pain treatment. Lectures are given on dental anesthesia (general anesthesia, local anesthesia, sedation, cardiopulmonary resuscitation), orofacial pain clinic, temporomandibular disorders (TMD), and bruxism. In the section on general anesthesia, students learn the physiology of respiration and circulation, and the pharmacological effects and mechanisms of inhaled anesthetics, intravenous anesthetics, and muscle relaxants. In the section on sedation, students learn about the differences between general anesthesia and sedation. As a first aid training, students learn not only basic life support but also advanced life support using a cardiopulmonary resuscitation training system. In ofofacial pain clinic, students are instructed on the basis of physiology and pharmacology as a field of neuroscience. In TMD and bruxism, we teach not only anatomy and dentistry of temporomandibular joint and masticatory muscles, but also social and psychological factors that may be involved in TMD and bruxism.

(4) Clinical Services & Other Works

In the operating room, about 1,000 cases of general anesthesia are performed annually for oral surgery. These include lengthy surgeries like as reconstruction with free flap, and 2 jaw osteotomies. In the outpatient dental anesthesia clinic, we perform more than 2,000 sedation procedures per year to treat patients, who is difficult to receive in general dentistry, as well as long procedures such as implant-related procedures. In addition, we respond promptly to emergencies that occur in our hospital on average several times a month, and if necessary, we collaborate with the ER of the medical school hospital. The Department of Orofacial Pain Clinic and the Department of Temporomandibular Joint Treatment are two of the few specialized outpatient clinics in Japan, and we accept referrals from inside and outside the hospital. In the Orofacial Pain Clinic, we mainly treat neuropathic pain and trigeminal neuralgia, and provide multidisciplinary treatment with medication, nerve blocks, oriental medicine and physical therapy. In the outpatient clinic for temporomandibular joint, after definitive diagnosis by imaging, we provide treatment based on lifestyle and self-management approaches.

(5) Publications

[Original Articles]

1. Takaya Ito, Atsushi Sakai, Motoyo Maruyama, Yoshitaka Miyagawa, Takashi Okada, Haruhisa Fukayama, Hidenori Suzuki. Dorsal Root Ganglia Homeobox downregulation in primary sensory neurons contributes to neuropathic pain in rats. *Mol Pain*. 2020.01; 16; 1744806920904462
2. Nguyen Ngan G. K., Nishiyama Akira, Shimada Masahiko. A rat model for inducing temporomandibular anterior disc displacement experimentally *JOURNAL OF ORAL SCIENCE*. 2020.01; 62(1); 70-74
3. Satokawa C, Nishiyama A, Suzuki K, Uesugi S, Kokai S, Ono T. Evaluation of tissue oxygen saturation of the masseter muscle during standardised teeth clenching. *Journal of oral rehabilitation*. 2020.01; 47(1); 19-26
4. Nguyen Ngan G.K., Nishiyama Akira, Shimada Masahiko. A rat model for inducing temporomandibular anterior disc displacement experimentally *Journal of Oral Science*. 2020.01; 62(1); 70-74
5. Ayuse Takao, Okayasu Ichiro, Tachi-Yoshida Mizuki, Sato Jun, Saisu Hironori, Shimada Masahiko, Yamazaki Yoko, Imura Hiroko, Hosogaya Naoki, Nakashima Sawako. Examination of pain relief effect of Goreisan for glossodynia *MEDICINE*. 2020.08; 99(33); e21536

6. Ikeda N, Matsumura T, Kono H, Baba Y, Hanaoka M, Fukayama H. Combined Use of a Gum Elastic Bougie and Video Laryngoscopy for Intubating a Patient With an Unexpected Laryngeal Papilloma. *Anesthesia progress*. 2020.12; 67(4); 230-232
7. Nanako Ikeda, Tomoka Matsumura, Haruna Kono, Yukiko Baba, Miho Hanaoka, Haruhisa Fukayama. Combined use of a gum elastic bougie and video laryngoscopy for intubating a patient with an unexpected laryngeal papilloma *Anesthesia Progress*. 2020.12; 67(4); 230-232

[Misc]

1. Hideshima M, Ishihara N, Ishiyama H. Oral appliance therapy for sleep apnea and development of the prognosis model for treatment effect *Cell*. 2020.09; 52 (697); 570-573

[Conference Activities & Talks]

1. Ito Takaya, Sakai Atsushi, Maruyama Motoyo, Miyagawa Yoshitaka, Okada Takashi, Fukayama Haruhisa, Suzuki Hidenori. Dorsal Root Ganglia Homeobox (DRGX) in the DRG neurons is involved in neuropathic pain. The 93rd Annual Meeting of the Japanese Pharmacological Society 2020.03.18 PACIFICO Yokohama
2. Tomoka Matsumura, Yoshiyuki Ishida, Daisuke Watanabe. Dental anesthesia and society. The 48th Annual Meeting of the Japanese Dental Society of Anesthesiology 2020.10 on line
3. A case of using Japanese traditional medicine for treatment of mandibular osteomyelitis. 2020.10

Pediatric Dentistry/ Special Needs Dentistry

Professor

Tsutomu Iwamoto (May-)

Associate Professor

Michiyo Miyashin (-Mar)

Junior Associate Professor

Satoko Kakino

Assistant Professor

Yasuka Kusumoto, Tomoki Uehara, Kanae Wada

Project assistant professor

Atsushi Oishi, Taiji Hoshiai

Hospital staff

Yuko Seki, Shigeki Nagahiro(Apr-), Haruka Naito(Apr-), Kaori Konuma(Apr-), Kaori Kohi, Taki Sekiya(-Mar),
Emi Furusawa(-Mar), Kenichi Miura(-Mar),
Kie Aida, Anna Kumakura, Kana Hayashi

Graduate Student

Erika Kubota, Shigeki Nagahiro(-Mar), Aiko Hoshiai, Rika Kodama, Manami Takenoshita,
Amrita Widyagarini Subagyo(-Mar), Cho Li, Yujeong Shin, Yusuke Iwabuchi

Research Student

Emi Kanai, Kaori Konuma(-Mar), Haruka Naito(-Mar), Karen Inoue, Daishi Saito, Yumiko Nakashima(Apr-),
Yoshihito Yamakawa(Apr-)

Special Research Student

Rika Kurogoshi

Adjunct Lecturer

Ryu Matsubara, Natsumi Tsuchihashi, Takeshi OKamura, Shoji Takahashi, Asuri Jayawarudeina, Yuko Matumura,
Makiko Takashi, Taki Sekiya(Apr-), Kennichi Miura(Apr-),
Jo Inada, Yosuke Kinoshita, Seiji Sakurai, Osamu Shinozuka, Tomo Suzuki, Goro Sekiguchi, Yohei Takeuchi, Shohei Tamura,
Moriyuki Nakamura

(1) Publications

[Original Articles]

1. Shigeki Nagahiro, Tomoki Uehara, Mariko Yamamoto Kawai, Preksa Keo, Toshimi Sato, Hiroki Ochi, Shingo Sato, Shinji Kuroda, Takashi Ono, Michiyo Miyashin, Kazuhiro Aoki. RANKL-binding peptide promotes ectopic bone formation induced by BMP-2 gene transfer in murine gastrocnemius muscle Dental, Oral and Maxillofacial Research. 2020.01; 6(1); 1-6

2. Komuro Hiroaki, Wint Wit Y., Horiuchi Naohiro, Nozaki Kosuke, Sasano Tetsuo, Miyashin Michiyo, Yamashita Kimihiro, Nagai Akiko. An oriented hydroxyapatite film with arrayed plate-like particles enhance chondrogenic differentiation of ATDC5 cells JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A. 2020.03; 108(3); 537-544
3. Kusumoto Yasuka, Imai Kohsuke, Ohyama Yoshio, Fukayama Haruhisa, Shinozuka Osamu. Oral management of a patient with down syndrome and agammaglobulinemia: a case report BMC ORAL HEALTH. 2020.03; 20(1);
4. Funada K, Yoshizaki K, Miyazaki K, Han X, Yuta T, Tian T, Mizuta K, Fu Y, Iwamoto T, Yamada A, Takahashi I, Fukumoto S. microRNA-875-5p plays critical role for mesenchymal condensation in epithelial-mesenchymal interaction during tooth development. Scientific reports. 2020.03; 10(1); 4918
5. Nakamura T, Iwamoto T, Nakamura HM, Shindo Y, Saito K, Yamada A, Yamada Y, Fukumoto S, Nakamura T. Regulation of miR-1-Mediated Connexin 43 Expression and Cell Proliferation in Dental Epithelial Cells. Frontiers in cell and developmental biology. 2020.03; 8; 156
6. Keo P, Matsumoto Y, Shimizu Y, Nagahiro S, Ikeda M, Aoki K, Ono T. . A pilot study to investigate the histomorphometric changes of murine maxillary bone around the site of mini-screw insertion in regenerated bone induced by anabolic reagents. European journal of orthodontics. . 2020.03;
7. N Ogasawara, F Kano, N Hashimoto, H Mori, Y Liu, L Xia, T Sakamaki, H Hibi, T Iwamoto, E Tanaka, A Yamamoto. Factors secreted from dental pulp stem cells show multifaceted benefits for treating experimental temporomandibular joint osteoarthritis. Osteoarthritis Cartilage. 2020.06; 28(6); 831-841
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9. Chiba Y, Yoshizaki K, Saito K, Ikeuchi T, Iwamoto T, Rhodes C, Nakamura T, de Vega S, Morell RJ, Boger ET, Martin D, Hino R, Inuzuka H, Bleck CKE, Yamada A, Yamada Y, Fukumoto S. G-protein coupled receptor Gpr115 (Adgrf4) is required for enamel mineralization mediated by ameloblasts. The Journal of biological chemistry. 2020.08;
10. Ijbara Manhal, Wada Kanae, Wada Junichiro, Jayawardena Jayanetti Amiri, Miyashin Michiyo. Replica-based inspection of enamel wear microfeatures Bio-Medical Materials and Engineering. 2020.11; 31(5); 279-290
11. Dar Oo Thaw, Kakino Satoko, Kusano Masahiko, Ikeda Hideharu, Miyashin Michiyo, Okiji Takashi. Transmitted-light plethysmography detects changes in human pulpal blood flow elicited by innocuous tooth cooling and foot heating ARCHIVES OF ORAL BIOLOGY. 2020.11; 119; 104881
12. Nakamura T, Iwabuchi Y, Hirayama S, Narisawa N, Takenaga F, Nakao R, Senpuku H. Roles of membrane vesicles from Streptococcus mutans for the induction of antibodies to glucosyltransferase in mucosal immunity. Microbial pathogenesis. 2020.12; 149; 104260
13. Ryoko Hino, Aya Yamada, Yuta Chiba, Keigo Yoshizaki, Emiko Fukumoto, Tsutomu Iwamoto, Yuriko Maruya, Keishi Otsu, Hidemitsu Harada, Kan Saito, Satoshi Fukumoto. Melnick-Needles syndrome associated molecule, Filamin-A regulates dental epithelial cell migration and root formation Pediatric Dental Journal. 2020.12; 30(3); 208-214

[Books etc]

1. Miyashin Michiyo. Clinical approach for dental trauma of children. Quintessens Publishing Japan, 2020.12 (ISBN : 978-4781207865)

[Conference Activities & Talks]

1. Satoko Kakino, Yuko Seki, Karen Inoue, Michiyo Miyashin. Intentional replantation for Dens Invaginatus with endodontic-periodontal disease. 2020.05.21
2. Miyashin Michiyo. CAPS educational activity in Dental Hospital. 2020.08.02

[Works]

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

Orthodontic Science

Professor	Takashi ONO
Associate Professor	
Junior Associate Professor	Yoshiro MATSUMOTO, Zusei KANNO (-Mar), Jun HOSOMICHI
Assistant Professor	Kazuo SHIMAZAKI (-Mar), Ippei WATARI, Ikuo YONEMITSU Yuji ISHIDA, Takayoshi ISHIDA, Risa USUMI
Project Assistant Professor	Chiho KATO, Shuji OISHI (-Mar), Hidemasa OKIHARA (Apr-)
Dental Resident	Hiroko OHMORI (Apr-), Hidemasa OKIHARA (-Mar), Yasunori ABE (-Mar) Takuya OGAWA, Asuka MANABE
Graduate Students	Eri SAITO, Edward CHO, Erika OZAWA, Shin-Sheng Yang (-Mar), Thi Kim Uyen DONG Yuta UCHIKAWA (-Mar), Akihiro KOYAMA (-Mar), Sun-min KIM Thura AUNG PHYO (-Jun), Ryo KIMURA, Shahriar Mohd SHAMS, Haixin HONG Anindya Kamaratih GUNARSO, Kai LI Sasin SRITARA, Hideyuki ISHIDORI, Seiko ISHIIHARA Aiko TAKADA, Yoshiyuki HAMADA Akiyo FUJITA, Ahmad F J M SH ALSULAILI Saranya SERIRUKCHUTARUNGSEE, Yixin LOU Keita ISHIZUKA, Mirei KEITOKU, Rikima TAKANO Eri MISAWA, Kitanon ANGKANAWARAPHAN (-Jul) Ruixin LI, Chun Shuo HUANG, Wenqian SUN Masato AKAKURA (Apr-), Shuntaro IWAKI (Apr-), Takumi SUZUKI (Apr-) Yuka TANAKA (Apr-), Moe TANIGAWA (Apr-), Naomi TOYAMA (Apr-)
Graduate School Research Students	Yukano FUKUSHIMA (-Mar), Yuta NAKAI Masamu INOUE, Moe SATO, Kasumi HATANO, Keiko HATANO, Makiko OKUZAWA Masako KAWADA, Shuko ARAI, Aiko ISHIZAKI, Misa TAKAHASHI Kazuki SAWAYA, Chiyo SHIMIZU, Naoaki MIKAMI Yumi NAKANO (Apr-), Saori WATAYA (Apr-), Doyoon KIM (Oct-), Jia QI (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. Satokawa C, Nishiyama A, Suzuki K, Uesugi S, Kokai S, Ono T. Evaluation of tissue oxygen saturation of the masseter muscle during standardised teeth clenching. *Journal of oral rehabilitation*. 2020.01; 47(1); 19-26
2. Aung PT, Kato C, Abe Y, Ogawa T, Ishidori H, Fujita A, Okihara H, Kokai S, Ono T. Functional analysis of rhythmic jaw movements evoked by electrical stimulation of the cortical masticatory area during low occlusal loading in growing rats. *Frontiers in Physiology*. 2020.01; 11; 34
3. Kita S, Fujita K, Imai H, Aoyagi M, Shimazaki K, Yonemitsu I, Omura S, Ono T. Postoperative stability of conventional bimaxillary surgery compared with maxillary impaction surgery with mandibular autorotation for patients with skeletal class II retrognathia. *British Journal of Oral and Maxillofacial Surgery*. 2020.01; 58(1); 57-61
4. Yang W, Podyma-Inoue KA, Yonemitsu I, Watari I, Ikeda Y, Guo X, Watabe T, Ono T. Mechanoresponsive and lubricating changes of mandibular condylar cartilage associated with mandibular lateral shift and recovery in the growing rat. *Clinical Oral Investigations*. 2020.02;
5. Guo X, Watari I, Ikeda Y, Yang W, Ono T. Effect of functional lateral shift of the mandible on hyaluronic acid metabolism related to lubrication of temporomandibular joint in growing rats. *European Journal of Orthodontics*. 2020.02;
6. Wu Yang, Katarzyna Anna Podyma-Inoue, Ikuo Yonemitsu, Ippei Watari, Yuhei Ikeda, Xiyuan Guo, Tetsuro Watabe & Takashi Ono . Mechanoresponsive and lubricating changes of mandibular condylar cartilage associated with mandibular lateral shift and recovery in the growing rat *Clinical Oral Investigations*. 2020.02;
7. Yang SS, Ishida T, Fujita K, Nakai Y, Ono T, Okazawa H. PQBP1, an intellectual disability causative gene, affects bone development and growth. *Biochem Biophys Res Commun*. 2020.03; 523(4); 894-899
8. Keo P, Matsumoto Y, Shimizu Y, Nagahiro S, Ikeda M, Aoki K, Ono T. A pilot study to investigate the histomorphometric changes of murine maxillary bone around the site of mini-screw insertion in regenerated bone induced by anabolic reagents. *European journal of orthodontics*. 2020.03;
9. Hong H, Hosomichi J, Maeda H, Lekvijittada K, Oishi S, Ishida Y, Usumi-Fujita R, Kaneko S, Suzuki JI, Yoshida KI, Ono T. Intermittent hypoxia retards mandibular growth and alters RANKL expression in adolescent and juvenile rats. *European Journal of Orthodontics*. 2020.03;
10. Koyama A, Ono T, Uo M, Kiyokawa H, Ohira N, Shima Y, Kanno Z. Improvement of binding friction between stainless steel orthodontic wire and bracket by performing Rh-PTFE composite plating on the wire. *Orthodontic Waves*. 2020.03; 79(1); 39-47
11. Kato C, Kokai S, Ono T. Orthodontic movement of a contralateral maxillary central incisor across the midpalatal suture. *APOS Trends in Orthodontics*. 2020.03; 10(1); 50-59
12. Sakaguchi-Kuma T, Ishida Y, Oishi S, Kurabayashi T, Ono T. Cone-beam computed tomography-based quantitative analysis of the thickness of mandibular alveolar bone in adult females with different vertical facial patterns. *APOS Trends in Orthodontics*. 2020.03; 10; 25-31
13. Imamura T, Uesugi S, Ono T. Unilateral maxillary central incisor root resorption after orthodontic treatment for Angle Class II, division 1 malocclusion with significant maxillary midline deviation: A possible correlation with root proximity to the incisive canal. *Korean Journal of Orthodontics*. 2020.05; 50(3); 216-226
14. Oishi S, Ishida Y, Matsumura T, Kita S, Sakaguchi-Kuma T, Imamura T, Ikeda Y, Kawabe A, Okuzawa M, Ono T. A cone-beam computed tomographic assessment of the proximity of the maxillary canine and posterior teeth to the maxillary sinus floor: Lessons from 4778 roots. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2020.06; 157(6); 792-802

15. Saito E, Watari I, Mizumachi-Kubono M, Hsu-Hayashi S, Ono T. Occlusional modifications reversibly alter aquaporin 5 expression and localization in rat salivary glands. *Frontiers in Physiology*. 2020.06; 11; 528
16. Okuzawa-Iwasaki M, Ishida Y, Ikeda Y, Imamura T, Oishi S, Kita S, Matsumura T, Sakaguchi-Kuma T, Ono T. Alveolar bone morphology in patients with a unilateral palatally displaced maxillary lateral incisor: A cone-beam computed tomography study. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2020.07; 158(1); 28-34
17. Okihara H, Ono T. Correction of bilateral heavily impacted second molar with improved super-elastic nickel-titanium alloy wires. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2020.07; 158(1); 114-125
18. Imai H, Fujita K, Yamashita Y, Yajima Y, Takasu H, Takeda A, Honda K, Iwai T., Mitsudo K., Ono T, Omura S. Accuracy of mandible-independent maxillary repositioning using pre-bent locking plates: a pilot study *International Journal of Oral and Maxillofacial Surgery*. 2020.07; 49(7); 901-907
19. Suga T, Tu TTH, Takenoshita M, Higashihori N, Kabasawa Y, Ono T, Moriyama K, Toyofuku A. Psychosocial Indication for Orthognathic Surgery in Patients with Psychiatric Comorbidities. *Psychiatry and clinical neurosciences*. 2020.08;
20. Kuma YI, Hosomichi J, Maeda H, Oishi S, Usumi-Fujita R, Shimizu Y, Kaneko S, Suzuki JI, Yoshida KI, Ono T. Intermittent hypoxia induces turbinate mucosal hypertrophy via upregulating the gene expression related to inflammation and EMT in rats. *Sleep and Breathing*. 2020.08;
21. Miki H, Okito A, Akiyama M, Ono T, Tachikawa N, Nakahama KI. Genetic and epigenetic regulation of osteopontin by cyclic adenosine 3' 5'-monophosphate in osteoblasts. *Gene*. 2020.08; (763); 145059
22. Keiichi Hosaka, Antonin Tichy, Yasuji Motoyama, Koji Mizutani, Wei-Jen Lai, Zusei Kanno, Junji Tagami, Masatoshi Nakajima. Post-orthodontic recontouring of anterior teeth using composite injection technique with a digital workflow. *J Esthet Restor Dent*. 2020.10; 32(7); 638-644
23. Ono T. Should the "envelope of discrepancy" be revised in the era of three-dimensional imaging? *Journal of the World Federation of Orthodontists*. 2020.10; 9(3S); S59-S66
24. Shima Y, Takemoto K, Koyama A, Uo M, Ono T. Comparative evaluation of square and rectangular slot three-point play behavior. *Dental Materials Journal*. 2020.10; 39(5); 735-741
25. Miwa K, Tsutsumi M, Fukino K, Eguchi K, Okada R, Akita K. An anatomical atudy of the anterior wall of the hypopharyngeal and the cervical esophageal junction. *Auris Nasus Larynx*. 2020.10; 47(5); 849-855
26. Sritara S, Tsutsumi M, Fukino K, Matsumoto Y, Ono T, Akita K. Evaluating the morphological features of the lateral pterygoid insertion into the medial surface of the condylar process. *Clinical and experimental dental research*. 2020.11;
27. Naito S, Kato C, Yabushita T, Ono T. Functional changes in the temporomandibular joint mechanoreceptors associated with experimentally induced condylar resorption in rats. *Angle Orthodontist*. 2020.11; 90(6); 831-836

[Conference Activities & Talks]

1. Phyo Thura Aung, Chiho Kato, Yasunori Abe, Takuya Ogawa, Hideyuki Ishidori, Akiyo Fujita, Ruixin Li, Hidemasa Okihara, Satoshi Kokai, Takashi Ono. LOW OCCLUSAL LOADING AFFECTS THE NEUROMUSCULAR CONTROL OF JAW MOVEMENTS INDUCED BY ANTERIOR PART OF CORTICAL MASTICATORY AREA IN GROWING RATS. 9th International Orthodontic Congress 2020.10.04 Pacific Yokohama
2. Imai H, Fujita K, Honda K, Minamiyama S, Yamashita Y, Tasuku H, Omura S, Hirota M, Mitsudo K, Ono T . Accuracy of mandible-independent maxillary repositioning with pre-bent locking plates and CAD/CAM osteotomy guides. The 9th International Orthodontic Congress 2020.10.04
3. Okihara H, Ono T. Mandibular advancement of a patient with a retruded mandible secondary to trauma by sagittal split ramus osteotomy. The 9th International Orthodontic Congress 2020.10.04

4. Kato C, Watari I, Arai S, Ono T. Factors associated with eruption periods of impacted third molars showing complete root formation after second molar extraction. The 9th International Orthodontic Congress 2020.10.04
5. Saito E, Watari I, Mizumachi-kubono M, Hsu-Hayashi S, Ono T. Occlusional modifications reversibly alter aquaporin 5 expression and localization in rat salivary glands. The 9th International Orthodontic Congress 2020.10.04
6. Angkanawaraphan K, Hosomichi J, Maeda H, Changsiripun C, Haixin H, Ono T. Effects of intermittent hypoxia on learning and memory functions in infant rats. The 9th International Orthodontic Congress 2020.10.04
7. Lekvijittada K, Hosomichi J, Maeda H, Hong H, Changsiripun C, Kuma Y, Oishi S, Suzuki JI, Yoshida KI, Ono T. Intermittent hypoxia inhibits mandibular cartilage growth by reducing TGF- β and SOX9 expression levels in infant rats. The 9th International Orthodontic Congress 2020.10.04
8. Ohmori H, Kirimoto H, Ono T. The relationship among food textures, the autonomic nervous system activity and cerebral circulation during mastication. The 9th International Orthodontic Congress 2020.10.04
9. Fujita K, Omura S, Imai H, Honda K, Takeda A, Minamiyama S, Yamashita Y, Takasu H, Usumi-Fujita R, Iwai T, Hirota M, Mitsudo K, Ono T. Prospective condylar changes of MAC surgery (maxillary impaction surgery with mandibular autorotation) compared with conventional bimaxillary surgery for skeletal Class II retrognathia patients. The 9th International Orthodontic Congress 2020.10.04
10. Yonemitsu I, Omura S, Fujita K, Kimizuka S, Imai H, Honda K, Shimazaki K, Ono T. Accurate postero-superior movement of the maxilla using an SLM technique to treat a patient with skeletal class II malocclusion with a gummy smile. The 9th International Orthodontic Congress 2020.10.04

Cariology and Operative Dentistry

Professor: Junji Tagami

Associate Professor: Masayuki Otsuki

Junior Associate Professor: Masatoshi Nakajima, Noriko Hiraish (January ~)

Assistant Professor: Takako Yoshikawa, Go Inoue, Keiichi Hosaka, Rena Takahashi, Naoko Mastui (~ March)

Hospital Staff: Takaaki Sato, Kento Sato, Takashi Hatayama (~ March), Nami Takashino, Ayako Nakamoto,

Daisuke Araoka (~ March), Akifumi Takahashi (~ March), Yusuke Kuno (April ~), Daiki Nagano (April ~), Shigeki Uchinuma (April ~),

Specially Appointed Assistant Professor: N. H. M. Khairul Matin, Hisaichi Nakagawa (April ~), Tomoko Tabata (April ~)

Staff Assistant: Shiori Ogi, Takako Nakagawa (~ December)

Graduate Student: Sae Akehashi (~ March), Nao Kominami (~ March), Yuna Kanamori (~ March),

Yukina Ochiai (~ March), Kurumi Ide (~ March), Yusuke Kuno (~ March), Yuki Ito (~ March), Shigeki Uchinuma (~ March), Daiki Nagano (~ March), Yusuke Kakiuchi (~ March), Akira Nakane (~ March),

RIMA ZAKZOUK (~ September), HALABI SOMAYAH ABDULRAHMAN A, RUMMANI GHASSAN MAHMOOD S, ALQAHTANI ALI AWAD M, ARAVETI SANDEEP

KUMAR (~ September), HOSEA LAL RIN MUANA (~ September),

SAI KHAM LYANN (~ September), 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,

Motoi Takahashi, Kim Seunggun, Kyoko Ishikawa, Toyoaki Kobayashi, Miyuki Shimizu,

Mayu Hasegawa, Shun Kobayashi, Nanako Ueda, Misa Kashiwa, Saki Uchiyama, Yosuke Minato,

Yuta Baba, LEILA NASIRY KHANLAR, VICHEVA MARTINA GEORGIEVA, Citra Kusumasari,

Min Khant Ko Ko, Pa Pa Kay Khine, MULTUZA AYED ALI (April ~), WAHYUNI SUCI DWIANDHANY,

Mayuri Nshimaki, Ryuta Andou, Shiori Yamamoto, Ayaka Sato, Yorichika Shioya, Yusuke Koshimitsu,

Chin Akane, Yutaro Oda, SAEED, NOORULDEEN ALI, MURTUZA AYED ALI, TICHY ANTONIN,

Yutaro Motoyama (April ~), Ako YAamashita (April ~), Kiyoka Furusawa (April ~), Satoshi Akiya

(April ~), Yuko Ogawa (April ~), Aya Ishizaka (April ~ September), Seiki Nakano (April ~ June),

KITTISAK SANON (April ~), SOE KAY THWE NAING (October ~), QI FENG (April ~),

TAGHREED ABDULRAHMAN ALREFAIE (April ~), Research Student: Shinji Ogura, Mineo Kijima,

WEI DIANTONG, RIMA ZAKZOUK (October ~)

(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 dentistry. 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. [Cariology and Operative Dentistry : Hasegawa Mayu] Mayu HASEGAWA, Antonin TICHY, Keiichi HOSAKA, Yusuke KUNO, Masaomi IKEDA, Kosuke NOZAKI, Ayaka CHIBA, Masatoshi NAKAJIMA*, Junji TAGAMI. Degree of conversion and dentin bond strength of light-cured multi-mode adhesives pretreated or mixed with sulfinate agents *Dental Materials Journal* . 2020;
2. [Oral Prosthetic Engineering : IKEDA Masaomi] Ko AK, Matsui N, Nakamoto A, Ikeda M, Nikaido T, Burrow MF, Tagami J. Effect of silver diammine fluoride application on dentin bonding performance. *Dental materials journal*. 2020.01;
3. [Cariology and Operative Dentistry : TAGAMI Junji] Sandeep Kumar Araveti, Noriko Hiraishi, Nao Kominami, Masayuki Otsuki, Yasunori Sumi, Cynthia K Y Yiu, Junji Tagami. Swept-source optical coherence tomographic observation on prevalence and variations of cemento-enamel junction morphology. *Lasers Med Sci*. 2020.02; 35(1); 213-219
4. [Advanced Biomaterials : WADA Takahiro] Kusumasari C, Abdou A, Tichy A, Hatayama T, Hosaka K, Foxton RM, Wada T, Sumi Y, Nakajima M, Tagami J. Effect of smear layer deproteinization with chemo-mechanical caries removal agents on sealing performances of self-etch adhesives. *Journal of dentistry*. 2020.02; 103300
5. [Operative Dentistry and Endodontics : TAKAHASHI Rena] ROZAN Shin, TAKAHASHI Rena, ODA Yutaro, NIKAIDO Toru, TAGAMI Junji. The effect of the thickness of resin coating layer and CAD/CAM resin block on bond strength of resin cement with single visit treatment *Japanese Journal of Dental Esthetics*. 2020.03; 32(2); 111-118
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8. [- : TICHY Antonin] Tichy A, Hosaka K, Abdou A, Nakajima M, Tagami J. Degree of Conversion Contributes to Dentin Bonding Durability of Contemporary Universal Adhesives. *Oper Dent*. 2020.04;
9. [Cariology and Operative Dentistry : TAGAMI Junji] Alireza Sadr, Behnoush Bakhtiari, Juri Hayashi, Minh N Luong, Yen-Wei Chen, Grant Chyz, Daniel Chan, Junji Tagami. Effects of fiber reinforcement on adaptation and bond strength of a bulk-fill composite in deep preparations. *Dent Mater*. 2020.04; 36(4); 527-534
10. [- : TICHY Antonin] Paing SY, Tichy A, Hosaka K, Nagano D, Nakajima M, Tagami J. Effect of smear layer deproteinization with HOCl solution on the dentin bonding of conventional and resin-modified glass-ionomer cements. *European journal of oral sciences*. 2020.05; 128(3); 255-262
11. [Cariology and Operative Dentistry : HOSAKA Keiichi] Taweesak Prasansuttiporn, Ornnicha Thanatvarakorn, Teerapong Mamane, Keiichi Hosaka, Junji Tagami, Richard M. Foxton, Masatoshi Nakajima. Effect of antioxidant/reducing agents on the initial and long-term bonding performance of a self-etch adhesive to caries-affected dentin with and without smear layer-deproteinizing *International Journal of Adhesion and Adhesives*. 2020.05; 102;
12. [- : TICHY Antonin] Yonekura K, Hosaka K, Tichy A, Taguchi K, Ikeda M, Thanatvarakorn O, Prasansuttiporn T, Nakajima M, Tagami J. Air-blowing strategies for improving the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *Dental materials journal*. 2020.05;
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15. [- : TICHY Antonin] Hosaka K, Tichy A, Motoyama Y, Mizutani K, Lai WJ, Kanno Z, Tagami J, Nakajima M. Post-orthodontic recontouring of anterior teeth using composite injection technique with a digital workflow. *Journal of esthetic and restorative dentistry : official publication of the American Academy of Esthetic Dentistry ... [et al.]* . 2020.06;
16. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Khanlar LN, Takagaki T, Inokoshi M, Ikeda M, Nikaido T, Tagami J. The effect of carboxyl-based monomers on resin bonding to highly translucent zirconia ceramics. *Dent Mater J*. 2020.07;
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20. [Cariology and Operative Dentistry : TAGAMI Junji] Sho Obayashi, Hidenori Hamba, Keiki Nakamura, Toru Nikaido, Junji Tagami. Preventive effect of experimental polymer-based desensitizers with NaF on demineralization of root dentin -observed using micro-CT. *Dent Mater J*. 2020.07;
21. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka, Antonin Tichy, Yuichi Hasegawa, Yasuji Motoyama, Manabu Kanazawa, Junji Tagami, Masatoshi Nakajima. Replacing mandibular central incisors with a direct resin-bonded fixed dental prosthesis by using a bilayering composite resin injection technique with a digital workflow: A dental technique *J Prosthet Dent*. 2020.08;
22. [Cariology and Operative Dentistry : YOSHIKAWA Takako] Takako Yoshikawa, Alireza Sadr, Junji Tagami . Polymerization behavior of resin composites using different irradiance lights *Asian Pac J Dent*. 2020.08; 20; 25-28
23. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Koko M, Takagaki T, Abdou A, Inokoshi M, Ikeda M, Wada T, Uo M, Nikaido T, Tagami J. Effects of the ratio of silane to 10-methacryloyloxydecyl dihydrogenphosphate (MDP) in primer on bonding performance of silica-based and zirconia ceramics. *J Mech Behav Biomed Mater*. 2020.08; 112; 104026
24. [Cariology and Operative Dentistry : AHMED Mohamed Abdelrahman Abdou] Heba H. Alsherbiney, Heba A. El-deeb, Ahmed H. Alsherbiney, Ahmed A. Abdou, Enas H. Mobarak, Omaima S. Hamza. Effect of calcium sodium phosphosilicate-containing compared to nanohydroxyapatite-containing toothpastes on dentinal tubule occlusion: A randomized clinical in situ study. *Journal of International Oral Health*. 2020.08; 12(4); 305-312
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27. [Cariology and Operative Dentistry : TAGAMI Junji] Toru Nikaido, Tomohiro Takagaki, Takaaki Sato, Michael F Burrow, Junji Tagami. The concept of super enamel formation -Relationship between chemical interaction and enamel acid-base resistant zone at the self-etch adhesive/enamel interface. *Dent Mater J*. 2020.08; 39(4); 534-538

28. [Cariology and Operative Dentistry : HOSAKA Keiichi] Diana Lb Borghetti, Roberto Zimmer, Fernando F Portella, Eduardo G Reston, Celso A Klein-Junior, Daniel R Marinowic, Keiichi Hosaka. Effect of preheating on cytotoxicity and physicochemical properties of light-cured calcium-based cements. *Acta Odontol Latinoam*. 2020.09; 33(2); 82-89
29. [Cariology and Operative Dentistry : TAGAMI Junji] Seung-Hoon Han, Yasushi Shimada, Alireza Sadr, Junji Tagami, Kee-Yeon Kum, Sung-Ho Park. Effect of Pretreatment and Activation Mode on the Interfacial Adaptation of Nanoceramic Resin Inlay and Self-adhesive Resin Cement. *Dent Mater*. 2020.09; 36(9); 1170-1182
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31. [Cariology and Operative Dentistry : TAGAMI Junji] Shiori Yamamoto, Mahmoud Sayed, Motoi Takahashi, Khairul Matin, Noriko Hiraishi, Toru Nikaido, Michael F Burrow, Junji Tagami. Effects of a surface prereacted glass-ionomer filler coating material on biofilm formation and inhibition of dentin demineralization. *Clin Oral Investig*. 2020.09;
32. [Cariology and Operative Dentistry : AHMED Mohamed Abdelrahman Abdou] Sherif Adel, Takahiro Wada, Nobuyuki Kawashima, Ahmed Abdou, Hiroshi Watanabe, Tohru Kurabayashi, Takashi Okiji, Motohiro Uo. Preparation and properties of tristrontium aluminate as an alternative component of mineral trioxide aggregate (MTA) cement. *Dental materials journal*. 2020.09;
33. [Cariology and Operative Dentistry : HOSAKA Keiichi] Shimada Y, Burrow MF, Araki K, Zhou Y, Hosaka K, Sadr A, Yoshiyama M, Miyazaki T, Sumi Y, Tagami J. 3D imaging of proximal caries in posterior teeth using optical coherence tomography. *Scientific reports*. 2020.09; 10(1); 15754
34. [Oral Prosthetic Engineering : IKEDA Masaomi] Yonekura Kazuhide, Hosaka Keiichi, Tichy Antonin, Taguchi Keita, Ikeda Masaomi, Thanatvarakorn Ornnicha, Prasansuttiporn Taweesak, Nakajima Masatoshi, Tagami Junji. Air-blowing strategies for improving the microtensile bond strength of one-step self-etch adhesives to root canal dentin(和訳中) *Dental Materials Journal*. 2020.09; 39(5); 892-899
35. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka, Antonin Tichy, Yasuji Motoyama, Koji Mizutani, Wei-Jen Lai, Zuisei Kanno, Junji Tagami, Masatoshi Nakajima. Post-orthodontic recontouring of anterior teeth using composite injection technique with a digital workflow. *J Esthet Restor Dent*. 2020.10; 32(7); 638-644
36. [Operative Dentistry and Endodontics : NAKAJIMA Masatoshi] Rima Zakzuk Alshahni, Kento Sato, Keiichi Hosaka, Takashi Hatayama, Ayaka Chiba, Richard M. Foxton, Junji Tagami, Yasunori Sumi, Yasushi Shimada, Masatoshi Nakajima . Effect of smear layer deproteinization with enzyme solutions on bonding efficacy of one-step self-etch adhesives *International Journal of Adhesion & Adhesives*. 2020.10; 102; 102672
37. [Cariology and Operative Dentistry : HOSAKA Keiichi] PaPa Kaykhine, Antonin Tichy, Ahmed Abdou, Keiichi Hosaka, Richard M Foxton, Yasunori Sumi, Masatoshi Nakajima, Junji Tagami. Long-term evaluation of warm-air treatment effect on adaptation of silane-containing universal adhesives to lithium disilicate ceramic. *Dent Mater J*. 2020.10;
38. [Pharmacology : TAMURA Yukihiro] Nassar M, Dargham A, Jamleh A, Tamura Y, Hiraishi N, Tagami J. The Hormetic Effect of Arsenic Trioxide on Rat Pulpal Cells: An In Vitro Preliminary Study. *European journal of dentistry*. 2020.10;
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43. [Operative Dentistry and Endodontics : TAKAHASHI Rena] Mikako Hayashi, Yasuko Momoi, Morioki Fujitani, Masayoshi Fukushima, Satoshi Imazato, Yuichi Kitasako, Shisei Kubo, Shoji Nakashima, Toru Nikaido, Akihiko Shimizu, Kenichi Sugai, Rena Takahashi, Masako Unemori, Chinami Yamaki. Evidence-based consensus for treating incipient enamel caries in adults by non-invasive methods: recommendations by GRADE guideline. *Jpn Dent Sci Rev.* 2020.11; 56(1); 155-163
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47. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Shimizubata M, Inokoshi M, Wada T, Takahashi R, Uo M, Minakuchi S. Basic properties of novel S-PRG filler-containing cement. *Dent Mater J.* 2020.12; 39(6); 963-969
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49. [Cariology and Operative Dentistry : HOSAKA Keiichi] Celso Afonso Klein-Junior, Kathleen Sobieray, Roberto Zimmer, Fernando Freitas Portella, Eduardo Galia Reston, Daniel Marinowic, Keiichi Hosaka. Effect of heat treatment on cytotoxicity and polymerization of universal adhesives. *Dent Mater J.* 2020.12; 39(6); 970-975
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51. [Oral Prosthetic Engineering : IKEDA Masaomi] Koshimitsu Yusuke, Inoue Go, Sayed Mahmoud, Saad Amr, Ikeda Masaomi, Tagami Junji. Transverse Micro Radiography Analysis of the Effect of Experimental Calcium-Containing Primer System on Demineralized Enamel CRYSTALS. 2020.12; 10(12);
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53. [Cariology and Operative Dentistry : TAGAMI Junji] Anonint Tichy, Marek Brabec, Pavel Brandna, Keiichi Hosaka, Ayaka Chiba, Junji Tagami. Influence of central and peripheral dentin on micro-tensile bond strength estimated using a competing risk model. *J Mech Behav Biomed.* 2020.12;

[Misc]

1. [Operative Dentistry and Endodontics : TAKAHASHI Rena] Toru Nikaido, Tomohiro Takagaki, Syusuke Kusakabe, Rena Takahashi, Junji Tagami. Basic knowledge on the resin coating technique -Development of thin-film coating materials- The Journal of the Japanese Society for Dental Materials and Devices. 2020.05; 39(2); 143-146

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3. [Cariology and Operative Dentistry : TAGAMI Junji] Tagami Junji, Shimada Yasushi, Sadr Alireza, Yoshiyama Masahiro, Sumi Yasunori. New findings on Internal Tooth Structure Obtained by OCT Analysis 2020.08; 63(4); 267-271

[Conference Activities & Talks]

1. [Cariology and Operative Dentistry : HOSAKA Keiichi] Kusumasari Citra, Nakajima Masatoshi, Abdou Ahmed, Hatayama Takashi, Tichy Antonin, Hosaka Keiichi, Tagami Junji. Papacarie and Carisolv Pretreatments Improve Dentin Bonding Using Self-etch Adhesives. 2020 IADR/AADR/CADR General Session 2020 Washington, D.C., USA
2. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka. Bond: with Esthetic Outcome. "Esthetic Beyond Frontier", Global Young Dental Leaders Meeting 2020.02.11 Movenpick BDMS Wellness Resort Bangkok, Thailand
3. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka. The Direct composite Restoration with a digital work flow for Tooth Wear Cases. Invited Lecture, Thammasat University 2020.02.12 Bangkok, Thailand
4. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. Operative dentistry I . Lecture of operative dentistry I 2020.02.14 department of dentistry in Hokkaido University
5. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Hatano K, Inokoshi M, Tamura M, Shimizubata M, Wada T, Uo M, Takahashi R, Imai K, Minakuchi S. Antimicrobial effect of a novel denture adhesive containing S-PRG filler. 98th General Session & Exhibition of the IADR 2020.03
6. [Cariology and Operative Dentistry : HIRAISHI Noriko] Noriko Hiraishi, Fumiaki Hayashi, Junji Tagami. Solid-state NMR Study on S-PRG Releasing Ions Reacted with Dentin. 98th General Session & Exhibition of the IADR/AADR 2020.03 Washington, DC, USA
7. [Cariology and Operative Dentistry : YOSHIKAWA Takako] T. Yoshikawa, A. Sadr, J. Tagami. Polymerization Behavior of Composites at Top/Bottom of Cavity using Various-Lights . 98th, IADR 2020.03.18 Washington
8. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Tonprasong W, Inokoshi M, Shimizubata M, Hatano K, Uo M, Wada T, Takahashi R, Minakuchi S. Multi ion release from S-PRG nanofiller containing tissue conditioner. The 75th General Session of the Japanese Society for Dental Materials and Devices 2020.04
9. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. History and recent Developments in Adhesive dentistry. 2020 IADR Meeting: "Adhesive and Digital Dentistry" 2020.07.31 Seattle
10. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. Art and Science of Direct Aesthetic Restoration. Online lecture by brunch of FDI in Africa 2020.08.22 Zimbabwe
11. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. S-PRG TECHNOLOGY: SCIENTIFIC EVIDENCE AS THE BIO-ACTIVE MATERIAL AND IMPACT ON THE CLINIC. BRAZILIAN DIVISION OF IADR(SBPQO) 2020.09.12 Brazil
12. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. From basic to advanced for enjoy CR restoration . Dental health associate 2020.09.20 Japan
13. [Cariology and Operative Dentistry : TAGAMI Junji] prof Junji Tagami. New findings on tooth decay provided by OCT studies. Minimally Invasive Dentistry(MID) webinar series 2020.09.22 London
14. [Cariology and Operative Dentistry : HOSAKA Keiichi] Development of a novel online oral health management system using AI -Outline of survey system-. 2020.10.03

15. [Gerodontology and Oral Rehabilitation : INOKOSHI Masanao] Yamamoto M, Inokoshi M, Tamura M, Shimizubata M, Nozaki K, Takagaki T, Takahashi R, Yoshihara K, Minakuchi S. Antimicrobial effects of 4-META/MMA-TBB resin containing antibacterial agents. 30th Annual Congress of the European College of Gerodontology 2020.10.09 web
16. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. Micro cracks have potential to initiate proximal caries. The 2nd International Cooperation Symposium 2020.10.15 beijing
17. [Cariology and Operative Dentistry : TAGAMI Junji] Junji Tagami. what is happening in the cavity during composite resin filling?. Biomimetic 2020 2020.11.14 Netherlands
18. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka. Direct composite injection technique, Thammasat University Master Course Special Lecture. 2020.11.16 Online
19. [Cariology and Operative Dentistry : HOSAKA Keiichi] Keiichi Hosaka. Recent research findings in adhesive dentistry, Thammasat University Master Course Special Lecture. 2020.11.30 Online
20. [Cariology and Operative Dentistry : TAGAMI Junji] 田上順次. 保存修復学実習 講義. 2020.12.09 岡山

[Awards & Honors]

1. [Cariology and Operative Dentistry : TAGAMI Junji] Honorary Member, Myanmar Dental Association (Junji TAGAMI), Myanmar Dental Association, 2020.02

Pulp Biology and Endodontics

Professor:

Takashi OKIJI

Associate Professor:

Mitsuhiro SUNAKAWA

Junior Associate Professor:

Nobuyuki KAWASHIMA, Tomoatsu KANEKO(～December)

Assistant Professor:

Arata EBIHARA, Satoshi WATANABE, Kento TAZAWA(～September, October ～Leave for research),
Kentaro HASHIMOTO, Yoshiko IINO (March ～), Keisuke NARA(October ～)

Specially Appointed Assistant Professor

Yoshiko IINO(～February)

Hospital Staff:

Keisuke NARA(～September), Sonoko NODA, Tomoyuki HONGO(～March), Mayuko FUJII,
Keiichiro MAKI, Yuki KASAHARA(April ～September), Syunsuke KIMURA(April ～),
Masashi KURAMOTO(April ～September), Bin GU(April ～September), Miharu SHIMIZU(～July),
Akira KOUNO(April ～), Yasuhiro HOSHIHARA(October ～), Shinya YAMAUCHI(October ～),
Nanami NIKAIDO(October ～), Hiroko SOEDA(October ～), Taro NAKATSUKASA(October ～)

Graduate Student:

Mayuko FUJII(～September), Yuki KASAHARA(～March), Shunsuke KIMURA(～March),
Masashi KURAMOTO(～September), Bin GU(～March), Akira KOUNO(～March),
Yasuhiro HOSHIHARA, Keiichiro MAKI(～March), Shinya YAMAUCHI,
Thaw Dar Oo(～September), Phyoo Pyai Sone(～September), Su Yee Myo Zaw(～September),
Pyae Hein Htun(～September), Taro NAKATSUKASA, Hiroki MURANO, Yadanar Su Phyoo,
Xu AO, Aung Nyein Pyae Sone, Htoo Shwe Sin Thein, Sherif Adel Abd El-Fattah SALEH,
Zar Chi Thein Zaw, Yamato OKADA, Shion ORIKASA, Dumrogvute KUNLANUN,
Myint Thu, KIEU Quoc Thoai, Hayate UNNO, Satoshi OMORI, Hiroki OKUDA, Jiayi LIU,
Aseel Alchawoosh, Han Peifeng, Moe Sandar Kyaw, Yuka KASUGA(April ～),
Souta MOCHIDUKI(April～), Nyein Chan Ko(October～)

Research Student:

Sonoko YABUMOTO(～March), Nanami NIKAIDO(～September), Sousuke IZAWA,
Hiroko SOEDA(～September), Yu Ziniu(April ～), Wang Shihan(October ～)

(1) Outline

The Department of Pulp Biology and Endodontics provides research, education and patient care 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 this tissue 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. Biology of dentin/pulp complex and dental pulp tissue regeneration
 - Establishment of an experimental model of rat dental pulp tissue engineering using mesenchymal stem cells
 - Immunohistochemical and gene expression analysis of stem-cell-associated markers in rat dental pulp
 - Expression and function of transient receptor potential channels in dental pulp cells
 - Involvement of hypoxia inducible factor I α (HIF1 α) in the pulpal inflammation
 - Effects BCL9 signaling on osteo-/odontoblastic differentiation of dental pulp stem cells
2. Root canal irrigation
 - Evaluation of efficacy- and safety-related properties of laser-activated root canal irrigation
3. Evaluation of newly developed endodontic sealers and pulp capping materials
 - Anti-inflammatory effects of mineral trioxide aggregate
 - Cytocompatibility of an experimental sealer containing surface reaction type pre-reacted glassionomer (S-PRG) to osteoblastic cells
 - Evaluation of strontium ranelate as a direct pulp capping material
 - Development of new tricalcium silicate-based endodontic materials
4. Nickel-titanium rotary root canal instrumentation
 - Cleaning and shaping ability of Gentlefile, HyFlex EDM, and ProTaper Next instruments: a combined micro-computed tomographic and scanning electron microscopic study.
 - Cyclic fatigue resistance of rotary and reciprocating nickel-titanium instruments subjected to static and dynamic tests.
 - Comparative evaluation of mechanical properties and shaping performance of heat-treated nickel titanium rotary instruments used in the single-length technique.
5. Endodontic diagnosis
 - Detection of periapical bone defects and vertical root fracture with cone beam computed tomography
6. Dental pulp injury-induced gene expression in the central nervous system
 - Alteration of pain-associated gene expression in the thalamus following dental pulp stimulation in rats

(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 therapy,
- Nonsurgical root canal therapy
- Root canal retreatment,
- Endodontic microsurgery,
- Internal tooth bleaching,
- Post-endodontic restoration.

(5) Clinical Performances

The latest development of endodontics is remarkable as seen in root canal instrumentation with super-elastic Ni-Ti rotary files, diagnosis with 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. Fujii M, Kawashima N, Tazawa K, Hashimoto K, Nara K, Noda S, Nagai S, Okiji T. Hypoxia-inducible factor 1 α promotes interleukin 1 β and tumour necrosis factor α expression in lipopolysaccharide-stimulated human dental pulp cells. *International Endodontic Journal*. 2020.01;53(5):636-646
2. Fujii M, Kawashima N, Tazawa K, Hashimoto K, Nara K, Noda S, Kuramoto M, Orikasa S, Nagai S, Okiji T. HIF1 α inhibits LPS-mediated induction of IL-6 synthesis via SOCS3-dependent CEBP β suppression in human dental pulp cells. *Biochemical and Biophysical Research Communications*. 2020.02;522(2):308-314
3. Kimura S, Ebihara A, Maki K, Nishijo M, Tokita D, Okiji T. Effect of optimum torque reverse motion on torque and force generation during root canal instrumentation with crown-down and single-length techniques. *Journal of Endodontics*. 2020.02;46(2):232-237
4. Maki K, Ebihara A, Kimura S, Nishijo M, Tokita D, Miyara K, Okiji T. Enhanced root canal-centering ability and reduced screw-in force generation of reciprocating nickel-titanium instruments with a post-machining thermal treatment. *Dental Materials Journal*. 2020.03;39(2):251-255
5. Aoki A, Takeuchi Y, Mizutani K, Katagiri S, Ikeda Y, Maekawa S, Watanabe K, Ebihara A, Hideshima M, Nikaido T, Oda S, Araki K, Iwata K, Izumi Y. Current status of clinical practice of periodontal therapy by predoctoral dental students at Tokyo Medical and Dental University (TMDU). *The Journal of Japanese Society of Periodontology*. 2020.03;62(1):38-46
6. Htun PH, Ebihara A, Maki K, Kimura S, Nishijo M, Tokita D, Okiji T. Comparison of torque, force generation and canal shaping ability between manual and nickel-titanium glide path instruments in rotary and optimum glide path motion. *Odontology*. 2020.04;108(2):188-193
7. Kouno A, Watanabe S, Hongo T, Yao K, Satake K, Okiji T. Effect of pulse energy, pulse frequency, and tip diameter on intracanal vaporized bubble kinetics and apical pressure during laser-activated irrigation using Er: YAG laser. *Photobiomodulation, Photomedicine, and Laser Surgery*. 2020.07;38(7):431-437
8. Aung NPS, Watanabe S, Kouno A, Hongo T, Yao K, Satake K, Okiji T. Fluid movement in the apical area beyond the ledge during Er: YAG laser-activated irrigation: A particle image velocimetry analysis. *Photobiomodulation, Photomedicine, and Laser Surgery*. 2020.07;38(7):438-446
9. Sone PP, Kaneko T, Zaw SYM, Sueyama Y, Gu B, Murano H, Zaw ZCT, Okada Y, Han P, Katsube KI, Okiji T. Neural regeneration/remodeling in engineered coronal pulp tissue in the rat molar. *Journal of Endodontics*. 2020.07;46(7):943-949

10. Kasahara Y, Iino Y, Ebihara A, Okiji T. Differences in the coronal-apical location of sinus tracts and buccal cortical bone defects between vertically root-fractured and non-root-fractured teeth based on periradicular microsurgery. *Journal of Oral Science*. 2020.07;62(3);327-330
11. Htun PH, Ebihara A, Maki K, Kimura S, Nishijo M, Okiji T. Cleaning and shaping ability of Gentle file, HyFlex EDM, and ProTaper Next instruments: a combined micro-computed tomographic and scanning electron microscopic study. *Journal of Endodontics*. 2020.07;46(7);973-979
12. Iino Y, Izawa T, Yao K, Okiji T. Surgical endodontic treatment of radicular cyst associated with periapical osteoperiostitis in a maxillary molar: a case report. *Japanese Journal of Conservative Dentistry*. 2020.08;63(4);332-337
13. Maki K, Ebihara A, Nakatsukasa T, Kimura S, Okiji T. Comparative evaluation of the shaping ability of nickel-titanium rotary and stainless steel hand root canal instrumentation performed by undergraduate students. *Japanese Journal of Conservative Dentistry*. 2020.08;63(4);305-311
14. Kouno A, Watanabe S, Yao K, Satake K, Okiji T. Intracanal vaporized bubble kinetics and apical pressure during root canal irrigation activated by Er:YAG laser: Effect of tip configuration and irradiation time. *Journal of Japanese Society for Laser Dentistry*. 2020.08;30(2);57-62
15. Zaw SYM, Kaneko T, Zaw ZCT, Sone PP, Murano H, Gu B, Okada Y, Han P, Katsube KI, Okiji T. Crosstalk between dental pulp stem cells and endothelial cells augments angiogenic factor expression. *Oral Diseases*. 2020.09;26(6);1275-1283
16. Kawashima N, Hashimoto K, Kuramoto M, Bakhit A, Wakabayashi Y, Okiji T. A novel bioactive endodontic sealer containing surface-reaction-type prereacted glass-ionomer filler induces osteoblast differentiation. *Materials*. 2020.10;13(20);4477
17. Hoshihara Y, Watanabe S, Kouno A, Yao K, Okiji T. Effect of tip insertion depth and irradiation parameters on the efficacy of cleaning calcium hydroxide from simulated lateral canals using Er:YAG laser or ultrasonic activated irrigation. *Journal of Dental Sciences*. 2020.10; in press
18. Thu M, Ebihara A, Maki K, Nishijo M, Okiji T. Cyclic fatigue resistance of rotary and reciprocating nickel-titanium instruments subjected to static and dynamic tests. *Journal of Endodontics*. 2020.11;46(11);1752-1757
19. Thaw Dar O, Kakino S, Kusano M, Ikeda H, Miyashin M, Okiji T. Transmitted-light plethysmography detects changes in human pulpal blood flow elicited by innocuous tooth cooling and foot heating. *Archives of Oral Biology*. 2020.11;119;104881
20. Tazawa K, Kawashima N, Kuramoto M, Noda S, Fujii M, Nara K, Hashimoto K, Okiji T. Transient receptor potential ankyrin 1 is up-regulated in response to lipopolysaccharide via p38/mitogen-activated protein kinase in dental pulp cells and promotes mineralization. *American Journal of Pathology*. 2020.12;190(12);2417-2426
21. Kuramoto M, Kawashima N, Tazawa K, Nara K, Fujii M, Noda S, Hashimoto K, Nozaki K, Okiji T. Mineral trioxide aggregate suppresses pro-inflammatory cytokine expression via the calcineurin/nuclear factor of activated T cells/early growth response 2 pathway in lipopolysaccharide-stimulated macrophages. *International Endodontic Journal*. 2020.12;53(12);1653-1665
22. Edanami N, Yoshida K, Shirakashi M, Ibn Belal RS, Yoshida N, Ohkura N, Tohma A, Takeuchi R, Okiji T, Noiri Y. Impact of remnant healthy pulp and apical tissue on outcomes after simulated regenerative endodontic procedure in rat molars. *Scientific Reports*. 2020.12;10(1);20967

23. Fukumori Y, Nakatshukasa T, Maki K, Kimura S, Ebihara A, Okiji T. Effect of taper of nickel-titanium rotary instruments on cyclic fatigue resistance in a dynamic model. *Japanese Journal of Conservative Dentistry*. 2020.12;63(6); 512-518

[Books etc]

1. Paradigm shift in endodontics. Quintessence Publishing, 2020.06 (ISBN : 978-4781207520)

[Misc]

1. Murano H, Kaneko T, Okiji T. Root dentinal microcracks: a post-extraction experimental phenomenon? *The Nippon Dental Review*. 2020.01; 927(80); 146-147
2. Okiji T. Mineral trioxide aggregate: current trends and future perspectives. *The Nippon Dental Review*. 2020.01; 80(1); 20-21
3. Watanabe S, Okiji T. Association between the Root canal configuration, endodontic treatment technical errors, and periapical hypodensities in molar teeth: a cone-beam computed tomographic study. *The Quintessence*. 2020.05; 80(5); 154-155
4. Iino Y, Sunakawa M, Tsuruoka H, Okihata R, Takahashi Y, Araki K. Preventive measures in dental conservative treatment associated with the spread of severe acute respiratory syndrome Corona -Virus 2 (SARS-CoV-2) infection. *Japanese Journal of Conservative Dentistry*. 2020.08 ;63(4);272-279
5. Unno H, Kaneko S, Okiji T. Evaluation of dentine thickness of middle mesial canals of mandibular molars prepared with rotary instruments: a micro-CT study. *The Nippon Dental Review*. 2020.09;80(9); 146-147
6. Omori S, Kaneko T, Okiji T. Association between the root canal configuration, endodontic treatment technical errors, and periapical hypodensities in molar teeth: a cone-beam computed tomographic study. *The Quintessence*. 2020.09;49(9);154-155
7. Okiji T. Dentin/pulp complex. *The Nippon Dental Review*. 2020.10; 80(Special Issue); 8-16
8. Kasuga Y, Watanabe S, Okiji T. Proximity of vascular bone channel in the lateral sinus wall to root apices of maxillary first molars: A cone-beam computed tomographic analysis. *The Quintessence*. 2020.11;39(11);212-213
9. Okiji T. Endodontics treatment of the late elderly. *Dental Diamond*. 2020.12; 45(16); 72-76

[Conference Activities & Talks]

1. Thaw Dar Oo, Kakino S, Kusano M, Ikeda H, Miyashin M, Okiji T. Systemic circulatory influence on pulpal circulation in young adult human teeth. The 9th Conference of the Asian International Association of Dental Traumatology. 2020 Virtual Meeting
2. Orikasa S, Kawashima N, Fujii M, Yamamoto M, Hashimoto K, Tazawa K, Okiji T. Hypoxia-inducible factor 1 α induces osteo-/odontoblast differentiation of mouse dental papillae cells via Bcl 9 and Bcl 9l, Wnt / β -catenin transcriptional cofactors. Balance Unit young researcher workshop 2020. 2020.02.07 Tokyo
3. Thaw Dar Oo, Kakino S, Kusano M, Ikeda H, Miyashin M, Okiji T. Transmitted-light plethysmography detects changes in human pulpal blood flow elicited by innocuous foot heating. The 152nd Meeting of the Japanese Society of Conservative Dentistry. 2020.06.11 Virtual Meeting
4. Phyo Pyai Sone, Kaneko T, Su Yee Myo Zaw, Bin G, Murano H, Zar Chi Thein Zaw, Okada Y, Peifeng HAN, Okiji T. Time course analysis of neural regeneration /remodeling in engineered coronal pulp tissue in the rat molar. The 152nd Meeting of the Japanese Society of Conservative Dentistry. 2020.06.11 Virtual Meeting

5. Su Yee Myo Zaw , Kaneko T, Zar Chi Thein Zaw , Phyo Pyai Sone , Murano H, Bin G, Okada Y, Peifeng HAN , Okiji T. Crosstalk between dental pulp stem cells and endothelial cells promoted via nuclear factor kappa B signaling pathways . The 152nd Meeting of the Japanese Society of Conservative Dentistry . 2020 .06 .11 Virtual Meeting
6. Myint Thu , Ebihara A, Nishijo M, Maki K, Okiji T. Cyclic fatigue resistance of rotary and reciprocating NiTi instruments subjected to static and dynamic tests . The 152 nd Meeting of the Japanese Society of Conservative Dentistry . 2020.06.11 Virtual Meeting
7. Maki K, Ebihara A, Unno H, Omori S, Nakatsukasa T, Kimura S, Okiji T. Evaluation of shaping ability of NiTi rotary files used by undergraduate students . The 41 st Annual Scientific Meeting of Japan Endodontic Association . 2020.06.27 Virtual Meeting
8. Nyein Pyae Sone Aung , Watanabe S, Kouno A, Yao K, Satake K, Okiji T. Cleaning efficacy of different irrigant activation techniques in the apical area beyond the ledge in curved root canals . The 41st Annual Scientific Meeting of Japan Endodontic Association . 2020.06.27 Virtual Meeting
9. Liu J, Watanabe S, Kouno A, Yao K, Satake K, Okiji T. Intracanal vaporized cavitation bubble kinetics in the apical area beyond the fractured instrument during Er :YAG laser -activated irrigation . The 41 st Annual Scientific Meeting of Japan Endodontic Association . 2020.06.27 Virtual Meeting
10. Pyae Hein Htun , Maki K, Kimura S, Nishijo M, Ebihara A, Okiji T . Root canal cleaning efficacy and shaping ability of Gentle file . The 41 st Annual Scientific Meeting of Japan Endodontic Association . 2020 .06 .27 Virtual Meeting
11. Unno H, Maki K, Kimura S, Nakatsukasa T, Omori S, Ebihara A, Okiji T. Evaluation of mechanical properties of a newly developed niti rotary instrument, TruNatomy . The 41st Annual Scientific Meeting of Japan Endodontic Association . 2020.06.27 Virtual Meeting
12. Kanamori Y, Noritake K, Umemori S, Iwaki M, Kido D, Hideshima M, Kimura Y, Hattori A, Tonami K, Ebihara A, Araki K, Nitta H. TMDU trainee residents' feedback on the trial of objective clinical skills examinations . The 39th General and Scientific Meeting of the Japanese Dental Education Association . 2020 .09 .26
13. Kieu Quoc T, Tazawa K, Kawashima N, Nara K, Fujii M, Noda S, Hashimoto K, Okiji T . Lyve -1+ pulpal macrophages: M2-polarization and response to cavity preparation . The 68th Annual Meeting of Japanese Association for Dental Research . 2020 .11 .07 Virtual Meeting
14. Kouno A, Watanabe S, Yamauchi S, Okiji T. Effect of heating on the physical properties of paste-type root canal sealers . The 153rd Meeting of the Japanese Society of Conservative Dentistry . 2020 .11 .16 Virtual Meeting
15. Omori S, Maki K, Kimura S, Nakatsukasa T, Unno H, Nishijo M, Ebihara A, Okiji T . Effect of various rotational modes on the stress generation during nickel-titanium rotary root canal instrumentation . The 153rd Meeting of the Japanese Society of Conservative Dentistry . 2020 .11 .16 Virtual Meeting
16. Maki K, Ebihara A, Kasuga Y, Omori S, Unno H, Nakatsukasa T, Kimura S, Okiji T . Effect of different apical load on shaping ability, stress generation, and instrumentation time of nickel titanium rotary instruments . The 153rd Meeting of the Japanese Society of Conservative Dentistry . 2020 .11 .16 Virtual Meeting

17. Moe Sandar Kyaw, Maki K, Kimura S, Pyae Hein Htun, Ebihara A, Okiji T. Influence of rotational speed on torque /force generation and shaping ability during root canal instrumentation with continuous rotation and optimum torque reverse motion. The 153rd Meeting of the Japanese Society of Conservative Dentistry. 2020.11.16 Virtual Meeting
18. Zar Chi Thein Zaw, Kaneko T, Su Yee Myo Zaw, Okada Y, Murano H, Peifeng Han, Okiji T. Comparison of NF- κ B pathway-related angiogenic factor expression between rat incisor dental pulp stem cells and rat bone marrow mesenchymal stem cells. The 153rd Meeting of the Japanese Society of Conservative Dentistry. 2020.11.16 Virtual Meeting
19. Okada Y, Kaneko T, Su Yee Myo Zaw, Murano H, Zar Chi Thein Zaw, Peifeng Han, Okiji T. Expression analysis of VEGF-dependent angiogenic signaling pathway-related genes in dental pulp stem cells co-cultured with endothelial cells: A comprehensive microarray analysis. The 153rd Meeting of the Japanese Society of Conservative Dentistry. 2020.11.16 Virtual Meeting
20. Yadanar SP, Hashimoto K, Kawashima N, Kuramoto M, Okiji T. Evaluation of the cytocompatibility of methacrylate resin - based sealers with osteoblast -like cells . Korean Academy of Endodontics Online Annual Congress & 18th JEA-KAE Joint Meeting. 2020.11.28 Virtual Meeting
21. Htoo SST, Hashimoto K, Kawashima N, Kuramoto M, Noda S, Nara K, Fujii M, Okiji T. Evaluation of anti-inflammatory effect of Surface-Reaction-Type Prereacted Glass-Ionomer filler containing root canal sealer in lipopolysaccharide-stimulated RAW264.7 macrophages. Korean Academy of Endodontics Online Annual Congress & 18th JEA-KAE Joint Meeting. 2020.11.28 Virtual Meeting

[Awards & Honors]

1. Tazawa K. The first place in Balance Unit young researcher workshop 2020, 2020.02
2. Ao Xiang. The second place in Balance Unit young researcher workshop 2020, 2020.02
3. Orikasa S. The third place in Balance Unit young researcher workshop 2020, 2020.02
4. Hongo T. Annual excellent award of the Japanese Journal of Conservative Dentistry, 2020.11
5. Kouno A. Annual excellence article award, Japanese Society for Laser Dentistry, 2020.11

Removable Partial Prosthodontics

Professor - Noriyuki Wakabayashi

Associate professor - Kenji Fueki

Junior associate professor - Takeshi Ueno

Assistant professors

- Eiko Kohno, Junnichi Wada, Natsuko Murakami, Atsushi Takaichi, Yuki Arai, Yuka Inamochi

Specially Appointed Assistant Professors

- Kensuke Takakusaki, Toshiki Yamazaki

Hospital staff

- Hideaki Inagawa, Keigo Isoshima, Keiichiro Uchikura, Hisami Okawara, Taihei Kasai, Hirokazu Sato, Gen Nabeshima, Masahiro Hirasawa, Yasuo Nakajima, Tomiharu Nagayama, Shiro Hibi, Daiki Hikita

Graduate students

- AMR GAMAL, Yurika Ishioka, Hirofumi Uchida, Wang Zuo, Kim Eung Yeol, QU WENRUI, Wu huaze, K Zin Myint, Yoshio Kobayashi, Hiroki Saito, Kazuki Sakamoto, SAN WIN THANT, Yuka Shichiri, Tenhaku Tan, Gu Zheng, Zhao Qian, Taku Nemoto, Yoko Hayashi, Hao Jialin, Hein Linn Htat, Hitomi Matsuno, Hla Htoot Wai Cho, Yu Huaxin, Abdullah Kamel, Hideaki Umi, Tetsu Sato, Zou Shiqi, CUI XIAOWEI, Chai Xinyi, Ding Zhiyuan, Deng Fan, Yoko Mashimo, Yang Shiyi, Li Yajie

(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. Nagayama T, Wada J, Watanabe C, Murakami N, Takakusaki K, Uchida H, Utsumi M, Wakabayashi N.. Influence of retainer and major connector designs of removable partial dentures on the stabilization of mobile teeth: a preliminary study. *Dental Materials Journal*. 2020.01; 39(1); 89-100
2. Kenji Fueki, Eiko Yoshida-Kohno, Yuka Inamochi, Noriyuki Wakabayashi. Patient satisfaction and preference with thermoplastic resin removable partial dentures: a randomised cross-over trial. *J Prosthodont Res*. 2020.01; 64(1); 20-25
3. Myint Oo KZ, Fueki K, Yoshida-Kohno E, Hayashi Y, Inamochi Y, Wakabayashi N. Minimal clinically important differences of oral health-related quality of life after removable partial denture treatments. *Journal of dentistry*. 2020.01; 92(1); 103246
4. Iwanaga J, Cleveland MK, Wada J, Tubbs RS.. How to avoid iatrogenic lingual nerve injury in the retromolar area: an anatomical study of retromolar pad and lingual nerve. *Surg Radiol Anat*. . 2020.01;
5. The first JPS student clinical skills competition *Annals of Japan Prosthodontic Society*. 2020.01; 12(1); 5-15
6. Atsushi Takaichi, Yuka Kajima, Nuttaphon Kittikundecha, Hein Linn Htat, Hla Htoot Wai Cho, Takao Hanawa, Takayuki Yoneyama, Noriyuki Wakabayashi. Effect of heat treatment on the anisotropic microstructural and mechanical properties of Co-Cr-Mo alloys produced by selective laser melting. *J Mech Behav Biomed Mater*. 2020.02; 102;
7. Yuka Kajima, Atsushi Takaichi, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi, Akira Kawasaki. Influence of magnetic susceptibility and volume on MRI artifacts produced by low magnetic susceptibility Zr-14Nb alloy and dental alloys. *Dent Materials Journal*. 2020.03; 39(2); 256-261
8. 王 佐, 河野 英子, 笛木 賢治, 稲用 友佳, 上野 剛史, 若林 則幸. The effect of flipped classroom on learning outcomes: randomized controlled trial in prosthodontic class(和訳中) *口腔病学会雑誌*. 2020.03; 87(1); 17-18
9. Ogawa M, Katagiri S, Koyanagi T, Maekawa S, Shiba T, Ohsugi Y, Takeuchi Y, Ikawa T, Takeuchi S, Sekiuchi T, Arai Y, Kazama R, Wakabayashi N, Izumi Y, Iwata T. Accuracy of cone beam computed tomography in evaluation of palatal mucosa thickness *Journal of Clinical Periodontology*. 2020.04; 47(4); 479-488
10. K Zin Myint Oo, Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Yoko Hayashi, Noriyuki Wakabayashi. Pre-treatment impairment of oral health-related quality of life is associated with variations in minimal clinically important differences among patients with removable partial denture treatment. *J Oral Rehabil*. 2020.07; 47(7); 902-909
11. Yuka Inamochi, Kenji Fueki, Yusuke Matsuyama, Eiko Yoshida-Kohno, Takeo Fujiwara, Noriyuki Wakabayashi. Does oral dryness influence pressure pain sensitivity in the oral mucosa of removable denture wearers? *Clinical Oral Investigations*. 2020.08; 24(8); 2603-2609
12. Ijbara Manhal, Wada Kanae, Wada Junichiro, Jayawardena Jayanetti Amiri, Miyashin Michiyo. Replica-based inspection of enamel wear microfeatures *Bio-Medical Materials and Engineering*. 2020.11; 31(5); 279-290

13. Kenji Fueki, Yuka Inamochi, Eiko Yoshida-Kohno, Yoko Hayashi, Noriyuki Wakabayashi. Responsiveness of methods to evaluate chewing ability after removable partial denture treatments. *J Oral Rehabil.* 2020.11;
14. Yuka Kajima, Atsushi Takaichi, Nuttaphon Kittikundecha, Hein Linn Htat, Hla Htoot Wai Cho, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi, Takayuki Yoneyama. Reduction in anisotropic response of corrosion properties of selective laser melted Co-Cr-Mo alloys by post-heat treatment. *Dental Materials.* 2020.11;

[Misc]

1. Keiichi Sasaki, Kenji Fueki. Current status, prosthodontic treatment and a perspective on future researches for dementia *Ann Jpn Prosthodont.* 2020.04; 12(2); 120-121
2. Fueki Kenji. Digital removable dentures: A challenge in a super-aged society *JOURNAL OF PROSTHODONTIC RESEARCH.* 2020.07; 64(3); VI

[Conference Activities & Talks]

1. Hao Jialin, Murakami Natsuko, Yamazaki Toshiki, Iwasaki Naohiko, Yatabe Masaru, Takahashi Hidekazu, Wakabayashi Noriyuki. Flexural Behavior of Machinable Polyester Denture Material Under Cyclic Loading. 2020 IADR/AADR/CADR General Session 2020.03 Washington, D.C., USA
2. ケジミ ミツウー オ, 笛木賢治, 河野英子, 林 葉子, 稲用友佳, 若林則幸. 部分床義歯治療における口腔関連 QoL の臨床的な最小重要差. 第 129 回日本補綴歯科学会学術大会 2020.06 Web 会議
3. Yuka Inamochi, Kenji Fueki, Eiko Yoshida-Kohno, Youko Hayashi, K Zin Myint Oo, Noriyuki Wakabayashi. Critical factors for removable partial denture treatments from patients perspective. The 129th Annual Meeting of the Japan Prosthodontic Society 2020.06.27 online conference
4. Hla Htoot Wai Cho, Kajima Yuka, Takaichi Atsushi, Hein Linn Htat, Wakabayashi Noriyuki. Effects of cooling conditions during heat treatments on microstructures and mechanical properties of the Co-Cr-Mo alloy prepared by SLM. The 129th Scientific Meeting of Japan Prosthodontic Society 2020.06.27
5. Murakami N, Takaichi A, Fueki K, Ueno T, Inamochi Y, Wada J, Arai Y, Wakabayashi N. A systematic review of digital removable partial dentures Part II. Meta-analysis. 24th Annual Scientific Meeting of Japan Prosthodontic Society Tokyo Branch 2020.11.29
6. 稲用友佳, 笛木賢治, 和田淳一郎, 村上奈津子, 新井祐貴, 河野英子, 上野剛史, 若林則幸. コロナ禍での歯科補綴学教育における遠隔授業の学習効果. 口腔病学会第 85 回学術大会 2020.12.05 東京医科歯科大学

[Social Contribution]

1. Associate editor of *Annals of Dentistry University of Malaya*, 2019.04 - Now
2. Associate editor of *Journal of Prosthodontic Research*, the Japan Prosthodontic Society, 2019.07 - Now

Oral Implantology and Regenerative Dental Medicine

Professor Shohei KASUGAI
Associate Professor Makoto SHIOTA
Senior Lecturer Noriko TACHIKAWA, Sinji KURODA
Assistant Professor Hidemi NAKATA, Kazuhiro KON, Masahiro SHIMOGISHI
Clinical Fellow Maiko YAMAMOTO, You-Kyoung KIM, Munemitsu MIYASAKA
Seiji OHARA, Maki SHIBASAKI, Reo IKUMI

(1) Outline

Prosthetic treatment with dental implants (dental implant treatment) is very effective. We are conducting researches and educations of clinical procedures, materials and tissue regeneration related to dental implant treatment. In addition, we are treating patients with dental implants in the university dental hospital.

(2) Research

We conducted the following studies: Development of bone substitute stimulating bone formation, development of implant surface stimulating bone formation and preventing infection, stimulation of bone formation with dissociated soft tissue, development of resorbable DBG membrane and effects of liposomal chondronate on osteoblastic differentiation.

(3) Education

We gave lectures about basic knowledge necessary for implant treatment to dental students. Dental students also practiced treatment planning using computer soft wear and real patient data. In dental implant clinic, dental students also learned every step of dental implant treatment: Examinations, implant placement surgery and bone augmentation, prosthetic treatment and maintenance. We also gave lectures about advanced knowledge of dental implant treatment and regenerative medicine to post-graduate students.

(4) Lectures & Courses

Acquire basic knowledge and an attitude of thinking continuously.

(5) Clinical Services & Other Works

In dental implant clinic we treated patients, who missed teeth, with dental implants recovering aesthetics and functions. We further observed and followed these patients after the treatments (Maintenance Procedure).

(6) Clinical Performances

In dental implant clinic in TMDU, the number of clinical cases of dental implant treatments is the most in 29 dental schools in Japan. Difficult cases of dental implant treatments in other hospitals and clinics and problem

cases, which have been treated by other dentists, are increasing. We can handle most of these difficult and problem cases.

(7) Publications

[Original Articles]

1. Xiaolong Sun, Hidemi Nakata, Shohei Kasugai, Shinji Kuroda. Effects of three-day Fibroblast growth factors-2 (FGF-2) supplementation on proliferation and osteogenic differentiation of cultured adipose-derived and bone marrow-derived stromal cells *Journal of Oral Tissue Engineering*. 2020;
2. Motoi Miura, Hidemi Nakata, Shohei Kasugai, Shinji Kuroda. Fibroblast and osteoblast differentiation characteristics of periosteum-derived cells in mouse calvaria *Journal of Bio-Integration*. 2020.01; 10(1); 24-46
3. Wai Myo Maung, Hidemi Nakata, Maiko Yamamoto, You-kyoung Kim, Munemitsu Miyasaka, Shohei Kasugai, Shinji Kuroda. Effects of Low-intensity pulsed ultrasound in osteogenic differentiation of murine periosteum-derived cells *Journal of Bio-Integration*. 2020.01; 10(1); 47-60
4. Shigeki Nagahiro, Tomoki Uehara, Mariko Yamamoto Kawai, Preksa Keo, Hiroki Ochi, Shingo Sato, Shinji Kuroda, Takashi Ono, Michiyo Miyashin, Kazuhiro Aoki. RANKL-binding peptide promotes ectopic bone formation induced by BMP-2 gene transfer in murine gastrocnemius muscle *Dental, Oral and Maxillofacial Research*. 2020.01; 6(1);
5. Date Yuki, Kondo Hisatomo, Yamashita Atsuko, Iseki Sachiko, Kasugai Shohei, Ota Masato S.. Combined in silico analysis identified a putative tooth root formation-related gene, Chd3, which regulates DNA synthesis in HERS01a cells *ODONTOLOGY*. 2020.02;
6. Maung WM, Nakata H, Miura M, Miyasaka M, Kim YK, Kasugai S, Kuroda S. Low intensity pulsed ultrasound stimulates osteogenic differentiation of periosteal cells in vitro. *Tissue engineering. Part A*. 2020.03;
7. Maung Wai Myo, Nakata Hidemi, Miura Motoi, Miyasaka Munemitsu, Kim You-Kyoung, Kasugai Shohei, Kuroda Shinji. Low-Intensity Pulsed Ultrasound Stimulates Osteogenic Differentiation of Periosteal Cells In Vitro *TISSUE ENGINEERING PART A*. 2020.03; 27(1-2); 63-73
8. Kaori Fujiwara-Takahashi, Takayasu Watanabe, Masahiro Shimogishi, Masaki Shibasaki, Makoto Umeda, Yuichi Izumi, Ichiro Nakagawa. Phylogenetic diversity in fim and mfa gene clusters between *Porphyromonas gingivalis* and *Porphyromonas gulae*, as a potential cause of host specificity. *J Oral Microbiol*. 2020.06; 12(1); 1775333
9. Thiha Tin Kyaw, Hidemi Nakata, Miyahara Takayuki, Shinji Kuroda, Shohei Kasugai. Evaluation of residual contamination on the healing abutments after cleaning with a protein-denaturing agent and detergent *Quintessence International*. 2020.06; 51(6); 474-478
10. Miki H, Okito A, Akiyama M, Ono T, Tachikawa N, Nakahama KI. Genetic and epigenetic regulation of osteopontin by cyclic adenosine 3' 5'-monophosphate in osteoblasts. *Gene*. 2020.08; (763); 145059
11. Yoko Yamaguchi, Makoto Shiota, Masaki Fujii, Masahiro Shimogishi, Motohiro Munakata. Effects of implant thread design on primary stability-a comparison between single- and double-threaded implants in an artificial bone model. *Int J Implant Dent*. 2020.08; 6(1); 42
12. Yee Mon Shwe, Kensuke Inoue, Maiko Yamamoto, Nakata Hidemi, Shinji Kuroda, Shohei Kasugai. Microbial and inflammatory parameters before and after non-surgical treatment of peri-implantitis *Journal of Interdisciplinary Clinical Dentistry*. 2020.08; 2(1); 1-6
13. Sasaki T, Nakata H, Suzuki A, Hada T, Kasugai S, Kuroda S. Comparison of splinted and non-splinted superstructures of three implants placed in a mandibular distal extension model with missing teeth using modal analysis *Journal of the Mechanical Behavior of Biomedical Materials*. 2020.09; 112; 104050
14. Sun Xiaolong, Nakata Hidemi, Kasugai Shohei, Kuroda Shinji. Effects of Three-dayFibroblast Growth Factors-2(FGF-2) Supplementation on Proliferation and Osteogenic Differentiation of Cultured Adipose-derived and Bone Marrow-derived Stromal Cells(和訳中) *Journal of Oral Tissue Engineering*. 2020.09; 18(1); 1-12

15. Komatsu K, Shiba T, Takeuchi Y, Watanabe T, Koyanagi T, Nemoto T, Shimogishi M, Shibasaki M, Katagiri S, Kasugai S, Iwata T. Discriminating Microbial Community Structure Between Peri-Implantitis and Periodontitis With Integrated Metagenomic, Metatranscriptomic, and Network Analysis *Frontiers in Cellular and Infection Microbiology*, Tokyo Medical and Dental University. 2020.12; 10; 596490

[Conference Activities & Talks]

1. Shimogishi M, Watanabe T, Shibasaki M, Nakano Y, Kasugai S, Nakagawa I. Compositional change of peri-implant microbiota after the implant placement. The 93rd Annual Meeting of Japanese Society for Bacteriology 2020.02.19 Nagoya, Japan
2. Komatsu K, Shiba T, Nemoto T, Shimogishi M, Shibasaki M, S, Takeuchi Y, Kasugai S, Iwata T. Metagenomic analysis of peri-implant microbiome and its relation to disease severity. 2020.02.26 Niigata
3. Sabbagh AA, Nakata H, Abdou AMA, Kasugai S, Kuroda S. Fluctuation of salivary Alpha-Amylase level and vital signs during dental implant surgeries. Congress of Myanmar Dental Association 2020.09.05
4. SHIMOGISHI M, SHIBASAKI M, KAWAKAMI S, KURODA S, NAKATA H, TACHIKAWA N, KASUGAI S, SHIOTA M. Compositional change of peri-implant microbiota. The 50th Anniversary Annual Meeting of the Japanese Society of Oral Implantology 2020.09.19
5. Sasaki T, Nakata H, Suzuki A, Kasugai S, Kuroda S. Comparison of splinted and non-splinted superstructures of three implants placed in a mandibular distal extension missing tooth model by using modal analysis. The 30th Annual Scientific Meeting of European Association for Osseointegration 2020.10.08
6. Komatsu K, Takeuchi Y, Shiba T, Watanabe T, Shimogishi M, Shibasaki M, Nemoto T, Koyanagi T, Katagiri S, Iwata T. Omics analysis defines differences in microbial community structure between periimplantitis and periodontitis. 第 68 回 国際歯科研究学会 日本部会 総会・学術大会 2020.11.07 オンライン開催
7. Afnan Ahmed Sabbagh, Hidemi Nakata, Ahmed Mohamed Abdelrahman Abdou, Shohei Kasugai, Shinji Kuroda. Salivary Alpha-Amylase as a stress marker during dental implant surgeries. The 68th Annual Meeting of Japanese Association for Dental Research 2020.11.07
8. Taninokuchi H, Nakata H, Takahashi Y, Inoue K, Kasugai S, Kuroda S. Resistance of *P. gingivalis*, *S. aureus*, *P. aeruginosa* to a Cetylpyridinium Chloride -based Mouthwash. The 31st SEAAE&34th IADR-SEA 2020.11.24
9. Inoue K, Nakata H, Taninokuchi T, Takahashi Y, Kasugai S, Kuroda S. Microbiological evaluation of sealing materials the access holes of implant restorations. The 31st SEAAE&34th IADR-SEA 2020.11.24
10. Hirohito Miki et al. Genetic and epigenetic regulation of osteopontin promoter by cAMP in osteoblasts. 2020.12
11. SHIMOGISHI Masahiro, TACHIKAWA Noriko, FUJII Masaki, YAMAGUCHI Yoko, KUSUMOTO Yuki, MUNAKATA Motohiro. Risk factor of early dental implant failure in reconstructed mandible. 2020.12.05

Plastic and Reconstructive Surgery

Professor(Chairman):Mori Hiroki

Professor:Tanaka Kentaro

Assistant Professor (Hospital Staff):Uemura Noriko

Project Assistant Professor (Hospital Staff) :Inoue Makiko

Graduate Student:Homma Tsutomu,Suesada Nobuko,Hamanaga Mayuko,Ogawa Kazuya,Yamamoto Mao,Ishida Naoya

(1) Research

Plastic and Reconstructive Surgery :

MORI Hiroki

1. Pre and post operative breast or facial contour evaluation using 3D camera
2. Sensory recovery in the nipple-sparing or skin-sparing mastectomy
3. Development of classification and algorithm in blepharoptosis and blepharospasm surgery
4. Elucidation of the role of TRP channel and the midline in the interaction between keratinocyte and peripheral nervous system
5. Blood circulation study of the surgical flap using indocyanine green angiography and multi slice CT

Functional Reconstruction :

TANAKA Kentaro

1. Development of functional and aesthetic reconstruction following cancer ablation in head and neck
2. Does the improvement of capillary patency rate contribute to the preservation of transferred fatty tissue volume ?
3. Evaluation of blood supply to various flaps using ICG fluorescence angiography
4. Development of ambulatory functional reconstruction for refractory ulcer especially in CLI patients
5. Development of functional and aesthetic reconstruction for facial paralysis

(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 remodeling 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. Usami S, Kawahara S, Inami K. Vascularized Second Metacarpal Bone Graft for the Treatment of Idiopathic Osteonecrosis of the Capitate. *Hand (N Y)*. 2020.01; 15(1); NP22-NP25
2. Usami S, Inami K, Hirase Y, Mori H. An ulnar parametacarpal perforator flap for volar digital soft tissue reconstruction *JOURNAL OF HAND SURGERY-EUROPEAN VOLUME*. 2020.07; 1753193420939379
3. Ogawa K, Okazaki M, Tanaka K, Uemura N, Homma T. One-Stage Simultaneous Augmentation of 2 Regions of 3 Facial Reanimations After Mid Skull Base Surgery by Using a Neurovascular Latissimus Dorsi Chimeric Flap. *J Craniofac Surg*. 2020.11;

[Conference Activities & Talks]

1. Usami S, Kawahara S, Takemitsu M, Shimizu H, Inami K. Clinical outcome of ear cartilage resurfacing arthroplasty together with suture-button suspensionplasty for symptomatic thumb carpometacarpal joint arthritis. *FSSH-EFSHT2020* 2020.09.03 Basel
2. Tanaka K, Uemura N, Homma T, Mori H, Sugawara T, Asakage T, Okazaki M. The role of plastic surgeons in skull base surgery the lectures from one anterior skull base reconstruction case. 15th Asia-Oceanian International Congress on Skull Base Surgery Virtual Congress 2020.10.26 Fukushima, Japan

Head and Neck Surgery

Professor: Takahiro Asagkage
Junior Associate Professor: Yosuke Ariizumi, Kazuchika Ohno
Assistant Professor: Akihisa Tasaki
Specially Appointed Assistant Professor: Yumiko Tateishi
Senior Resident: Hiroaki Kawabe, Nobuaki Koide, Ryosuke Takahashi
Graduate Student: Masaharu Kishikawa, Toshifumi Tomioka, Sadahiro Kishishita

(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. Wakiyama H, Furusawa A, Okada R, Inagaki F, Kato T, Maruoka Y, Choyke PL, Kobayashi H.. Increased Immunogenicity of a Minimally Immunogenic Tumor after Cancer-Targeting Near Infrared Photoimmunotherapy. *Cancers (Basel)*. 2020; 12(12); E3747
2. Maruoka Y, Furusawa A, Okada R, Inagaki F, Wakiyama H, Kato T, Nagaya T, Choyke PL, Kobayashi H. Interleukin-15 after Near-Infrared Photoimmunotherapy (NIR-PIT) Enhances T Cell Response against Syngeneic Mouse Tumors. *Cancers (Basel)*. 2020; 10(12(9)); 2575
3. Fujimura D, Inagaki F, Okada R, Rosenberg A, Furusawa A, Choyke PL, Kobayashi H. Conjugation Ratio, Light Dose, and pH Affect the Stability of Panitumumab-IR700 for Near-Infrared Photoimmunotherapy. *ACS Medicinal Chemistry Letters*. 2020; 6(11(8)); 1598-1604
4. Kohtaro Eguchi, Shigeo Kawai, Masayoshi Mukai, Hiroaki Nagashima, Satoshi Shirakura, Taro Sugimoto, Takahiro Asakage. Medial lingual lymph node metastasis in carcinoma of the tongue. *Auris Nasus Larynx*. 2020.02; 47(1); 158-162
5. Xui-Fen Liu, Junxia Wei, Qi Zhou, Bruce A Molitoris, Ruben Sandoval, Hisataka Kobayashi, Ryuhei Okada, Tadanobu Nagaya, Baktiar Karim, Donna Butcher, Ira Pastan. Immunotoxin SS1P is rapidly removed by proximal tubule cells of kidney, whose damage contributes to albumin loss in urine. *Proc Natl Acad Sci U S A*. 2020.03; 117(11); 6086-6091
6. Yasuhiro Maruoka, Aki Furusawa, Ryuhei Okada, Fuyuki Inagaki, Daiki Fujimura, Hiroaki Wakiyama, Takuya Kato, Tadanobu Nagaya, Peter L Choyke, Hisataka Kobayashi. Combined CD44- and CD25-Targeted Near-Infrared Photoimmunotherapy Selectively Kills Cancer and Regulatory T Cells in Syngeneic Mouse Cancer Models. *Cancer Immunol Res*. 2020.03; 8(3); 345-355
7. Zeliang Zheng, Ryuhei Okada, Hisataka Kobayashi, Tadanobu Nagaya, Junxia Wei, Qi Zhou, Fred Lee, Tapan K Bera, Yun Gao, William Kuhlman, Chin-Hsien Tai, Ira Pastan. Site-Specific PEGylation of Anti-Mesothelin Recombinant Immunotoxins Increases Half-life and Antitumor Activity. *Mol Cancer Ther*. 2020.03; 19(3); 812-821
8. Takeshi Shinozaki, Chikatoshi Katada, Kiyoto Shiga, Takahiro Asakage, Tetsuji Yokoyama, Tomonori Yano, Ichiro Oda, Yuichi Shimizu, Kenichi Takemura, Hideki Ishikawa, Akira Yokoyama, Manabu Muto. Effectiveness of planned surveillance for detecting second primary head and neck cancers after endoscopic resection of esophageal squamous cell carcinoma. *Jpn. J. Clin. Oncol.* 2020.06;
9. 井上 剛志, 野村 文敬, 清川 佑介, 朝蔭 孝宏. 特徴的な嚥下障害をきたした Zenker 憩室の一例 口腔・咽頭科. 2020.06; 33(2); 131-135
10. Fuyuki F Inagaki, Daiki Fujimura, Sara Ansteatt, Ryuhei Okada, Aki Furusawa, Peter L Choyke, Marcin Ptaszek, Hisataka Kobayashi. Effect of Short PEG on Near-Infrared BODIPY-Based Activatable Optical Probes. *ACS Omega*. 2020.06; 5(25); 15657-15665
11. Yuki Saito, Ryuichi Hayashi, Yoshiyuki Iida, Takatsugu Mizumachi, Takashi Fujii, Fumihiko Matsumoto, Takeshi Beppu, Masafumi Yoshida, Hiroataka Shinomiya, Ryosuke Kamiyama, Mutsukazu Kitano, Kazuhiko Yokoshima, Yasushi Fujimoto, Takanori Hama, Taku Yamashita, Kenji Okami, Kouki Miura, Takuo Fujisawa, Daisuke Sano, Hisayuki Kato, Shujiro Minami, Masashi Sugawara, Muneyuki Masuda, Ichiro Ota, Shigemichi Iwae, Ryo Kawata, Nobuya Monden, Takayuki Imai, Takahiro Asakage, Masafumi Okada, Takanori Yoshikawa, Kensuke Tanioka, Megumi Kitayama, Mariko Doi, Satoshi Fujii, Masato Fujii, Nobuhiko Oridate, Munenaga Nakamizo, Seiichi Yoshimoto, Akihiro Homma, Ken-Ichi Nibu, Katsunari Yane. Optimization of therapeutic strategy for p16-positive oropharyngeal squamous cell carcinoma: Multi-institutional observational study based on the national head and neck cancer registry of Japan. *Cancer*. 2020.07; 126(18); 4177-4187
12. Kanako Ichikura, Nao Nakayama, Shiho Matsuoka, Yosuke Ariizumi, Takuro Sumi, Taro Sugimoto, Yuko Fukase, Norio Murayama, Hirokuni Tagaya, Takahiro Asakage, Eisuke Matsushima. Efficacy of stress management program for depressive patients with advanced head and neck cancer: A single-center pilot study *International Journal of Clinical and Health Psychology*. 2020.07; 20; 213-221

13. Adrian Rosenberg, Daiki Fujimura, Ryuhei Okada, Aki Furusawa, Fuyuki Inagaki, Hiroaki Wakiyama, Takuya Kato, Peter L Choyke, Hisataka Kobayashi. Real-Time Fluorescence Imaging Using Indocyanine Green to Assess Therapeutic Effects of Near-Infrared Photoimmunotherapy in Tumor Model Mice. *Mol Imaging*. 2020.07; 19; 1536012120934965
14. Yokota T, Homma A, Kiyota N, Tahara M, Hanai N, Asakage T, Matsuura K, Ogawa T, Saito Y, Sano D, Kodaira T, Motegi A, Yasuda K, Takahashi S, Tanaka K, Onoe T, Okano S, Imamura Y, Ariizumi Y, Hayashi R, Japan Clinical Oncology Group (JCOG) Head and Neck Cancer Study Group.. Immunotherapy for squamous cell carcinoma of the head and neck. *Japanese journal of clinical oncology*. 2020.08;
15. Adrian Rosenberg, Fuyuki Inagaki, Takuya Kato, Ryuhei Okada, Hiroaki Wakiyama, Aki Furusawa, Peter L Choyke, Hisataka Kobayashi. Wound healing after excision of subcutaneous tumors treated with near-infrared photoimmunotherapy. *Cancer Med*. 2020.08; 9(16); 5932-5939
16. Yokoyama Kota, Manabe Osamu, Tsuchiya Jyunichi, Oyama Jun, Kawabe Hiroaki, Tateishi Yumiko, Asakage Takahiro, Yamamoto Kouhei, Tateishi Ukihide. A rare case of cranial and spinal leptomeningeal dissemination of recurrent ethmoid carcinoma detected by [18F]-FDG PET/CT *EUROPEAN JOURNAL OF NUCLEAR MEDICINE AND MOLECULAR IMAGING*. 2020.09;
17. Ichikura K, Nakayama N, Matsuoka S, Ariizumi Y, Sumi T, Sugimoto T, Fukase Y, Murayama N, Tagaya H, Asakage T, Matsushima E. Efficacy of stress management program for depressive patients with advanced head and neck cancer: A single-center pilot study. *International journal of clinical and health psychology : IJCHP*. 2020.09; 20(3); 213-221
18. Maruoka Y, Furusawa A, Okada R, Inagaki F, Fujimura D, Wakiyama H, Kato T, Nagaya T, Choyke PL, Kobayashi H. Near-Infrared Photoimmunotherapy Combined with CTLA4 Checkpoint Blockade in Syngeneic Mouse Cancer Models *Vaccines (Basel)*. 2020.09; 8(3); 528
19. Miwa K, Tsutsumi M, Fukino K, Eguchi K, Okada R, Akita K. An anatomical study of the anterior wall of the hypopharyngeal and the cervical esophageal junction. *Auris, nasus, larynx*. 2020.10; 47(5); 849-855
20. Takahashi R, Kawabe H, Koide N, Tasaki A, Ohno K, Ariizumi Y, Kobayashi D, Asakage T. Superior mediastinal paraganglioma initially suspected of being a mediastinal thyroid goiter. *Auris, nasus, larynx*. 2020.11;
21. Baba S, Akashi T, Kayamori K, Ohuchi T, Ogawa I, Kubota N, Nakano K, Nagatsuka H, Hasegawa H, Matsuzaka K, Tomii S, Uchida K, Katsuta N, Sekiya T, Ando N, Miura K, Ishibashi H, Ariizumi Y, Asakage T, Michi Y, Harada H, Sakamoto K, Eishi Y, Okubo K, Ikeda T. Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma. *Pathology international*. 2020.12;
22. Kiyokawa Y, Ariizumi Y, Ohno K, Ito T, Kawashima Y, Tsunoda A, Kishimoto S, Asakage T, Tsutsumi T. Indications for and extent of elective neck dissection for lymph node metastasis from external auditory canal carcinoma. *Auris, nasus, larynx*. 2020.12;
23. 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. Hitoshi Hirakawa, Takeshi Shinozaki, Mitsuru Ebihara, Wataru Shimbashi, Tomoyuki Kamijo, Makito Okamoto, Takeshi Beppu, Junichiro Ohori, Kazuto Matsuura, Motoyuki Suzuki, Hiroshi Nishino, Yuichiro Sato, Hiroto Ishiki. Symptom prevalence and functional status in patient with terminal phase of head and neck cancer –multi institutional research. 第30回日本頭頸部外科学会 2020.01.31 沖縄

Radiation Therapeutics and Oncology

Professor Ryoichi Yoshimura

Lecturers Kazuma Toda

Research Associates Hirofumi Kuwabara(~ Mar.)

Hospital Staff members Takuya Nagano(Apr. ~),
Aya Usami(Apr. ~), Daigoro Matsubara (Oct. ~)

Resident Meika Koide(~ Mar.)

Graduate Students

Yoshinao Takada, Masahiro Yoshida, Kazuma Sasamura

(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 791 patients, including 240 head and neck cancer patients, 89 prostate cancer patients, 60 breast cancer patients, 35 lung cancer patients, and 37 esophageal cancer patients, were treated at our hospital in 2019.

(6) Clinical Performances

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

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

1. Kunogi H, Hsu IC, Yamaguchi N, Kusunoki S, Nakagawa K, Sugimori Y, Fujino K, Terao Y, Ogishima D, Yoshimura R, Sasai K. CT-Guided Pelvic Lymph Nodal Brachytherapy. *Frontiers in oncology*. 2020; 10; 532555
2. Iijima Kotaro, Okamoto Hiroyuki, Takahashi Kana, Aikawa Ako, Wakita Akihisa, Nakamura Satoshi, Nishioka Shie, Harada Ken, Notake Ryoichi, Sugawara Akimoto, Yoshimura Ryoichi, Kunieda Etsuo, Itami Jun. Inter-fractional variations in the dosimetric parameters of accelerated partial breast irradiation using a strut-adjusted volume implant *JOURNAL OF RADIATION RESEARCH*. 2020.01; 61(1); 123-133
3. Iijima Kotaro, Okamoto Hiroyuki, Takahashi Kana, Aikawa Ako, Wakita Akihisa, Nakamura Satoshi, Nishioka Shie, Harada Ken, Notake Ryoichi, Sugawara Akimoto, Yoshimura Ryoichi, Kunieda Etsuo, Itami Jun. strut-adjusted volume implant を用いた加速乳房部分照射の線量パラメータにおける inter-fractional variation(Inter-fractional variations in the dosimetric parameters of accelerated partial breast irradiation using a strut-adjusted volume implant) *Journal of Radiation Research*. 2020.01; 61(1); 123-133
4. Hirai H, Ohsako T, Kugimoto T, Tomioka H, Michi Y, Kayamori K, Yoda T, Miura M, Yoshimura R, Harada H. Comparison of 50- and 66-Gy total irradiation doses for postoperative cervical treatment of patients with oral squamous cell carcinoma. *Oral oncology*. 2020.04; 107; 104708
5. Hirota Hiroshi, Ito Kei, Kageyama Shun-Ichiro, Tamamoto Fumihiko, Karasawa Katsuyuki, Yoshimura Ryouichi. Safety of radiotherapy for hemodialysis patients with cancer *INTERNATIONAL JOURNAL OF CLINICAL ONCOLOGY*. 2020.05; 25(5); 978-983
6. Yoshida S, Takahara T, Arita Y, Toda K, Yoshimura R, Fujii Y. Patterns of failure after progressive site-directed therapy in oligo-progressive castration-resistant prostate cancer. *International journal of urology : official journal of the Japanese Urological Association*. 2020.07; 27(7); 634-635
7. Sasamura K, Suzuki R, Kozuka T, Yoshimura R, Yoshioka Y, Oguchi M. Outcomes after reirradiation of spinal metastasis with stereotactic body radiation therapy (SBRT): a retrospective single institutional study. *Journal of radiation research*. 2020.08;
8. Yoshida S, Takahara T, Yokoyama M, Matsuoka Y, Yoshimura R, Fujii Y. Can progressive site-directed therapy prolong the efficacy of subsequent androgen receptor axis-targeted drugs in oligometastatic castration-resistant prostate cancer? *International journal of urology : official journal of the Japanese Urological Association*. 2020.11;
9. Towithelertkul C, Chugh A, Hattori M, Yoshimura R, Sumita YI. A custom-made brachytherapy applicator for recurrent endometrial and vaginal cancer: A dental technique for prosthesis fabrication. *The Journal of Prosthetic Dentistry*. 2020.11; online;

Maxillofacial Anatomy

Professor Shunichi SHIBATA
Associate Professor Masaki TAKECHI (from October, 2020)
Graduate Student Maki HASEGAWA
Graduate Student Angamma RANDILINI
Lecturer Rei SATO

(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) Hyaluronan synthesis in tooth germ.
- 6) Studies on regeneration of jaw bone.
- 7) 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. Shibata S, Amano H, Nagayama M, Takahashi M, Watanabe M, Tanaka M. Immunohistochemical and ultrastructural evaluation of matrix components in mandibular condylar cartilage in comparison with growth plate cartilage in cartilage calcification insufficient rats. *Anatomical science international*. 2020.01; 95(1); 54-66
2. Yamada, T, Takechi M (Co-first), Yokoyama N, Hiraoka Y, Ishikubo H, Usami T, Furutera T, Taga Y, Hirate Y, Kanai-Azuma M, Yoda T, Ogawa-Goto K, Iseki S. Heterozygous mutation of the splicing factor Sf3b4 affects development of the axial skeleton and forebrain in mouse. *Developmental Dynamics*. 2020.01;
3. Randilini A, Fujikawa K, Shibata S. Expression, localization and synthesis of small leucine-rich proteoglycans in developing mouse molar tooth germ *European Journal of Histochemistry*. 2020.02; 64(1); 3092
4. Funato N, Srivastava D, Shibata S, Yanagisawa H. TBX1 regulates chondrocyte maturation in the spheno-occipital synchondrosis *Journal of Dental Research*. 2020.05;
5. Fujikawa K, Shibata S, Nakamura M. An in situ hybridization study of the Syndecan family in the developing condylar cartilage of fetal mouse mandible *Anatomical Record*. 2020.06;
6. Kim JH, Jin ZW, Shibata S, Murakami G, Hayashi S, Rodríguez-Vázquez JF. Vermiform appendix during the repackaging process from umbilical herniation to fixation onto the right posterior abdomen: a study of human fetal horizontal sections *Clinical Anatomy*. 2020.07; 33(5); 667-677
7. Honkura Y, Hayashi S, Abe H, Murakami G, Rodríguez-Vázquez JF, Shibata S. The third vascular route of the inner ear or the canal of Cotugno: its topographical anatomy, fetal development, and contribution to ossification of the otic capsule cartilage *Anatomical Record*. 2020.08;
8. Randilini A, Fujikawa K, Shibata S. An in situ hybridization study of decorin and biglycan mRNA in mouse osteoblasts in vivo *Anatomical Science International*. 2020.11; on line;

[Conference Activities & Talks]

1. Horigome Y, Ida-Yonemochi H, Waguri S, Shibata S, Komatsu M. Loss Of Autophagy In Chondrocytes Causes Severe Growth Retardation . Orthopedic Research Society 2020 Annual Meeting 2020.02.10 Phoenix Convention Center Phoenix, Arizona, USA
2. 井関祥子, 柳澤昇平, Arun Kumar Rajendran, 有坂慶紀, 塗隆志, 原田敦子, 小林真司, 上田晃一, 武智正樹, 由井伸彦. 臨床応用を目指した骨芽細胞分化のコントロール . 第 29 回日本形成外科学会基礎学術集会 2020.10.08
3. Tabata Makoto J, Sugiura Makoto, Shibata shunichi . Attempt of histology training using virtual slides and future prospects. 2020.12.04 TMDU

Cognitive Neurobiology

Professor:
Naofumi Uesaka
Lecturer:
Daisuke Tanaka
Assistant Professor
Atsuya Takeuchi
Moe Tanigawa
Nozomi Utsumi
Ryo Masumura
Yang Sun
Ibin Han

(1) Outline

Our goal is to understand how each brain cell or group of brain cells generates complex brain functions and how dysfunction of each cell causes brain diseases. To answer these questions, we use a variety of techniques, including neurophysiology, molecular biology, and genetics. We promote researches and aim to find novel concepts in brain development, brain function, and brain diseases.

(2) Research

1. Functional development of the brain

We are studying the mechanism of selective strengthening and elimination of synapses (synapse elimination) during postnatal development.

2. Glial function

We aim to discover novel functions of glial cells.

3. Crosstalk between oral function and brain function in the health and disease.

We aim to elucidate the information processing of oral sensation in the brain and brain disease caused by oral dysfunction.

4) Brain diseases

We aim to elucidate the mechanisms by which brain diseases develop and become malignant.

(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. 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

We plan to actively accept a diverse range of students and staff from various backgrounds, including biology, engineering, dentistry, and medicine, regardless of academic field. We will educate them to be able to either develop innovative methods, hit innovative hypotheses, or make innovative discoveries. For this reason, we place importance on creating an environment and atmosphere where staff and students can actively share their opinions in daily discussions and study sessions. By reading our papers and papers on the latest research findings and conducting research with staff and senior students, students can learn how to acquire and analyze data, conduct research, and write papers. Let's work together to make innovative discoveries by cooperating with each other and doing research every day toward the major goal of elucidating brain development, brain function, and brain diseases.

(5) Publications

[Original Articles]

1. Saito R, Koebis M, Nagai T, Shimizu K, Liao J, Wulaer B, Sugaya Y, Nagahama K, Uesaka N, Kushima I, Mori D, Maruyama K, Nakao K, Kurihara H, Yamada K, Kano M, Fukada Y, Ozaki N, Aiba A. Comprehensive analysis of a novel mouse model of the 22q11.2 deletion syndrome: a model with the most common 3.0-Mb deletion at the human 22q11.2 locus. *Translational psychiatry*. 2020.02; 10(1); 35
2. Watanabe Takaki, Suzuki Honoka, Sakoori Kazuto, Inoue Shutaro, Akamatsu Tsubasa, Abe Manabu, Sakimura Kenji, Uesaka Naofumi, Kano Masanobu. Protocadherin 10 delays developmental climbing fiber synapse elimination in a subset of aldolase C-positive Purkinje cells in the cerebellum(和訳中) *The Journal of Physiological Sciences*. 2020.03; 70(Suppl.1); S97
3. Rai Y, Watanabe T, Matsuyama K, Sakimura K, Uesaka N, Kano M. Phospholipase C β 3 is Required for Climbing Fiber Synapse Elimination in Aldolase C-positive Compartments of the Developing Mouse Cerebellum. *Neuroscience*. 2020.04;
4. Nagumo Yasuyuki, Ueta Yoshifumi, Nakayama Hisako, Osaki Hironobu, Takeuchi Yuichi, Uesaka Naofumi, Kano Masanobu, Miyata Mariko. Tonic GABAergic Inhibition Is Essential for Nerve Injury-Induced Afferent Remodeling in the Somatosensory Thalamus and Ectopic Sensations *CELL REPORTS*. 2020.06; 31(12); 107797
5. Sacai H, Sakoori K, Konno K, Nagahama K, Suzuki H, Watanabe T, Watanabe M, Uesaka N, Kano M. Autism spectrum disorder-like behavior caused by reduced excitatory synaptic transmission in pyramidal neurons of mouse prefrontal cortex. *Nature communications*. 2020.10; 11(1); 5140
6. Yamashiro K, Hori K, Lai ESK, Aoki R, Shimaoka K, Arimura N, Egusa SF, Sakamoto A, Abe M, Sakimura K, Watanabe T, Uesaka N, Kano M, Hoshino M. AUTS2 Governs Cerebellar Development, Purkinje Cell Maturation, Motor Function and Social Communication. *iScience*. 2020.12; 23(12); 101820

[Conference Activities & Talks]

1. 渡邊 貴樹^{1,2}, 佐郡 和人¹, 鈴木 穂香¹, 赤松 翼¹, 松山 恭子¹, 井上 秀太郎¹, 阿部 学³, 崎村 建司³, 上阪直史^{1,2}, 狩野 方伸^{1,2}. Protocadherin 10 は一部のアルドラーゼC陽性の小脳プルキンエ細胞において発達期の登上線維シナプスの刈り込みを遅延させる. 2020.07.29
2. 上阪直史. 運動機能を司る小脳の発達：咀嚼嚥下の機能発達の理解を目指して. 第62回 歯科基礎医学会学術大会 2020.09.22 日本 (Web シンポジウム)

3. 上阪直史. Astrocytes regulate synapse elimination in the developing cerebellum. 遺伝研研究会「哺乳類脳の機能的神経回路の構築メカニズム」 2020.12.11 日本 (Web シンポジウム)

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 Toshiko FURUTERA Shigeru Okuhara

Graduate Students

Erika KUBOTA
RAJENDRAN Arun kumar
Takahiko YAMADA
Shohei YANAGISAWA
VU HOANG Tri
Manami TAKENOSHITA
Rika TAKEUCHI
NAMANGKALAKUL Worachat
Yukiko HOSHINO

Research students

(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. Yamada, T, Takechi M (Co-first), Yokoyama N, Hiraoka Y, Ishikubo H, Usami T, Furutera T, Taga Y, Hirate Y, Kanai-Azuma M, Yoda T, Ogawa-Goto K, Iseki S. Heterozygous mutation of the splicing factor Sf3b4 affects development of the axial skeleton and forebrain in mouse. *Developmental Dynamics*. 2020.01;
2. Saadat KASM, Bozgeyik E, Arman K, Bozgeyik I, Ikeda MA. ARID3A-mediated modulation of TP73 and TP73-AS1 in osteosarcoma cells *Gene Reports*. 2020.04; 20; 100683
3. Yamada T, Takechi M, Yokoyama N, Hiraoka Y, Ishikubo H, Usami T, Furutera T, Taga Y, Hirate Y, Kanai-Azuma M, Yoda T, Ogawa-Goto K, Iseki S. . Heterozygous mutation of the splicing factor Sf3b4 affects development of the axial skeleton and forebrain in mouse. *Developmental Dynamics*. 2020.05; 249(5); 622-635

4. 3. Bozgeyik E, Saadat KASM, Arman K, Bozgeyik I, Ikeda MA. Enhanced E2F1 activity increases invasive and proliferative activity of breast cancer cells through non-coding RNA CDKN2B-AS1 Meta Gene. 2020.06; 24; 100691
5. Ohki S, Oka K, Ogata K, Okuhara S, Rikitake M, Toda-Nakamura M, Tamura S, Masao Ozaki, Iseki S, Sakai T. . Transforming Growth Factor-Beta and Sonic Hedgehog Signaling in Palatal Epithelium Regulate Tenascin-C Expression in Palatal Mesenchyme During Soft Palate Development Frontiers in Physiology. 2020.06; 11; 532
6. Sanchez J, Miyake R, Cheng A, Liu T, Iseki S, Kume T. . Conditional inactivation of Foxc1 and Foxc2 in neural crest cells leads to cardiac abnormalities Genesis. 2020.07; 58(7); e23364
7. Date Yuki, Kondo Hisatomo, Yamashita Atsuko, Iseki Sachiko, Kasugai Shohei, Ota Masato S.. Combined in silico analysis identified a putative tooth root formation-related gene, Chd3, which regulates DNA synthesis in HERS01a cells(和訳中) Odontology. 2020.07; 108(3); 386-395
8. Arman Kaifee, Saadat Khandakar A. S. M., Igci Yusuf Z., Bozgeyik Esra, Ikeda Masa-Aki, Cakmak Ecir A., Arslan Ahmet. Long noncoding RNA ERICD interacts with ARID3A via E2F1 and regulates migration and proliferation of osteosarcoma cells CELL BIOLOGY INTERNATIONAL. 2020.08; 11434;

[Misc]

1. Arun Kumar Rajendan, Yoshinori Arisaka, Nobuhiko Yui, Sachiko Iseki. Polyrotaxanes as emerging biomaterials for tissue engineering applications: A brief review Inflammation and Regeneration. 2020.11; 40(1); 27

[Conference Activities & Talks]

1. Arun Kumar Rajendran, Yoshinori Arisaka, Shohei Yanagisawa, Takashi Nuri, Atsuko Harada, Koichi Ueda, Masaki Takechi, Nobuhiko Yui, Sachiko Iseki. Regulating osteogenic differentiation by supramolecular mobility-a treatment for craniosynostosis?. Gordon Research Conference, Craniofacial Morphogenesis and Tissue Regeneration II Ciocco 2020.02.27 Italy
2. 先天性顎顔面形成不全研究の現在と展望 神経堤細胞由来頭部間葉の分化について . 日本歯科基礎医学会 2020.09.11 鹿児島 (オンライン)
3. Seki N, Moross J, Kanamori Y, Kanazawa M, Komagamine Y, Mizutani K, Liao S, Kabasawa Y, Iseki S, Morio I. Importance of preparatory courses for international/global dental student exchange programs. Annual Meeting of the 39th Japanese Dental Education Association 2020.09.25 Paper/Online Base
4. 井関祥子, 柳澤昇平, Arun Kumar Rajendran, 有坂慶紀, 塗隆志, 原田敦子, 小林真司, 上田晃一, 武智正樹, 由井伸彦. 臨床応用を目指した骨芽細胞分化のコントロール . 第 29 回日本形成外科学会基礎学術集会 2020.10.08
5. 井関祥子, 柳澤昇平, Arun Kumar Rajendran, 有坂慶紀, 塗隆志, 原田敦子, 小林真司, 上田晃一, 武智正樹, 由井伸彦. 臨床応用を目指した骨芽細胞分化のコントロール. 第 29 回日本形成外科学会基礎学術集会 2020.10.09 横浜
6. Sachiko ISEKI. Classification and pathological mechanisms of Craniosynostosis based on the differentiation pattern of iPS cells. 第 68 回国際歯科研究学会 日本部会総会・学術大会 2020.11.07

Cellular Physiological Chemistry

Associate Professor Ken-ichi Nakahama

Junior Associate Professor Hiroshi Fujita, Yasuki Ishizaki, Masahiro Shinohara

Research Student : Hong Ding Liu
: Hirohito Miki
: SUN WEIMING
: Shiho Hidaka
: Risa Kawakura

Collaborator :Yuki Kasahara

(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. Miki H, Okito A, Akiyama M, Ono T, Tachikawa N, Nakahama KI. Genetic and epigenetic regulation of osteopontin by cyclic adenosine 3' 5'-monophosphate in osteoblasts. *Gene*. 2020.08; (763); 145059

[Conference Activities & Talks]

1. Shohei Yanagisawa, Sachiko Iseki, Rajendran Arun Kumar, Nobuhiko Yui, Yoshinori Arisaka, Kenichi Nakahama, Hiroyuki Harada, Koichi Ueda, Takashi Nuri, Atsuko Harada, Shinji Kobayashi, Tadashi Kaname, Youichirou Ninomiya. Mechanical cues of polyrotaxanes control osteogenic differentiation for adjunct treatment of craniosynostosis. The 43rd Annual Meeting of the Molecular Biology Society of Japan 2020.12.02

Maxillofacial Surgery

Professor: Tetsuya YODA
Associate Professor: Eriko MARUKAWA, Yoshiyuki SASAKI
Junior Associate Professor: Keiiti MORITA
Assistant Professor: Hiroyuki YOSHITAKE, Kouichi NAKAKUKI, Namiaki TAKAHARA,
Nobuyoshi TOMOMATSU
Special Assistant Professor: Yasuhiro KURASAWA, Tsubasa KIHARA, Yosuke HARAZONO,
Masahiko TERAUCHI, Hirokazu KACHI
Hospital Staff: Daisuke YAMAMOTO, Takahiko YAMADA, Kentaro SUGIYAMA,
Takuya IWASAKI, Erina NAKAMURA, Tomomi SAKUMA, Atsushi KIMURA,
Eri ANZAI
Graduate Student: Eri SHIBATA, Hiroki MASUDA, Yuu AKAIKE, Kouhi SYU,
Noboru MARUTA, Shintarou YAMAZAKI, Rina TAJIMA
Social Graduate Student: Mari SHIBATA
Student: Tizuko KOMURO, Junya KUMAGAI, Yuuko KATSUKI, Chika MIURA
Part-time Lecturer: Hiroyuki WAKE, Masashi YAMASHIRO, Jin SATO, Hideo MIYACHI,
Akiko KOBAYASHI, Fumiaki SATO, Tetsuo SUZUKI, Yutaka SATO,
Takashi MISHIMAGI, Kazuto KUROHARA,
Katuya AIKOU, Yosio OYAMA, Shigehiro ABE, Chieko MICHIKAWA,
Ryosuke NAGAOKA, Toshiyuki YAMADA, Erina TONOUCI,
Katsuya HYODO

(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 injuries 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. Nguyen CTK, Sawangarun W, Mandasari M, Morita KI, Harada H, Kayamori K, Yamaguchi A, Sakamoto K. AIRE is induced in oral squamous cell carcinoma and promotes cancer gene expression. *PloS one*. 2020; 15(2); e0222689
2. Kaneko A, Marukawa E, Harada H. Hydroxyapatite Nanoparticles as Injectable Bone Substitute Material in a Vertical Bone Augmentation Model IN VIVO. 2020; 34(3); 1053-1061
3. Mikami R, Mizutani K, Sasaki Y, Iwata T, Aoki A. Patient-reported outcomes of laser-assisted pain control following non-surgical and surgical periodontal therapy: A systematic review and meta-analysis. *PloS one*. 2020; 15(9); e0238659
4. Shibata E, Morita K, Kayamori K, Maruiwa M, Michi Y, Sato Y, Takeuchi K, Ikeda T, Harada H, Yoda T. Report Secretory carcinoma around Stensen's duct misdiagnosed as salivary duct cyst *INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL PATHOLOGY*. 2020; 13(8); 2211-2217
5. Yamada, T, Takechi M (Co-first), Yokoyama N, Hiraoka Y, Ishikubo H, Usami T, Furutera T, Taga Y, Hirate Y, Kanai-Azuma M, Yoda T, Ogawa-Goto K, Iseki S. Heterozygous mutation of the splicing factor Sf3b4 affects development of the axial skeleton and forebrain in mouse. *Developmental Dynamics*. 2020.01;
6. Dulguun B, Akiko K, Kumagai J, Yamaguchi S, Yoda T. Clinical observation of patients with inferior alveolar nerve sensory disturbance *JOURNAL OF ORAL SCIENCE*. 2020.01; 62(1); 112-118
7. Kim Yusoon, Hayashi Mikihito, Ono Takehito, Yoda Tetsuya, Takayanagi Hiroshi, Nakashima Tomoki. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation(和訳中) *Modern Rheumatology*. 2020.01; 30(1); 85-92
8. Fukushima Y, Kitamura T, Ikami E, Yumoto M, Sano Y, Sato T, Yoda T. A case of burning mouth syndrome leading to suicide 10 days after self-cutting of tongue *Psychogeriatrics*. 2020.01; 20(1); 126-128
9. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer Sci*. 2020.02; 111(2); 700-712
10. Yagihara K, Ishii J, Shibata M, Anzai E, Yagishita H, Ishikawa A. A case of carcinoma ex pleomorphic adenoma occurred in the sublingual gland *Oral science international*. 2020.02; 17(3); 174-178
11. Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Simple treatment of cell culture surfaces with water-dimethyl sulfoxide mixtures impacts YAP localization in vascular endothelial cells *Materials Letters*. 2020.03; 263; 127245
12. Yokokawa M, Morita KI, Oikawa Y, Kayamori K, Sakamoto K, Ikeda T, Harada H. Co-expression of EGFR and MET has a synergistic effect on the prognosis of patients with oral squamous cell carcinoma *J Oral Pathol Med*. 2020.03; 49(3); 235-242

13. Yahara H, Horita S, Yanamoto S, Kitagawa Y, Asaka T, Yoda T, Morita K, Michi Y, Takechi M, Shimasue H, Maruoka Y, Kondo E, Kusukawa J, Tsujiguchi H, Sato T, Kannon T, Nakamura H, Tajima A, Hosomichi K, Yahara K. A Targeted Genetic Association Study of the Rare Type of Osteomyelitis. *J Dent Res.* 2020.03; 99(3); 271-276
14. Kurasawa Y, Maruoka Y, Sekiya H, Negishi A, Mukohyama H, Shigematsu , Sugizaki J, Karakida K, Ohashi M, Ueno M, Michiwaki Y. Pneumonia prevention effects of perioperative oral management in approximately 25,000 patients following cancer surgery. *Clin Exp Dent Res.* 2020.04; 6(2); 165-173
15. Masuda H, Arisaka Y, Sekiya-Aoyama R, Yoda T, Yui N. Biological Effects of Polyrotaxane Surfaces on Cellular Responses of Fibroblast, Preosteoblast and Preadipocyte Cell Lines. *Polymers (Basel).* 2020.04; 12(4);
16. Hirai H, Ohsako T, Kugimoto T, Tomioka H, Michi Y, Kayamori K, Yoda T, Miura M, Yoshimura R, Harada H. Comparison of 50- and 66-Gy total irradiation doses for postoperative cervical treatment of patients with oral squamous cell carcinoma. *Oral oncology.* 2020.04; 107; 104708
17. Kitamura T, Tomoda, T Ikami E, Hayash N, Horishima Y, Yokota K, Mimura T, Fukushima Y, Yoda T, Sato T,. A case of giant cell arteritis with jaw claudication and trismus treated with early steroid therapy *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology.* 2020.05; 32(1); 222-225
18. Takahara N, Kimura A, Tomomatsu N, Nakakuki K, Yoda T. Does the amount of mandibular setback during bimaxillary surgery correlate with the degree of surgical relapse? *Oral surgery, oral medicine, oral pathology and oral radiology.* 2020.05; 129(5); 447-452
19. Tomoda K , Sato T, Ikami E, Fukushima Y, S Kokabub S, Yoda T. Contact co-culture of osteoblasts and sympathetic neuronal cells enhances osteoblast differentiation *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology.* 2020.07; 32(4); 307-312
20. Kinoshita N, Sasaki Y, Marukawa E, Hirose R, Sawada SI, Harada H, Akiyoshi K. Crosslinked nanogel-based porous hydrogel as a functional scaffold for tongue muscle regeneration *J Biomater Sci Polym Ed.* 2020.07; 31(10); 1254-1271
21. Eri Shibata, Kei-Ichi Morita, Kou Kayamori, Mayuko Maruiwa, Yasuyuki Michi, Yukiko Sato, Kengo Takeuchi, Tohru Ikeda, Hiroyuki Harada, Tetsuya Yoda. Secretory carcinoma around Stensen's duct misdiagnosed as salivary duct cyst. *Int J Clin Exp Pathol.* 2020.08; 13(8); 2211-2217
22. Ikami E, Sato T, Tomoda T, Fukushima Y, Kokabu S, Yoda T . Soluble factors mediate the interaction between Schwann cells and osteocytes *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology .* 2020.09; 32(5); 394-399
23. Yoda T, Ogi N, Yoshitake H, Kawakami T, Takagi R, Murakami K, Yuasa H, Kondoh T, Tei K, Kurita K. Clinical guidelines for total temporomandibular joint replacement. *Jpn Dent Sci Rev.* 2020.11; 56(1); 77-83
24. Sekiya-Aoyama R, Arisaka Y, Hakariya M, Masuda H, Iwata T, Yod T, Yui N. Dual effect of molecular mobility and functional groups of polyrotaxane surfaces on the fate of mesenchymal stem cells *Biomaterials Science.* 2020.12;
25. Mizutani K, Mikami R, Gohda T, Gotoh H, Aoyama N, Matsuura T, Kido D, Takeda K, Izumi Y, Sasaki Y, Iwata T. Poor oral hygiene and dental caries predict high mortality rate in hemodialysis: a 3-year cohort study. *Scientific reports.* 2020.12; 10(1); 21872
26. Miki K, Aizawa Y, Fujii S, Karakama J, Fujita K, Sasaki Y, Nemoto S, Sumita K. Combined technique thrombectomy with a long balloon guiding catheter and long sheath aids in rapid and stable recanalization in patients with anterior circulation acute ischemic stroke. *Journal of Neuroendovascular Therapy.* 2020.12;

Maxillofacial Orthognathics

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Yasuo ISHIWATA, Yoshiyuki BABA, Toshimoto TENGAN,
Masahiko YOKOZEKI, Shigetoshi HIYAMA,
Shigeki TAKAHASHI, Maristela Sayuri ARAI,
Junichi TAKADA, Rina HIKITA, Yosuke ITO,
Yuko YASUDA

(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. Hiratsuka T, Uezono M, Takakuda K, Kikuchi M, Oshima S, Sato T, Suzuki S, Moriyama K. Enhanced bone formation onto the bone surface using a hydroxyapatite/collagen bone-like nanocomposite. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*. 2020.02; 108(2); 391-398
2. Ogawa T, Cheng ES, Muramoto K, Moriyama K. Long-Term Management and Maxillofacial Growth in a Klippel-Trenaunay Syndrome Patient. *The Cleft Palate-Craniofacial Journal*. 2020.06; 57(6); 782-790
3. Purevjav E, Ganburged G, MukhtarY, Bazar A, Moriyama K. Arnett Facial Soft Tissue Cephalometric Analysis between the Ages of 6 and 15 Years in Mongolian Children *International Journal of Clinical Preventive Dentistry* . 2020.06; 16(2); 68-79
4. Purevjav E, Ganburged G, Bazar A, Mukhtar Y, Moriyama K. Arnett Facial Soft-tissue Cephalometric Analysis Norms for Mongolian Children *Central Asian Journal of Medical Sciences*. 2020.06; 6(2); 55-65
5. Tsuji M, Suzuki H, Suzuki S, Moriyama K. Three-dimensional evaluation of morphology and position of impacted supernumerary teeth in cases of cleidocranial dysplasia. *Congenital Anomalies*. 2020.07; 60(4); 106-114
6. Suga T, Tu TTH, Takenoshita M, Higashihori N, Kabasawa Y, Ono T, Moriyama K, Toyofuku A. Psychosocial Indication for Orthognathic Surgery in Patients with Psychiatric Comorbidities. *Psychiatry and clinical neurosciences*. 2020.08;

7. Teramoto A, Suzuki S, Higashihori N, Ohbayashi N, Kurabayashi T, Moriyama K. 3D evaluation of the morphological and volumetric changes of the tongue and oral cavity before and after orthognathic surgery for mandibular prognathism: a preliminary study. *Progress in Orthodontics* . 2020.08; 21(1); 30
8. Suga T, Tu TTH, Takenoshita M, Higashihori N, Kabasawa Y, Ono T, Moriyama K, Toyofuku A. Psychosocial indication for orthognathic surgery in patients with psychiatric comorbidities. *Psychiatry and Clinical Neurosciences*. 2020.08; 74(11); 621-623
9. Nakahara N, Matsuyama Y, Kino S, Badrakhkhoo N, Ogawa T, Moriyama K, Fujiwara T, Kawachi I. The Consumption of Sweets and Academic Performance among Mongolian Children. *International Journal of Environmental Research and Public Health*. 2020.11; 17(23); 8912

[Conference Activities & Talks]

1. Minswe NM, Kobayashi Y, Kamimoto H, Moriyama K . Aberrant Wnt/ β -catenin Signaling in Coronal Sutures of Apert Mouse Model. 2020 IADR/AADR/CADR General Session 2020.03.18 special online only issue of the *Journal of Dental Research*
2. Kadota-Watanabe C, Ogawa T, Funahashi K, Morita K, Yoda T, Moriyama K. A case of EEC syndrome treated by maxillary distraction osteogenesis and mandibular setback surgery. *The 44th Annual Meeting of Japanese cleft Palate Association* 2020.06.04
3. Ogawa T. Undergraduate Education on Cleft Lip and/or Palate at TMDU. *The 44th Annual Meeting of Japanese cleft Palate Association* 2020.06.04
4. Ogawa T, Baba Y, Uezono M, Mibu M, Sumita Y, Morita K, Yoda T, Moriyama K. Changes of pharyngeal morphology and speech function after maxillary distraction in cases of CLP. *The 44th Annual Meeting of Japanese Cleft Palate Association* 2020.06.04
5. Miyamoto J. Advancemens in the evaluation of orofacial function: aiming to improve treatment results. *The 30th Annual Meeting of the Society for Jaw Deformities* 2020.06.24
6. Kadota-Watanabe C, Higashihori N, Ogasawara T, Kamimoto H, Akiyama S, Matsumoto T, Moriyama K. Relationship between postoperative stability and condylar changes after mandibular advancement. *The 30th Annual Meeting of the Japanese Society for Jaw Deformities* 2020.06.24 Webinar
7. Kano S, Higashihori N, Ogura K, Kadota C, Matsumoto T, Takahara N, Yoda T, Moriyama K. Case reports of skeletal mandibular retrognathia treated by surgical-orthodontic treatment combined with maxillary osteotomy and genioplasty. *The 30th Annual Meeting of the Japanese Society for Jaw Deformities* 2020.06.24 Webinar
8. Higashihori N. Consideration of the difficulty of surgical orthodontic treatment for skeletal mandibular prognathism from the perspective of orthodontists. *The 30th Annual Meeting of the Society for Jaw Deformities* 2020.06.24
9. Katagiri W, Kobayashi T, Sasaki A, Susami T, Suda N, Tanaka E, Chikazu D, Tominaga K, Moriyama K, Yamashiro T, Saito I, Takahashi T. A nationwide survey for surgical orthognathic treatment in Japan. *The 30th Annual Meeting of the Japanese Society for Jaw Deformities* 2020.06.24 Webinar
10. Kobayashi Y, Min Swe Nay Myo, Kamimoto H, Moriyama K. Analysis of the Wnt/ β -catenin signaling pathway in craniosynostosis of a mouse model of Apert syndrome. *The 60th Annual Meeting of the Japanese Teratology Society* 2020.07.11
11. Nakagawa Kang J, Unnai Yasuda Y, Ogawa T, Sato M, Yamagata Z, Fujiwara T, Moriyama K. Association between Maternal Smoking during Pregnancy and Missing Teeth in Offspring. *The 9th Internarional Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society* 2020.10.04 ondemand
12. Teramoto A, Sagawa Y, Akiyama S, Funahashi K, Kobayashi Y, Moriyama K. Interdisciplinary Approach for an Adult Orthodontic Patient with Angle Class III Malocclusion Complicated with Severe Periodontitis. *The 9th Internarional Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society* 2020.10.04 ondemad

13. Yokouchi R, Ogawa T, Fukumoto Y, Komaki H, Moriyama K. Orthodontic Treatment of a Patient with Ullrich Congenital Muscular Dystrophy. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
14. Yohsizawa H, Miyamoto JJ, Hanakawa T, Shitara H, Honda M, Moriyama K. Reciprocal cortical activation patterns during molar and incisal biting correlated with bite force levels: an fMRI study. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
15. Arimura M, Yoshizawa Araki M, Unnai Yasuda Y, Higashihori N, Ogawa T, Moriyama K. A Survey of Unilateral Cleft Lip and Palate Patients Who Missed Orthodontic Management Until the Permanent Dentition Stage. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
16. Kaisaka Y, Uezono M, Inoue M, Takakuda K, Moriyama K. Bone formation around the experimental orthodontic anchorage devices fixed onto cortical bone. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
17. Kano S, Higashihori N, Ogura K, Kadota-Watanabe C, Matsumoto T, Takahara N, Yoda T, Moriyama K. Skeletal mandibular retrognathic cases in which occlusion and respiratory function during sleep were improved after surgical-orthodontic treatment . The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
18. Niki Y, Kobayashi Y, Moriyama K. Expression pattern of transcriptional enhanced associate domain family member 1in developing mouse molar tooth. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
19. Lin Tun Oo, Miyamoto JJ, Takada J, Moriyama K. Correlation Between the Position of the Glenoid Fossa and Condylar Movement in Mandibular Asymmetry Patients. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
20. Kamimoto H, Higashihori N, Akiyama S, Ogasawara T, Kadota-Watanabe C, Matsumoto T, Moriyama K. Usefulness of the Index of Orthognathic Functional Treatment Need in Surgical-Orthodontic Treatment for Japanese Skeletal Class III Patients: A Retrospective Study. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
21. Matsumura K, Miyamoto JJ, Ogura K, Unnai Y, Takada J, Baba Y, Moriyama K. Clinical study of Marfan syndrome patients: craniofacial morphology including frontal and maxillary sinuses. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
22. Funahashi K, Kobayashi Y, Niki Y, Higashihori N, Nakakuki K, Yoda T, Moriyama K. A Case Report of Severe Class II Malocclusion Treated with Anterior Segmental Maxillary Osteotomy and Genioplasty. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
23. Tsuji M, Nakakuki K, Hirabayashi K, Moriyama K. Spontaneous tooth eruption after early enucleation of supernumerary teeth in a patient with cleidocranial dysplasia. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
24. Kobayashi Y, Minswe NM, Kamimoto H, Moriyama K. Aberrant Wnt/ β -catenin Signaling in Coronal Sutures of Apert Mouse Model. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand

25. Uezono M, Takakuda K, Ogasawara T, Inoue M, Kaisaka Y, Moriyama K. Bone bonding efficacy of a newly developed orthodontic micro-screw evaluated with miniature swine model. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
26. Teekavanich C, Uezono M, Techalertpaisarn P, Moriyama K. Effect of pilot hole size on miniscrew insertion torque and stress generation of synthetic cortical bone. The 9th International Orthodontic Congress, The 12th Asian Pacific Orthodontic Conference, The 79th Annual Meeting of the Japanese Orthodontic Society 2020.10.04 ondemand
27. Kadota-Watanabe C, Higashihori N, Kang J, Ogawa T, Yoda T, Moriyama K. A skeletal Class II open bite case in which functional disharmony was improved after surgical-orthodontic treatment. The 59th Congress of the Korean Association of Maxillofacial Plastic and Reconstructive Surgeons 2020.10.29 e-conference
28. Thiha P, Higashihori N, Kano S, Moriyama K. Histone methyltransferase SETDB1 negatively regulates PTH/PTHrP receptor in chondrocytes. The 68th Annual Meeting of Japanese Association for Dental Research 2020.11.07 virtual congress
29. Miyamoto J. The human brain and mastication; broad impact on systemic functions. The 68th Annual Meeting of Japanese Association for Dental Research 2020.11.07 virtual congress
30. Inagaki Y, Ogawa T, Tabata M, Nagata Y, Watanabe R, Kawamoto T, Moriyama K, Tanaka T. Whole exome analysis of non-syndromic oligodontia in Japanese. The 65th Annual Meeting of the Japan Society of Human Genetics 2020.11.18 virtual congress

[Social Contribution]

1. Research Activities at Department of Maxillofacial Orthognathics in TMDU, Joint Degree Program with Chulalongkorn University, 2020.08.04

Maxillofacial Prosthetics

2020 April

Junior Associate Professor
SUMITA Yuka

Assistant Professor
HATTORI Mariko
OTOMARU Takafumi (~ December)

Contract Assistant Professor
HARAGUCHI Mihoko
MURASE Mai

Clinical Staff
MINAMISAWA Naoko (~ June)
NAGAI Hana (September ~ February, 2021)

Graduate Student
AWUTI Shater (~ September)
FUJITA haruka (~ March, 2021)
ZHANG Manjin
LIU Rongguang
TANI Hiroko
GAO Yuan
WANG Yujia
TOWITHELERTKUL Cheewin
YU Hongli (April ~)
CHUGH Anshu (April ~)
HAN Xuwei (October ~)
FARAG Islam (October ~)

Part-time Special Student
HU Junhui (~ March, 2021)
HAN Xuwei (~ September)
BAI Ziyi (April ~ March, 2021)
WANG Jiangyu (April ~ March, 2021)
ZHANG Fan (October ~ March, 2021)

Part-time Lecturer (Faculty of Dentistry)
SATO Iwao
IFUKUBE Akira
ARAI Takayuki
UZAWA Shinobu
ELBASHTI Mahmoud Ellarousi
HATANO Noriko
KANAZAKI Ayako (~ March, 2021)
INOHARA Ken (April ~)
TERUYAMA Yuko (April ~)

Part-time Lecturer (Graduated School)
OZAWA Shogo
KOSAKA Moe
TANIGAWA Chihiro

Speech-Language-Hearing Therapist
MASAKI Keita

(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.

1. Research for prosthetic diagnosis in patients with a maxillofacial defect
2. Research for functional rehabilitation of patients with a maxillofacial defect
3. Research for masticatory function in patients with a maxillofacial defect
4. Research for speech evaluation in patients with a maxillofacial defect
5. Research for development of new materials for facial prosthesis

(3) Publications

[Original Articles]

1. Hoshiai A, Yoshida N, Hoshiai T, Iida T, Adachi T, Sumita YI, Siozuka O. A case of radiotherapy patient that solved various issues using the dental hygiene process. *The Journal of Japan Society for Dental Hygiene*. 2020.02; 14(2); 93-101
2. Awuti S, Sumita YI, Hattori M, Yoshi S, Kelimu S, Ohbayashi N, Kurabayashi T, Taniguchi H. Morphological comparison of artificial teeth position utilising denture space in glossectomy patients. *Gerodontology*. 2020.03; 37(1); 72-77
3. Kelimu S, Sumita YI, Hattori M, Elbashti ME, Awuti S, Kanazaki A. A nonconventional approach to prevent mouth dryness in a patient with a complex maxillofacial defect. *Int J Maxillofac Prosthetics*. 2020.04; 3; 7-11
4. Yu H, Wang Y, Sumita YI, Hattori M. Maxillofacial prosthetic rehabilitation in a patient with a high-arched palate. *Open J Clin Med Case Rep*. 2020.04; 6(8); 1657
5. Kamiyanagi A, Sumita YI, Hattori M, Otomaru T, Murase M, Haraguchi M, Watanabe M, Taniguchi H. Clinical survey about immediate surgical obturator at the clinic for Maxillofacial Prosthetics Tokyo Medical and Dental University. *J Prosthodont Res*. 2020.04; 64(2); 237-238
6. Sumita YI, Maruoka R, Kamikuri Y, Watanabe M. 2019 Young Researchers Short-term Overseas Training Report. *Journal of Japanese Cleft Palate Association*. 2020.04; 45(1); 42-47
7. Zhang M, Hattori M, Elbashti ME, Sumita YI. Feasibility of Intraoral Scanning for Data Acquisition of Maxillectomy Defects. *Int J Prosthodont*. 2020.07; 33(4); 452-456
8. Liu Y, Hattori M, Sumita YI. A technique of speech aid adjustment with the assistance of nasalance values for non-nasal and nasal sounds. *Int J Maxillofac Prosthetics*. 2020.08; 3; 23-27
9. Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita YI, Uddin Chowdhury R, Uddin Chowdhury N, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment: A case report. *J Prosthodont Res*. 2020.09; online;
10. Murase M, Tani H, Ino S, Sumita YI. Nutrition assessment of an elderly patient with recurrent advanced carcinoma of the maxilla: A case report. *Int J Maxillofac Prosthetics*. 2020.10; 3; 28-31
11. Elbashti ME, Itamiya T, Aswehlee AM, Sumita YI, Ella B, Naveau A. Augmented Reality for Interactive Visualization of 3D Maxillofacial Prosthetic Data. *Int J Prosthodont*. 2020.11; 33(6); 680-683

12. Towithelertkul C, Chugh A, Hattori M, Yoshimura R, Sumita YI. A custom-made brachytherapy applicator for recurrent endometrial and vaginal cancer: A dental technique for prosthesis fabrication. *J Prosthet Dent.* 2020.11; online;
13. Fujita H, Otomaru T, Takahashi H, Iwasaki N, Said MM, Abdel-Khalek EA, Sumita YI. Effect of direct retainer types for a dento-maxillary prosthesis on abutment teeth of maxillectomy patients: In vitro study. *Maxillofacial Prosthetics.* 2020.12; 43(2); 73-84

[Books etc]

1. prosthodontics III. 2020.01 (ISBN : 978-4-8160-1373-7)

[Misc]

1. Nakabayashi S, Ohyama T, Shioiri S, Murakami K, Hata M, Miyamae S, Haraguchi M, Hattori M, Nakajima J, Minagi Y, Fujiwara S, Ono T. Effectiveness for functional recovery on wearing prosthesis with defective mandibular jaw. *Maxillofacial Prosthetics.* 2020.06; 43(1); 19-25

[Conference Activities & Talks]

1. Murase M, Tani H, Sumita YI. Nutrition assessment of postoperative head and neck cancer patients using a brief self-administered diet-history questionnaire (BDHQ). The 35th Annual Meeting of Japanese Society for Clinical Nutrition and Metabolism 2020.02.27 Kyoto (Japan) (on the Journal)
2. Tani H, Murase M, Sumita YI. Examination of changes in resting energy expenditure in patients with head and neck cancer using an indirect calorimetry. The 35th Annual Meeting of Japanese Society for Clinical Nutrition and Metabolism 2020.02.27 Kyoto (Japan) (on the Journal)
3. Zhang M. The possibility of the data acquisition using intraoral scanner on maxillectomy patients. 2020 生体環境応答学系大学院交流セミナー・難病（がん）ユニットワークショップ 2020.03.13 東京医科歯科大学（紙上開催）
4. Sumita YI, Moriyama K. Symposium 3:. The 44th Annual Meeting of Japanese Cleft Palate Association 2020.06.04 Nagoya (Japan) (on the Journal)
5. Sumita YI. Symposium 3: The prosthetic treatment for the cleft and lip palate patients at the special clinic for maxillofacial prosthetics. The 44th Annual Meeting of Japanese Cleft Palate Association 2020.06.04 Nagoya (Japan) (on the Journal)
6. Ogawa T, Baba Y, Uezono M, Mibu M, Sumita YI, Morita K, Yoda T, Moriyama K. Changes of pharyngeal morphology and speech function after maxillary distraction in cases of CLP. The 44th Annual Meeting of Japanese Cleft Palate Association 2020.06.04 Nagoya (Japan) (on the Journal)
7. 張 満金, 服部麻里子, 隅田由香. 口唇口蓋裂患者における口腔内スキャンによるデータ採取. 第44回日本口蓋裂学会総会・学術集会 2020.06.04 ウィンクあいち（愛知・名古屋市）（誌面開催）
8. Haraguchi M, Sumita YI, Kanazaki A. Over denture treatment for patients with cleft lip and palate difficult to do orthodontic treatment. The 44th Annual Meeting of Japanese Cleft Palate Association 2020.06.04 Nagoya (Japan) (on the Journal)
9. Hideshima M, Otomaru T, Kanazaki A, Ozawa S, Matsui K, Takahashi T, Shirota T, Danjo A, Yamashita Y. Symposium 5: Formulating clinical practice guidelines for the prosthodontic treatment of cleft lip & palate patients. The 44th Annual Meeting of Japanese Cleft Palate Association 2020.06.05 Nagoya (Japan) (on the Journal)
10. Sumita YI. Prosthodontic Specialist Seminar: The Competence that Prosthodontists Should Acquire; Part2 Maxillofacial prosthetic support for patients' dietary intake. The 129th Annual Meeting of the Japan Prosthodontic Society 2020.06.28 Web broadcast and by the Abstracts
11. Gao Y, Hattori M, Sumita YI. Performing and analyzing digital impression of a mandibulectomy model with simulated trismus condition. The 67th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2020.10.17 (Webinar)

12. Zhang M, Hattori M, Elbashti ME, Sumita YI. Comparison of data acquisition for maxillectomy patients using two different intraoral scanners. The 67th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2020.10.17 (Webinar)
13. Liu R, Hattori M, Sumita YI. Use of nasal speaking valve and voice measurement in maxillofacial restoration. The 67th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2020.10.17 (Webinar)
14. Wang Y, Hattori M, Garg P, Wesemann C, Ariff TFTM, Fredes CL, Sumita YI. Two- steps fabrication of an obturator prosthesis for a large maxillary defect with digital speech analysis. The 67th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2020.10.17 (Webinar)
15. Towithelertkul C, Sumita YI, Hattori M, Otomaru T. Processed record base technique obturator for edentulous patient with extensive maxillary defect. The 67th Annual Meeting of the American Academy of Maxillofacial Prosthetics 2020.10.17 (Webinar)
16. Yagihara K, Ishii J, Sumino J, Katsurano M, Shibata M, Kim Y, Haraguchi M, Izumo T, Yagishita H, Ishikawa A. Treatment and outcome of tongue cancer in our department . 2020.10.22 Kyoto (Japan) (Hybrid)

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. Shimizu T, Nakamura T, Inaba H, Iwasa H, Maruyama J, Arimoto-Matsuzaki K, Nakata T, Nishina H, Hata Y. The RAS-interacting chaperone UNC119 drives the RASSF6-MDM2-p53 axis and antagonizes RAS-mediated malignant transformation. *The Journal of biological chemistry*. 2020.06;

[Conference Activities & Talks]

1. Tomohiro Ishii, Xiyin Deng, Takao Nakata. Development of optogenetic tools and induction of cell differentiation. The 125th Annual Meeting of the Japanese Association of Anatomists 2020.03.25 ANA Crowne Plaza Ube
2. Toshifumi Asano, Takao Nakata. Control of intracellular calcium in skeletal muscle myoblasts. The 19th Congress of the Japanese Society for Regenerative Medicine 2020.05.18 Online
3. Hironori Inaba, Takao Nakata. Analyses of the regulation of PLC ϵ activity by small GTPases using optogenetics. The 72nd Annual Meeting of the Japan Society for Cell Biology 2020.06
4. Hironori Inaba, Qianqian Miao, Takao Nakata. Optogenetic control of small GTPases reveals RhoA-mediated intracellular calcium signaling. Cell Bio Virtual 2020 - An Online ASCB/EMBO Meeting 2020.12.14 Online

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. Watanabe Naoshi, Morimatsu Masatoshi, Fujita Ayano, Teranishi Mika, Sudevan Surabhi, Watanabe Masaru, Iwasa Hiroaki, Hata Yutaka, Kagi Hiroyuki, Nishiyama Masayoshi, Naruse Keiji, Higashitani Atsushi. Increased hydrostatic pressure induces nuclear translocation of DAF-16/FOXO in *C. elegans* BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 2020.03; 523(4); 853-858
2. Kodaka Manami, Mao Fengju, Arimoto-Matsuzaki Kyoko, Kitamura Masami, Xu Xiaoyin, Yang Zeyu, Nakagawa Kentaro, Maruyama Junichi, Ishii Kana, Akazawa Chihiro, Oyaizu Takuya, Yamamoto Naoki, Ishigami-Yuase Mari, Tsuemoto Nozomi, Ito Shigeru, Kagechika Hiroyuki, Nishina Hiroshi, Hata Yutaka. Characterization of a novel compound that promotes myogenesis via Akt and transcriptional co-activator with PDZ-binding motif (TAZ) in mouse C2C12 cells PLOS ONE. 2020.04; 15(4); e0231265
3. Shimizu T, Nakamura T, Inaba H, Iwasa H, Maruyama J, Arimoto-Matsuzaki K, Nakata T, Nishina H, Hata Y. The RAS-interacting chaperone UNC119 drives the RASSF6-MDM2-p53 axis and antagonizes RAS-mediated malignant transformation. The Journal of biological chemistry. 2020.06;

[Books etc]

1. Iwasa H, Shimizu T, Hata Y.. Encyclopedia of Signaling Molecules RASSF6. Springer, (ISBN : 978-1-4419-0460-7)
2. Xu X, Kodaka M, Iwasa H, Hata Y. Encyclopedia of Signaling Molecules MAGI2/S-SCAM. Springer,
3. 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,

[Patents]

1. Myogenesis Promotor, Muscle Atrophy Inhibitor, Medical Composition and Taz Activator, Patent Number : US10653672

Joint Surgery and Sports Medicine

Hideyuki Koga
Tomomasa Nakamura, Kazumasa Miyatake, Masaki Amemiya

Department of Cartilage Regeneration
Kunikazu Tsuji
Yusuke Nakagawa

Naoko Araya, JaeSung An, Kazumasa Kawata, Shinji Hagio,
Masaaki Isono, Aritoshi Yoshihara, Tang Guo, Kei Sato,
Yusuke Amano, Shoichi Hasegawa, Tetsuya Tachibana,
Zhu Ling, Qu Zhen, Yang Yang

Miyoko Ojima, Miho Okada

(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

(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 unrepairable 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-menisectomy 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 unrepairable meniscal tear since August 2014.

(5) Publications

[Original Articles]

1. Nobutake Ozeki, Hideyuki Koga, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Tomoyuki Saito, Takeshi Muneta, Ichiro Sekiya. Biomechanical analysis of the centralization procedure for extruded lateral menisci with posterior root deficiency in a porcine model. *J Orthop Sci.* 2020.01; 25(1); 161-166
2. Mai Katakura, Kaori Nakamura, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *Knee.* 2020.01; 27(1); 95-101

3. Yasuyuki Ishibashi, Nobuo Adachi, Hideyuki Koga, Eiji Kondo, Ryosuke Kuroda, Tatsuo Mae, Yuji Uchio. Japanese Orthopaedic Association (JOA) clinical practice guidelines on the management of anterior cruciate ligament injury - Secondary publication. *J Orthop Sci.* 2020.01; 25(1); 6-45
4. Kaori Nakamura, Tomomasa Nakamura, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Masaki Amemiya, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Anatomic femoral tunnel placement is difficult by the transtibial technique: comparison of three different femoral tunnel drilling techniques in double-bundle anterior cruciate ligament reconstructions. *Knee Surg Sports Traumatol Arthrosc.* 2020.02; 28(2); 584-593
5. Masaki Amemiya, Kunikazu Tsuji, Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Synovial fluid-derived mesenchymal cells have non-inferior chondrogenic potential and can be utilized for regenerative therapy as substitute for synovium-derived cells. *Biochem. Biophys. Res. Commun.* 2020.03; 523(2); 465-472
6. Daniel Nemirov, Yusuke Nakagawa, Zhexion Sun, Amir Lebaschi, Susumu Wada, Camila Carballo, Xiang-Hua Deng, David Putnam, Lawrence J Bonassar, Scott A Rodeo. Effect of Lubricin Mimetics on the Inhibition of Osteoarthritis in a Rat Anterior Cruciate Ligament Transection Model. *Am J Sports Med.* 2020.03; 48(3); 624-634
7. Akimasa Kimura, Tetsuya Jinno, Sachi-yuki Tsukada, Masaaki Matsubara, Hideyuki Koga. Detection of total hip prostheses at airport security checkpoints. *J Orthop Sci.* 2020.03; 25(2); 255-260
8. Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Masafumi Horie, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Validity of intraoperative observation of graft length change pattern for medial patellofemoral ligament reconstruction. *J Orthop.* 2020.03; 21; 131-136
9. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Ichiro Sekiya. The effect of a centralization procedure for extruded lateral meniscus on load distribution in porcine knee joints at different flexion angles. *BMC Musculoskelet Disord.* 2020.04; 21(1); 205
10. Leyang Li, Hiroyuki Yokoyama, Hidetoshi Kaburagi, Takashi Hirai, Kunikazu Tsuji, Mitsuhiro Enomoto, Yoshiaki Wakabayashi, Atsushi Okawa. Remnant neuromuscular junctions in denervated muscles contribute to functional recovery in delayed peripheral nerve repair. *Neural Regen Res.* 2020.04; 15(4); 731-738
11. Toshifumi Watanabe, Hideyuki Koga, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Takeshi Muneta, Ichiro Sekiya, Tetsuya Jinno. Correction to: Coronal and sagittal laxity affects clinical outcomes in posterior-stabilized total knee arthroplasty: assessment of well-functioning knees. *Knee Surg Sports Traumatol Arthrosc.* 2020.05; 28(5); 1410
12. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Atsushi Okawa. Portable imageless navigation system and surgeon's estimate for accurate evaluation of acetabular cup orientation during total hip arthroplasty in supine position. *Eur J Orthop Surg Traumatol.* 2020.05; 30(4); 707-712
13. Tingting Zhang, Nanako Kawaguchi, Kunikazu Tsuji, Emiko Hayama, Yoshiyuki Furutani, Hisashi Sugiyama, Toshio Nakanishi. Silibinin Upregulates CXCR4 Expression in Cultured Bone Marrow Cells (BMCs) Especially in Pulmonary Arterial Hypertension Rat Model. *Cells.* 2020.05; 9(5); 1276
14. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Kei Inomata, Mio Udo, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Fibrotic changes in the infrapatellar fat pad induce new vessel formation and sensory nerve fiber endings that associate prolonged pain. *J. Orthop. Res.* 2020.06; 38(6); 1296-1306
15. So Suzuki, Mitsuru Mizuno, Yuriko Sakamaki, Ayako Mimata, Kentaro Endo, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Morphological changes in synovial mesenchymal stem cells during their adhesion to the meniscus. *Lab. Invest.* 2020.07; 100(7); 916-927

16. Naoko Araya, Kazumasa Miyatake, Kunikazu Tsuji, Hiroki Katagiri, Yusuke Nakagawa, Takashi Hoshino, Hiroaki Onuma, Saisei An, Hirofumi Nishio, Yoshitomo Saita, Ichiro Sekiya, Hideyuki Koga. Intra-articular Injection of Pure Platelet-Rich Plasma Is the Most Effective Treatment for Joint Pain by Modulating Synovial Inflammation and Calcitonin Gene-Related Peptide Expression in a Rat Arthritis Model. *Am J Sports Med.* 2020.07; 48(8); 2004-2012
17. Kenji Hirohata, Junya Aizawa, Hidetaka Furuya, Sho Mitomo, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Kate E Webster. The Japanese version of the anterior cruciate ligament-return to sport after injury (ACL-RSI) scale has acceptable validity and reliability. *Knee Surg Sports Traumatol Arthrosc.* 2020.08; 28(8); 2519-2525
18. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Koga Hideyuki, Okawa Atsushi, Jinno Tetsuya, Yagishita Kazuyoshi. The Gap Between Subjective Return to Sports and Subjective Athletic Performance Intensity After Anterior Cruciate Ligament Reconstruction *ORTHOPAEDIC JOURNAL OF SPORTS MEDICINE.* 2020.09; 8(9); 2325967120947402
19. Takahisa Ogawa, Toshitaka Yoshii, Mutsuko Moriwaki, Shingo Morishita, Yoto Oh, Kazumasa Miyatake, Ara Nazarian, Koichiro Shiba, Atsushi Okawa, Kiyohide Fushimi, Takeo Fujiwara. Association between Hemiarthroplasty vs Total Hip Arthroplasty and Major Surgical Complications among Patients with Femoral Neck Fracture. *J Clin Med.* 2020.10; 9(10); 3203
20. Yoshie Seki, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga. Investigation of association between the preoperative intra-articular anesthetic test and persistent pain after total knee arthroplasty. *J Orthop Sci.* 2020.11; 25(6); 1055-1060
21. Hideyuki Koga, Tomomasa Nakamura, Hiroki Katagiri, Yusuke Nakagawa, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya. Two-Year Outcomes After Meniscopectomy by Capsular Advancement With the Application of Arthroscopic Centralization Technique for Lateral Compartment Knee Osteoarthritis. *Am J Sports Med.* 2020.11; 48(13); 3154-3162
22. Aizawa J, Hirohata K, Ohji S, Ohmi T, Koga H, Yagishita K. Factors Associated With Psychological Readiness to Return to Sports With Cutting, Pivoting, and Jump-Landings After Primary ACL Reconstruction. *Orthopaedic journal of sports medicine.* 2020.11; 8(11); 2325967120964484
23. Masanobu Hirao, Kazumasa Miyatake, Daisuke Koga, Ryohei Takada, Gaku Koyano, Atsushi Okawa, Tetsuya Jinno. Comparison of 5-year postoperative results between standard-length stems and short stems in one-stage bilateral total hip arthroplasty: a randomized controlled trial. *Eur J Orthop Surg Traumatol.* 2020.11;
24. Naoto Watanabe, Kentaro Endo, Keiichiro Komori, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Yuji Kohno, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Mesenchymal Stem Cells in Synovial Fluid Increase in Knees with Degenerative Meniscus Injury after Arthroscopic Procedures through the Endogenous Effects of CGRP and HGF. *Stem cell reviews and reports.* 2020.12; 16(6); 1305-1315
25. Yoshihisa Kushida, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Koichiro Kishima, Yoshio Soma, Ichiro Sekiya. Two- and three-dimensional optical coherence tomography to differentiate degenerative changes in a rat meniscectomy model. *J Orthop Res.* 2020.12; 38(12); 2592-2600

[Misc]

1. N. Araya, H. Katagiri, Y. Nakagawa, T. Ohara, M. Shioda, Y. Kohno, M. Amemiya, I. Sekiya, H. Koga. Predictors of residual mechanical symptoms after meniscus surgery: data from the maks group Osteoarthritis and Cartilage. 2020.04; 28(1); S221-S223
2. 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.* 2020.05; 25(3); 537-543
3. Mai Katakura, Adam W M Mitchell, Justin C Lee, James D Calder. Is it time to replace CT with T1-VIBE MRI for the assessment of musculoskeletal injuries? *Bone Joint J.* 2020.11; 102-B(11); 1435-1437

[Conference Activities & Talks]

1. Hideyuki Koga, Hiroko Ueki, Yusuke Nakagawa, Hiroki Katagiri. Contribution of Additional Anterolateral Structure Augmentation to Controlling Pivot Shift in anterior cruciate ligament reconstruction based on objective evaluation of pivot shift phenomenon using triaxial accelerometer. ACL Study Group Meeting 2020.01.27 Kitzbuhel, Austria
2. Yusuke Nakagawa, Kunikazu Tsuji, Hideyuki Koga. Infra-patellar fat pad fibrosis is associated with elevation of inflammatory cytokines level in the synovial fluid and delays functional recovery in ACL-reconstructed patients. 2020 ACL Study Group Meeting 2020.01.27 Kitzbuhel, Austria
3. Masaki Amemiya. Downregulation Of Cd140b/pdgfrb Is Associated With The Less Proliferative Potential Of Mesenchymal Stem Cells Derived From Synovial Fluid. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
4. Naoko Araya, Kazumasa, Miyatake, Kunikazu Tsuji, Hiroaki Onuma, Saisei An, Ichiro Sekiya, Hideyuki Koga. Pure Platelet-rich Plasma Is Most Effective For The Treatment Of Arthritis. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
5. Jae-Sung An, Kunikazu Tsuji, Hiroaki Onuma, Takashi Hoshino, Kei Inomata, Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Jun Hino, Hiroshi Hosoda, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Pain Persistence And Articular Cartilage Degeneration Were Significantly Alleviated By An Anti-fibrotic Drug Treatment In Monoiodoacetate Induced Rat Arthritis Model. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
6. Kazumasa Kawata . Enhancement Of Proliferation And Migration Abilities Of Mesenchymal Stem Cells And Chondrocytes By Exosomes Derived From Mesenchymal Stem Cells From Four Different Tissues. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
7. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Kei Inomata, Saisei An, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Fibrotic Changes Of Infrapatellar Fat Pad Induce New Vessel Formation And Sensory Nerve Fiber Endings That Cause Persistent Knee Pain.. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
8. Tomoamsa Nakamura, Price TM, DiNenna MA, Linde MA, van Eck CF, Smolinski P, Fu FH. Suture With Graft Augmentation For MCL Grade 3 Injury Provides Sufficient Knee Kinematic Restoration In Concomitant With ACL Reconstruction. 2020 Orthopaedic Research Society 2020.02.08 Phonex, AZ, USA
9. Tomoamsa Nakamura, Price TM, DiNenna MA, Linde MA, van Eck CF, Smolinski P, Fu FH. The Effect Of Graft Augmentation With MCL Suture Repair On Medial Tissue Forces In Combined ACL And Grade 3 MCL Injury. 2020 Orthopaedic Research Society 2020.02.08 Phonex, AZ, USA
10. Tomoamsa Nakamura, DiNenna MA, Price TM, Linde MA, Smolinski P, Fu FH. Classifying The Shape Of The Acl Cross Section. 2020 Orthopaedic Research Society 2020.02.08 Phonex, AZ, USA
11. Tomoamsa Nakamura, Price TM, DiNenna MA, Linde MA, Smolinski P, Fu FH. Geometric Analysis Of The Native Anterior Cruciate Ligament. 2020 Orthopaedic Research Society 2020.02.08 Phonex, AZ, USA
12. Hideyuki Koga. Meniscal Repair Part II: Radial tear. 2020 Knee Webinar 2020.04.23 WEB
13. Tomoamsa Nakamura, Price TM, DiNenna MA, Linde MA, van Eck CF, Smolinski P, Fu FH. Combined Graft augmentation for medial collateral ligament repair may improve knee kinematics. 2020 AANA annual meeting 2020.05.07 Grapevine, TX, USA
14. Tomoamsa Nakamura, Linde MA, Koga H, Smolinski P, Fu FH. Lateral meniscus centralization in ACL reconstructed knee restores the rotational stability. 2020 The 93th JOA online 2020.06.11
15. Tomoamsa Nakamura, Linde MA, van Eck CF, Smolinski P, Fu FH. Graft Augmentation Combined with MCL Suture Repair Provides Sufficient Knee Kinematic Restoration in Concomitant ACL Reconstruction and MCL Grade 3 Injury. 2020 The 93th JOA online 2020.06.11
16. Hideyuki Koga. Clinical Outcomes after Meniscopectomy by Capsular Advancement with Centralization Technique for Knee Osteoarthritis due to Lateral Meniscal Defects. International Knee Day 2020.06.12

17. Mai Katakura, Nick Allen, Angela Kedgley, James Calder. Injury patterns over a three-year period in a professional ballet company : Change and trends 10 years on. 2020 International Association for Dance Medicine & Science (web) 2020.07.01
18. Hideyuki Koga. Cases sharing, discussion and experiences with JuggerStitch™ in Japan. Case Experience sharing and discussion with JuggerStitch™ (webinar) 2020.10.27
19. Hideyuki Koga. Concept of meniscal repair. vol.33 Zimmer Biomet Times (Web) 2020.11
20. Tomomasa Nakamura, Monica Linde, Patrick Smolinski, Freddie Fu. The Effect of Graft Augmentation in Concomitant with Suturing for MCL Grade 3 Injury on in situ Force Distribution of the Knee - a Biomechanical Study in Human Cadaveric Knees. JOSKAS-JOSSM 2020 2020.12.17
21. Yusuke Nakagawa, Toshiyuki Ohara, Aritoshi Yoshihara, Hiroko Ueki, Takashi Hoshino, Tsuyoshi Nagase, Masaya Hayashi, Takashi Ogiuchi, Takeshi Muneta, Hideyuki Koga, TMDU MAKS group. Evidences from TMDU MAKS study. JOSKAS-JOSSM 2020 2020.12.17

Biostructural Science

Associate Professor: Makoto TABATA

Technician: Makoto SUGIURA

Graduate Student: Momoko SAKAGUCHI

(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

[Books etc]

1. Makoto J. Tabata. Comparative Oral Anatomy on the 12 Animals of Oriental Zodiac. Ishiyaku Publishers, inc, 2020.06 (ISBN : 978-4-263-46161-7)

2. Makoto J. Tabata, Masato Endou, Daisuke SHioguri, Yuuichirou Yasukawa, Takeo Kuriyama, Gen Morimoto. Natural History of the Scale. Graphi-sha, 2020.10 (ISBN : 978-4-7661-3369-1)

[Conference Activities & Talks]

1. Sugiura-Nakazato Makoto, Tabata Makoto J. Good effect of Well-Organized Tissue Sections for Practice of Histology. The 61st Annual meeting of the Japanese Society of Neuropathology 2020.10.12 Kanazawa,web
2. Tabata Makoto J, Sugiura Makoto, Shibata shunichi . Attempt of histology training using virtual slides and future prospects. 2020.12.04 TMDU

Pharmacology

Staffs and Students

Assistant Professor Yukihiro TAMURA

Researchers

Tomoki UEHARA (Pediatric Dentistry)

Shigeki NAGAIHIRO (Pediatric Dentistry)

Yuki ARAI (Removable Prosthodontics)

Noriko HIRAIISHI (Cariology and Operative Dentistry)

Yasuka KUSUMOTO (Pediatric Dentistry)

Graduate Students

Kenya YONEDA (Regenerative Dental Medicine)

Michiko OZAWA

C.Supachatwong (Regenerative Dental Medicine)

Jason Hou (Regenerative Dental Medicine)

Meng Sikun (Regenerative Dental Medicine)

Lecturers

Yoshihiro WAKI

Etsuko TAKAHASHI

Kenichi NAGANO

Hiroyuki SETO

Toshimi SATO

Genki KATO

Kiichi NONAKA

Fumie SATO

(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) 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. Mohannad NASSAR, Ahmad DARGHAM, Noriko HIRAISHI, Yukihiro TAMURA, Junji TAGAMI. In Vitro Mitigation of Arsenic-Induced Toxicity by Reduced Glutathione in Rat Pulpal Cells *European Endodontic Journal*. 2020.05; 139-143
2. Nassar M, Dargham A, Jamleh A, Tamura Y, Hiraishi N, Tagami J. The Hormetic Effect of Arsenic Trioxide on Rat Pulpal Cells: An In Vitro Preliminary Study. *European journal of dentistry*. 2020.10;

[Conference Activities & Talks]

1. Sikun Meng, Jingyang Kang, Yukihiro Tamura, Shohei Kasugai. The Direct Effect of Several Different Concentration of Lithium on Osteogenic Cells from Mouse Bone Marrow. *Academic of Osseointegration 35th Annual Meeting 2020* 2020.03.18 オンライン
2. Jingyang Kang, Sikun Meng, Yukihiro Tamura, Shohei Kasugai. The Direct Effect of Lithium Concentration on Mouse Osteogenic Cells. *Academic of Osseointegration 35th Annual Meeting 2020* 2020.03.18 オンライン

Biochemistry

Professor Testuro Watabe

Associate Professor Miki Yokoyama

Assistant Professor Katarzyna Anna Podyma-Inoue, Miho Kobayashi

Technical staff Megumi Naito, Kazue Terasawa

Part-time Lecturer Yasuhiro Yoshimatsu

Graduate student Kazuki Takahashi, Shiori Kimuro, Rina Takayama, Hitomi Takahashi, Ikumi Wakabashi, Maki Saito, Kashio Fujiwara

(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. In addition, we elucidated the molecular mechanism for anti-angiogenesis by vasohibin-1 (VASH1). We are conducting basic research aimed at suppressing tumor progression through the functional analysis of VASH1.

(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) Unraveling of the physiological role of VASH1 as a detyrosination enzyme

VASH1, which is induced expression by VEGF stimulation in endothelial cells, was re-identified as a enzyme

of detyrosination. Detyrosination is one of the post-translational modification of microtubules, It is known that detyrosinated microtubules play key role for several physiological phenomena, such as chromosome partition in mitosis or functional beating of heart. We are conducting basic research aimed at molecularly elucidating of role as a detyrosination enzyme in physiological function of VASH1.

(5) 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-2 with mutation in multimerization. By using the LAMP-2 mutants, we are now investigating the functional aspect of lysosomal membrane during intracellular degradation.

(6) HSPGs, Exosomes and EMT

Metastasis is the cause of the death in a majority of human cancers. Tumor-derived, small extracellular vesicles (exosomes) are suggested to play important roles in different steps of metastatic cascade. Tumor-derived exosomes has been shown to participate in tumor progression by mediating epithelial-to-mesenchymal transition (EMT), stimulating the invasion, migration, angiogenesis. Heparan sulfate proteoglycans (HSPGs) are strategically localized on the cell surface and serves as receptors for a number of extracellular ligands. HSPG-dependent signals regulate tumor proliferation, angiogenesis and metastasis. HSPGs have been also implicated in the formation/uptake of tumor-derived exosomes, but the detailed mechanisms still remain to be characterized. We are working on the characterization of exosomal cargo and identification of the molecules responsible for exosome-recipient cell interactions as well as pathways involved in the internalization of exosomes focusing on the role of HSPGs in those events.

(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. Yuji Kato, Satoko Arakawa, Kazue Terasawa, Jin-Ichi Inokuchi, Takanori Iwata, Shigeomi Shimizu, Tetsuro Watabe, Miki Hara-Yokoyama. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. *Bioorg. Med. Chem. Lett.* 2020; 30(3); 126891
2. Yamamoto D, Kayamori K, Sakamoto K, Tsuchiya M, Ikeda T, Harada H, Yoda T, Watabe T, Hara-Yokoyama M. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer Sci.* 2020.02; 111(2); 700-712
3. Yang W, Podyma-Inoue KA, Yonemitsu I, Watari I, Ikeda Y, Guo X, Watabe T, Ono T. Mechanoresponsive and lubricating changes of mandibular condylar cartilage associated with mandibular lateral shift and recovery in the growing rat. *Clinical Oral Investigations.* 2020.02;
4. Daisuke Yamamoto, Kou Kayamori, Kei Sakamoto, Maiko Tsuchiya, Tohru Ikeda, Hiroyuki Harada, Tetsuya Yoda, Tetsuro Watabe, Miki Hara-Yokoyama. Intracellular claudin-1 at the invasive front of tongue squamous cell carcinoma is associated with lymph node metastasis. *Cancer Sci.* 2020.02; 111(2); 700-712
5. Yoshimatsu Y, Kimuro S, Pauty J, Takagaki K, Nomiyama S, Inagawa A, Maeda K, Podyma-Inoue KA, Kajiya K, Matsunaga YT, Watabe T. TGF-beta and TNF-alpha cooperatively induce mesenchymal transition of lymphatic endothelial cells via activation of Activin signals. *PloS One.* 2020.05; 15(5); e0232356
6. Ojima C, Noguchi Y, Miyamoto T, Saito Y, Orihashi H, Yoshimatsu Y, Watabe T, Takayama K, Hayashi Y, Itoh F. Peptide-2 from mouse myostatin precursor protein alleviates muscle wasting in cancer-associated cachexia. *Cancer science.* 2020.06; 111(8); 2954-2964
7. Yoshimatsu Y, Wakabayashi I, Kimuro S, Takahashi N, Takahashi K, Kobayashi M, Maishi N, Podyma-Inoue KA, Hida K, Miyazono K, Watabe T. TNF- α enhances TGF- β -induced endothelial-to-mesenchymal transition via TGF- β signal augmentation. *Cancer Science.* 2020.07; 111(7); 2385-2399
8. Kazuki Takahashi, Yuichi Akatsu, Katarzyna A Podyma-Inoue, Takehisa Matsumoto, Hitomi Takahashi, Yasuhiro Yoshimatsu, Daizo Koinuma, Mikako Shirouzu, Kohei Miyazono, Tetsuro Watabe. Targeting all transforming growth factor- β isoforms with an Fc chimeric receptor impairs tumor growth and angiogenesis of oral squamous cell cancer. *J. Biol. Chem.* 2020.09; 295(36); 12559-12572
9. 榎谷 振太郎, 井上 カタジナアンナ, 高橋 和樹, 原田 浩之, 渡部 徹郎. β 2-アドレナリン受容体シグナルは口腔扁平上皮癌の進行を阻害する 日本癌学会総会記事. 2020.10; 79 回; OJ10-2

[Conference Activities & Talks]

1. Shintaro Sakakitani, Katarzyna A. Inoue, Takeshi Kuroshima, Hirofumi Tomioka, Kei Sakamaoto, Tohru Ikeda, Hiroyuki Harada and Tetsuro Watabe. Identification of transcription factor that controls the progression of oral squamous carcinoma cells. The 38th Annual Meeting of Japanese Society of Oral Oncology 2020.01.24 Tokyo
2. Yuji Kato, Satoko Arakawa, Kazue Terasawa, Jin-ichi Inokuchi, Takanori Iwata, Shigeomi Shimizu, Tetsuro Watabe, and Miki Hara-Yokoyama. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. The 62nd Japan Lipid Chemistry Society 2020.05.14 Funabori
3. Miho Kobayashi, Ikumi Wakabayashi, Yasuhiro Suzuki, Yasufumi Sato, Tetsuro Watabe. Vasohibin-1 Inhibits Angiogenesis via the Increase of Detyrosinated α -Tubulin. The 21st International Vascular Biology Meeting (IVBM2020) 2020.09.09 Korea (WEB hybrid)
4. Tetsuro Watabe. Roles of TGF- β family signals during formation and maintenance of blood and lymphatic vascular systems. International Vascular Biology Meeting 2020 2020.09.11 Seoul, Korea

5. Kazue Terasawa, Yuji Kato, Yuta Ikami, Kensaku Sakamoto, Kazumasa Ohtake, Tetsuro Watabe, Shigeyuki Yokoyama, and Miki Hara-Yokoyama. Homophilic interaction of the luminal domain of LAMP-2 is important for chaperone-mediated autophagy. The 93rd Annual Meeting of the Japanese Biochemical Society 2020.09.14 Web holding
6. Katarzyna A. Inoue, Kazuki Takahashi, Maki Saito, Atsushi Kaida, Akinari Sugauchi, Toshihiro Uchihashi, Yasuhiro Yoshimatsu, Susumu Tanaka, Masahiko Miura, Mikihiko Kogo, Tetsuro Watabe. Oral squamous carcinoma cells under TGF- β -induced cell cycle arrest represent highly motile and invasive population. AACR Virtual Special Conference: Tumor Heterogeneity: From Single Cells to Clinical Impact 2020.09.17
7. Kazuki Takahashi, Katarzyna A. Inoue, Atsushi Kaida, Akinari Sugauchi, Toshihiro Uchihashi, Yasuhiro Yoshimatsu, Susumu Tanaka, Masahiko Miura, Mikihiko Kogo, Tetsuro Watabe. TGF- β -induced cell cycle arrest is associated with increased migration and metastasis of oral squamous carcinoma cells. 第79回日本癌学会学術総会 2020.10.01 広島
8. Shintaro Sakakitani, Katarzyna A. Podyma-Inoue, Kazuki Takahashi, Hiroyuki Harada, Tetsuro Watabe. Inhibition of oral squamous carcinoma cell progression by targeting β 2-adrenergic receptor signals. The 97th Annual Meeting of the Japanese Cancer Association 2020.10.01 Hiroshima
9. Yasuhiro Yoshimatsu, Ikumi Wakabayashi, Shiori Kimuro, Naoya Takahashi, Kazuki Takahashi, Miho Kobayashi, Katarzyna A. Inoue, Kohei Miyazono, Tetsuro Watabe. Endothelial-derived TGF- β signals activated during ednothelial-to-mesenchymal transition induce EMT of oral cancer cells. 第79回日本癌学会学術総会 2020.10.01
10. Katarzyna A. Inoue, Shintaro Sakakitani, Kazuki Takahashi, Hiroyuki Harada, Tetsuro Watabe. Novel approach for treatment of oral squamous cell carcinoma. 第79回日本癌学会学術総会 2020.10.03 広島
11. Miho KOBAYASHI, Ikumi Wakabayashi, Yasuhiro Suzuki, Kashio Fujiwara, Masanori Nakayama, Yasufumi Sato, Tetsuro Watabe. Vasohibin-1 induced post-translational modification of microtubules mediates VEGF-signaling in angiogenesis. 第42回日本分子生物学会年会 (MBSJ2020) 2020.12.03 WEB
12. Shintaro Sakakitani, Katarzyna A. Podyma-Inoue, Kazuki Takahashi, Hiroyuki Harada, Tetsuro Watabe. Inhibition of oral squamous carcinoma cell progression by β 2-adrenergic receptor signals. The 85th Annual Meeting of the Japanese Stomatological Society, Japan 2020.12.04 Tokyo

[Awards & Honors]

1. The JVBMO/IVBM 2020 Best E-poster Awards (1st Place), JVBMO, IVBM, 2020.09

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. Fumiyuki Sasaki, Mikihito Hayashi, Yuki Mouri, Satoshi Nakamura, Taiji Adachi, Tomoki Nakashima. Mechanotransduction via the Piezo1-Akt pathway underlies Sost suppression in osteocytes. *Biochem Biophys Res Commun.* 2020.01; 521(3); 806-813
2. Kim Yusoon, Hayashi Mikihito, Ono Takehito, Yoda Tetsuya, Takayanagi Hiroshi, Nakashima Tomoki. Suppression of hematopoietic cell kinase ameliorates the bone destruction associated with inflammation(和訳中) *Modern Rheumatology.* 2020.01; 30(1); 85-92
3. Fumiyuki Sasaki, Mikihito Hayashi, Yuki Mouri, Satoshi Nakamura, Taiji Adachi, Tomoki Nakashima. Mechanotransduction via the Piezo1-Akt pathway underlies Sost suppression in osteocytes. *Biochemical and Biophysical Research Communications.* 2020.01; 521(3); 806-813
4. Y Kameo, Y Miya, M Hayashi, T Nakashima, T Adachi. In silico experiments of bone remodeling explore metabolic diseases and their drug treatment. *Sci Adv.* 2020.03; 6(10); eaax0938

5. Yoshitaka Kameo, Yuki Miya, Mikihiro Hayashi, Tomoki Nakashima, Taiji Adachi. In silico experiments of bone remodeling explore metabolic diseases and their drug treatment. *Science Advances*. 2020.03; 6(10); eaax0938
6. Yosuke Tsuchiya, Mikihiro Hayashi, Katashi Nagamatsu, Takehito Ono, Masaki Kamakura, Takanori Iwata, Tomoki Nakashima. The key royal jelly component 10-hydroxy-2-decenoic acid protects against bone loss by inhibiting NF- κ B signaling downstream of FFAR4. *J. Biol. Chem.*. 2020.07;
7. Nasir K Bashiruddin, Mikihiro Hayashi, Masanobu Nagano, Yan Wu, Yukiko Matsunaga, Junichi Takagi, Tomoki Nakashima, Hiroaki Suga. Development of cyclic peptides with potent in vivo osteogenic activity through RaPID-based affinity maturation. *Proc Natl Acad Sci U S A*. 2020.12; 117(49); 31070-31077

[Books etc]

1. Mikihiro Hayashi, Takehito Ono, Tomoki Nakashima. *Encyclopedia of Bone Biology* 1st Edition. Elsevier, 2020.06 (ISBN : 9780128140819)

[Misc]

1. Takehito Ono, Mikihiro Hayashi, Fumiyuki Sasaki, Tomoki Nakashima. RANKL biology: bone metabolism, the immune system, and beyond. *Inflammation and Regeneration*. 2020.02; 40(2);
2. Takehito Ono, Mikihiro Hayashi, Fumiyuki Sasaki, Tomoki Nakashima. RANKL biology: bone metabolism, the immune system, and beyond. *Inflammation and Regeneration*. 2020.02; 40; 2
3. Hayashi M, Ono T, Nakashima T.. Signaling in osteoblast differentiation. *Encyclopedia of Bone Biology*. 2020.07; 416-426

[Conference Activities & Talks]

1. Takehito Ono. Revisit of the regulatory mechanisms of brain functions by mastication from the viewpoint of locomotion science. The 62nd Annual Meeting of Japanese Association for Oral Biology 2020.09.22 Held online

[Awards & Honors]

1. U.S. National Academy of Medicine Catalyst Award, U.S. National Academy of Medicine (NAM), 2020.10

Periodontology

From January.2020

【Professor】 Takanori Iwata

【Associate Professor】 Akira Aoki

【Junior Associate Professor】 Yasuo Takeuchi, Sayaka Katagiri(Apr~)

【Assistant Professor】 Koji Mizutani, Yuichi Ikeda, Takahiko Shiba(Sep~)

【Project Assistant Professor】 Yuuka Tsumanuma

【Specially appointed Assistant Professor】 Takeaki Sudo(Apr ~ Aug), Risako Tanimoto(Apr~), Hideyuki Takamatsu(Apr~)

【Clinical Fellow】

Shunsuke Fukuba(Apr~), Kohei Takeda, Yujin Ohsugi, Yousuke Tsuchiya(Apr~), Munehiro Okada(Apr~), Aya Suzuki(Jan~Mar), Shotaro Mori(Jan~Mar), Tomoaki Kariya(Sep~), Mai Kitamura(Sep~)

【Graduate Students】 Chihiro Kano(~Mar), Yuji Kato(~Mar), Rie Kawamura(~Mar), Keitesu Kure(~ Mar), Yutaro Kitanaka, Kohei Nohara, Kazuki Watanabe, Keiji Komatsu, Ryo Satou, Daiki Tanaka, Takashi Nemoto, Hiromi Kominato, Natsumi Saito, Ryo Mikami, TsuyoshiShimohira(Apr~), Shunsuke Takeuchi(Apr~), Masahiro Hatasa(Apr~), Anhao LIU, Shu Takemura(Apr~), Keita Nakagawa(Apr~), Takahiko Nagai(Apr~), Masahiro Hakariya(Apr~), Kazuki Morita(Apr~), Lisa Yagasaki(Apr~), Mako Yokose(Apr~), Sumiko Yoshida(Apr~), Sakura Hayashi(Apr~), Jiacheng Wang(Oct~), Peiya Lin(Oct~)

【Adult graduate student】

Akiko Kobayashi(~ Mar), Miho Ogawa(~ Mar)

【Graduate Research Student】

Takeshi Iida, Ayako Kawada, Yuri Ito, Aiko Fujino, Kazuki Miyata, Miki Dobashi, Akane Ochiai(Apr~), Sakurako Kawamoto(Apr~), Yumine Kiuchi(Apr~), Hiroe Nakashima(Apr~),(Apr~), Yuya Hamada(Apr~), Shiwei Sun(Apr~)

【Clinical Professor】 Hiroaki Kobayashi, Shigenari Kikuchi, Hiroaki Tsutioka

【Adjunct Lecturer】 36

【Registered dentist】 34

【Assistant Administrative Staff】 Tomomi Anai, Saori Hashimoto(Oct~)

(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 application of lasers/LEDs in periodontal therapy

(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. Mikami R, Mizutani K, Sasaki Y, Iwata T, Aoki A. Patient-reported outcomes of laser-assisted pain control following non-surgical and surgical periodontal therapy: A systematic review and meta-analysis. *PloS one*. 2020; 15(9); e0238659
2. Hatasa M, Ohsugi Y, Katagiri S, Yoshida S, Niimi H, Morita K, Tsuchiya Y, Shimohira T, Sasaki N, Maekawa S, Shiba T, Hirota T, Tohara H, Takahashi H, Nitta H, Iwata T.. Endotoxemia by *Porphyromonas gingivalis* alters endocrine functions in brown adipose tissue *Frontiers in Cellular and Infection Microbiology*. 2020; 10; 580577
3. Kobayashi T, Torii D, Iwata T, Izumi Y, Nasu M, Tsutsui TW. Characterization of proliferation, differentiation potential, and gene expression among clonal cultures of human dental pulp cells. *Human Cell*. 2020.03; 33(3); 490-501
4. Ye C, Kobayashi H, Katagiri S, Miyasaka N, Takeuchi Y, Kuraaji R, Izumi Y. The relationship between the anti-*Porphyromonas gingivalis* immunoglobulin G subclass antibody and small for gestational age delivery: a longitudinal study in pregnant Japanese women. *International dental journal*. 2020.03; 70(4); 296-302
5. Kasai S, Onizuka S, Katagiri S, Nakamura T, Hanatani T, Kudo T, Sugata Y, Ishimatsu M, Usui M, Nakashima K. Associations of cytokine levels in gingival crevicular fluid of mobile teeth with clinical improvement after initial periodontal treatment *Journal of oral science*. 2020.03; 62(2); 189-196
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30. Lin T, Taniguchi Y, Aoki A, Chang YC. Clinical evaluation of ridge preservation and augmentation with buccal bone deficiency by Er:YAG laser-assisted bone regenerative therapy *Journal of Dental Science*. 2020.12; 15(4); 560-561
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[Books etc]

1. Aoki A, Mizutani K, Iwata T. Chapter 30: Laser therapy, *Clinical Periodontology 3rd Edition*. Ishiyaku Publishers Inc., 2020.01
2. Aoki A. Root debridement by Er:YAG laser, Vol.2: SRP and subgingival debridement. *Interaction*, 2020.06
3. Aoki A. Volume of Japan Oral Implantology Meeting, Glossary of oral implantology. Ishiyaku Publishers, Inc., 2020.06

[Misc]

1. Shiba T, Watanabe T. Polymicrobial Peri-Implant Infection Risk Factor for Peri-implant Diseases. 2020;

2. Inagaki K, Kikuchi T, Noguchi T, Mitani A, Naruse K, Matsubara T, Kawanami M, Negishi J, Furuichi Y, Nemoto E, Yamada S, Yoshie H, Tabeta K, Tomita S, Saito A, Katagiri S, Izumi Y, Nitta H, Iwata T, Numabe Y, Yamamoto M, Yoshinari N, Fujita T, Kurihara H, Nishimura F, Nagata T, Yumoto H, Naito T, Noguchi K, Ito K, Murakami S, Nishimura R, Tajima N. A large-scale observational study to investigate the current status of diabetic complications and their prevention in Japan (JDCP study 6): baseline dental and oral findings *Diabetology International*. 2020.10; e-pub;
3. Ohsugi Y, Niimi H, Shimohira T, Hatasa M, Katagiri S, Aoki A, Iwata T. In vitro cytological responses against laser photobiomodulation for periodontal regeneration *International Journal of Molecular Sciences*. 2020.11; 21(23); 9002
4. Aoki A. Development of a novel periodontal pocket therapy which employs the Er:YAG laser *The Journal of the Stomatological Society*. 2020.12; 87(2,3); 31-39
5. Aoki A. Potential of laser dentistry: 4 types of lasers, the differences and their use *Clinical library, web*. 2020.12;
6. Aoki A. Application of Er:YAG laser in minimally invasive flapless periodontal pocket surgery *Journal of the Japanese Academy of Clinical Periodontology*. 2020.12; 38(2); 19-27
7. Aoki A. Periodontal pocket therapy using a laser *Dental Hygien*. 2020.12; 41(1); 43-45

[Conference Activities & Talks]

1. Aoki A, Tsubokawa M, Kakizaki S, Ohsugi Y, Kitanaka Y. Application of OCT in periodontal examination. The 3rd Review Committee in 2019 fiscal year for developing periodontal examination technique using OCT 2020.01.14 Tokyo
2. Aoki A. Application of Er:YAG laser in periodontal therapy. Dental Association of Mitaka Academic Meeting 2020.01.28 Mitaka City
3. Aoki A. Application of Er:YAG Laser in Minimally Invasive Flapless Periodontal Surgery . The 16th International Congress of WFLD-AEEDC 2020.02.04 Dubai
4. Aoki A. Er:YAG laser in esthetic management of periodontal soft tissues. The 16th International Congress of WFLD-AEEDC 2020.02.05 Dubai
5. Shimohira T, Katagiri S, Ohsugi Y, Hirota T, Mizutani K, Watanabe K, Niimi H, Hatasa M, Meinzer W, Iwata T, Aoki A . Comprehensive and Sequential Gene expression analysis of bone healing process following Er:YAG laser ablation. World Federation of Laser Dentistry Dubai Congress 2020 2020.02.05 Dubai
6. Aoki A. Periodontitis and systemic diseases. Association for insurance doctor in Chiba-ken, Inba Branch Academic Meeting 2020.02.19
7. Komatsu K, Shiba T, Nemoto T, Simogishi M, Shibazaki M, S, Takeuchi Y, Kasugai S, Iwata T. Metagenomic analysis of peri-implant microbiome and its relation to disease severity. 2020.02.26 Niigata
8. Aoki A. Debridement with Er:YAG laser. 2nd Consensus meeting for periodontal therapy 2020.02.29 Hall of Essam Kanda, Tokyo, Japan
9. Yuji Kato, Satoko Arakawa, Kazue Terasawa, Jin-ichi Inokuchi, Takanori Iwata, Shigeomi Shimizu, Tetsuro Watabe, and Miki Hara-Yokoyama. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. The 62nd Japan Lipid Chemistry Society 2020.05.14 Funabori
10. Kawada A, Ikeda Y, Tanaka D, Ikeda E, Kobayashi H, Iwata T. A Questionnaire Study on Satisfactory Level of Magnet Type . The 63rd Spring Meeting of the Japanese Society of Periodontology 2020.05.29 Virtual
11. Nemoto T, Shiba T, Watanabe T, Koyanagi T, Komatsu K, Katagiri S, Takeuchi Y, Iwata T. Comparison of microbial network structure and functional composition of various periodontal conditions by using metatranscriptomic analysis. The 152nd Meeting of the Japanese Society of Conservative Dentistry 2020.06.11

12. Tanabe G, Hasunuma T, Inai Y, Churei H, Hayashi K, Kamiya N, Fukasawa S, Takeuchi Y, Kobayashi H, Moriya N, Iwata T, Ueno T. The influence of changes in the subjective fatigue and salivary immunological parameter during high-intensity training on periodontal inflammation. The 152nd Meeting of the Japanese Society of Conservative Dentistry 2020.06.11
13. Aoki A, Tsubokawa M, Ohsugi Y, Kitanaka Y, Shimohira T. Application of OCT in periodontal examination. The first meeting in 2020 for the development of OCT application in dentistry 2020.06.16 Virtual
14. Shimohira T, Katagiri S, Ohsugi Y, Hirota T, Hatasa M, Mizutani K, Watanabe K, Niimi H, Iwata T, Aoki A. Comprehensive and sequential gene expression analysis during bone healing process following Er:YAG laser ablation. The 63rd Spring Meeting of the Japanese Society of Periodontology 2020.07.13
15. Aoki A. Application of Hepatocyte growth factor (HGF) in periodontal diagnosis. 2020.07.13 Virtual
16. Aoki A. Application of lasers on periodontal therapy. 2020.07.13 Virtual
17. Aoki A, Tsubokawa M, Ohsugi Y, Kitanaka Y, Shimohira T. Application of OCT in periodontal examination. The second meeting in 2020 for the development of OCT application in dentistr 2020.07.21 Virtual
18. Aoki A. Periodontology and periodontal therapy. Open trial lecture for Dentistry of Tokyo Medical and Dental University 2020.08.09 Virtual
19. Seki N, Moross J, Kanamori Y, Kanazawa M, Komagamine Y, Mizutani K, Liao S, Kabasawa Y, Iseki S, Morio I. Importance of preparatory courses for international/global dental student exchange programs. Annual Meeting of the 39th Japanese Dental Education Association 2020.09.25 Paper/Online Base
20. Aoki A. Application of Er:YAG laser in minimally invasive flapless periodontal pocket surgery. 2020.10.01 Virtual
21. Aoki A, Tsubokawa M, Ohsugi Y, Kitanaka Y, Shimohira T. Application of OCT in periodontal examination. The third meeting in 2020 for the development of OCT application in dentistr 2020.10.06 Virtual
22. Ohsugi Y, Katagiri S, Hirota T, Niimi H, Hatasa M, Watanabe K, Shimohira T, Mizutani K, Kitazawa M, Matsuzawa A, Kadokura H, Yokose S, Iwata T, Aoki A . Er:YAG laser irradiation decreases sclerostin expression in bone and osteogenic cell. The 63th Autumn Meeting of The Japanese Society of Periodontology 2020.10.16 Virtual
23. The impact of diabetes on the capillaries in marginal gingiva. 2020.10.16
24. A case of a patient with severe chronic periodontitis treated with periodontal regenerative therapy and plastic surgery. 2020.10.16
25. Tanaka D, Ikeda Y, Ikeda E, Yokose M, Iwata T. The effect of Amelotin on bone regeneration in mice calvarial defect model.. The 63rd Autumn Meeting of the Japanese Society of Periodontology 2020.10.16 Virtual
26. Kobayashi H, Kawashima N, Sudo T, Kano C, Mikami R, Katagiri S, Takeuchi Y, Iwata T. 1. Bacterial examination for diagnosing healing periodontal endodontic lesions. 2020.10.16
27. The effect of antimicrobial photodynamic therapy using yellow-green LED and rose bengal on *Porphyromonas gingivalis*. 2020.10.16
28. Aoki A, Katagiri S, Ohsugi Y, Mizutani K, Nitta H, Iwata T. Effects of single visit full mouth disinfection (FMD) in advanced periodontitis using ultrasonic debridement in combination with systemic azithromycin administration. 2020.10.16 Virtual
29. Effects of low-level Er:YAG laser irradiation on proliferation and calcification of primary osteoblast-like cells isolated from rat calvaria. 2020.10.16
30. Endotoxemia by *Porphyromonas gingivalis* alters endocrine functions in brown adipose tissue. 2020.10.16 Virtual

31. Ohsugi Y, Katagiri S, Hirota T, Niimi H, Hatasa M, Watanabe K, Shimohira T, Mizutani K, Kitazawa M, Matsuzawa A, Kadokura H, Yokose S, Iwata T, Aoki A. Laser irradiation decreases Sost expression in bone and osteogenic cells. The 106th Annual meeting American Academy of Periodontology 2020.11.06 Virtual
32. Komatsu K, Shiba T, Watanabe T, Nemoto T, Koyanagi T, Iwata T. Non-surgical treatment and microbiome of periodontitis and peri-implantitis: seven-year. The 106th Annual Meeting of the American Academy of Periodontology in collaboration with the Japanese Society of Periodontology and Japanese Academy of Clinical Periodontology 2020.11.06 Virtual
33. Niimi H, Ohsugi Y, Katagiri S, Watanabe K, Hatasa M, Shimohira T, Tsuchiya Y, Maekawa S, Hirota T, Kadokura H, Yokose S, Iwata T, Aoki A. The effects of Er:YAG laser irradiation on primary osteoblast-like cells. The 106th Annual meeting American Academy of Periodontology 2020.11.06 Virtual
34. Hatasa M, Ohsugi Y, Katagiri S, Hirota T, Yoshida S, Morita K, Niimi H, Shimohira T, Watanabe K, Sasaki N, Maekawa S, Nitta H, Iwata T. Endotoxemia by *Porphyromonas gingivalis* aggravates inflammation in brown adipose tissue. The 106th Annual meeting American Academy of Periodontology 2020.11.06 Virtual
35. Komatsu K, Takeuchi Y, Shiba T, Watanabe T, Shimogishi M, Shibasaki M, Nemoto T, Koyanagi T, Katagiri S, Iwata T. Omics analysis defines differences in microbial community structure between peri-implantitis and periodontitis. The 68th Annual Meeting of Japan Dental Research 2020.11.07 Virtual
36. Aoki A. The current concepts and methods for periodontal therapy. 2020.11.26 Virtual
37. Aoki A. Application of Er:YAG laser in periodontology. 2020.11.28 Virtual
38. Effects of low-level Er:YAG laser irradiation on proliferation and calcification of primary osteoblast-like cells isolated from rat calvaria. 2020.11.28
39. Aoki A. Er:YAG laser application in periodontal therapy: effects on bone regeneration. TMDU International Symposium 2020.12.04
40. Yamaguchi Y, Fukada K, Tatsumi K, Aoki A, Ohshima M. The possibility of Chinese herbal medicine as a candidate drug for peri-implantitis treatment. 2020.12.07 Virtual
41. Aoki A, Tsubokawa M, Ohsugi Y, Kitanaka Y, Shimohira T. Application of OCT in periodontal examination. The fourth meeting in 2020 for the development of OCT application in dentistr 2020.12.15 Virtual
42. Aoki A. Periodontal Er:YAG laser operation - Less pain, good healing, and fast healing . Tokyo Medical and Dental University Alumni Association: CDE workshop course 2020.12.20 Tokyo

[Awards & Honors]

1. First Best Poster (Tsuyoshi Shimohira), World Federation for Laser Dentistry Dubai Congress 2020, 2020.02

Inorganic Biomaterials

Professor Masakazu Kawashita
Associate Prof. Taishi Yokoi

(1) Outline

In this department, we are conducting research on biomaterials (especially ceramic biomaterials) that contribute to the treatment of cancer and bone diseases. Specifically, various material synthesis methods such as the sol-gel method are used to synthesize cancer therapeutic materials (particularly fine particles) and bone filling materials, and evaluate their chemical, physical, and biological properties. By doing so, we aim to obtain knowledge that will lead to clinical application.

(2) Research

1. Development of Biomaterials for Intra-arterial Treatment of Cancer

Radioactive microspheres 20-30 μ m in diameter are useful for the radiotherapy of cancers, especially for tumors located deep inside the body. Also, ferromagnetic microspheres 20-30 μ m in diameter are useful as thermoseeds for inducing hyperthermia in deep-seated cancers under alternating magnetic field. In this department, we try to develop novel biomaterials for minimally invasive treatment of cancer by using various synthetic techniques.

2. Development of Bioactive Materials for Bone Repair

It has been found from 1970 that some ceramics can bond to living bone without fibrous tissues. They are called "bioactive" ceramics and clinically used as important bone substitutes. However, in a clinical field, novel bioactive materials showing excellent bone-bonding ability are required. In this laboratory, we try to develop novel bioactive materials by using various synthetic techniques.

3. Study on Osteoconductive Mechanism of Hydroxyapatite

Hydroxyapatite (HAp) is widely used as an artificial bone or a coating material for metallic biomaterials because it bonds to living bone (shows osteoconductivity). However, the details of the expression mechanism of its osteoconductivity have not been clarified yet. In this department, we are focusing on the initial adsorption of serum proteins such as albumin, fibronectin (Fn) and laminin (Ln) on HAp and hypothesize that some serum protein which specifically adsorbs on HAp causes the osteoconductivity of HAp.

4. Study on Organically Modified Octacalcium Phosphates

Octacalcium phosphate (OCP) is a precursor phase of hydroxyapatite (HAp) in bones and teeth, and has a high affinity for the hard tissues. OCP has been studied as bioabsorbable artificial bones. OCP has a layered structure, and various organic molecules can be incorporated into the OCP interlayers. We develop functional bone-repairing materials and ceramic materials that achieve both diagnosis and therapy utilizing the unique property of OCP.

(3) Lectures & Courses

Students aim to be able to comprehensively and comprehensively understand the structure, physical properties, chemical properties, reactions with biomolecules and cells, etc. of ceramic biomaterials. Their final goal is to

learn cutting-edge science and technology related to ceramic biomaterials and to acquire the ability to propose and design ceramic biomaterials that are useful for medical treatment.

(4) Publications

[Original Articles]

1. Kawashita Masakazu, Ueno Shoji, Handa Shoma, Furuya Maiko, Yokota Kotone, Kanetaka Hiroyasu. In vitro evaluation of doxorubicin-eluting porous titania microspheres for transcatheter arterial chemoembolization *Journal of Asian Ceramic Societies*. 2020.01; 8(1); 10-20
2. Iwatsu M, Kanetaka H, Mokudai T, Ogawa T, Kawashita M, Sasaki K. Visible light-induced photocatalytic and antibacterial activity of N-doped TiO₂ *Journal of Biomedical Materials Research. Part B, Applied Biomaterials*. 2020.02; 108(2); 451-459
3. Chigama Hiroki, Yokoi Taishi, Furuya Maiko, Yokota Kotone, Kanetaka Hiroyasu, Kawashita Masakazu. Apatite formation and bacterial growth on raw silk fabric heated in argon gas *Journal of Materials Science: Materials in Medicine*. 2020.05; 31(6); 49
4. Yokoi Taishi, Goto Tomoyo, Kato Takeharu, Takahashi Seiji, Nakamura Jin, Sekino Tohru, Ohtsuki Chikara, Kawashita Masakazu. Hydroxyapatite formation from octacalcium phosphate and its related compounds: A discussion of the transformation mechanism *Bulletin of the Chemical Society of Japan*. 2020.05; 93(5); 701-707
5. Miyazaki Toshiki, Tange Takayuki, Kawashita Masakazu, Jeyadevan Balachandran. Structural control of magnetite nanoparticles for hyperthermia by modification with organic polymers: effect of molecular weight *RSC Advances*. 2020.07; 10(44); 26374-26380
6. Myat-Htun Myat, Noor Ahmad-Fauzi Mohd, Kawashita Masakazu, Ismail Yanny Marliana Baba. Enhanced sinterability and in vitro bioactivity of barium-doped akermanite ceramic *Ceramics International*. 2020.08; 46(11); 19062-19068
7. Moe Kubota, Taishi Yokoi, Tomoyuki Ogawa, Shin Saito, Maiko Furuya, Kotone Yokota, Hiroyasu Kanetaka, Balachandran Jeyadevan, Masakazu Kawashita. Setting behavior, mechanical properties, and heat generation under AC magnetic fields of Fe₃O₄/TiO₂/PMMA composite bone cement *Medical Devices & Sensors*. 2020.08; 3; e10114
8. Tomoyo Goto, Jeehoon Shin, Taishi Yokoi, Sung Hun Cho, Tohru Sekino. Photocatalytic properties and controlled morphologies of TiO₂-modified hydroxyapatite synthesized by the urea-assisted hydrothermal method *Powder Technology*. 2020.08; 373; 468-475
9. Taishi Yokoi, Tatsuki Ujiyama, Jin Nakamura, Masakazu Kawashita, Chikara Ohtsuki. Behaviour of calcium phosphate ester salts in a simulated body fluid modified with alkaline phosphatase: a new concept of ceramic biomaterials *Materials Advances*. 2020.11; 1(9); 3215-3220

[Books etc]

1. Taishi Yokoi, Jin Nakamura, Chikara Ohtsuki. *Bioceramics from macro to nanoscale*. 2020.09

[Conference Activities & Talks]

1. H. Chigama, H. Kanetaka, M. Furuya, K. Yokota, T. Yokoi, M. Kawashita. Antibacterial activity of calcium-doped raw silk fabric. *International Joint Symposium 2020: The 15th International Workshop on Biomaterials in Interface Science and The 11th Symposium on Innovative Dental-Engineering Alliance (IDEA)* 2020.12.15

Global Health Promotion

Professor: Takeo Fujiwara, MD, MPH, PhD

Junior Associate Professor: Ayako Morita, PhD

Assistant Professor: Yukako Tani, PhD; Yusuke Matsuyama, PhD;

Nobutoshi Nawa, MD, MPH, PhD (Department of Medical Education Research and Development)

Research Fellow of Japan Society for the Promotion of Science: Aya Isumi, PhD; Satomi Doi, PhD

Project Assistant Professor: Yui Yamaoka, PhD

Specially Appointed Assistant Professor: Yu Funakoshi (Institute of Education) , MD, MPH

(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. Mental health (antenatal and postnatal mental health, mental health after a disaster, and child mental health)
5. Nutritional epidemiology (childhood nutrition from prenatal to early school-years and the food environment)
6. Environmental health (the physical environment and climate change)
7. Occupational health (harassment and work-place social capital)
8. Infectious Disease Epidemiology (descriptive epidemiology about COVID-19, research on behavioral change)

(3) 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.

(4) Publications

[Original Articles]

1. Jung SH, Han HW, Koh H, Yu SY, Nawa N, Morita A, Ong KIC, Jimba M, Oh J.. Patients help other patients: Qualitative study on a longstanding community cooperative to tackle leprosy in India. *PLOS Neglected Tropical Diseases*. 2020.01; 14(1); e0008016
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Environmental Parasitology

Professor : Shiroh IWANAGA
Lecturer : Takashi KUMAGAI, Hai Yen Doan
Assistant Professor : Naoaki SINZAWA, Sora Enya
PhD Course Students :
Michael Amoa-BOSOMPEM (D4)
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Rie KUBOTA (D2)
Master Course Students:
Takeshi SEKINE(M2)

(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.

(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.

(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 weekly 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. Teruya Shihono, Hiramatsu Yukihiro, Nakamura Keiji, Fukui-Miyazaki Aya, Tsukamoto Kentaro, Shinoda Noriko, Motooka Daisuke, Nakamura Shota, Ishigaki Keisuke, Shinzawa Naoaki, Nishida Takashi, Sugihara Fuminori, Maeda Yusuke, Horiguchi Yasuhiko. Bordetella Dermonecrotic Toxin Is a Neurotropic Virulence Factor That Uses Ca(v)3.1 as the Cell Surface Receptor MBIO. 2020; 11(2);
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3. Prah Isaac, Ayibieke Alafate, 井口 純, Mahazu Samiratu, 佐藤 和佳菜, 鈴木 敏彦, 山岡 昇司, 岩永 史朗, Ablordey Anthony, 齋藤 良一. Virulence Profile of Diarrheagenic E. coli from the Western region of Ghana(和訳中) 日本細菌学雑誌. 2020.01; 75(1); 118
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Forensic Medicine

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Associate Professor
Toshihiko AKI

Junior Associate Professor
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Assistant Professor
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Specially Appointed Assistant Professor
Kanao NORITAKE
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Moeka NOMURA
Tatsuhiko MURATA
Miu Kajihara
Miyu Komatsu
Hasumi Matsuyama

(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. Joji Kunihiro, Hiroaki Nabeka, Hiroyuki Wakisaka, Kana Unuma, Md Sakirul Islam Khan, Tetsuya Shimokawa, Farzana Islam, Takuya Doihara, Kimiko Yamamiya, Shouichiro Saito, Fumihiko Hamada, Seiji Matsuda. Prosaposin and its receptors GRP37 and GPR37L1 show increased immunoreactivity in the facial nucleus following facial nerve transection. *PLoS One*. 2020; 15(12); e0241315
2. Kitayama T, Fukagawa T, Watahiki H, Mita Y, Fujii K, Unuma K, Sakurada K, Uemura K, Sekiguchi K, Mizuno N. Evaluation of Rapid DNA system for buccal swab and disaster victim identification samples. *Legal medicine (Tokyo, Japan)*. 2020.05; 46; 101713
3. Toshihiko Aki, Takeshi Funakoshi, Kanako Noritake, Kana Unuma, Koichi Uemura. Extracellular glucose is crucially involved in the fate decision of LPS-stimulated RAW264.7 murine macrophage cells. *Sci Rep*. 2020.06; 10(1); 10581
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[Misc]

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Molecular Epidemiology

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Associate Professor : Noriko SATO
Assistant Professor : Chihiro Imai

Adjunct Instructor : Sumio Sugano, Tomio Arai

Graduate Student: Hiroo Fujitani, Tadaaki Katsuta,
Maidina Abudushataer, Ake Ko Ko Minn, Zong Yuan, Tong Daike
Master Student: Fuko Yamada

(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. Developmental Origin of Health and Diseases
3. Role of nutrition on epigenetic modification and health
4. Genetic factors that affect the severity of pathological atherosclerosis and the development of cancer
5. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
6. Application of personal genome to preemptive & preventive medicine.

(3) Education

[Doctor course]

Noriko Sato: Biomedical Science

[Master course]

Masaaki Muramatsu: Environmental Social Health

Masaaki Muramatsu: Health Care Informatics

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

Noriko Sato: Big Data Analytics

[Undergraduate]

Noriko Sato: Bioinformatics

(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. Sato N, Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Mizutani S, and Miyasaka N. Placenta mediates the effect of maternal hypertension polygenic score on offspring birth weight: a study of birth cohort with fetal growth velocity data *BMC Medicine*. 2021;
2. Sato N, Fudono A, Imai C, Takimoto H, Tarui I, Aoyama T, Yago S, Okamitsu M, Mizutani S, and Miyasaka N. Placenta mediates the effect of maternal hypertension polygenic score on offspring birth weight: a study of birth cohort with fetal growth velocity data *BMC Medicine*. 2021;
3. Zong Y, Tanaka M, Muramatsu M, Arai T. D-amino acid oxidase (DAO) rare genetic missense variant p.Pro103Leu and gastric cancer. *Molecular and clinical oncology*. 2021.03; 14(3); 58
4. Imai C, Takimoto H, Fudono A, Tarui I, Aoyama T, Yago S, Okamitsu M, Sasaki S, Mizutani S, Miyasaka N, Sato N. Application of the Nutrient-Rich Food Index 9.3 and the Dietary Inflammatory Index for assessing maternal dietary quality in Japan: a single-center birth cohort study *Nutrients*. 2021.08; 13; 2854
5. Imai C, Takimoto H, Fudono A, Tarui I, Aoyama T, Yago S, Okamitsu M, Sasaki S, Mizutani S, Miyasaka N, Sato N . Application of the Nutrient-Rich Food Index 9.3 and the Dietary Inflammatory Index for Assessing Maternal Dietary Quality in Japan: A Single-Center Birth Cohort Study *Nutrients*. 2021.08; 13(8);

[Conference Activities & Talks]

1. Satoshi Yago, Motoko Okamitsu, Noriko Sato, Hidemi Takimoto, Chihiro Imai, Ayako Fudono, Hiroshi Yomogida, Tomoko Aoyama, Naoyuki Miyasaka. Perinatal maternal mental health, sleep quality, and infant development: A Japanese prospective cohort study. World Association for Infant Mental Health(WAIMH) 17th Congress 2021.06.22
2. Analysis of diet quality in pregnant women using Nutrient-rich food index and Dietary inflammatory index. 2021.07.03

Research Development

Faculty Staff
Professor
Kozo TAKASE

Graduate Students
Doctor course
Kazushige ENDOH

Master course (Master of Medical Administration)
Tadayuki ARAI
Mika ARAI
Tetsufumi ISAYAMA
Kenji ISHIZAKI
Manabu KITAGAKI
Kotaro MOTOYOSHI

(1) Outline

Department of Research Development was established in 2000.
This department has been managing the course of Master of Medical Administration.

(2) 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

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

University

(4) 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.

(5) Clinical Services & Other Works

Kozo TAKASE

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

Committee member of Tokyo District Court

Editorial Board of Japanese Society for Clinical Pathway

(6) Publications

[Original Articles]

1. Hideki Teruya, Kozo Takase. Pediatric directors' perception of clinical research education in Japan
Pediatrics International. 2020.01; 62(1); 36-46

Health Policy and Informatics

Professor:Kiyohide FUSHIMI

Graduate Student : Akira HOMMA, Kyoko HIRANO, Mihoko OTA, Natsuko KANAZAWA, Senri WATANABE, Risa SUZUKI,

Graduate Research Student:Masahiro INOUE, Tomonori TAKEUCHI

(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. Mandai S, Sato H, Iimori S, Naito S, Tanaka H, Ando F, Susa K, Isobe K, Mori T, Nomura N, Sohara E, Okado T, Uchida S, Fushimi K, Rai T. Nationwide in-hospital mortality following major fractures among hemodialysis patients and the general population: An observational cohort study. *Bone*. 2020.01; 130; 115122
2. Itaru Hayakawa, Yusuke Okubo, Hiroki Nariai, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Recent treatment patterns and variations for pediatric acute encephalopathy in Japan. *Brain Dev.* 2020.01; 42(1); 48-55
3. Yusuke Ugata, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Periprocedural hypotension after conscious sedation versus local anesthesia during defibrillator implantation for left ventricular dysfunction: analysis of a national inpatient database in Japan. *Heart Vessels*. 2020.01; 35(1); 118-124
4. Yuko Mine, Yoshihisa Fujino, Ken Sabanai, Keiji Muramatsu, Makoto Otani, Tatsuhiko Kubo, Kiyohide Fushimi, Shinya Matsuda. Effectiveness of regional clinical pathways on postoperative length of stay for hip fracture patients: A retrospective observational study using the Japanese Diagnosis Procedure Combination database. *J Orthop Sci*. 2020.01; 25(1); 127-131

5. Shunsuke Edakubo, Kiyohide Fushimi. Mortality and risk assessment for anorexia nervosa in acute-care hospitals: a nationwide administrative database analysis. *BMC Psychiatry*. 2020.01; 20(1); 19
6. Yamaoka Y, Fujiwara T, Fujino Y, Matsuda S, Fushimi K. Incidence and age distribution of hospitalized presumptive and possible abusive head trauma of children under 12 months old in Japan. *JOURNAL OF EPIDEMIOLOGY*. 2020.02; 30(2); 91-97
7. Hiroyuki Ohbe, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early enteral nutrition in patients with severe traumatic brain injury: a propensity score-matched analysis using a nationwide inpatient database in Japan. *Am. J. Clin. Nutr.*. 2020.02; 111(2); 378-384
8. Takashi Sakamoto, Michimasa Fujiogi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. ASO Author Reflections: Anastomotic Complications are More Prevalent in Laparoscopic Total Gastrectomy than in Open Total Gastrectomy. *Ann. Surg. Oncol.*. 2020.02; 27(2); 527-528
9. Fusao Ikawa, Nobuaki Michihata, Koji Iihara, Yasuhiko Akiyama, Akio Morita, Kiyohide Fushimi, Hideo Yasunaga, Kaoru Kurisu. Risk Management of Aneurysmal Subarachnoid Hemorrhage by Age and Treatment Method from a Nationwide Database in Japan. *World Neurosurg.* 2020.02; 134; e55-e67
10. Takashi Sakamoto, Michimasa Fujiogi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Short-Term Outcomes of Laparoscopic and Open Total Gastrectomy for Gastric Cancer: A Nationwide Retrospective Cohort Analysis. *Ann. Surg. Oncol.*. 2020.02; 27(2); 518-526
11. Hideyuki Mouri, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Effect of Sugammadex on Postoperative Myasthenic Crisis in Myasthenia Gravis Patients: Propensity Score Analysis of a Japanese Nationwide Database. *Anesth Analg.*. 2020.02; 130(2); 367-373
12. Hiroyuki Ohbe, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Differences in effect of early enteral nutrition on mortality among ventilated adults with shock requiring low-, medium-, and high-dose noradrenaline: A propensity-matched analysis. *Clin Nutr.* 2020.02; 39(2); 460-467
13. Taisuke Jo, Hideo Yasunaga, Yasuhiro Yamauchi, Akihisa Mitani, Yoshihisa Hiraishi, Wakae Hasegawa, Yukiyo Sakamoto, Hiroki Matsui, Kiyohide Fushimi, Takahide Nagase. Inhaled corticosteroid withdrawal may improve outcomes in elderly patients with COPD exacerbation: a nationwide database study. *ERJ Open Res.* 2020.02; 6(1);
14. Kohei Muguruma, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Epidemiology and volume-outcome relationship of extracorporeal membrane oxygenation for respiratory failure in Japan: A retrospective observational study using a national administrative database. *Acute Med Surg.* 2020.02; 7(1); e486
15. Yoshito Hirota, Susumu Kunisawa, Kiyohide Fushimi, Yuichi Imanaka. Association between clinic physician workforce and avoidable readmission: a retrospective database research. *BMC Health Serv Res.* 2020.02; 20(1); 125
16. Mikio Nakajima, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Hyperbaric oxygen therapy and mortality from carbon monoxide poisoning: A nationwide observational study. *Am J Emerg Med.* 2020.02; 38(2); 225-230
17. Hideki Endo, Kiyohide Fushimi, Yasuhiro Otomo. The off-hour effect in severe trauma and the structure of care delivery among Japanese emergency and critical care centers: A retrospective cohort study. *Surgery*. 2020.03; 167(3); 653-660
18. Takahiro Kido, Masao Iwagami, Hideo Yasunaga, Toshikazu Abe, Yuki Enomoto, Hiroki Matsui, Kiyohide Fushimi, Hidetoshi Takada, Nanako Tamiya. Outcomes of paediatric out-of-hospital cardiac arrest according to hospital characteristic defined by the annual number of paediatric patients with invasive mechanical ventilation: A nationwide study in Japan. *Resuscitation*. 2020.03; 148; 49-56
19. Kensuke Nakamura, Hiroyuki Ohbe, Hiroki Matsui, Yuji Takahashi, Aiki Marushima, Yoshiaki Inoue, Kiyohide Fushimi, Hideo Yasunaga. Changes in Real-world Practice Patterns of Antiepileptic Drugs for Status Epilepticus: A Nationwide Observational Study in Japan. *Neurol. Med. Chir. (Tokyo)*. 2020.03; 60(3); 156-163

20. Yusuke Okubo, Masaru Miura, Tohru Kobayashi, Naho Morisaki, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. The Impact of Changes in Clinical Guideline on Practice Patterns and Healthcare Utilizations for Kawasaki Disease in Japan. *Front Pediatr.* 2020.03; 8; 114
21. Morishita S, Yoshii T, Okawa A, Fushimi K, Fujiwara T. Comparison of perioperative complications between anterior decompression with fusion and laminoplasty for cervical spondylotic myelopathy: Propensity score-matching analysis using Japanese diagnosis procedure combination database. *Clin Spine Surg.* 2020.04; 33(3); E101-E107
22. Fusao Ikawa, Nobuaki Michihata, Yasuhiko Akiyama, Koji Iihara, Akio Morita, Yoko Kato, Shuhei Yamaguchi, Kaoru Kurisu, Kiyohide Fushimi, Hideo Yasunaga. Propensity Score Matching Analysis for the Patients of Unruptured Cerebral Aneurysm from a Post Hoc Analysis of a Nationwide Database in Japan. *World Neurosurg.* 2020.04; 136; e371-e379
23. Ikuyo Tsutsumi, Susumu Kunisawa, Chikashi Yoshida, Masanori Seki, Takuya Komeno, Kiyohide Fushimi, Satoshi Morita, Yuichi Imanaka. Correction to: Impact of oral voriconazole during chemotherapy for acute myeloid leukemia and myelodysplastic syndrome: a Japanese nationwide retrospective cohort study. *Int. J. Clin. Oncol.* 2020.04; 25(4); 782-783
24. Fusao Ikawa, Nobuaki Michihata, Toshinori Matsushige, Masaru Abiko, Daizo Ishii, Jumpei Oshita, Takahito Okazaki, Shigeyuki Sakamoto, Ryota Kurogi, Koji Iihara, Kunihiro Nishimura, Akio Morita, Kiyohide Fushimi, Hideo Yasunaga, Kaoru Kurisu. In-hospital mortality and poor outcome after surgical clipping and endovascular coiling for aneurysmal subarachnoid hemorrhage using nationwide databases: a systematic review and meta-analysis. *Neurosurg Rev.* 2020.04; 43(2); 655-667
25. Morishita S, Yoshii T, Okawa A, Inose H, Hirai T, Ogawa T, Fushimi K, Fujiwara T. Comparison of Perioperative Complications Between Anterior Fusion and Posterior Fusion for Osteoporotic Vertebral Fractures in Elderly Patients: Propensity Score-Matching Analysis Using Nationwide Inpatient Database. *Clin Spine Surg.* 2020.04;
26. Toru Takiguchi, Mikio Nakajima, Hiroyuki Ohbe, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Shiei Kim, Hiroyuki Yokota, Hideo Yasunaga. Vasodilator Therapy and Mortality in Nonocclusive Mesenteric Ischemia: A Nationwide Observational Study. *Crit. Care Med.* 2020.05; 48(5); e356-e361
27. Takashi Sakamoto, Michimasa Fujiogi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Clinical features and outcomes of nonocclusive mesenteric ischemia after cardiac surgery: a retrospective cohort study. *Heart Vessels.* 2020.05; 35(5); 630-636
28. Takaaki Konishi, Michimasa Fujiogi, Takayoshi Niwa, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Comparison of outcomes after differentiated thyroid cancer surgery performed with and without energy devices: A population-based cohort study using a nationwide database in Japan. *Int J Surg.* 2020.05; 77; 198-204
29. Daisuke Shigemi, Miho Ishimaru, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Suicide Attempts Among Pregnant and Postpartum Women in Japan: A Nationwide Retrospective Cohort Study. *J Clin Psychiatry.* 2020.05; 81(3); 19m12993
30. Hiroaki Abe, Masahiko Sumitani, Hiroki Matsui, Shotaro Aso, Reo Inoue, Kiyohide Fushimi, Kanji Uchida, Hideo Yasunaga, Yoshitsugu Yamada. Comparing outcomes after peripheral nerve block versus general anesthesia for lower extremity amputation: a nationwide exploratory retrospective cohort study in Japan. *Reg Anesth Pain Med.* 2020.06; 45(6); 399-404
31. Kohei Hironaka, Shotaro Aso, Masanori Suzuki, Fumihiko Matano, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Akio Morita. Outcomes in Elderly Japanese Patients Treated for Aneurysmal Subarachnoid Hemorrhage: A Retrospective Nationwide Study. *J Stroke Cerebrovasc Dis.* 2020.06; 29(6); 104795
32. Yujiro Hattori, Shigeyuki Tahara, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Akio Morita. Pituitary surgery's epidemiology using a national inpatient database in Japan. *Acta Neurochir (Wien).* 2020.06; 162(6); 1317-1323
33. Mikio Nakajima, Shotaro Aso, Hiroki Matsui, Richard H Kaszynski, Kiyohide Fushimi, Yoshihiro Yamaguchi, Hideo Yasunaga. Prevalence of myocardial injury requiring percutaneous coronary intervention after acute carbon monoxide poisoning. *Eur J Emerg Med.* 2020.06; 27(3); 213-216

34. Yohei Hashimoto, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Makoto Aihara. Reoperation rates after Ex-PRESS versus trabeculectomy for primary open-angle or normal-tension glaucoma: a national database study in Japan. *Eye (Lond)*. 2020.06; 34(6); 1069-1076
35. Ryo Iketani, Shinobu Imai, Hiromasa Horiguchi, Daisuke Furushima, Kiyohide Fushimi, Hiroshi Yamada. Risk stratification for physical morbidity using factors associated with atypical antipsychotic treatment in Parkinson's disease: A retrospective observational study using administrative claims data. *J Clin Neurosci*. 2020.06; 76; 189-194
36. Tetsuji Minami, Hayato Yamana, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Postoperative Outcomes after Tubeless, Totally Tubeless, Standard, and Standard with Ureteral Stent Percutaneous Nephrolithotomy: A Nationwide Retrospective Study in Japan. *Urol. Int.*. 2020.06; 104(5-6); 445-451
37. Akira Okada, Hayato Yamana, Satoko Yamaguchi, Kayo Ikeda Kurakawa, Hiroki Matsui, Kiyohide Fushimi, Masaomi Nangaku, Takashi Kadowaki, Hideo Yasunaga. Outcomes of lactulose plus branched-chain amino acid infusion and lactulose alone for hepatic encephalopathy: A retrospective cohort study using a national inpatient database. *Hepatol. Res.*. 2020.06; 50(6); 693-703
38. Takashi Sakamoto, Michimasa Fujiogi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Timing of cholecystectomy after percutaneous transhepatic gallbladder drainage for acute cholecystitis: a nationwide inpatient database study. *HPB (Oxford)*. 2020.06; 22(6); 920-926
39. Yui Yamaoka, Takeo Fujiwara, Yoshihisa Fujino, Shinya Matsuda, Kiyohide Fushimi. Response to the Letter to Editor: "Do Inter-Country Differences in the Frequency of Abusive Head Trauma Reflect Different Proportions of Overdiagnosis of Abuse or True Differences in Abuse?" *J Epidemiol*. 2020.06; 30(6); 278-279
40. Yasuhiko Miyakuni, Mikio Nakajima, Hiroyuki Ohbe, Yusuke Sasabuchi, Richard H Kaszynski, Miho Ishimaru, Hiroki Matsui, Kiyohide Fushimi, Yoshihiro Yamaguchi, Hideo Yasunaga. Angiography versus colonoscopy in patients with severe lower gastrointestinal bleeding: a nation-wide observational study. *Acute Med Surg*. 2020.06; 7(1); e533
41. Tatsuya Hosoi, Hayato Yamana, Hiroyuki Tamiya, Hiroki Matsui, Kiyohide Fushimi, Masahiro Akishita, Hideo Yasunaga, Sumito Ogawa. Association between comprehensive geriatric assessment and short-term outcomes among older adult patients with stroke: A nationwide retrospective cohort study using propensity score and instrumental variable methods. *EClinicalMedicine*. 2020.06; 23; 100411
42. Takeshi Kitamura, Mikio Nakajima, Iwanari Kawamura, Hiroyuki Ohbe, Yusuke Sasabuchi, Hiroki Matsui, Kiyohide Fushimi, Seiji Fukamizu, Hideo Yasunaga. Patient characteristics, procedure details including catheter devices, and complications of catheter ablation for ventricular tachycardia: a nationwide observational study. *J Arrhythm*. 2020.06; 36(3); 464-470
43. Akihito Uda, Hiroyo Kuwabara, Sayuri Shimizu, Ryuichi Iwakiri, Kiyohide Fushimi. Optimal use of biologics with endoscopic balloon dilatation for repeated intestinal strictures in Crohn's disease. *JGH Open*. 2020.06; 4(3); 532-540
44. Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Vasopressin versus epinephrine as adjunct vasopressors for septic shock. *Intensive Care Med*. 2020.07; 46(7); 1484-1485
45. Akira Endo, Atsushi Shiraishi, Kiyohide Fushimi, Yasuhiro Otomo. Reply to the comment by Osuka et al. *J Intensive Care*. 2020.07; 8; 48
46. Senda A, Endo A, Tachimori H, Fushimi K, Otomo Y. Early administration of glucocorticoid for thyroid storm: analysis of a national administrative database. *Critical care (London, England)*. 2020.07; 24(1); 470
47. Kensuke Nakamura, Hiroyuki Ohbe, Hiroki Matsui, Yuji Takahashi, Aiki Marushima, Yoshiaki Inoue, Kiyohide Fushimi, Hideo Yasunaga. Levetiracetam vs. Fosphenytoin for Second-Line Treatment of Status Epilepticus: Propensity Score Matching Analysis Using a Nationwide Inpatient Database. *Frontiers in neurology*. 2020.07; 11; 615
48. Daisuke Takada, Susumu Kunisawa, Takeshi Matsubara, Kiyohide Fushimi, Motoko Yanagita, Yuichi Imanaka. Developing and validating a multivariable prediction model for in-hospital mortality of pneumonia with advanced chronic kidney disease patients: a retrospective analysis using a nationwide database in Japan. *Clin. Exp. Nephrol.*. 2020.08; 24(8); 715-724

49. Yuki Miyamoto, Hiroyuki Ohbe, Miho Ishimaru, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. The Effect of Carbazochrome Sodium Sulfonate in Patients with Colonic Diverticular Bleeding: Propensity Score Matching Analyses Using a Nationwide Inpatient Database. *Intern. Med.*. 2020.08; 59(15); 1789-1794
50. Toshitaka Yoshii, Shingo Morishita, Hiroyuki Inose, Masato Yuasa, Takashi Hirai, Atsushi Okawa, Kiyohide Fushimi, Takeo Fujiwara. Comparison of Perioperative Complications in Anterior Decompression With Fusion and Posterior Decompression With Fusion for Cervical Ossification of the Posterior Longitudinal Ligament: Propensity Score Matching Analysis Using a Nation-Wide Inpatient Database. *Spine*. 2020.08; 45(16); E1006-E1012
51. Kensuke Nakamura, Hiroyuki Ohbe, Hiroki Matsui, Hiromu Naraba, Hidehiko Nakano, Yuji Takahashi, Kiyohide Fushimi, Hideo Yasunaga. Phenytoin versus fosphenytoin for second-line treatment of status epilepticus: propensity score matching analysis using a nationwide inpatient database. *Seizure*. 2020.08; 80; 124-130
52. Takeshi Hatachi, Nobuaki Michihata, Muneyuki Takeuchi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early steroid pulse therapy among children with influenza virus-associated encephalopathy. *Journal of intensive care*. 2020.08; 8; 62
53. Yoshihisa Miyamoto, Shotaro Aso, Masao Iwagami, Hideo Yasunaga, Hiroki Matsui, Kiyohide Fushimi, Yoshifumi Hamasaki, Masaomi Nangaku, Kent Doi. Association Between IV Thiamine and Mortality in Patients With Septic Shock: A Nationwide Observational Study. *Critical care medicine*. 2020.08; 48(8); 1135-1139
54. Hiroyuki Tanaka, Hayato Yamana, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Proportion and risk factors of cholesterol crystal embolization after cardiovascular procedures: a retrospective national database study. *Heart Vessels*. 2020.09; 35(9); 1250-1255
55. Hideyuki Mouri, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Impact of glucocorticoid supplementation on reducing perioperative complications in patients on long-term glucocorticoid medication: A propensity score analysis using a nationwide inpatient database. *Am. J. Surg.*. 2020.09; 220(3); 648-653
56. Shunichi Otaka, Shotaro Aso, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Early Versus Late Rib Fixation in Patients With Traumatic Rib Fractures: A Nationwide Study. *The Annals of thoracic surgery*. 2020.09; 110(3); 988-992
57. Natsuko Kanazawa, Hiroaki Iijima, Kiyohide Fushimi. In-hospital cardiac rehabilitation and clinical outcomes in patients with acute myocardial infarction after percutaneous coronary intervention: a retrospective cohort study. *BMJ open*. 2020.09; 10(9); e039096
58. Yutaka Kondo, Hiroyuki Ohbe, Hiroki Matsui, Kiyohide Fushimi, Hiroshi Tanaka, Hideo Yasunaga. Proton pump inhibitors versus histamine-2 receptor antagonists for stress ulcer prophylaxis during extracorporeal membrane oxygenation: a propensity score-matched analysis. *BMJ open*. 2020.09; 10(9); e037534
59. Kohei Taniguchi, Hiroyuki Ohbe, Kazuma Yamakawa, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Antithrombin use and mortality in patients with stage IV solid tumor-associated disseminated intravascular coagulation: a nationwide observational study in Japan. *BMC cancer*. 2020.09; 20(1); 867
60. Shinichi Tomioka, Megumi Rosenberg, Kiyohide Fushimi, Shinya Matsuda. An analysis of equity in treatment of hip fractures for older patients with dementia in acute care hospitals: observational study using nationwide hospital claims data in Japan. *BMC health services research*. 2020.09; 20(1); 830
61. Kunio Tarasawa, Kenji Fujimori, Kiyohide Fushimi. Recombinant Human Soluble Thrombomodulin Contributes to a Reduction In-Hospital Mortality of Acute Cholangitis with Disseminated Intravascular Coagulation: A Propensity Score Analyses of a Japanese Nationwide Database. *The Tohoku journal of experimental medicine*. 2020.09; 252(1); 53-61
62. T Sakamoto, M Fujiogi, A K Lefor, H Matsui, K Fushimi, H Yasunaga. Stent as a bridge to surgery or immediate colectomy for malignant right colonic obstruction: propensity-scored, national database study. *Br J Surg*. 2020.09; 107(10); 1354-1362

63. Kensuke Matsuda, Jo Taisuke, Masashi Miyauchi, Kazuhiro Toyama, Kumi Nakazaki, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Mineo Kurokawa. Primary prophylaxis with pegfilgrastim in patients with newly-diagnosed diffuse large B-cell lymphoma: propensity score and instrumental variable analyses. *Leuk. Lymphoma*. 2020.10; 61(10); 2435-2441
64. Hiroyuki Ohbe, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Stress ulcer prophylaxis plus enteral nutrition versus enteral nutrition alone in critically ill patients at risk for gastrointestinal bleeding: a propensity-matched analysis. *Intensive care medicine*. 2020.10; 46(10); 1948-1949
65. Megumi Koizumi, Sayaka Suzuki, Hiroki Matsui, Kiyohide Fushimi, Tatsuya Yamasoba, Hideo Yasunaga. Trends in complications after functional endoscopic sinus surgery in Japan: A comparison with a previous study (2007-2013vs. 2013-2017). *Auris, nasus, larynx*. 2020.10; 47(5); 814-819
66. Taku Inohara, Jacqueline Saw, Shun Kohsaka, Keiichi Fukuda, Kiyohide Fushimi. Treatment pattern and outcome of spontaneous coronary artery dissection in Japan. *International journal of cardiology*. 2020.10; 316; 13-18
67. Takahiro Ando, Masahiro Kawashima, Taisuke Jo, Kimihiko Masuda, Yasuhiro Yamauchi, Goh Tanaka, Hidenori Kage, Maho Suzukawa, Hideaki Nagai, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga, Takahide Nagase. Early Arterial Embolization and Mortality in Mechanically Ventilated Patients With Hemoptysis: A Nationwide Retrospective Cohort Study. *Critical care medicine*. 2020.10; 48(10); 1480-1486
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69. Yusuke Okubo, Kazuhiro Uda, Noriko Kinoshita, Yuho Horikoshi, Isao Miyairi, Nobuaki Michihata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. National trends in appropriate antibiotics use among pediatric inpatients with uncomplicated lower respiratory tract infections in Japan. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2020.11; 26(11); 1122-1128
70. Takaaki Konishi, Michimasa Fujiogi, Nobuaki Michihata, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Treatments and outcomes of encapsulating peritoneal sclerosis in patients undergoing peritoneal dialysis: 295 cases from a nationwide inpatient database in Japan. *Perit Dial Int*. 2020.11; 40(6); 593-599
71. Takanori Suzuki, Nobuaki Michihata, Tetsushi Yoshikawa, Tadayoshi Hata, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. High-dose versus low-dose intravenous immunoglobulin for treatment of children with Kawasaki disease weighing 25 kg or more. *Eur J Pediatr*. 2020.12; 179(12); 1901-1907
72. Takaaki Konishi, Michimasa Fujiogi, Nobuaki Michihata, Kojiro Morita, Hiroki Matsui, Kiyohide Fushimi, Masahiko Tanabe, Yasuyuki Seto, Hideo Yasunaga. Impact of Body Mass Index on Outcomes After Breast Cancer Surgery: Nationwide Inpatient Database Study in Japan. *Clin Breast Cancer*. 2020.12; 20(6); e663-e674
73. Kensuke Shoji, Nobuaki Michihata, Isao Miyairi, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Recent epidemiology of Pneumocystis pneumonia in Japan. *J Infect Chemother*. 2020.12; 26(12); 1260-1264
74. Naoki Yonezawa, Taisuke Jo, Hiroki Matsui, Kiyohide Fushimi, Hideo Yasunaga. Effect of Early Tracheostomy on Mortality of Mechanically Ventilated Patients with Guillain-Barré Syndrome: A Nationwide Observational Study. *Neurocrit Care*. 2020.12; 33(3); 759-768

Life Sciences and Bioethics

Masayuki Yoshida
Yusuke Ebana
Hiroko Kohbata
Mizuko Osaka

(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. Takahiro Fukaiishi, Isao Minami, Seizaburo Masuda, Yasutaka Miyachi, Kazutaka Tsujimoto, Hajime Izumiyama, Koshi Hashimoto, Masayuki Yoshida, Sayako Takahashi, Kenichi Kashimada, Tomohiro Morio, Kenjiro Kosaki, Yoshiro Maezawa, Koutaro Yokote, Takanobu Yoshimoto, Tetsuya Yamada. A case of generalized lipodystrophy-associated progeroid syndrome treated by leptin replacement with short and long-term monitoring of the metabolic and endocrine profiles. *Endocr. J.* 2020.02; 67(2); 211-218
2. Higashijima Y, Matsui Y, Shimamura T, Nakaki R, Nagai N, Tsutsumi S, Abe Y, Link VM, Osaka M, Yoshida M, Watanabe R, Tanaka T, Taguchi A, Miura M, Ruan X, Li G, Inoue T, Nangaku M, Kimura H, Furukawa T, Aburatani H, Wada Y, Ruan Y, Glass CK, Kanki Y. Coordinated demethylation of H3K9 and H3K27 is required for rapid inflammatory responses of endothelial cells. *The EMBO journal.* 2020.03; e103949
3. Terui-Kohbata Hiroko, Egawa Makiko, Yura Kei, Yoshida Masayuki. Knowledge and attitude of hereditary breast cancer among Japanese university female students *Journal of Human Genetics.* 2020.07; 65(7); 591-599
4. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a stimulation of differentiated HL60 induces THP-1 chemotaxis via MCP-1 dependent pathway(和訳中) 日本動脈硬化学会総会プログラム・抄録集. 2020.07; 52 回; 268
5. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a Elevates MCP-1 Expression in Neutrophil-like Differentiated HL60 via NF- κ B Signaling Pathway(和訳中) 日本循環器学会学術集会抄録集. 2020.07; 84 回; OE122-6

6. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver(和訳中) 日本循環器学会学術集会抄録集. 2020.07; 84回; PE28-2
7. Hiroko Terui-Kohbata, Masami Ikeda, Kei Yura. The reliability and validity of the Japanese version of Revised Illness Perception Questionnaires for Healthy people (IPQ-RH-J) British Journal of Cancer Research. 2020.08; 3(2); 341-348
8. Xiaoxi Yang, Tetsuo Sasano, Yusuke Ebana, Jun K Takeuchi, Kensuke Ihara, Masahiro Yamazoe, Tetsushi Furukawa. Functional Role of the L396R Mutation of Tks5 Identified by an Exome-Wide Association Study in Atrial Fibrillation. Circ J. 2020.10;
9. Tsuru H, Osaka M, Hiraoka Y, Yoshida M. HFD-induced hepatic lipid accumulation and inflammation are decreased in Factor D deficient mouse. Scientific reports. 2020.10; 10(1); 17593
10. Inoue Reiko, Nishi Hiroshi, Osaka Mizuko, Yoshida Masayuki, Nangaku Masaomi. NEUTROPHIL INTERFERON-INDUCED, DOUBLE-STRANDED RNA-ACTIVATED PROTEIN KINASE (EIF2AK2) PROMOTES ADHESION IN NON-VIRAL INFLAMMATORY KIDNEY DISEASE NEPHROLOGY. 2020.10; 25; 35

[Conference Activities & Talks]

1. Hiroko Terui-Kohbata. Genetic testing with a multi-gene hereditary cancer panel and genetic counseling. 2020.07.05 web
2. 大坂 瑞子、出牛 三千代、吉田 雅幸. 選択的 PPAR α アゴニスト、ペマフィブラートは LDL 受容体欠損マウス大腿動脈における高中性脂肪血症を改善し、白血球接着を抑制する. 第 52 回日本動脈硬化学会総会・学術集会 2020.07.17 名古屋
3. Syed Masudur Rahman Dewan, Michiyo Deushi, Mizuko Osaka, Masayuki Yoshida. C5a elevates MCP-1 expression in neutrophil-like differentiated HL60 via NF- κ B signaling pathway. 第 84 回日本循環器学会学術集会 2020.07.27 京都
4. Hiromi Tsuru, Mizuko Osaka, Masayuki Yoshida. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver . 第 84 回日本循環器学会学術集会 2020.07.27 Kyoto
5. 大坂瑞子. 動脈硬化症関連血管炎症反応における好中球でのヒストンシトルリン化の重要性. 第 43 回日本分子生物学会年会 2020.12.02

Forensic Dentistry

Professor Koichi SAKURADA
Assistant Professor Hajime UTSUNO
Graduate Student Saki MINEGISHI
Graduate Student Jun OHTA
Graduate Student Shuuji NAMIKI
Graduate Student Maiko TOYA

(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. Jun Ohta, Nanaka Noda, Saki Minegishi, Koichi Sakurada. Application of DNA repair for *Streptococcus salivarius* DNA-based identification of saliva from ultraviolet-exposed samples. *Forensic Sci. Int.* 2020.01; 306; 110077
2. Tomoko Akutsu, Isao Yokota, Ken Watanabe, Koichi Sakurada. Development of a multiplex RT-PCR assay and statistical evaluation of its use in forensic identification of vaginal fluid. *Leg Med (Tokyo)*. 2020.05; 45; 101715
3. Kitayama T, Fukagawa T, Watahiki H, Mita Y, Fujii K, Unuma K, Sakurada K, Uemura K, Sekiguchi K, Mizuno N. Evaluation of Rapid DNA system for buccal swab and disaster victim identification samples. *Legal medicine (Tokyo, Japan)*. 2020.05; 46; 101713
4. Hiroko Oka, Akiko Takeuchi, Toshihiko Suzuki, Rieka Katsuragi-Go, Hisako Saitoh, Koichi Sakurada, Hiromi Yamashita. Current status of the forensic dentistry section at the cause of death investigation research and education hub centers *Forensic Dental Science*. 2020.09; 13(1); 8-13
5. Nagai M, Sakurada K, Imaizumi K, Ogawa Y, Uo M, Funakoshi T, Uemura K. Evaluation of Parameters for Estimating the Postmortem Interval of Skeletal Remains Using Bovine Femurs: A Pilot Study. *Diagnostics*. 2020.12; 10(12);
6. Chihiro Tanaka, Hajime Utsuno, Yohsuke Makino, Saki Minegishi, Jun Ota, Hirotaro Iwase, Koichi Sakurada. Facial soft tissue thickness of the Japanese population determined using post mortem computed tomography images *Forensic Imaging*. 2020.12; 23; 200423

[Misc]

1. Saki Minegishi, Koichi Sakurada. Forensic odontological methods for age estimation from one tooth *J. Stomatol. Soc., Jpn.* 2020.03; 87(1); 8
2. Sakurada K, Ohta H. No promising antidote 25 years after the Tokyo subway sarin attack: A review. *Legal medicine (Tokyo, Japan)*. 2020.07; 47; 101761
3. Koichi Sakurada, Ken Watanabe, Tomoko Akutsu. Current Methods for Body Fluid Identification Related to Sexual Crime: Focusing on Saliva, Semen, and Vaginal Fluid. *Diagnostics*. 2020.09; 10(9);

[Conference Activities & Talks]

1. Utsuno H, Makino Y, Saitoh H, Minegishi S, ohta J, Iwase H, Sakurada K. Study on three-dimensional facial soft tissue thickness of Japanese adults. The 104th Congress of the Japanese Society of Legal Medicine 2020.09.24 Kyoto
2. Yamaguchi R, Sakurada K, Saitoh H, Yoshida M, Makino Y, Torimitsu S, Mizuno S, Tsuneya S, Kira K, Iwase H. An autopsy case of asphyxiating from airway narrowing due to severe dental infection that spread to the floor of the mouth, deep neck, and face. The 104th Congress of the Japanese Society of Legal Medicine 2020.09.24 Kyoto
3. 大田隼, 峰岸沙希, 宇都野創, 櫻田宏一. Comparison of bacterial DNA and human RNA markers for identification of saliva from forensic samples. 第104次日本法医学会学術全国集会 2020.09.24 京都
4. Minegishi S, Utsuno H, Ohta J, Ishii N, Sakuma A, Namiki S, Tota M, Saitoh H, Makino Y, Sakurada K. Study on the relationship between dental findings and various situation in unidentified cadavers (1st report). 14th Annual Meeting of Japanese Society of Forensic Dental Science 2020.10.04 Iwate

5. Utsuno H, Makino Y, Namiki S, Minegishi S, ohta J, Toya M, Iwase H, Sakurada K.. Study on estimation method of nasal wing position in the skull of Japanese men. The 89th Kanto District Meeting of the Japanese Society of Legal Medicine 2020.10.10 Bunkyo-ku
6. Jun Ohta, Yuko Katoh, Saki Minegishi, Koichi Sakurada. Bacterial DNA-based identification of human and canine saliva-Development of a molecular biological bite mark analysis.. 26th Annual Meeting of Japanese Association of Forensic Science and Technology 2020.11.12 Online
7. Koichi Sakurada. Crime of Heisei and forensic dentistry for Reiwa . The 57th Annual Meeting of the Japanese Association of Criminology 2020.11.28 Online
8. Koichi Sakurada, Naoko Seki, Sachi Umemori. Project for Promoting Leading-edge Research in Oral Science, Society and Education . The 85th Annual Meeting of the Stomatological Society of Japan 2020.12.05 Tokyo Medical and Dental University

[Awards & Honors]

1. Outstanding Performance Award of Student Poster Forum in the 104th Congress of the Japanese Society of Legal Medicine (Jun Ohta) , 2020.09

[Social Contribution]

1. Personal identification using dental findings and others (60cases) , 2020.01.01 - 2020.12.31
2. Arakawa Dental Association Lecture (Koichi Sakurada), Arakawa Dental Association , Online , 2020.12.02

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

Dental Education Development

Professor: Ikuko MORIO
 Assistant Professor Naoko SEKI
 Graduate Student: Mio NAITO
 Graduate Student: Ai OHSATO
 Graduate Student: Shin-ru LIAO
 Graduate Student: Kittichai SIREERAT

(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 6 (online seminar, TMDU). August 24 - September 2.
2. Discussion Cafe (online, TMDU Global Education). August 26.
3. International Symposium 2020 (online, TMDU). December 4.
4. Essential Expertise for Clinical Dentistry 6.5 (online session for treatment planning, TMDU). December 18.

(4) Publications

[Original Articles]

1. Seki N, Moross J, Otsuka H, Sunaga M, Naito M, Kondo K, Shinada K, Morio I, Kinoshita A. Dental Hygiene Learning Outcomes Obtained Through Computer-Assisted Simulation Modules The Journal of Dental Hygiene. 2020.02; 94(1); 32-38

[Conference Activities & Talks]

1. Seki N, Moross J, Kanamori Y, Kanazawa M, Komagamine Y, Mizutani K, Liao S, Kabasawa Y, Iseki S, Morio I. Importance of preparatory courses for international/global dental student exchange programs. Annual Meeting of the 39th Japanese Dental Education Association 2020.09.25 Paper/Online Base

2. Yuna Kanamori, Naoko Seki, Kanako Noritake, Masayo Sunaga, Janelle Moross, Ikuko Morio, Kouji Araki, Atsuhiko Kinoshita, Hiroshi Nitta. Assessment of TMDU trainee residents' dental English ability. The 85th annual meeting of the Stomatological Society 2020.12.05 Tokyo
3. Liao S, Seki N, Akiyama M, Shinada K, Morio I . Perceived stress and career planning of undergraduate dental hygiene students. The 85th Annual Meeting of the Stomatological Society 2020.12.05 Tokyo
4. Ohsato A, Seki N, Moross J, Sunaga M, Kabasawa Y, Kinoshita A, Morio I. Development of e-learning materials and their international provision. The 85th Annual Meeting of the Stomatological Society 2020.12.05 Tokyo

Oral Health Promotion

Professor	Yoko Kawaguchi(till 2020.3)
Jun Aida(from 2020.8)	
Assistant Professor	Takashi Zaitso
Assistant Professor	Akiko Oshiro
Assistant Professor	Masato Nagai(from 2021.4)
Office administrator	Nami Kokuryu(till 2021.3)
	Ayaka Yasuda(from 2021.4)
Registered Resident	Hiromi Nishiyama
Graduate Student	Takashi Tanemura
	Jin Aoki
	Zar Chi Kyaw Myint(till 2020.9)
	Nguyen Thi Nhat Vy (till 2021.9)
	Tomoya Saito
	Srinarupat Jarassri
	Yuko Inoue

(1) Research

- Epidemiological research on oral diseases and prevention of oral diseases
- Oral health care systems and public health dentistry
- Relationship between oral health and general health
- Research on community dental health and oral health promotion
- International comparative studies on oral health

(2) 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.

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

1. [Oral Health Promotion : AIDA Jun] Kawachi I, Aida J, Hikichi H, Kondo K. Disaster Resilience in Aging Populations: Lessons from the 2011 Great East Japan Earthquake & Tsunami. *Journal of the Royal Society of New Zealand.* 2020; 50(2); 263-278
2. [Oral Health Promotion : AIDA Jun] Matsuo G, Aida J, Osaka K, Rozier RG. . Effects of Community Water Fluoridation on Dental Caries Disparities in Adolescents. *International Journal of Environmental Research and Public Health* 2020;17(6):2020.. 2020; 17(6); 2020
3. [Oral Health Promotion : AIDA Jun] Mizuta A, Aida J, Nakamura M, Ojima T. Does the Association between Guardians' Sense of Coherence and their Children' s Untreated Caries Differ According to Socioeconomic Status? *International Journal of Environmental Research and Public Health .* 2020; 17(5); 1619
4. [Oral Health Promotion : AIDA Jun] Sasaki Y, Tsuji T, Koyama S, Tani Y, Saito T, Kondo K, Kawachi I, Aida J. . Neighborhood Ties Reduced Depressive Symptoms in Older Disaster Survivors: Iwanuma Study, a Natural Experiment. *Int J Environ Res Public Health .* 2020; 17(1);
5. [Oral Health Promotion : AIDA Jun] Hoshi M, *Aida J, Kusama T, Yamamoto T, Kiuchi S, Yamamoto T, Ojima T, Kondo K, Osaka K. . Is the Association between Green Tea Consumption and the Number of Remaining Teeth Affected by Social Networks?: A Cross-Sectional Study from the Japan Gerontological Evaluation Study Project. *International Journal of Environmental Research and Public Health* 2020;17(6):2052.. 2020; 17(6); 2052
6. [Oral Health Promotion : AIDA Jun] Kiuchi S, *Aida J, Kusama T, Yamamoto T, Hoshi M, Yamamoto T, Kondo K, Osaka K.. Does public transportation reduce inequalities in access to dental care among older adults? *Japan Gerontological Evaluation Study. Community Dent Oral Epidemiol .* 2020; 48(2); 109-118
7. [Oral Health Promotion : AIDA Jun] Sato Y, *Tsuboya T, Aida J, Saijo Y, Yoshioka E, Osaka K. Effort-reward imbalance at work and tooth loss: a cross-sectional study from the J-SHINE project. *Ind Health.* 2020; 58(1); 26-34
8. [Oral Health Promotion : AIDA Jun] Yoshida Y, *Hiratsuka Y, Kawachi I, Murakami A, Kondo K, Aida J. Association between visual status and social participation in older Japanese:The JAGES cross-sectional study. *Soc Sci Med* 2020;253:112959.. 2020;
9. [Oral Health Promotion : AIDA Jun] Hikichi H, Aida J, Matsuyama Y, Tsuboya T, Kondo K, Kawachi I.. Community-level social capital and cognitive decline after a natural disaster: A natural experiment from the 2011 Great East Japan Earthquake and Tsunami. *Soc Sci Med* 2020;257:111981.. 2020;
10. [Oral Health Promotion : AIDA Jun] Goodwin R, Sugiyama K, Sun S, Aida J, Ben-Ezra M.. Psychological distress after the Great East Japan Earthquake: Two multilevel 6-year prospective analyses. *British Journal of Psychiatry .* 2020; 216(3); 144-150
11. [Oral Health Promotion : AIDA Jun] Sasaki Y, Aida J, Miura H.. Social capital in disaster affected areas. *Journal of the National Institute of Public Health .* 2020; 69(1); 25-32
12. [Oral Health Promotion : AIDA Jun] Koyama S, Tabuchi T, Aida J, Osaka K, Miyashiro I. . Determinants of Increased Tobacco Consumption Following a Major Disaster. *Disaster Medicine and Public Health Preparedness .* 2020; 1-5
13. [Oral Health Promotion : AIDA Jun] *Disaster Medicine and Public Health Preparedness* 2020:1-5.. Disaster resilience in aging populations: lessons from the 2011 Great East Japan earthquake and tsunami. *Journal of the Royal Society of New Zealand .* 2020; 1-16
14. [Oral Health Promotion : AIDA Jun] Sato Yukihiro, Tsuboya Toru, Aida Jun, Saijo Yasuaki, Yoshioka Eiji, Osaka Ken. Effort reward imbalance at work and tooth loss: a cross-sectional study from the J-SHINE project *INDUSTRIAL HEALTH.* 2020; 58(1); 26-34

15. [Oral Health Promotion : AIDA Jun] Shiba K, Hanazato M, Aida J, Kondo K, Arcaya M, James P, Kawachi I. Cardiometabolic Profiles and Change in Neighborhood Food and Built Environment Among Older Adults: A Natural Experiment *Epidemiology*. 2020; 31(6); 758-767
16. [Oral Health Promotion : AIDA Jun] Hoshi M, Aida J, Kusama T, Yamamoto T, Kiuchi S, Yamamoto T, Ojima T, Kondo K, Osaka K. Is the Association between Green Tea Consumption and the Number of Remaining Teeth Affected by Social Networks?: A Cross-Sectional Study from the Japan Gerontological Evaluation Study Project *International Journal of Environmental Research and Public Health*. 2020; 17(6); 2052
17. [Oral Health Promotion : AIDA Jun] Mizuta A, Aida J, Nakamura M, Ojima T. Does the Association between Guardians' Sense of Coherence and their Children's Untreated Caries Differ According to Socioeconomic Status? *International Journal of Environmental Research and Public Health*. 2020; 17(5); 1619
18. [Global Health Promotion : TANI YUKAKO] Sasaki Y, Tsuji T, Koyama S, Tani Y, Saito T, Kondo K, Kawachi I, Aida J. Neighborhood Ties Reduced Depressive Symptoms in Older Disaster Survivors: Iwanuma Study, a Natural Experiment. *International journal of environmental research and public health*. 2020.01; 17(1);
19. [Oral Health Promotion : AIDA Jun] Sato Yukihiro, Tsuboya Toru, Aida Jun, Saijo Yasuaki, Yoshioka Eiji, Osaka Ken. Effort-reward imbalance at work and tooth loss: a cross-sectional study from the J-SHINE project(和訳中) *Industrial Health*. 2020.01; 58(1); 26-34
20. [Oral Health Promotion : ZAITSU Takashi] Takashi Zaitsu, Tomoya Saito, Akiko Oshiro, Takeo Fujiwara, Yoko Kawaguchi. The Impact of Oral Health on Work Performance of Japanese Workers. *J. Occup. Environ. Med.*. 2020.02; 62(2); e59-e64
21. [Oral Health Promotion : AIDA Jun] Koyama S, Tabuchi T, Aida J, Osaka K, Miyashiro I. Determinants of Increased Tobacco Consumption Following a Major Disaster. *Disaster medicine and public health preparedness*. 2020.03; 1-5
22. [Oral Health Promotion : AIDA Jun] Hoshi Manami, Aida Jun, Kusama Taro, Yamamoto Takafumi, Kiuchi Sakura, Yamamoto Tatsuo, Ojima Toshiyuki, Kondo Katsunori, Osaka Ken. Is the Association between Green Tea Consumption and the Number of Remaining Teeth Affected by Social Networks?: A Cross-Sectional Study from the Japan Gerontological Evaluation Study Project *INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*. 2020.03; 17(6);
23. [Oral Health Promotion : AIDA Jun] Matsuo Go, Aida Jun, Osaka Ken, Rozier Richard Gary. Effects of Community Water Fluoridation on Dental Caries Disparities in Adolescents *INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*. 2020.03; 17(6);
24. [Oral Health Promotion : AIDA Jun] Mizuta Akiko, Aida Jun, Nakamura Mieko, Ojima Toshiyuki. Does the Association between Guardians' Sense of Coherence and their Children's Untreated Caries Differ According to Socioeconomic Status? *INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*. 2020.03; 17(5);
25. [Oral Health Promotion : AIDA Jun] Goodwin Robin, Sugiyama Kemmyo, Sun Shaojing, Aida Jun, Ben-Ezra Menachem. Psychological distress after the Great East Japan Earthquake: two multilevel 6-year prospective analyses *BRITISH JOURNAL OF PSYCHIATRY*. 2020.03; 216(3); 144-150
26. [Oral Health Promotion : ZAITSU Takashi] Akiko Oshiro, Takashi Zaitsu, Masayuki Ueno and Yoko Kawaguchi. Characterization of oral bacteria in the tongue coating of patients with halitosis using 16S rRNA analysis *ACTA ODONTOLOGICA SCANDINAVICA*. 2020.04;
27. [Oral Health Promotion : AIDA Jun] Kiuchi Sakura, Aida Jun, Kusama Taro, Yamamoto Takafumi, Hoshi Manami, Yamamoto Tatsuo, Kondo Katsunori, Osaka Ken. Does public transportation reduce inequalities in access to dental care among older adults? *Japan Gerontological Evaluation Study COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY*. 2020.04; 48(2); 109-118
28. [Oral Health Promotion : ZAITSU Takashi] Zar Chi Kyaw Myint, Takashi Zaitsu, Akiko Oshiro, Masayuki Ueno, Ko Ko Soe, Yoko Kawaguchi. Risk Indicators of Dental Caries and Gingivitis among 10-11-year-old Students in Yangon, Myanmar *International Dental Journal* . 2020.05; 70; 167-175

29. [Oral Health Promotion : ZAITSU Takashi] Zar Chi Kyaw Myint, Takashi Zaitzu, Akiko Oshiro, Ko Ko Soe, Yoko Kawaguchi. Reliability and validity of the Myanmar version of the child oral health impact profile – short form 19 *Annals of Epidemiology & Public Health*. 2020.05; 1-7
30. [Oral Health Promotion : AIDA Jun] Yoshida Yuto, Hiratsuka Yoshimune, Kawachi Ichiro, Murakami Akira, Kondo Katsunori, Aida Jun. Association between visual status and social participation in older Japanese: The JAGES cross-sectional study *SOCIAL SCIENCE & MEDICINE*. 2020.05; 253; 112959
31. [Oral Health Promotion : AIDA Jun] Goodwin R, Sugiyama K, Sun S, Aida J, Ben-Ezra M. Psychological distress after the Great East Japan Earthquake: two multilevel 6-year prospective analyses - CORRIGENDUM. *The British journal of psychiatry : the journal of mental science*. 2020.05; 1
32. [Oral Health Promotion : ZAITSU Takashi] Zar Chi Kyaw Myint, Takashi Zaitzu, Akiko Oshiro, Ko Ko Soe and Yoko Kawaguchi. Effectiveness of a School Oral Health Education Program in Yangon, Myanmar Interventions in Pediatric Dentistry *Open Access Journal* . 2020.06; 4(1); 291-299
33. [Oral Care for Systemic Health Support : ITO Kanade] Kanade Ito, Noriko Cable, Tatsuo Yamamoto, Kayo Suzuki, Katsunori Kondo, Ken Osaka, Georgios Tsakos, Richard G Watt, Jun Aida. Wider Dental Care Coverage Associated with Lower Oral Health Inequalities: A Comparison Study between Japan and England. *International journal of environmental research and public health*. 2020.07; 17(15);
34. [Oral Health Promotion : AIDA Jun] Cooray U., Aida J., Watt R. G., Tsakos G., Heilmann A., Kato H., Kiuchi S., Kondo K., Osaka K.. Effect of Copayment on Dental Visits: A Regression Discontinuity Analysis *JOURNAL OF DENTAL RESEARCH*. 2020.07;
35. [Oral Health Promotion : AIDA Jun] Ikeda T, Cable N, Saito M, Koyama S, Tsuji T, Noguchi T, Kondo K, Osaka K, Aida J. Association between social isolation and smoking in Japan and England. *Journal of epidemiology*. 2020.08;
36. [Oral Health Promotion : AIDA Jun] Kino S, Aida J, Kondo K, Kawachi I. Persistent mental health impacts of disaster. Five-year follow-up after the 2011 great east Japan earthquake and tsunami: Iwanuma Study. *Journal of psychiatric research*. 2020.08;
37. [Oral Health Promotion : AIDA Jun] Kino Shiho, Aida Jun, Kondo Katsunori, Kawachi Ichiro. Long-term Trends in Mental Health Disorders After the 2011 Great East Japan Earthquake and Tsunami *JAMA NETWORK OPEN*. 2020.08; 3(8); e2013437
38. [Oral Health Promotion : AIDA Jun] Tsuji T, Saito M, Ikeda T, Aida J, Cable N, Koyama S, Noguchi T, Osaka K, Kondo K. Change in the prevalence of social isolation among the older population from 2010 to 2016: A repeated cross-sectional comparative study of Japan and England. *Archives of gerontology and geriatrics*. 2020.08; 91; 104237
39. [Oral Health Promotion : ZAITSU Takashi] Junzo Funaki, Seiko Funaki, Takashi Zaitzu, Brian S. Noguchi, and Fajar H. Nasution. International Comparison of Perceived Smile Attractiveness and Consciousness *International Journal of Clinical Preventive Dentistry*. 2020.09; 16(4); 209-214
40. [Oral Health Promotion : AIDA Jun] Goodwin Robin, Sugiyama Kemmyo, Sun Shaojing, Takahashi Masahito, Aida Jun. Trajectories of Distress Following the Great East Japan Earthquake: A Multiwave Prospective Study *CLINICAL PSYCHOLOGICAL SCIENCE*. 2020.09;
41. [Oral Health Promotion : AIDA Jun] Ikeda T, Aida J, Kawachi I, Kondo K, Osaka K. Causal effect of deteriorating socioeconomic circumstances on new-onset arthritis and the moderating role of access to medical care: A natural experiment from the 2011 great east Japan earthquake and tsunami. *Social science & medicine (1982)*. 2020.09; 264; 113385
42. [Oral Diagnosis and General Dentistry : UMEMORI Sachi] Umemori S, Aida J, Tsuboya T, Tabuchi T, Tonami K, Nitta H, Araki K, Kondo K. Does the second-hand smoking associate with tooth loss among older Japanese?: JAGES cross-sectional study. *International Dental Journal*. 2020.10; 70(5); 388-395
43. [Oral Health Promotion : AIDA Jun] Hosokawa Rikuya, Ojima Toshiyuki, Myojin Tomoya, Aida Jun, Kondo Katsunori, Kondo Naoki. Associations between Healthcare Resources and Healthy Life Expectancy: A Descriptive Study across Secondary Medical Areas in Japan *INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*. 2020.10; 17(20);

44. [Oral Health Promotion : AIDA Jun] Shiba K, Aida J, Kondo K, Nakagomi A, Arcaya M, James P, Kawachi I. Mediation of the relationship between home loss and worsened cardiometabolic profiles of older disaster survivors by post-disaster relocation: A natural experiment from the Great East Japan earthquake and tsunami. *Health & place*. 2020.10; 66; 102456
45. [Oral Health Promotion : AIDA Jun] Gero Krisztina, Hikichi Hiroyuki, Aida Jun, Kondo Katsunori, Kawachi Ichiro. Associations Between Community Social Capital and Preservation of Functional Capacity in the Aftermath of a Major Disaster *AMERICAN JOURNAL OF EPIDEMIOLOGY*. 2020.11; 189(11); 1369-1378
46. [Oral Health Promotion : AIDA Jun] Kusama T, Todoriki H, Osaka K, Aida J. Majority of New Onset of Dental Caries Occurred from Caries-Free Students: A Longitudinal Study in Primary School Students. *International journal of environmental research and public health*. 2020.11; 17(22);
47. [Oral Health Promotion : AIDA Jun] Gero K, Aida J, Kondo K, Kawachi I. Evaluation of Trust Within a Community After Survivor Relocation Following the Great East Japan Earthquake and Tsunami. *JAMA network open*. 2020.11; 3(11); e2021166
48. [Oral Health Promotion : AIDA Jun] Saito M, Shimazaki Y, Fukai K, Furuta M, Aida J, Ando Y, Miyazaki H, Kambara M. A multilevel analysis of the importance of oral health instructions for preventing tooth loss: The 8020 Promotion Foundation Study of Japanese Dental Patients. *BMC oral health*. 2020.11; 20(1); 328

[Books etc]

1. [Oral Health Promotion : AIDA Jun] Aida J, Kondo K. *Social Determinants of Health in Non-communicable Disease: Case Studies from Japan*. Springer, 2020.11

[Conference Activities & Talks]

1. [Fresh Breath Clinic : OSHIRO Akiko] Srinarupat Jarassri, Zaitzu Takashi, Oshiro Akiko, Aung Ei Ei, Kawaguchi Yoko. タイ国の高齢者集団における咀嚼能力とその関連要因 (Chewing ability and its related factors among elderly population in Thailand). *口腔衛生学会雑誌* 2020.03.01
2. [Fresh Breath Clinic : OSHIRO Akiko] Nguyen Thi Nhat Vy, Zaitzu Takashi, Oshiro Akiko, Kawaguchi Yoko. ベトナムにおける12歳の生徒に対する口腔保健教育プログラムの有効性 (Effectiveness of oral health education program on 12-year-old students in Vietnam). *口腔衛生学会雑誌* 2020.03.01
3. [Fresh Breath Clinic : OSHIRO Akiko] Zar Chi Kyaw Myint, Zaitzu Takashi, Oshiro Akiko, Kawaguchi Yoko. ミャンマーにおける学校ベースの口腔保健教育プログラムの影響 (Impact of school-based oral health education program in Myanmar). *口腔衛生学会雑誌* 2020.03.01

Sports Medicine and Dentistry

- [Associate Professor] Toshiaki Ueno
- [Assistant Professor] Hiroshi Churei
- [Specially Appointed Assistant Professor] Kairi Hayashi
- [Graduate Student] Nana Kamiya-Shiota, Phyu Sin Tun, Rio Kinjo, Thet Khaing Aung, Yuumi Takahashi, Keishi Fujimoto, Chenyuan Li, Masato Sakai, Shintaro Shimizu
- [Research Student] Kaito Togawa
- [Part-time Instructor] Goshi Kondo, Yukio Sasaki, Ryo Sato, Takuto Yamanaka, Sachiko Fujino, Yuriko Yoshida, Gen Tanabe, Takefumi Negoro, Kazushi Watanabe, Shintarou Fukasawa, Takahiro Shirako, Chiho Shibata, Mai Ikegawa, Misaki Suzaka
- [Part-time Resident] Takaaki Fukuda, Chie Ichihara, Yoko Ohara, Akira Nagai, Asami Sakuma

(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-Ensyu
- 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 facilities>

Department of Sports Medicine/Dentistry: Mouthguard training facility certified by Japanese Academy of Sports Dentistry(JASD)

Clinic of Sports Dentistry in University Hospital: Medical Check-up Facility certified by Japan Paralympic Committee

< Certified specialists>

Toshiaki Ueno (1.JSPO Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 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 Dental Materials and Devices), 4.Dental specialist certified by Japanese Academy of Dental Traumatology, 7.JPSA Sports Doctor certified by Japanese Para-Sports Association

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

Kairi Hayashi (1.JSPO Sports Dentist certified by Japan Sports Association, 2.Dental specialist certified by JASD, 3. MG technical instructor certified by JASD)

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

Yuriko Yoshida (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Gen Tanabe (1.Dental specialist certified by JASD, 2.MG technical instructor certified by JASD)

Nana Kamiya-Shiota (1.JSPO Sports Dentist certified by Japan Sports Association, 2. MG technical instructor certified by JASD)

Rio Kinjo (MG technical instructor certified by JASD)

(7) Publications

[Original Articles]

1. Tanabe Gen, Churei Hiroshi, Wada Takahiro, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine JOURNAL OF ORAL SCIENCE. 2020.01; 62(1); 23-27
2. Tanabe G, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine J Oral Sci. 2020.01; 62(1); 23-27
3. Aung Thet Khaing , Churei Hiroshi, Kinjo Rio, Tun Phyu Sin , Tanabe Gen, Ueno Toshiaki. フェイスガードの異なるクッション材料の換気率と衝撃吸収能の比較 (Ventilation rate and shock absorbing ability of different types of cushion materials in face guard) スポーツ歯学. 2020.02; 23(2); 88-89
4. Tun Phyu Sin , Tanabe Gen, Kamijo Shingo, Aung Thet Khaing , Oki Meiko, Churei Hiroshi, Hikita Kazuhiro, Ueno Toshiaki. 光学3Dスキャナーを用いて個別調整したマウスガード適合性に関するデジタル評価法 (Digital evaluation of the fit of custom-made mouthguard using optical 3D scanner) スポーツ歯学. 2020.02; 23(2); 94-95
5. Kairi Hayashi, Hiroshi Churei, Gen Tanabe, Kaito Togawa, Ruman Uddin Chowdhury, Toshiaki Ueno. Improving the Wearing Rate of Mouthguards in the Youth Rugby Category Affects the Total Future Mouthguard Wearing Rate. Dent J (Basel). 2020.07; 8(3); e77
6. Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita YI, Chowdhury RU, Chowdhury NU, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment: A case report Journal of Prosthodontic Research. 2020.09; Sep 15 published online;
7. Tun PS, Churei H, Hikita K, Kamijo S, Oki M, Tanabe G, Hayashi K, Aung TK, Win A, Hlaing S, Takahashi H, Ueno T. Fabrication of shock absorbing photopolymer composite material for 3D printing sports mouthguard JOURNAL OF PHOTOPOLYMER SCIENCE AND TECHNOLOGY. 2020.12; 33(6); 615-622
8. Takahiro Wada, Hiroshi Churei, Mako Yokose, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Application of Glass Fiber and Carbon Fiber-Reinforced Thermoplastics in Face Guards. Polymers (Basel). 2020.12; 13(1); 18

[Conference Activities & Talks]

1. Churei H. Sports Dentistry. University of Dental Medicine, Yangon/Special Lecture 2020.02.06 Yangon, Myanmar
2. Aung TK, Churei H, Kinjo R, Tun PS, Tanabe G, Ueno T . Shock absorbing ability of different cushion materials used in face guard. 40th Myanmar Dental Conference 2020.02.07
3. Tun PS, Churei H, Tanabe G, Aung TK, Kamijo S, Oki M, Takahashi H, Hikita K, Ueno T. Shock-absorbing capability of laminated type of 3D printing materials compared to conventional mouthguard materials. 40th Myanmar Dental Conference 2020.02.07
4. Takahiro Wada, Yasuhito Takashima, Rio Kinjo, Kasei Aoyagi, Hiroshi Churei, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takashi, Fumiyoshi Minami, Motohiro Uo. Strain distribution analysis of face guards made of carbon fiber-reinforced thermoplastics during shock absorption test using high-speed camera and digital image correlation. 4th open forum for "Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development" 2020.03.04 Tokyo, Japan
5. Wada Takahiro, Kinjo Rio, Uo Motohiro. Ion-Releasing and Shock-Absorbing Properties of Surface Pre-reacted Glass-ionomer Filler in Multilayer Mouth Guards. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)
6. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Uo Motohiro, Ueno Toshiaki. Development of wearable mouth-guard device for monitoring teeth clenching during exercise. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)

7. Aung TK, Churei H, Kinjo R, Tun PS, Tanabe G, Takahashi Y, Hayashi T, Ueno T. Shock absorbing ability of 3D printed thermoplastic ABS compatible with face guard material. 第31回日本スポーツ歯科医学会 2020.12.05 広島市+ WEB 開催
8. Tun PS, 中禮宏, 疋田一洋, 上條真悟, 大木明子, 田邊元, 林海里, Aung TK, 高橋英和, 上野俊明. Production of shock absorbing photopolymer composite material for 3D printing sports mouthguard. 第31回日本スポーツ歯科医学会 2020.12.05 広島市+ WEB 開催

Educational System in Dentistry

Professor Kouji ARAKI
Associate Professor Jun TSURUTA
Junior Associate Professor(non-full time) Kouji IIDA
Hiroki KATAOKA
Graduate Student Akitaka HATTORI
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. Le SH, Tonami K, Umemori S, Nguyen LT, Ngo LT, Araki K, Nitta H. Relationship between pre-operative dental anxiety and short-term inflammatory response following oral surgery. *Australian dental journal*. 2020.09;
2. Umemori S, Aida J, Tsuboya T, Tabuchi T, Tonami K, Nitta H, Araki K, Kondo K. Does the second-hand smoking associate with tooth loss among older Japanese?: JAGES cross-sectional study. *International Dental Journal*. 2020.10; 70(5); 388-395

[Misc]

1. Iino Y, Sunakawa M, Tsuruoka H, Okihata R, Takahashi Y, Araki K. Preventive measures in dental conservative treatment associated with the spread of severe acute respiratory syndrome Corona-Virus 2 (SARS-CoV-2) infection *The japanese journal of conservative dentistry*. 2020.08; 63(4); 272-279

[Conference Activities & Talks]

1. UMEMORI Sachi, TONAMI Ken-ichi, NORITAKE Kanako, IWAKI Maiko, KIMURA Yasuyuki, NITTA Hiroshi, ARAKI Kouji. The Analysis of Unprofessional behavior in the class of "behavioral science" in Tokyo Medical and Dental University (TMDU). 2020.07
2. KANAMORI Yuna, NORITAKE Kanako, UMEMORI Sachi, IWAKI Maiko, KIDO Daisuke, HIDEHIMA Masayuki, KIMURA Yasuyuki, HATTORI Akitaka, TONAMI Ken-ichi, EBIHARA Arata, ARAKI Kouji, NITTA Hiroshi. TMDU trainee residents' feedback on the trial of objective clinical skills examinations. 2020.09.26
3. Tonami K, Umemori S, Noritake K, Iwaki M, Kimura Y, Araki K, Nitta H. Relation between unprofessional behavior and score of medical ethics examination. The 39th congress of Japanese Dental Education Association 2020.09.26 online
4. Yuna Kanamori, Naoko Seki, Kanako Noritake, Masayo Sunaga, Janelle Moross, Ikuko Morio, Kouji Araki, Atsuhiko Kinoshita, Hiroshi Nitta. Assessment of TMDU trainee residents' dental English ability. The 85th annual meeting of the Stomatological Society 2020.12.05 Tokyo

[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 Atsuhiko
Assistant Professor SUNAGA Masayo
Graduate Student AKIYAMA Kyoko
Graduate Student HARADA Yusuke
Graduate Student TAKENOUCI Akane
Graduate Student URAKAWA Ayaka
Graduate Research Student YANG Shengsen(~ September)

(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.

(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-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. Naoko Seki, Janelle Moross, Hiromi Otsuka, Masayo Sunaga, Mio Naito, Keiko Kondo, Kayoko Shinada, Ikuko Morio, Atsuhiko Kinoshita. Dental Hygiene Learning Outcomes Obtained Through Computer-Assisted Simulation Modules. *J Dent Hyg.* 2020.02; 94(1); 32-38
2. Nobutoshi Nawa, Mitsuyuki Numasawa, Mina Nakagawa, Masayo Sunaga, Takeo Fujiwara, Yujiro Tanaka, Atsuhiko Kinoshita. Differential effects of individual and school factors on the academic trajectories of Japanese dental students. *J Dent Educ.* 2020.03;
3. Nawa N, Numasawa M, Nakagawa M, Sunaga M, Fujiwara T, Tanaka Y, Kinoshita A. Associations between demographic factors and the academic trajectories of medical students in Japan. *PloS one.* 2020.05; 15(5); e0233371
4. Takenouchi A, Otani E, Sunaga M, Toyama T, Uehara H, Akiyama K, Kawashima T, Ito K, Izuno H, Kinoshita A. Development and evaluation of e-learning materials for dental hygiene students in six schools: using smartphones to learn dental treatment procedures. *International journal of dental hygiene.* 2020.06;

Insured Medical Care Management

Professor Masumi AI
Associate Professor Minato YOKOYAMA
Graduate Student Masako ARIMOTO

(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.

A doctor course student is in her third 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. Kitazawa Toru, Seino Hiroaki, Ohashi Hiroshi, Inazawa Takeshi, Inoue Masahiro, Ai Masumi, Fujishiro Midori, Kuroda Hisamoto, Yamada Masayo, Anai Motonobu, Ishihara Hisamitsu. Comparison of tofogliflozin versus glimepiride as the third oral agent added to metformin plus a dipeptidyl peptidase-4 inhibitor in Japanese patients with type 2 diabetes: A randomized, 24-week, open-label, controlled trial (STOP-OB) DIABETES OBESITY & METABOLISM. 2020.09; 22(9); 1659-1663
2. Ikezaki Hiroaki, Furusyo Norihiro, Yokota Yuya, Ai Masumi, Asztalos Bela F., Murata Masayuki, Hayashi Jun, Schaefer Ernst J.. Small Dense Low-Density Lipoprotein Cholesterol and Carotid Intimal Medial Thickness Progression Journal of Atherosclerosis and Thrombosis. 2020.10; 27(10); 1108-1122

[Others]

1. IRB Member, Sony Corporation 2012-

Department of Global Health Entrepreneurship

Professor: Keiko Nakamura, MD, PhD
Junior Associate Professor: Kaoruko Seino, PhD
Research Fellow: AL-SOBAlHI Saber, RN, MPH, PhD;
Yuri Tashiro, MPharm, MPH, PhD

Graduate Student:
Deogratius Bintabara, MD, MPH;
TJ Robison Moncatar, RN, MPH;
Kathryn Lizbeth Lucena Siongco, RN, RM;
Tran Dai Tri Han, MD, MPH; Hue Man Vo, MD;
HASAN S M Mahmudul Hasan, DMD;
Shayo Festo Kasmir, MD; Alemi Sharifullah, MD;
Romnalin Thonglor, MPH;
Ayano Miyashita, MSc; Kouki Akahoshi, MD;
Yasushi Sakuramoto MD, MPH, MPA;
Rueda Saleh Alojaimy, RN;
Hideko Sato, RN, MPH;
Anderson Bendera, MD;
Kamila Dost, MD;
Eugene Meshi, MSc;
Zia-ul-haq Safi, MD;
Minh Tri Tran Xuan, MD;
Thao Vi, MD;
Jobir Khan, PD;
Uyanga Munkhdavaa;
Nalusha Quadros, DMD

(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. Vo THM, Nakamura K, Seino K, Nguyen HTL, Vo TV. Fear of falling and cognitive impairment in elderly with different social support levels: findings from a community survey in Central Vietnam. *BMC Geriatrics*. 2020.03; 20; 141
2. Rahman M, Nakamura K, Hasan SMM, Seino K, Mostofa G. Mediators of the association between low socioeconomic status and poor glyceemic control among type 2 diabetics in Bangladesh. *Scientific Reports*. 2020.03; 10; 6690
3. Nguyen HTL, Nakamura K, Seino K, Vo VT . Relationships among cyberbullying, parental attitudes, self-harm and suicidal behavior among adolescents: results from a school-based survey in Vietnam. *BMC Public Health*. 2020.03; 20; 476

4. Vo Thi Hue Man, Nakamura Keiko, Seino Kaoruko, Nguyen Hoang Thuy Linh, Vo Thang Van. Fear of falling and cognitive impairment in elderly with different social support levels: findings from a community survey in Central Vietnam BMC GERIATRICS. 2020.04; 20(1); 141
5. Rahman M, Nakamura K, Hasan SMM, Seino K, Mostofa G. Mediators of the association between low socioeconomic status and poor glycemic control among type 2 diabetics in Bangladesh. Scientific reports. 2020.04; 10(1); 6690
6. Nguyen Hoang Thuy Linh, Nakamura Keiko, Seino Kaoruko, Vo Van Thang. Relationships among cyberbullying, parental attitudes, self-harm and suicidal behavior among adolescents: results from a school-based survey in Vietnam BMC PUBLIC HEALTH. 2020.04; 20(1); 476
7. Siongco KLL, Nakamura K, Seino K. Reduction in inequalities in health insurance coverage and healthcare utilization among older adults in the Philippines after mandatory national health insurance coverage: trend analysis for 2003-2017. Environmental health and preventive medicine. 2020.06; 25(1); 17
8. Alemi S, Nakamura K, Rahman M, Seino K. Male participation in antenatal care and its influence on their pregnant partners' reproductive health care utilization: insight from the 2015 Afghanistan Demographic and Health Survey. Journal of biosocial science. 2020.06; 1-23
9. Moncatar TJR, Nakamura K, Siongco KL, Rahman M, Seino K. Prevalence and Determinants of Self-Reported Injuries among Community-Dwelling Older Adults in the Philippines: A 10-Year Pooled Analysis. International journal of environmental research and public health. 2020.06; 17(12);
10. Siongco Kathryn Lizbeth Lucena, Nakamura Keiko, Seino Kaoruko. 強制加入国民健康保険適用後のフィリピンの高齢者における健康保険適用範囲とヘルスケア利用の不平等是正 2003~2017年の傾向分析 (Reduction in inequalities in health insurance coverage and healthcare utilization among older adults in the Philippines after mandatory national health insurance coverage: trend analysis for 2003-2017) Environmental Health and Preventive Medicine. 2020.06; 25; 1 of 13-13 of 13
11. Munseri P, Said J, Amour M, Magohe A, Matee M, Rees CA, Mackenzie T, Tvaroha S, Bailey-Kellogg C, Maro I, Wieland-Alter W, Adams LV, Horsburgh CR, Nakamura K, Arbeit RD, Pallangyo K, von Reyn CF. DAR-901 vaccine for the prevention of infection with Mycobacterium tuberculosis among BCG-immunized adolescents in Tanzania: A randomized controlled, double-blind phase 2b trial. Vaccine. 2020.09; 38; 7239-7245
12. Sumino K, Sato N, Nakashiba K, Ohisa K, Fujii K, Hashimoto A, Kataoka M, Sato H, Kobayashi Y, Masuda R, Zhang J, Kijima Y, Nakamura K, Hashimoto H.. Collaboration between academic institutes and public health centers under public health emergency; lessons learnt through COVID-19 epidemic. 2020.09;
13. Alemi Sharifullah, Nakamura Keiko, Seino Kaoruko, Mashal Mohammad Omar, Arab Ahmad Shekib, Hemat Shafiqullah. アフガニスタンの女性教師における非感染性疾患の危険因子プロファイル (Noncommunicable disease risk factor profile among Afghan female school teachers) 日本公衆衛生学会総会抄録集. 2020.10; 79回; 500
14. Nakamura Keiko, Seino Kaoruko, Kibusi Stephen, Maro Isaac, Bintabara Deogratius, Shayo Festo Kasmir, Miyashita Ayano, Tashiro Yuri. タンザニアでの高血圧/糖尿病管理に対する実施評価 (Implementation assessment for management of hypertension/diabetes in Tanzania) 日本公衆衛生学会総会抄録集. 2020.10; 79回; 512
15. Miyashita Ayano, Nakamura Keiko, Kibusi Stephen M., Seino Kaoruko, Bintabara Deogratius, Shayo Festo K, Maro Isaac, Tashiro Yuri. タンザニアにおける mHealth を用いた NCD 管理への受容性 (Assessing acceptability of mHealth for NCD management in Tanzania) 日本公衆衛生学会総会抄録集. 2020.10; 79回; 504
16. Siongco Kathryn Lizbeth L., Nakamura Keiko, Moncatar TJ Robinson T., Canila Carmelita, Lorenzo Felyl Marilvn, Seino Kaoruko, Takano Takehito. フィリピンの医療現場における協働に対する態度の改善 (Improvement in collaborative attitudes in the Philippine healthcare setting) 日本公衆衛生学会総会抄録集. 2020.10; 79回; 500
17. Tran Thi Hue Man, Nakamura Keiko, Seino Kaoruko, Vo Thi Hue Man, Vo Van Thang, Takano Takehito. ベトナムの高齢者における聴覚障害と認知機能 (Hearing impairment and cognitive function among older adults in Viet Nam) 日本公衆衛生学会総会抄録集. 2020.10; 79回; 499

18. Vo Thi Hue Man, Nakamura Keiko, Seino Kaoruko, Tran Dai Tri Han, Vo Van Thang, Takano Takehito. ベトナム人高齢者における一人暮らしと転倒恐怖感との関連性 (Association between living alone and fear of falling among Vietnamese elderly) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 494
19. Moncatar TJ Robinson, Nakamura Keiko, Siongco Kathryn Lizbeth, Seino Kaoruko, Canila Carmelita, Javier Richard, Lorenzo Fely Marilyn, Takano Takehito. 医療資源不足下での高齢者ケアの連携における決定要因 (Determinants of collaboration for elderly care in a low-resource context) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 493
20. Thonglor Romnalin, Nakamura Keiko, Seino Kaoruko. 子どもとの同居がタイの高齢者の心理的健康に及ぼす影響 (Does co-residence with children matters for Thai elderly psychological health?) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 499
21. Hasan S.M. Mahmudul, Nakamura Keiko, Seino Kaoruko, Rahman Mosiur. 心理症状が2型糖尿病患者の歯周病に及ぼす影響 (Psychological symptoms impact on periodontal disease among Type2 diabetes Patient) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 495
22. Shayo Festo Kasmir, Nakamura Keiko, Al-Sobaihi Saber, Seino Kaoruko. 汚染から保護されていない家庭用の水源と高いマラリア有病率との関連 (Does an unimproved source of domestic water linked to high malaria prevalence?) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 503
23. Seino Kaoruko, Nakamura Keiko, Siongco Kathryn Lizbeth L., Moncatar TJ Robinson, Canila Carmelita, Lorenzo Felyl Marilyn, Javier Richard, Takano Takehito. 高齢者ケアのための専門職間研修プログラム (In-service inter professional training program for geriatric care) 日本公衆衛生学会総会抄録集. 2020.10; 79 回; 500

[Books etc]

1. Kaoruko Seino. Relational Studies on Global Crises Vol. 7: Global Crises on the Boundaries. Iwanami Shoten Publishers, 2020.10

[Misc]

1. Nakamura K, Maro II, Kibusi SM. Community mHealth integrated care (ComHIC) to manage hypertension/diabetes in Tanzania's overburdened health system. Tanzania Medical Journal. 2020.04;
2. Nakamura K. Network of cities and academic institutions to promote Healthy Cities: WHO Collaborating Centre for Healthy Cities and Urban Policy Research Friends of WHO in Japan. 2020.07; 2020(Summer);

[Conference Activities & Talks]

1. Kaoruko Seino. Urban Heat Stress: individual and community level risks and mitigating factors. 90th Annual Scientific Conference, The Japanese Society for Hygiene 2020.03.28
2. Nakamura K. Urban governance in response to COVID-19 . Annual Meeting of Australian Chapter of the Alliance for Healthy Cities 2020.06.26
3. Maro II, Nakamura K, Kibusi S, Seino K. Community mHealth Integrated Care (ComHIC) to manage hypertension/diabetes in Tanzania' s overburdened health system. Global Alliance for Chronic Disease Annual Scientific Meeting 2020 2020.11.11 London
4. Nakamura K. Healthy Cities in the Western Pacific Region: Network of the Alliance for Healthy Cities. WHO European Healthy Cities Annual Business Meeting and Technical Conference, Healthy Cities Around the World 2020.12.10 Copenhagen

[Awards & Honors]

1. Fellowship of Faculty of Public Health, Faculty of Public Health, 2020.04

Rehabilitation Medicine

Professor	Atsushi OKAWA
Assistant Professor	Tomoko SAKAI
Associate Professor	Tetsuya JINNO
Assistant Professor	Chisato HOSHINO
Assistant Professor	Masanobu HIRAO(-Sep.)
Assistant Professor	Reiko YAMAGUCHI

Graduate Student

Kazuko ISSHIKI
Shunsuke OHJI
Ryo ONUMA
Yuji TAKAHASHI
Kenji HIROHATA
Tomoko KAWASAKI
Keigo NANJO
Koji IKEMATSU

(1) Research

Research Subjects

- 1) Rehabilitation for total joint arthroplasty
- 2) Motion and gait analysis of healthy and disabled subjects
- 3) Biomechanical research for prevention of sports injury
- 4) Patient safety in rehabilitation medicine
- 5) Osteoporosis of children (individuals) with severe motor and intellectual disabilities

(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. Emily Suzuki, Tomoko Sakai, Chisato Hoshino, Masanobu Hirao, Reiko Yamaguchi, Rui Nakahara. Assessment of the Need for Early Initiation of Rehabilitation Treatments in Patients with Coronavirus Disease 2019. Prog Rehabil Med. 2020; 5; 20200018

2. Akimasa Kimura, Tetsuya Jinno, Sachiya Tsukada, Masaaki Matsubara, Hideyuki Koga. Detection of total hip prostheses at airport security checkpoints. *J Orthop Sci.* 2020.03; 25(2); 255-260
3. Tomoko Sakai, Shiho Honzawa, Makiko Kaga, Yuji Iwasaki, Tatsuo Masuyama. Osteoporosis pathology in people with severe motor and intellectual disability. *Brain Dev.* 2020.03; 42(3); 256-263
4. Watanabe Toshifumi, Aoki Akino, Hoshi Kenji, Gamada Kazuyoshi, Nakagawa Yusuke, Otabe Koji, Katagiri Hiroki, Koga Hideyuki, Sekiya Ichiro, Muneta Takeshi, Jinno Tetsuya, Okawa Atsushi. 人工膝関節全置換術後の良好な予後と kinematics との関連 (Is good kinematics related to better clinical outcomes after total knee arthroplasty?) *日本整形外科学会雑誌.* 2020.03; 94(3); S968
5. Minoda Yukihide, Ito Masayuki, Iwakiri Kentarou, Uchiyama Katsufumi, Kawasaki Masashi, Kanda Akio, Jinno Tetsuya, Sugama Ryo, Chiba Daisuke, Hasagawa Masahiro, Fujishiro Takaaki. 仰臥位の人工股関節全置換術における加速度計センサーを用いた携帯型ナビゲーションシステムの精度 3D-CT 計測による多施設共同研究 (Accuracy of an accelerometer-based portable navigation system in total hip arthroplasty for supine position: A multicenter study using 3D-CT measurement) *日本整形外科学会雑誌.* 2020.03; 94(2); S260
6. Kimura Akimasa, Jinno Tetsuya, Tsukada Sachiya, Matsubara Masaaki, Koga Hideyuki. 空港での保安検査場における人工股関節の検知 (Detection of total hip prostheses at airport security checkpoints) *Journal of Orthopaedic Science.* 2020.03; 25(2); 255-260
7. Takehiro OHMI, Junya AIZAWA, Kenji HIROHATA, Shunsuke OHJI, Kazuyoshi YAGISHITA. Developing Direct Arch Measurement under Quantitative Partial Weight Bearing and Reliability and Validity 2020.04; 35(2); 179-185
8. Ito D, Tanaka T, Kunieda Y, Kimura Y, Ishiyama D, Nishio N, Otobe Y, Koyama S, Ohji S, Suzuki M, Ichikawa T, Ogawa H, Narita Y, Yoshida T, Yamada M, Kondo K. Factors associated with post-stroke apathy in subacute stroke patients. *Psychogeriatrics : the official journal of the Japanese Psychogeriatric Society.* 2020.04;
9. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Okawa Atsushi, Testuya Jinno, Kazuyoshi Yagishita. The gap between dichotomous responses regarding return to sports and subjective athletic performance intensity after anterior cruciate ligament reconstruction 2020.04;
10. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Kazuyoshi Yagishita. The difference of ground reaction force during anterior step motion in collegiate male long-distance runners between with or without a history of medial tibial stress syndrome. *Japanese Journal of Clinical Sports Medicine.* 2020.04; 28(2); 313-320
11. Toshifumi Watanabe, Hideyuki Koga, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Takeshi Muneta, Ichiro Sekiya, Tetsuya Jinno. Correction to: Coronal and sagittal laxity affects clinical outcomes in posterior-stabilized total knee arthroplasty: assessment of well-functioning knees. *Knee Surg Sports Traumatol Arthrosc.* 2020.05; 28(5); 1410
12. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Atsushi Okawa. Portable imageless navigation system and surgeon's estimate for accurate evaluation of acetabular cup orientation during total hip arthroplasty in supine position. *Eur J Orthop Surg Traumatol.* 2020.05; 30(4); 707-712
13. Tomoko Sakai, Chisato Hoshino, Atsushi Okawa, Kenji Wakabayashi, Hidenobu Shigemitsu . The Safety and Effect of Early Mobilization in the Intensive Care Unit According to Cancellation Criteria. *Progress in Rehabilitation Medicine.* 2020.07; 5;
14. Kenji Hirohata, Junya Aizawa, Hidetaka Furuya, Sho Mitomo, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Kate E Webster. The Japanese version of the anterior cruciate ligament-return to sport after injury (ACL-RSI) scale has acceptable validity and reliability. *Knee Surg Sports Traumatol Arthrosc.* 2020.08; 28(8); 2519-2525
15. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Koga Hideyuki, Okawa Atsushi, Jinno Tetsuya, Yagishita Kazuyoshi. The Gap Between Subjective Return to Sports and Subjective Athletic Performance Intensity After Anterior Cruciate Ligament Reconstruction *ORTHOPAEDIC JOURNAL OF SPORTS MEDICINE.* 2020.09; 8(9); 2325967120947402

16. Tomoko Sakai, Chisato Hoshino, Reiko Yamaguchi, Masanobu Hirao, Rui Nakahara, Atsushi Okawa. Remote rehabilitation for patients with COVID-19. *J Rehabil Med.* 2020.09; 52(9); jrm00095
17. Ito Daisuke, Tanaka Tomoya, Kunieda Yota, Kimura Yosuke, Ishiyama Daisuke, Nishio Naohito, Otobe Yuhei, Koyama Shingo, Ohji Shunsuke, Suzuki Mizue, Ichikawa Takeo, Ogawa Hideyuki, Narita Yuya, Yoshida Taiki, Yamada Minoru, Kondo Kunitsugu. Factors associated with post-stroke apathy in subacute stroke patients(和訳中) *Psychogeriatrics.* 2020.09; 20(5); 780-781
18. Ryohei Takada, Tetsuya Jinno, Kazumasa Miyatake, Masanobu Hirao, Toshitaka Yoshii, Atsushi Okawa. Incidence of tensor fascia lata muscle atrophy after using the modified Watson-Jones anterolateral approach in total hip arthroplasty. *Eur J Orthop Surg Traumatol.* 2020.10;
19. Taniguchi N, Jinno T, Endo H, Wako M, Tatsuno R, Ochiai S, Haro H. Improvement of locomotive syndrome after total hip arthroplasty: A two-year longitudinal cohort study. *Modern rheumatology.* 2020.10; 1-9
20. Kimura Y, Ohji S, Nishio N, Abe Y, Ogawa H, Taguchi R, Otobe Y, Yamada M. The impact of wheelchair propulsion based physical activity on functional recovery in stroke rehabilitation: a multicenter observational study. *Disability and rehabilitation.* 2020.10; 1-6
21. Furuya H, Ito T, Hirohata K, Mitomo S, Yamasaki K, Igarashi H, Omori K, Hoshino M, Hart RA. Construct validity and reliability of the Japanese Version of the Lumbar Stiffness Disability Index. *Spine.* 2020.11;
22. Aizawa J, Hirohata K, Ohji S, Ohmi T, Koga H, Yagishita K. Factors Associated With Psychological Readiness to Return to Sports With Cutting, Pivoting, and Jump-Landings After Primary ACL Reconstruction. *Orthopaedic journal of sports medicine.* 2020.11; 8(11); 2325967120964484
23. Masanobu Hirao, Kazumasa Miyatake, Daisuke Koga, Ryohei Takada, Gaku Koyano, Atsushi Okawa, Tetsuya Jinno. Comparison of 5-year postoperative results between standard-length stems and short stems in one-stage bilateral total hip arthroplasty: a randomized controlled trial. *Eur J Orthop Surg Traumatol.* 2020.11;

Gerodontology and Oral Rehabilitation

Professor

MINAKUCHI Shunsuke

Junior Associate Professor

KUBOTA Kazumasa, KANAZAWA Manabu

Assistant Professor

INOKOSHI Masanao, KOMAGAMINE Yuriko, MOTOMURA Kazuo,
SATO Yusuki, HAMA Yohei

Project Assistant Professor

SOEDA Hitomi, SUZUKI Hiroyuki

Dental Resident

ASAMI Mari, UEDA Kaori, MIYAYASU Anna, SHIMIZUBATA Makoto,

Graduate Student

MIURA Akemi, SHIMADA Ryo, DOKE Midori, TUN Min Bo, SOEDA Yumika, NEGORO Masatoshi,
HADA Tamaki, HATANO Keita, THAW Di Cho Too, KATHENG Awutsadaporn, Guo Ruoyan,
UEHARA Yoko, OTAKE Ryosuke, ONUMA Kei, SHIROBE Maki, TAKAGI Daisuke,
YAMAMOTO Mao, SAI Tun Naing, TONPRASONG Watcharapong, KATADA Haruko,
SHIMIZU Kento, NAKAI Hiroto, YANAGIHARA Yuiko, YAMAGUCHI Kohei, WATANABE Masataka,
LIU Hengyi, BUI Ngoc Huyen Trang, AKIYAMA Yo, UEDA Kaori, OKADA Mitsuzumi,
KASHIWAZAKI Kenta, NAMANO Sahaprom, XU Kaiqi, QI Keyu

Students

ONO Airi, OGAWA Takahiko, KUNISAWA Kiko, TOMODA Taisei,
HAYAKAWA Wakako, FUKASE Madoka

Staff

TERADA Mito

Adjunct lecturer

AKIBA Norihisa, ARAKIDA Toshio, ANDO Kazuo, IKEBE Kazunori, IKKA Tsunakuni,
ITO Junji, INOUE Minoru, UCHIDA Tatsuro, OWADA Gaku, OWATARI Tsuneto,
OSADA Eiji, KAIBA Yoshinori, KAMOCHI Go, KIKUCHI Keisuke, KUROSAWA Yukiko,
KOBAYASHI Shoji, SAKAGUCHI Hideo, SATO Koetsu, TAKAHASHI Noboru, TAKEUCHI Satoshi,
TAKEUCHI Shuhei, TANIMOTO Hiroyuki, TANOUE Mariko, CHO Fuizu, TERANAKA Satoshi,
TOMIOKA Eiji, NAKANODA Shinichi, BABA Yuya, HIRATSUKA Tomohiro, HIRANO Shigezo,
HIRANO Yasuyoshi, HIRAYAMA Daisuke, FUSHIJIMA Ichiro, MATSUO Koichiro,
YAMAGA Eijiro, YOSHIZAKI Taro, YONEYAMA Takeyoshi, WATANABE Ikki

(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) Stress analyses of implant overdenture
- 9) Factorial analysis of complete denture prosthesis
- 10) Resilient denture lining material
- 11) CAD/CAM system for fabricating complete dentures
- 12) Evaluations of masticatory performance using color-changeable chewing gum
- 13) Development of novel restorative materials for root caries
- 14) Development of novel aesthetic, strong and ageing resistant highly translucent zirconia
- 15) 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.

(3) Clinical Performances

We manage the prosthodontic and special care departments.

(4) Publications

[Original Articles]

1. Mari Asami, Manabu Kanazawa, Thuy V Lam, Khaing M Thu, Daisuke Sato, Shunsuke Minakuchi. Preliminary study of clinical outcomes for single implant-retained mandibular overdentures. *J Oral Sci.* 2020; 62(1); 98-102
2. Inokoshi M, Nozaki K, Takagaki T, Okazaki Y, Yoshihara K, Minakuchi S, Van Meerbeek B. Initial curing characteristics of composite cements under ceramic restorations. *J Prosthodont Res.* 2020;
3. Miura Yuka, Nakagami Gojiro, Tohara Haruka, Ogawa Nami, Sanada Hiromi. The association between jaw-opening strength, geniohyoid muscle thickness and echo intensity measured by ultrasound MEDICAL ULTRASONOGRAPHY. 2020; 22(3); 299-304
4. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Minakuchi S.. CAD-CAM milled complete dentures with custom disks and prefabricated artificial teeth: A dental technique. *J Prosthet Dent.* 2020;
5. Hara Y, Nakane A, Tohara H, Kubota K, Nakagawa K, Hara K, Yamaguchi K, Yoshimi K, Minakuchi S. Cervical Interferential Current Transcutaneous Electrical Sensory Stimulation for Patients with Dysphagia and Dementia in Nursing Homes. *Clinical interventions in aging.* 2020; 15; 2431-2437
6. Kazumasa Kubota, Yuka Kyosaka, Kaori Ueda, Shunsuke Minakuchi. Increase in pulse pressure on administration of a dental local anesthetic solution, prilocaine hydrochloride with felypressin in male diabetic patients with coronary heart disease. *Clin Oral Investig.* 2020.01; 24(1); 239-246

7. Kagifuku Y, Tohara H, Wakasugi Y, Susa C, Nakane A, Toyoshima M, Nakakuki K, Kabasawa Y, Harada H, Minakuchi S. What Factors Affect Changes in Body Composition and Swallowing Function in Patients Hospitalized for Oral Cancer Surgery? *Clinical Interventions in Aging*. 2020.01; 15; 1-7
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[Books etc]

1. Nakagawa K, Hara K and Tohara H. *Aspiration Pneumonia the current clinical giant for respiratory physicians*. Springer, 2020.01 (ISBN : 978-981-15-4505-4)
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[Misc]

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[Conference Activities & Talks]

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2. Junji Tokunaga, Junichi Furuya, Hiroyuki Suzuki, Yasushi Tamada, Taro Nomura, Hisatomo Kondo. The relationship between nutrition intake and oral function in acute care hospital inpatients with dysphagia. The 12th Scientific Meeting of Japan Denture Care Society 2020.02.22 Nagoya
3. Watanabe M, Kanazawa M, Miyayasu A, Shimada R, Negoro M, Uehara Y, Sato D, Sato Y, Minakuchi S.. Comparison of masticatory performances between immediately loaded and conventionally loaded mandibular two-implant overdentures with magnetic attachments. The 19th International Conference on Magnetic Applications in Dentistry 2020.02.28 JSMAD web site
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10. Miura Y, Nakagami G, Tohara H, Ogawa N, Sanada H. The association between jaw-opening strength, geniohyoid muscle thickness and echo intensity measured by ultrasound.. Medical ultrasonography 2020.03.27
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23. Masataka Watanabe, Manabu Kanazawa, Anna Miyayasu, Mari Asami, Ryo Shimada, Masatoshi Negoro, Yoko Uehara, Daisuke Sato, Yuriko Kusumoto, Yuka Abe, Kazuyoshi Baba, Shunsuke Minakuchi.. Oral function of implant assisted removable partial denture with magnetic attachments using short implants. 30th Annual Congress of the European College of Gerodontology 2020.10.09
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25. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Rena Hidaka, Haruka Tohara, Shunsuke Minakuchi.. The features of oral health status and functions in Mild Cognitive Impairment (MCI) patients. 30th Annual congress of European College of Gerodontology 2020.10.10 Online
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27. Yoshiko Hara, Ayako Nakane, Haruka Tohara, Kazumasa Kuboita, Marie Sato, Yu Yoshizumi, Mariko Ando, Mana Obara, Shohei Hasegawa,. Cervical Interferential Current Transcutaneous Electrical Sensory Stimulation for Patients with Dysphagia in Nursing Homes. 2020.11.07 Web
28. Eijiro Yamaga, Yusuke Sato, Hitomi Soeda, Shunsuke Minakuchi. The relationships between oral hypofunction, perceived chewing ability, denture satisfaction and oral health related quality of life in complete denture wearers. The 31st Annual Meeting of Japanese Society of Gerodontology 2020.11.07 Online
29. Ruoyan Guo, Yohei Hama, Katheng Awutsadaporn, Watcharapong Tonprasong, Khaing Myat Thu, Shunsuke Minakuchi. Effects of two types of Denture adhesive on Oral Cavity . International Association for Dental Research-Southeast Asia Division 2020.11.26 Thailand

[Awards & Honors]

1. Inokoshi M. Incentive Research Award, Tokyo Medical and Dental University, 2020.03

[Social Contribution]

1. Inokoshi M. responsible person of the international program with the Chulalongkorn University, 2017.07.01 - Now

Dysphagia Rehabilitation

(1) Publications

[Original Articles]

1. Miura Yuka, Nakagami Gojiro, Tohara Haruka, Ogawa Nami, Sanada Hiromi. The association between jaw-opening strength, geniohyoid muscle thickness and echo intensity measured by ultrasound MEDICAL ULTRASONOGRAPHY. 2020; 22(3); 299-304
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4. Yoshimi K, Nakagawa K, Hara K, Yamaguchi K, Nakane A, Kubota K, Furuya J, Tohara H. Relationship between tongue pressure and back muscle strength in healthy elderly individuals. Aging Clinical and Experimental Research. 2020.01;
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10. Hara Koji, Namiki Chizuru, Yamaguchi Kohei, Kobayashi Kenichiro, Saito Takayuki, Nakagawa Kazuharu, Ishii Miki, Okumura Takuma, Tohara Haruka. Association between myotonometric measurement of masseter muscle stiffness and maximum bite force in healthy elders JOURNAL OF ORAL REHABILITATION. 2020.06; 47(6); 750-756

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15. Tamura A, Yamaguchi K, Chantaramanee A, Totoki H, Tohara H. Dysphagia in a persistently vegetative patient improved by orthodontic treatment of severe dental misalignment Special care in dentistry. 2020.12;

[Books etc]

1. Nakagawa K, Hara K and Tohara H. Aspiration Pneumonia the current clinical giant for respiratory physicians. Springer, 2020.01 (ISBN : 978-981-15-4505-4)

[Conference Activities & Talks]

1. Miura Y, Nakagami G, Tohara H, Ogawa N, Sanada H. The association between jaw-opening strength, geniohyoid muscle thickness and echo intensity measured by ultrasound.. Medical ultrasonography 2020.03.27
2. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yasuhiro Yamazaki, Rena Hidaka, Kanako Yoshimi, Haruka Tohara, Shunsuke Minakuchi. Oral status and function in Mild Cognitive Impairment patients. The 129th Annual Meeting of the Japan Prosthodontic Society 2020.06.28 Online
3. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Rena Hidaka, Haruka Tohara, Shunsuke Minakuchi.. The features of oral health status and functions in Mild Cognitive Impairment (MCI) patients. 30th Annual congress of European College of Gerodontology 2020.10.10 Online
4. Yoshiko Hara, Ayako Nakane, Haruka Tohara, Kazumasa Kuboita, Marie Sato, Yu Yoshizumi, Mariko Ando, Mana Obara, Shohei Hasegawa,. Cervical Interferential Current Transcutaneous Electrical Sensory Stimulation for Patients with Dysphagia in Nursing Homes. 2020.11.07 Web

Laboratory Medicine

Professor Shuji TOHDA

Assistant Professor Mai ITOH

Graduate Students Erika SHIRATORI, Tatsuya SAITO, Salwa MOHAMMAD, Yuri SONODA

(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 technique 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. Nogami A, Yamamoto M, Yamamoto K, Ito M, Umezawa Y, Tohda S, Miura O, Fukuda T. Marginal zone lymphoma-like primary bone marrow lymphoma with long-term pancytopenia preceding diagnosis Rinsho ketsueki. 2020; 61(10); 1469-1475
2. Yukino Usui, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Draft Genome Sequence of a *Clostridioides difficile* Sequence Type 97 Strain Belonging to Hypervirulent Clade 2. Microbiol Resour Announc. 2020.04; 9(14); e00245-20
3. Yukino Usui, Alafate Ayibieke, Yuko Kamiichi, Shu Okugawa, Kyoji Moriya, Shuji Tohda, Ryoichi Saito. Impact of deoxycholate on *Clostridioides difficile* growth, toxin production, and sporulation. Heliyon. 2020.04; 6(4); e03717
4. Tatsuya Saito, Mai Itoh, Shuji Tohda. Metformin suppresses the growth of leukemia cells partly through downregulation of AXL receptor tyrosine kinase. Leuk Res. 2020.05; 94; 106383
5. Salwa M Okasha, Mai Itoh, Shuji Tohda. Sirtuin 1 Activation Suppresses the Growth of T-lymphoblastic Leukemia Cells by Inhibiting NOTCH and NF- κ B Pathways. Anticancer Res. 2020.06; 40(6); 3155-3161

[Conference Activities & Talks]

1. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
2. Shimano S., Ohkawa R., Nambu M., Sasaoka M., Yamazaki A., Fujii Y., Igarashi K., Horiuchi Y., Lai SJ., Kameda T., Ichimura N., Fujita K., Tohda S. and Tozuka M. Dramatic change of high-density lipoprotein structure and serum amyloid A distribution after orthopedic surgery. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
3. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line

Intensive Care Medicine

Professor and Chairman
Hidenobu Shigemitsu (2016.9.1 -)

Specially Appointed Professor
Hideo Takahashi(2017.4.1 -)

Associate Professor
Toyomu Ugawa (2018.11.1 -)

Junior Associate Professor
Michio Nagashima (2017.4.1 -)
Hideo Yamauchi (2019.4.1 -)
Kenji Wakabayashi (2015.4.1 -)

Assistant Professor
Takahiro Masuda (Intensive Care Unit) (2014.4.1 -)
Fumi Maruyama (Intensive Care Unit) (2017.2.1 -)
Nobuyuki Nosaka (2020.4.1 -)

Specially Appointed Assistant Professor
Nobuhiro Shiota (2017.4.1 -)
Takuga Hinoshita (Intensive Care Unit) (2019.4.1 -)
Ryo Uchimido (Intensive Care Unit) (2020.4.1 -)
Yuka Mishima (Intensive Care Unit) (2017.4.1 -)

Fellow:
Toshihiro Kubo (Intensive Care Unit) (2019.10.1 -)
Kotaro Noda (Intensive Care Unit) (2020.4.1 -)
Koki Kiyama (Family Medicine) (2020.4.1 -)
Kotaro Noda (Anesthesiology) (2020.4.1 -)

Postgraduate students:
Shotaro Matsumoto (2016.4.1 -)
Nobuhiro Shiota (2017.4.1 -)
Yoichi Iki (2018.4.1 -)
Michiko Abe (2019.4.1 -)
Yuka Mishima (2019.4.1 -)
Ryo Uchimido (2020.4.1 -)

Adjunct lecturer
Yoshito Ujike (2017.4.1 -)
Eriko Takezawa (2017.4.1 -)
Research student:

(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.
- 2) Clinical implementation of US-style bundle in the ICU (Shigemitsu, funded by Grant-in-Aid for Scientific Research C)

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)
- 4) Impact of residual neuromuscular blockade in the ICU (Nagashima, funded by Grant-in-Aid for Young Scientists B)
- 5) Effect of nutrition status in the ICU (Masuda, funded by Grant-in-Aid for Young Scientists B)

(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. Sakai T, Hoshino C, Okawa A, Wakabayashi K, Shigemitsu H. The Safety and Effect of Early Mobilization in the Intensive Care Unit According to Cancellation Criteria. *Progress in rehabilitation medicine*. 2020; 5; 20200016
2. Papanikolaou IC, Shigemitsu H. Sarcoidosis and breast cancer: A retrospective case series. *Respiratory medicine case reports*. 2020; 31; 101190
3. Sakai Tomoko, Hoshino Chisato, Okawa Atsushi, Wakabayashi Kenji, Shigemitsu Hidenobu. The Safety and Effect of Early Mobilization in the Intensive Care Unit According to Cancellation Criteria(和訳中) *Progress in Rehabilitation Medicine*. 2020; 5; 1-12
4. Yoshida Takuo, Uchino Shigehiko, Sasabuchi Yusuke, Hagiwara Yasuhiro, Yoshida Tomonao, Nashiki Hiroshi, Suzuki Hajime, Takahashi Hiroshi, Kishihara Yuki, Nagasaki Shinya, Okazaki Tomoya, Katayama Shinshu, Sakuraya Masaaki, Ogura Takayuki, Inoue Satoki, Uchida Masatoshi, Osaki Yuka, Kuriyama Akira, Irie Hiromasa, Kyo Michihito, Shima Nozomu, Saito Junichi, Nakayama Izumi, Jingushi Naruhiro, Nishiyama Kei, Masuda Takahiro, Tsujita Yasuyuki, Okumura Masatoshi, Inoue Haruka, Aoki Yoshitaka, Kondo Takashi, Nagata Isao, Igarashi Takashi, Saito Nobuyuki, Nakasone Masato. Prognostic impact of sustained new-onset atrial fibrillation in critically ill patients *INTENSIVE CARE MEDICINE*. 2020.01; 46(1); 27-35
5. Irie Hiromasa, Okamoto Hiroshi, Uchino Shigehiko, Endo Hideki, Uchida Masatoshi, Kawasaki Tatsuya, Kumasawa Junji, Tagami Takashi, Shigemitsu Hidenobu, Hashiba Eiji, Aoki Yoshitaka, Kurosawa Hiroshi, Hatakeyama Junji, Ichihara Nao, Hashimoto Satoru, Nishimura Masaji. The Japanese Intensive care Patient Database (JIPAD): A national intensive care unit registry in Japan *JOURNAL OF CRITICAL CARE*. 2020.02; 55; 86-94
6. Mahida RY, Matsumoto S, Matthay MA. Extracellular Vesicles: A New Frontier for Research in Acute Respiratory Distress Syndrome. *American journal of respiratory cell and molecular biology*. 2020.02;
7. Nosaka Nobuyuki, Martinon Daisy, Moreira Debbie, Crother Timothy R., Arditi Moshe, Shimada Kenichi. Autophagy Protects Against Developing Increased Lung Permeability and Hypoxemia by Down Regulating Inflammasome Activity and IL-1 beta in LPS Plus Mechanical Ventilation-Induced Acute Lung Injury *FRONTIERS IN IMMUNOLOGY*. 2020.02; 11; 207
8. Shimada Kenichi, Nosaka Nobuyuki, Martinon Daisy, Crother Timothy R., Arditi Moshe. Therapeutic hypothermia rescues severe acute lung injury (ALI) by IL-1 beta-induced neutrophil extracellular traps (NETs) formation through down-regulation of Gasdermin D *JOURNAL OF IMMUNOLOGY*. 2020.05; 204(1);
9. Papanikolaou I, Shigemitsu H, Afthinos A. Immune status in sarcoidosis: one size does not fit all. *Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace*. 2020.07; 90(3);

10. Tsukahara K, Naitou H, Yorifuji T, Nosaka N, Yamamoto H, Osako T, Nakao A, JaRPAC Study Group.. Comparison of Two Different Intensive Care Unit Systems for Severely Ill Children in Japan: Data from the JaRPAC Registry. *Acta medica Okayama*. 2020.08; 74(4); 285-291
11. Saito J, Shoji K, Oho Y, Aoki S, Matsumoto S, Yoshida M, Nakamura H, Kaneko Y, Hayashi T, Yamatani A, Capparelli E, Miyairi I. Meropenem pharmacokinetics during extracorporeal membrane oxygenation and continuous haemodialysis: a case report *J Glob Antimicrob Resist*. 2020.09; 22; 651-655
12. Zeng Congli, Motta-Ribeiro Gabriel C., Hinoshita Takuga, Lessa Marcos Adriano, Winkler Tilo, Grogg Kira, Kingston Nathan M., Hutchinson John N., Sholl Lynette Marie, Fang Xiangming, Varelas Xaralabos, Layne Matthew D., Baron Rebecca M., Vidal Melo Marcos F.. Lung Atelectasis Promotes Immune and Barrier Dysfunction as Revealed by Transcriptome Sequencing in Female Sheep *ANESTHESIOLOGY*. 2020.11; 133(5); 1060-1076
13. Hinoshita Takuga, Ribeiro Gabriel Motta, Winkler Tilo, de Prost Nicolas, Tucci Mauro R., Vieira Costa Eduardo Leite, Wellman Tyler J., Hashimoto Soshi, Zeng Congli, Carvalho Alysson R., Melo Marcos Francisco Vidal. Inflammatory Activity in Atelectatic and Normally Aerated Regions During Early Acute Lung Injury *ACADEMIC RADIOLOGY*. 2020.12; 27(12); 1679-1690
14. Matsumoto S, Fang X, Traber MG, Jones KD, Langelier C, Hayakawa Serpa P, Calfee CS, Matthay MA, Gotts JE. Dose-Dependent Pulmonary Toxicity of Aerosolized Vitamin E Acetate *Am J Respir Cell Mol Biol*. 2020.12; 63(6); 748-757

[Conference Activities & Talks]

1. Wakabayashi K. Roles and mechanisms of microvesicles in critical illness. 47th meeting of Japanese Society of Intensive Care Medicine 2020.03 Nagoya
2. 山内 英雄, 長島 道生, 丸山 史, 三島 有華, 落合 香苗, 山下 直美, 溝江 亜紀子, 大友 康裕, 高橋 英夫, 重光 秀信. RAS (Risk Assessment System) で拾うことができなかった急変死亡症例の検討. 第 47 回日本集中治療医学会学術集会 2020.03.06 名古屋
3. Nobuhiro Shiota, et al. The Effect of Multidisciplinary Rounds on Early Mobilization in the Intensive Care Unit. The 47th Annual Meeting of the Japanese Society of Intensive Care Medicine 2020.03.07
4. Hinoshita T, Ribeiro GM, Winkler T, de Prost N, Tucci MR, Costa ELV, Wellman TJ, Hashimoto S, Zeng C, Carvalho AR, Melo MFV. Inflammatory Activity in Atelectatic and Normally Aerated Regions During Early Acute Lung Injury.. *Academic radiology* 2020.03.12
5. Matsumoto S. Dose-Dependent Pulmonary Toxicity of Aerosolized Vitamin E Acetate. Fall 2020 TCORS Grantee meeting 2020.10.19

[Awards & Honors]

1. The Journal of Intensive Care Award , 2020.03

[Social Contribution]

1. COVID-19: Our experience at TMDU, Imperial College Alumni Association Japan, 2020.06.14

Pharmacokinetics and Pharmacodynamics

Associate Professor Masashi Nagata
Postgraduate student Kohta Tsuge, Xue Bingyang, Tsubura Noda, Tomofumi Kobayashi

(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. Asada M, Nagata M, Mizuno T, Uchida T, Takahashi H, Makita K, Arai H, Kijima S, Echizen H, Yasuhara M. Population pharmacokinetics of cefazolin before, during and after cardiopulmonary bypass in adult patients undergoing cardiac surgery. *European journal of clinical pharmacology*. 2020.11;
2. Ishiwata Y, Nagata M, Kiuchi S, Ippongi C, Takeda H, Takahashi H. Intravenous Infusion of Fentanyl Has No Effect on Blood Concentration of Tacrolimus In Patients Receiving Hematopoietic Stem Cell Transplantation. *Therapeutic drug monitoring*. 2020.12;

Medical Education Research and Development

Professor Masanaga YAMAWAKI
 Professor Yujiro TANAKA
 Junior Associate Professor Eriko OKADA
 Junior Associate Professor Yasuhiro ITSUI
 Assistant Professor Nobutoshi NAWA
 Attending Staff Ayako KASHIMADA
 Graduate Student Hisashi SHIMOZONO

(1) Outline

Our aim is to carry out the mission of the university, "cultivating professionals with knowledge and humanity, thereby contributing to people's well-being," from the perspective of educational management. The basis of our department is to contribute to the education, research, clinical practice, and management & operation of the university in cooperation with other departments and sections. Medical education will continue from undergraduate education to lifelong learning. Our department is in charge of "coordination and support" of education for 6 years of undergraduate and 2 years of junior residency period, and of cultivating future Clinician Scientists and Scientific Clinicians.

Department of General Medicine was established in 2000, we have aimed to coordinate and support a wide range of 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 patient support system including social casework, 3) Establishing the Center for Cell Therapy, 4) Reforming the undergraduate medical education, 5) Establishing the working group for ward management 6) Managing the medical safety committee, 7) Providing second opinion support system. Recently we have been focusing on providing systems for undergraduate and postgraduate education, such as reforming the undergraduate educational curriculum (e.g. educational cooperation with Harvard Medical School) and clinical training system. The medical training center was established for the clinical residency program. In 2006, the department of General Medicine was transformed into the Department of Medical Education Research and Development. We are working in close cooperation with Center for Extraprofessional Education which we took in part of its establishment to materialize the interprofessional education introduced due to a revision of a new curriculum in 2011.

(2) Research

We are developing the following research from the perspective of medical education.

- Study on evaluation for clinical ability acquisition

We are studying educational and evaluation system on how to learn and continue to practice in under- and post-graduate clinical training.

- Research on career education

Research on career education for doctors is being conducted with development of entrepreneurship education program for doctors.

- Research on research ethics education of medical students and residents

Development and verification of a model evaluation program for research ethics education by an interdisciplinary approach.

- Research on patient medication and drug swallowing using design thinking

Research on patient medication and drug swallowing using design thinking is being conducted in search for new treatment strategy for dysphagia.

- Research on team medical care and multidisciplinary education

We are conducting research on team medical care and multidisciplinary collaborative education.

- Research on health prevention and patient education

We are conducting research on the development of patient education programs related to health promotion for the super-elderly. In addition, we are also conducting preventive research on lifestyle-related diseases in Kyo-tango Longevity Cohort Study.

- Other research on medical education

We are also conducting research on cognitive mechanism and cerebral processing in clinical reasoning, on competence evaluation in pre- and post-graduate clinical medical education, on multifaceted evaluation in medical communication and research on community-based medicine.

(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 the 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.

Besides, 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 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 Japan Residency Matching Program, our education program revealed one of the most competitive among all national teaching hospitals.

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

We are aiming to improve initial clinical training through the recruitment of medical interns, training management, holding various workshops, such as Evening Seminars, and operation of the "Tasukigake" training system with each partner hospital. We also hold clinical training sessions for supervising physicians to learn better teaching methods, and staff training classes about medical safety, infection control and medical information throughout the year. We 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.

(5) Publications

[Original Articles]

1. Jung SH, Han HW, Koh H, Yu SY, Nawa N, Morita A, Ong KIC, Jimba M, Oh J.: Patients help other patients: Qualitative study on a longstanding community cooperative to tackle leprosy in India. PLOS Neglected Tropical Diseases. 2020.01; 14 (1): e0008016.

2. Sato Ayako, Kakinuma Sei, Miyoshi Masato, Kamiya Akihide, Tsunoda Tomoyuki, Kaneko Shun, Tsuchiya Jun, Shimizu Taro, Takeichi Eiko, Nitta Sayuri, Kawai-Kitahata Fukiko, Murakawa Miyako, Itsui Yasuhiro, Nakagawa Mina, Azuma Seishin, Koshikawa Naohiko, Seiki Motoharu, Nakauchi Hiromitsu, Asahina Yasuhiro, Watanabe Mamoru: Vasoactive Intestinal Peptide Derived From Liver Mesenchymal Cells Mediates Tight Junction Assembly in Mouse Intrahepatic Bile Ducts. *HEPATOLOGY COMMUNICATIONS*. 2020.02; 4(2):235-254
3. Nobutoshi Nawa, Mitsuyuki Numasawa, Mina Nakagawa, Masayo Sunaga, Takeo Fujiwara, Yujiro Tanaka, Atsuhiko Kinoshita: Differential effects of individual and school factors on the academic trajectories of Japanese dental students. *J Dent Educ*. 2020.03;
4. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina: Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient. *Hepatology Research*. 2020.04; 50(4):524-531.
5. Garrison-Desany HM, Nawa N, Kim Y, Ji Y, Susan Chang HY, Hong X, Wang G, Pearson C, Zuckerman BS, Wang X, Surkan PJ: Polydrug Use During Pregnancy and Preterm Birth in a Low-Income, Multiethnic Birth Cohort, Boston, 1998-2018. *Public health reports (Washington, D.C. : 1974)*. 2020.04; 33354920915437.
6. Nawa N, Numasawa M, Nakagawa M, Sunaga M, Fujiwara T, Tanaka Y, Kinoshita A: Associations between demographic factors and the academic trajectories of medical students in Japan. *PloS one*. 2020.05; 15 (5): e0233371.
7. Nawa N, Garrison-Desany HM, Kim Y, Ji Y, Hong X, Wang G, Pearson C, Zuckerman BS, Wang X, Surkan PJ: Maternal Persistent Marijuana Use and Cigarette Smoking Are Independently Associated With Shorter Gestational Age. *Paediatric and perinatal epidemiology*. 2020.06;
8. Nawa N, Nakamura K, Fujiwara T: Oxytocin Response Following Playful Mother–Child Interaction in Survivors of the Great East Japan Earthquake. *Frontiers in Psychiatry*. 2020.06; 11 477.
9. Shimozone H, Nawa N, Takahashi M, Tomita M, Tanaka Y: A cognitive bias in diagnostic reasoning and its remediation by the “2-Dimensional Approach”. *MedEdPublish*. 2020.06; 9 (1): 123.
10. Hirata K, Nambara T, Kawatani K, Nawa N, Yoshimatsu H, Kusakabe H, Banno K, Nishimura K, Ohtaka M, Nakanishi M, Taniguchi H, Arahori H, Wada K, Ozono K, Kitabatake Y: 4-Phenylbutyrate ameliorates apoptotic neural cell death in Down syndrome by reducing protein aggregates. *Scientific reports*. 2020.08; 10 (1): 14047.
11. Mina Nakagawa, Nobutoshi Nawa, Eiko Takeichi, Taro Shimizu, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Takeo Fujiwara, Mamoru Watanabe, Yujiro Tanaka, Yasuhiro Asahina: Mac-2 binding protein glycosylation isomer as a novel predictive biomarker for patient survival after hepatitis C virus eradication by DAAs. *J Gastroenterol*. 2020.08; 55 990-999.
12. Nawa N, Kuramochi J, Sonoda S, Yamaoka Y, Nukui Y, Miyazaki Y, Fujiwara T: Seroprevalence of SARS - CoV - 2 in Utsunomiya City, Greater Tokyo, after the first pandemic in 2020. *Journal of General and Family Medicine*. 2020.12
13. Ishii E, Nawa N, Matsui H, Otomo Y, Fujiwara T: Comparison of disease patterns and outcomes between non-Japanese and Japanese patients at a single tertiary emergency care center in Japan. *Journal of epidemiology*. 2020.12

[Books]

1. Takeo Fujiwara, Nobutoshi Nawa, and Yusuke Matsuyama. Child Health in Japan In: Health in Japan: Social Epidemiology of Japan Since the 1964 Tokyo Olympics. Oxford University Press 2020.12

[Conference Activities & Talks]

1. Nobutoshi Nawa, Mitsuyuki Numasawa, Mina Nakagawa, Takeo Fujiwara, Yujiro Tanaka, Atsuhiko Kinoshita. Analysis of the effects of demographic factors on the academic trajectories of medical students in Japan using group-based trajectory modeling. The Association for Medical Education in Europe (AMEE) Conference 2020 2020.09 Online
2. Kumiko Yamaguchi, Nobutoshi Nawa, Takeo Fujiwara, Keiichi Akita. Importance of school social capital on learning medicine in Japanese medical students. 2020.09 Online
3. Yu Funakoshi, Nobutoshi Nawa, Kumiko Yamaguchi, Mitsuyuki Numasawa, Takeo Fujiwara, Keiichi Akita. The potentially favorable effect of early identification of and timely support to medical students with low-performance trajectories on succeeding academic performance. The Association for Medical Education in Europe (AMEE) Conference 2020 2020.09 Online
4. Hisashi Shimozono, Nobutoshi Nawa, Yujiro Tanaka. A cognitive bias in diagnostic reasoning and its remediation by the “2-Dimensional Approach”. The Association for Medical Education in Europe (AMEE) Conference 2020 2020.09 Online

General Dentistry

Professor Hiroshi Nitta
 Junior Associate Professor Masayuki HIDEISHIMA
 Junior Associate Professor Ken-ichi TONAMI
 Assistant Professor Sachi UMEMORI
 Assistant Professor Kanako NORITAKE
 Project Assistant Professor Maiko IWAKI
 Project Assistant Professor Shuhei NAKAMURA
 Project Assistant Professor Yasuyuki KIMURA
 Project Assistant Professor Naoko HARADA
 Hospital Staff Yuna KANAMORI
 Hospital Staff Daisuke KIDO
 Hospital Staff Yukako KUSUNOKI
 Hospital Staff Naoki SASAKI
 Hospital Staff Shogo TAKEUCHI
 Hospital Staff Mai MIYACHI

(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. Nour Ammar, Nourhan M Aly, Morenike O Folayan, Yousef Khader, Jorma I Virtanen, Ola B Al-Batayneh, Simin Z Mohebbi, Sameh Attia, Hans-Peter Howaldt, Sebastian Boettger, Diah A Maharani, Anton Rahardjo, Imran Khan, Marwa Madi, Maher Rashwan, Verica Pavlic, Smiljka Cicmil, Youn-Hee Choi, Easter Joury, Jorge L Castillo, Kanako Noritake, Anas Shamala, Gabriella Galluccio, Antonella Polimeni, Prathip Phantumvanit, Davide Mancino, Jin-Bom Kim, Maha M Abdelsalam, Arheiam Arheiam, Mai A Dama, Myat Nyan, Iyad Hussein, Mohammad M Alkeshan, Ana P Vukovic, Alfredo Iandolo, Arthur M Kemoli, Maha El Tantawi. Behavior change due to COVID-19 among dental academics-The theory of planned behavior: Stresses, worries, training, and pandemic severity. *PLoS One*. 2020; 15(9); e0239961
2. Soeda Y, Kanazawa M, Iwaki M, Arakida T, Minakuchi S.. CAD-CAM milled complete dentures with custom disks and prefabricated artificial teeth: A dental technique. *J Prosthet Dent*. 2020;
3. Ogawa M, Katagiri S, Koyanagi T, Maekawa S, Shiba T, Ohsugi Y, Takeuchi Y, Ikawa T, Takeuchi S, Sekiuchi T, Arai Y, Kazama R, Wakabayashi N, Izumi Y, Iwata T. Accuracy of cone beam computed tomography in evaluation of palatal mucosa thickness *Journal of Clinical Periodontology, Tokyo Medical and Dental University*. 2020.04; 47(4); 479-488
4. Hayashi S, Tamaoka M, Tateishi T, Murota Y, Handa I, Miyazaki Y. A New Feature with the Potential to Detect the Severity of Obstructive Sleep Apnoea via Snoring Sound Analysis. *International Journal of Environmental Research and Public Health*. 2020.04; 17(8); 2951
5. Awutsadaporn Katheng, Manabu Kanazawa, Maiko Iwaki, Shunsuke Minakuchi. Evaluation of dimensional accuracy and degree of polymerization of stereolithography photopolymer resin under different postpolymerization conditions: An in vitro study. *The Journal of prosthetic dentistry*. 2020.05;

6. Hada T, Kanazawa M, Iwaki M, Arakida T, Minakuchi S. Effect of printing direction on stress distortion of three-dimensional printed dentures using stereolithography technology. *Journal of the Mechanical Behavior of Biomedical Materials*. 2020.07;
7. Hada T, Kanazawa M, Iwaki M, Arakida T, Soeda Y, Katheng A, Otake R, Minakuchi S. Effect of printing direction on the accuracy of 3D-printed dentures using stereolithography technology. *Materials*. 2020.08; 13(15);
8. TONAMI Ken-ich, UMEMORI Sachi, NORITAKE Kanako, KANAMORI Yuna, KASAI Miki, KONISHI Tomiyo, SHIMOYAMA Kazuhiro, NITTA Hiroshi. Impact of public information media on attendance at dental health check-ups *Journal of the Japan Society of Oral Health Science*. 2020.08; 15(1); 10-15
9. Mikami R, Mizutani K, Gohda T, Gotoh H, Matsuyama Y, Aoyama N, Matsuura T, Kido D, Takeda K, Izumi Y, Fujiwara T, Iwata T. Association between circulating tumor necrosis factor receptors and oral bacterium in patients receiving hemodialysis: a cross-sectional study. *Clinical and experimental nephrology*. 2020.08; e-pub;
10. Maiko Iwaki, Manabu Kanazawa, Toshio Arakida, Shunsuke Minakuchi. Mechanical properties of a polymethyl methacrylate block for CAD/CAM dentures. *J Oral Sci*. 2020.09; 62(4); 420-422
11. Le SH, Tonami K, Umemori S, Nguyen LT, Ngo LT, Araki K, Nitta H. Relationship between pre-operative dental anxiety and short-term inflammatory response following oral surgery. *Australian dental journal*. 2020.09;
12. Umemori S, Aida J, Tsuboya T, Tabuchi T, Tonami K, Nitta H, Araki K, Kondo K. Does the second-hand smoking associate with tooth loss among older Japanese?: JAGES cross-sectional study. *International Dental Journal*. 2020.10; 70(5); 388-395
13. Awutsadaporn Katheng, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Shunsuke Minakuchi. Evaluation of trueness and precision of stereolithography-fabricated photopolymer-resin dentures under different postpolymerization conditions: An in vitro study. *The Journal of prosthetic dentistry*. 2020.10;
14. Koji Inagaki, Takeshi Kikuchi, Hiroshi Nitta, Naoko Tajima, et. al.. A large-scale observational study to investigate the current status of diabetic complications and their prevention in Japan (JDCP study 6): baseline dental and oral findings *Diabetology International* . 2020.10;
15. Kanako Noritake, Yuna Kanamori, Hiroshi Nitta.. A remote program for residents to solve clinical questions and improve presentation skills *Journal of Dental Education*. 2020.10;
16. Watanabe K, Katagiri S, Takahashi H, Sasaki N, Maekawa S, Komazaki R, Hatasa M, Kitajima Y, Maruyama Y, Shiba T, Komatsu K, Ohsugi Y, Tanaka K, Matsuzawa A, Hirota T, Tohara H, Eguchi Y, Anzai K, Hattori A, Iwata T. *Porphyromonas gingivalis* impairs glucose uptake in skeletal muscle associated with altering gut microbiota *The FASEB Journal*, Tokyo Medical and Dental University. 2020.11; 35(2); e21171
17. Rumi Tano, Hiroko Miura, Katsuo Oshima, Kanako Noritake and Hideki Fukuda. The Relationship between the Sense of Coherence of Dental Hygiene Students in Their Graduation Year and Their View of the Profession and Attitude to Work: A Cross-Sectional Survey in Japan *International journal of Environmental Research and Public Health*. 2020.12; 17(9594); 1-9

[Books etc]

1. *Periodontal Motivational Interviewing*. 2020.02 (ISBN : 978-4-7812-0732-2)

[Misc]

1. Mai Miyachi. The Perspective of Dental Sleep Medicine the Quintessence. 2020.07; 39(7); 90-113
2. Hiroshi Nitta. Introduction of Peiodontal Motivational Interviewing *The Journal of Dental Hygienist*. 2020.08; 44(8); 26-42
3. Hideshima M, Ishihara N, Ishiyama H. Oral appliance therapy for sleep apnea and development of the prognosis model for treatment effect *Cell*. 2020.09; 52 (697); 570-573

[Conference Activities & Talks]

1. A. Katheng, M. Kanazawa, M. Iwaki, T. Arakida, T. Hada, Y. Soeda, R. Otake, S. Minakuchi. Evaluation of trueness using different post-curing conditions achieved by stereolithography. the 2020 IADR/AADR/CADR General Session, Washington, DC USA 2020.03.16
2. Hada T, Kanazawa M, Iwaki M, Arakida T, Soeda Y, Otake R, Katheng A, Minakuchi S. Stress distortion of 3D printing dentures with different printing directions. The 2020 IADR/AADR/CADR General Session and Exhibition 2020.03.18 Washington, D.C. (Online)
3. Soeda Yumika, Kanazawa Manabu, Iwaki Maiko, Arakida Toshio, Hada Tamaki, Otake Ryosuke, Katheng Awutsadaporn, Ando Kazuo, Minakuchi Shunsuke. Accuracy of artificial teeth positions in the digital complete denture using the customized disk. The 11st Scientific Meeting of the Japan Academy of Digital Dentistry 2020.04.25
4. Iwaki M, Kanazawa, Kodama N, Matsuda K, Ikebe K, Minagi S, Minakuchi S. The results of a survey of complete denture education in 29 dental colleges in Japan. 2020.06.27 Online
5. UMEMORI Sachi, TONAMI Ken-ichi, NORITAKE Kanako, IWAKI Maiko, KIMURA Yasuyuki, NITTA Hiroshi, ARAKI Kouji. The Analysis of Unprofessional behavior in the class of "behavioral science" in Tokyo Medical and Dental University (TMDU). 2020.07
6. Development of Medical Interview Practice using web conference system at dental school. 2020.09
7. Mina Nakagawa, Kanako Noritake, Kumiko Yamaguchi, Chiharu Kawakami, Janelle Moross, Jun Tsuruta. Introduction of interprofessional education (IPE) for medical and dental students. AMEE2020 2020.09.07 Web 開催
8. AO A, TAKESHITA K, HAYASHIDA S, SADAMURA M, NORITAKE K, NITTA H, TAKAHASHI T. Model-free fabrication of implant prosthesis for mandibular bilateral molar missing using the intraoral scanner. The 50th Anniversary Annual Meeting of the Japanese Society of Oral Implantology 2020.09.19
9. Seki N, Moross J, Kanamori Y, Kanazawa M, Komagamine Y, Mizutani K, Liao S, Kabasawa Y, Iseki S, Morio I. Importance of preparatory courses for international/global dental student exchange programs. Annual Meeting of the 39th Japanese Dental Education Association 2020.09.25 Paper/Online Base
10. KANAMORI Yuna, NORITAKE Kanako, UMEMORI Sachi, IWAKI Maiko, KIDO Daisuke, HIDEHIMA Masayuki, KIMURA Yasuyuki, HATTORI Akitaka, TONAMI Ken-ichi, EBIHARA Arata, ARAKI Kouji, NITTA Hiroshi. TMDU trainee residents' feedback on the trial of objective clinical skills examinations. 2020.09.26
11. The effect of online practice for the digital teeth arrangement of complete dentures using web application.. 2020.09.26
12. Tonami K, Umemori S, Noritake K, Iwaki M, Kimura Y, Araki K, Nitta H. Relation between unprofessional behavior and score of medical ethics examination. The 39th congress of Japanese Dental Education Association 2020.09.26 online
13. Awutsadaporn Katheng, Manabu Kanazawa, Maiko Iwaki, Toshio Arakida, Tamaki Hada, Yumika Soeda, Ryosuke Otake, Shunsuke Minakuchi. Evaluation of stereolithography in different post-curing conditions on the precision of photopolymer 3D resins.. 30th Annual Congress of the European College of Gerodontology : "Health Smiles, Longer Lives" 2020.10.09
14. Aoki A, Katagiri S, Ohsugi Y, Mizutani K, Nitta H, Iwata T. Effects of single visit full mouth disinfection (FMD) in advanced periodontitis using ultrasonic debridement in combination with systemic azithromycin administration. 2020.10.16 Virtual
15. Endotoxemia by Porphyromonas gingivalis alters endocrine functions in brown adipose tissue. 2020.10.16 Virtual
16. Hatasa M, Ohsugi Y, Katagiri S, Hirota T, Yoshida S, Morita K, Niimi H, Shimohira T, Watanabe K, Sasaki N, Maekawa S, Nitta H, Iwata T. Endotoxemia by Porphyromonas gingivalis aggravates inflammation in brown adipose tissue. The 106th Annual meeting American Academy of Periodontology 2020.11.06 Virtual

17. Mai Miyachi, Masyuki Hideshima, R. Merrill, S. Arman. Clinical practice and education system for dental sleep medicine in the United States. The Japanese Academy of Dental Sleep Medicine 2020.11.22 online
18. Yuna Kanamori, Naoko Seki, Kanako Noritake, Masayo Sunaga, Janelle Moross, Ikuko Morio, Kouji Araki, Atsuhiko Kinoshita, Hiroshi Nitta. Assessment of TMDU trainee residents' dental English ability. The 85th annual meeting of the Stomatological Society 2020.12.05 Tokyo

[Others]

1. Maiko Iwaki. Grant-in-Aid for Scientific Research(C) (JSPS) , 2020.04
Prospective study of CAD/CAM complete denture for the Edentulous Patients. 2018-2020.

Psychosomatic Dentistry

Professor	Akira Toyofuku
Assistant Professor	Miho Takenoshita
Project Assistant Professor	Motoko Watanabe
Hospital Staff	Takayuki Suga, Chihiro Takao
Graduate Student	Takayuki Suga, Kazuya Watanabe, Mitsuhiro Asami, Chaoli Hong, Chihiro Takao, Liu Zhenyan Atsushi Ito, Kiyokazu Iwawaki
Lecturer (part-time)	Haruhiko Motomura, Jiro Kurata, Takahiko Naganine

(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-Dopamin 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. Kawasaki K, Sugawara S, Watanabe K, Hong C, Tu TTH, Watanabe T, Sakamoto J, Yoshino N, Suga T, Mikuzuki L, Takenoshita M, Takada S, Kurabayashi T, Toyofuku A. Differences in the Clinical Characteristics of Persistent Idiopathic Facial Pain (Atypical Odontalgia) Patients with or Without Neurovascular Compression of the Trigeminal Nerve. *Pain medicine* (Malden, Mass.). 2020.02;
2. Takayuki Suga, Miho Takenoshita, Akira Toyofuku. A case of an elderly patient with persistent idiopathic facial pain related to dental implants successfully treated with mirtazapine. *Psychogeriatrics*. 2020.03;
3. Yojiro Umezaki, Takashi Asada, Toru Naito, Akira Toyofuku. A case of oral cenesthopathy in which dementia with Lewy bodies developed during treatment. *Psychogeriatrics*. 2020.03;
4. T T H Tu, A Toyofuku, H Matsuoka. Coping well. *Br Dent J*. 2020.07; 229(2); 70

5. Suga T, Tu TTH, Takenoshita M, Higashihori N, Kabasawa Y, Ono T, Moriyama K, Toyofuku A. Psychosocial Indication for Orthognathic Surgery in Patients with Psychiatric Comorbidities. *Psychiatry and clinical neurosciences*. 2020.08;
6. Yojiro Umezaki, Motoko Watanabe, Yukiko Shinohara, Shiori Sugawara, Kaoru Kawasaki, Trang T H Tu, Takeshi Watanabe, Takayuki Suga, Anna Miura, Miho Takenoshita, Yusuke Sato, Ichiro Minami, Jun Oyama, Akira Torihara, Tatsuya Yoshikawa, Toru Naito, Haruhiko Motomura, Akira Toyofuku. Comparison of Cerebral Blood Flow Patterns in Patients with Phantom Bite Syndrome with Their Corresponding Clinical Features. *Neuropsychiatr Dis Treat*. 2020.11; 16; 2277-2284
7. Takayuki Suga, Chihiro Takao, Motoko Watanabe, Miho Takenoshita, and Akira Toyofuku, . A case of refractory glossodynia successfully remitted with combination therapy of sodium valproate and clonazepam *Jpn J Psychosom Oral Med*. 2020.12; 3 5 (1 · 2); 3 7 - 4 0

[Conference Activities & Talks]

1. Takayuki Suga, Trang T.H Tu, Miho Takenoshita, Akira Toyofuku. . Psychosocial Indication of Jaw Deformity Surgery in Patients with Psychiatric Comorbidities . 第 35 回日本歯科心身医学会学術大会 2020.06.20 福岡県歯科医師会館 福岡市

Professional Development in Health Sciences

Professor Kazuki Takada

(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 provide 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

(3) Education

Undergraduate schools

Courses

- School of medicine (1st year): Medical Introductory Courses
- Schools of medicine/dentistry (2nd/3rd years): Global Communication for Health Professionals
- School of medicine (4th year): Preparation for Clinical Clerkship
- School of medicine (5th/6th years): Clinical Clerkship
- Health Sciences Leadership Program: Moral and Political Philosophy
- Health Sciences Leadership Program: Applied Critical Thinking for Health Sciences
- Health Sciences Leadership Program: Problem-solving in the Health Sciences

Graduate school

Course

- 【Master level】 Public Health Biology

(4) Clinical Services & Other Works

Medical Hospital

Kazuki TAKADA (Rheumatology)

(5) Publications

[Misc]

1. Kazuki Takada,Atsuhiro Kinoshita,Kumiko Yamaguchi,Masayo Sunaga,Keiichi Akita,Noriyuki Wakabayashi,Yujiro Tanaka. Ideal medical education to be pursued in the post-COVID era, elucidated through the response to the COVID-19 pandemic 2020.06; 51(3); 372-374

[Conference Activities & Talks]

1. Kazuki Takada. Workplace-based formative assessment of clinical reasoning skills by visualizing learners' clinical reasoning process. ASIA PACIFIC MEDICAL EDUCATION CONFERENCE (APMEC) 2020 2020.01.10
2. Kazuki Takada. Vision of health professions education of the post-COVID-19 era. 2020.12.19 Online

Family Medicine

Yousuke C. Takemura
Toru Yamada
Masashi Beppu
Suguru Mabuchi
Yoshiro Hadano
Yu Akaishi
Kazuhisa Sakai
Shoko Yoshida
Risa Suzuki
Yuki Goto
Yuiko Nagamine
Mari Fukuhara

Masako Sugihara
Yuya Ando
Akane Futami
Hiroshi Koike
Mari Miya

Erina Aida
Shuji Ouchi
Hiroki Nin
Hiroki Sekiguchi
Maki Goto
Risa Narita
Kouki Kiyama

(1) Outline

Greetings from Professor Yousuke C. Takemura

“Ambition” and “Passion”
Keys for Family Medicine/General Medicine
Share your “Ambition” with us.
You may think it impossible to become true.
Believe me, we are here for you.
We can take it with all our strength and our heart
Exert your passionate ebullience
We are ready to support you.

Professor Yousuke C. Takemura
Department of Family Medicine
Graduate School of Medical and Dental Sciences
Tokyo Medical and Dental University

Backgrounds and Aims

TMDU General Medicine/Family Medicine Network (TMUDGM/FM-N) is a network of hospitals and clinics which engage in practice, education, and research related to general medicine/family medicine or primary health care. More than ten healthcare institutions join the TMUDGM/FM-N in Tokyo Ward and a few prefectures surrounding Tokyo, Japan. The TMUDGM/FM-N is also known as a network for physicians and other professionals who engage in these activities. Members of the TMUDGM/FM-N build a weak tie with each other or facility, and collaborate closely in each activity.

The TMUDGM/FM-N engages in following activities for people in community all over the world to stay in healthy and happy lives:

1. To conduct research more efficiently and provide effective practices in general medicine/family medicine and primary health care.
2. To foster general medicine, family physicians, general practitioners, and healthcare professionals, who can practice in the field of general medicine/family medicine and primary health care
3. To nurture more advanced personnel who can educate general medicine/family physicians, healthcare professionals, educators, or researchers in the field of general medicine/family medicine and primary health care.

Our Activity

Education

The TMUDGM/FM-N provide educations about general medicine/family medicine, and primary healthcare, for each generation of healthcare professionals, such as medical students, junior residents, and senior residents. As well, we provide inter-professional educations for the various medical professionals. Although some of our educations are provided in TMDU, lots of parts are undertaken in clinics and hospitals in community.

The TMUDGM/FM-N weighs importance on career-long education for general medicine/family physicians and other collaborating healthcare professionals. As well, we have activities of continuous medical education on themes related to general medicine/family medicine.

Graduate School

The TMUDGM/FM-N provides education and research for TMDU Graduate School of Medical and Dental Sciences. The TMUDGM/FM-N accepts international students from all over the world.

In our graduate school, we want students to learn how to resolve problems in the real community via research. Our research should not be mere finding or exploring the facts, but contribute towards people in communities. Research is only one of the tools for resolving problems in communities, improving clinical practices, and contributing to patients and people in community. Therefore, we should keep in our mind to implement the research findings into the real world.

To enable students to fulfill our aims above mentioned, we provide didactic lectures about general medicine/family medicine, biostatistics, clinical epidemiology, qualitative research, how to build questionnaire and so on. However, attending these lectures for students is not enough to resolve problems in communities and they should: approach the target community or field; get familiar with the people living there; feel known or unknown needs from the people living there; and suggest some resolution for their needs or problems. These processes require students not only technical and academic skills, but also communication or social skills. As well, these processes train students to learn by their own mistakes. Therefore, we provide students safe environments to think their own interests for themselves.

Research

The TMUDGM/FM-N conducts research several themes in general medicine/family medicine, communication, community medicine, and medical education. We especially focus on the behavioral aspects of patients and medical professionals, as well as collaborations between specialties or healthcare professionals. We use both quantitative and qualitative approaches.

The examples of ongoing research are as follows:

1. Research on the relationship between the characteristic of physicians and patients' medical seeking behavior or their health status
2. Research on non-verbal communication using artificial intelligence (AI)
3. reliability and validity of apparatus used in primary care setting (ultrasound, etc.)
4. Cost-effectiveness of the home care
5. Collaboration between primary care physicians and occupational physicians
6. To establish the method to build better team in medical setting

7. Relationship between the basis of the family medicine and health outcomes
8. Inter-professional education for students in medical school
9. Home visiting care for elderly in community
10. Other researches of family medicine/general medicine

Practice

The TMUDGM/FM-N provides care for the people living in their own community, in their own clinics or hospitals besides at outpatient department and wards in TMDU university hospital. Our practice is based on the principles and methods for the general medicine/family medicine, or primary healthcare. Additionally, we weigh importance on the collaboration between specialties, between healthcare professionals, between medical facilities, and between healthcare system and community. Moreover, we try to learn about the newest evidences for all the disease we can be involved.

(2) Publications

[Original Articles]

1. Ie Kenya, Narushima Masato, Goto Michiko, Merenstein Joel, Wilson Stephen, Takemura Yousuke. Developing and implementing a faculty development curriculum for Japanese family medicine residency faculty(和訳中) *Journal of General and Family Medicine*. 2020.05; 21(3); 71-76
2. Ie K, Narushima M, Goto M, Merenstein J, Wilson S, Takemura Y. Developing and implementing a faculty development curriculum for Japanese family medicine residency faculty. *Journal of general and family medicine*. 2020.05; 21(3); 71-76
3. Takasaki T, Yamada T, Kinoshita J, Motomura Y. Asymptomatic Colonic Anisakiasis: Is It So Rare? Case reports in gastroenterology. 2020.09; 14(3); 593-597
4. Akaishi Y, Okada Y, Lee-Jayaram J, Seo JS, Yamada T, Berg BW. Validity evidence of a task trainer for normal and difficult lumbar puncture: A cross-sectional study. *Medicine*. 2020.10; 99(41); e22622
5. Ie K, Murata A, Tahara M, Komiyama M, Ichikawa S, Takemura YC, Onishi H. Relationship between medical students' career priority and specialty choice: A nationwide multicenter survey. *Journal of general and family medicine*. 2020.11; 21(6); 219-225
6. Haya Marinda Asiah Nuril, Ichikawa Shuhei, Shibagaki Yukino, Wakabayashi Hideki, Takemura Yousuke. The "Healthy Akame!" community - government - university collaboration for health: a community-based participatory mixed-method approach to address health issue in rural Japan *BMC HEALTH SERVICES RESEARCH*. 2020.11; 20(1); 1100
7. Ie Kenya, Murata Akiko, Tahara Masao, Komiyama Manabu, Ichikawa Shuhei, Takemura Yousuke C., Onishi Hiroataka. Relationship between medical students' career priority and specialty choice: A nationwide multicenter survey(和訳中) *Journal of General and Family Medicine*. 2020.11; 21(6); 219-225

[Books etc]

1. NAMIKI Takao, AMANO Yosuke, BEPPU Masashi et al. *The Dicrionary of Kampo Medicine -Basic terms-*. 2020.05 (ISBN : 978-4901767385)

[Misc]

1. Kato Daisuke, Wakabayashi Hideki, Takamura Akiteru, Takemura Yousuke C.. Identifying the learning objectives of clinical clerkship in community health in Japan: Focus group(和訳中) *Journal of General and Family Medicine*. 2020.03; 21(2); 3-8
2. Kato D, Wakabayashi H, Takamura A, Takemura YC. Identifying the learning objectives of clinical clerkship in community health in Japan: Focus group. *Journal of general and family medicine*. 2020.03; 21(2); 3-8

[Conference Activities & Talks]

1. toru yamada. Multiple Mini-Interview for Postgraduate Medical Admissions. Asia Pacific Medical Education Conference (APMEC) 2020 2020.01.10
2. Toru Yamada. NDC-POCUS course. 2020.01.24

Neuroanatomy and Cellular Neurobiology

Professor: TERADA Sumio
Assistant Professor: KAWAGISHI Masahiko
Assistant Professor: SAITO Kenta
Assistant Professor: SATO Keisuke
Graduate Student, MD-PhD Course : NAKAI Nori
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

[Original Articles]

1. Yuko Iwasaki, Masahiko Kawagishi, Hiroshi Takase, Kyoko Ohno-Matsui. Discrimination of dissociated lymphoma cells from leukocytes by Raman spectroscopy. *Sci Rep.* 2020.09; 10(1); 15778

[Conference Activities & Talks]

1. Keisuke Sato, Ayana Sugizaki, Kenta Saito, Mehta Shalin, Mikako Shirouzu, Tomomi Tani, Sumio Terada. Development of POLArIS, a novel universal fluorescence polarization probe. The 125th Annual Meeting of the Japanese Association of Anatomists 2020.03.26 Ube (On Journal)
2. Ayana Sugizaki, Keisuke Sato, Kazuyoshi Chiba, Masahiko Kawagishi, Sumio Terada. Live-imaging analysis of actin dynamics in the starfish early development. The 125th Annual Meeting of the Japanese Association of Anatomists 2020.03.26 Ube (On Journal)
3. Nori Nakai, Keisuke Sato, Ayana Sugizaki, Kazuki Nagashima, Kenta Saito, Masahiko Kawagishi, Tomomi Tani, Sumio Terada. Trial for versatility expansion of POLArIS, a probe for live fluorescence polarization imaging. The 125th Annual Meeting of the Japanese Association of Anatomists 2020.03.26 Ube (On Journal)
4. 英文誌”Microscopy”が選んだ顕微鏡ホットトピック Genetically encoded orientation probes for F-actin for fluorescence polarization microscopy. 日本顕微鏡学会第 63 回シンポジウム顕微鏡オンラ インフォーラム 2020 2020.11.20

Systems Neurophysiology

Professor Izumi Sugihara
Associate Professor Yuri Sugiuchi
Lecturer Yoshiko Izawa
Assistant Professor Mayu Takahashi
Project Researcher Yuanjun Luo
Students (doctoral) 8

(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 two "elective research course" students.

(5) Publications

[Original Articles]

1. Ando Takahiro, Ueda Mitsuhiro, Luo Yuanjun, Sugihara Izumi. Heterogeneous vestibulocerebellar mossy fiber projections revealed by single axon reconstruction in the mouse JOURNAL OF COMPARATIVE NEUROLOGY. 2020.01; 528(10); 1775-1802
2. Panezai Saddam K., Luo Yuanjun, Vibulyaseck Suteera, Sarpong Gideon A., Nguyen-Minh Viet T., Nedelescu Hermina, Hirano Shinji, Sugihara Izumi. Reorganization of longitudinal compartments in the laterally protruding paraflocculus of the postnatal mouse cerebellum JOURNAL OF COMPARATIVE NEUROLOGY. 2020.01; 528(10); 1775-1802
3. Luo Y, Onozato T, Wu X, Sasamura K, Sakimura K, Sugihara I. Dense projection of Stilling's nucleus spinocerebellar axons that convey tail proprioception to the midline area in lobule VIII of the mouse cerebellum. Brain structure & function. 2020.03; 225(2); 621-638
4. Takahashi Mayu, Shinoda Yoshikazu. 随意性急速眼球運動系と前庭動眼反射系の共通座標軸について (Common coordinate of eye movements shared by saccadic and vestibulooculomotor systems) The Journal of Physiological Sciences. 2020.03; 70(Suppl.1); S75
5. Shimuta Misa, Sugihara Izumi, Ishikawa Taro. Multiple signals evoked by unisensory stimulation converge onto cerebellar granule and Purkinje cells in mice COMMUNICATIONS BIOLOGY. 2020.07; 3(1); 381
6. Zhang J, Tran-Anh K, Hirata T, Sugihara I. Striped Distribution Pattern of Purkinje Cells of Different Birthdates in the Mouse Cerebellar Cortex Studied with the Neurog2-CreER Transgenic Line. Neuroscience. 2020.07; 462; 122-140
7. Takahashi M, Shinoda Y. Neural Circuits of Inputs and Outputs of the Cerebellar Cortex and Nuclei Neuroscience. 2020.08;
8. Yoshiko Izawa, Hisao Suzuki. Suppressive Control of Optokinetic and Vestibular Nystagmus by the Primate Frontal Eye Field. J. Neurophysiol.. 2020.09; 124(3); 691-702
9. Tran-Anh K, Zhang J, Nguyen-Minh VT, Fujita H, Hirata T, Sugihara I. Common origin of the cerebellar dual somatotopic areas revealed by tracking embryonic Purkinje cell clusters with birthdate tagging. eNeuro. 2020.10; 7(6); 1-23

[Conference Activities & Talks]

1. Mayu Takahashi. Common coordinate of eye movements shared by saccadic and vestibulooculomotor systems. 第97回日本生理学会大会 (誌上開催) 2020.03.18
2. Zhang J, Tran-Anh K, Hirata T, Sugihara I. Birthdate-dependent compartmentalization of Purkinje cells in the cerebellar cortex in the mouse.. The 43rd Annual Meeting of the Japan Neuroscience Society 2020.07.30 Online
3. Mayu Takahashi. Brainstem neural circuits for initiation and maintenance of horizontal saccades. 第43回日本神経科学会 2020.07.31
4. Yoshiko Izawa, Hisao Suzuki. Eye movements and neck torques evoked by electrical stimulation of the monkey frontal eye field. The 43rd Annual Meeting of the Japan Neuroscience Society 2020.07.31 Web開催

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

[Original Articles]

1. Mikeli Maimaiti, Fujikawa Makoto, Nagahisa Kai, Yasuda Shuhei, Yamada Natsuhiko, Tanabe Tsutomu. Contribution of GPD2/mGPDH to an alternative respiratory chain of the mitochondrial energy metabolism and the stemness in CD133-positive HuH-7 cells GENES TO CELLS. 2020.01; 25(2); 139-148
2. Saegusa Hironao, Li Xu, Wang Xinshuang, Kayakiri Midori, Tanabe Tsutomu. Knockdown of microglial Cav2.2 N-type voltage-dependent Ca(2+)channel ameliorates behavioral deficits in a mouse model of Parkinson's disease FEBS LETTERS. 2020.06; 594; 2914-2922
3. Ikeda T, Kishikawa JI, Hayashida Y, Fujikawa M, Yokoyama K. Identification of chemical compounds as an inhibitor of mitochondrial ATP synthesis, leading to an increased stress resistance and an extended lifespan in *C. elegans*. Biochimica et biophysica acta. Bioenergetics. 2020.11; 1861(11); 148281
4. Tanaka DH, Li S, Mukae S, Tanabe T. Genetic recombination in disgust-associated bitter taste-responsive neurons of the central nucleus of amygdala in male mice. Neuroscience letters. 2020.12; 135456

Molecular Neuroscience

Professor Kohichi Tanaka
Assistant Professor Saeko Ishida
Assistant Professor Yuichi Hiraoka

Graduate Student (doctor course)
Takehisa Handa
Bi Haining

Graduate Student (master course)
Haruna Aikawa
Yuuta Sawada
Zhao Di
Ryo Matsuura
Minami Kato

Technical Staff
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. Migraines affect millions of people worldwide, often lasting days and severely disrupting lives. More than simply super-intense headaches, some migraines actually result from pathological excitation of neurons in the brain. We show that susceptibility to migraines could be related to a molecular transporter that normally works to prevent excessive excitation of neurons. Migraines are related to a condition called cortical depression, in which a large wave of hyperactivity spreads across the brain, followed by a wave of inhibition, or depressed brain activity. We hypothesized that susceptibility to cortical spreading depression (CSD) is related to disrupted transport of glutamate, the most common excitatory neurotransmitter. We found that when mice lacked the GLT-1 transporter, cortical spreading depression occurred more frequently and spread more quickly than in control mice or in the other knockout mice. If GLT-1 proves to be disrupted in people who have migraines, drug therapy that acts to increase glial reuptake of glutamate could be a reasonable therapeutic approach.

2. In vivo genome editing using AAV-CRISPR system

Genetically modified animals play critical roles in understanding neuronal development, function and disease. Conventional methods to establish transgenic animals have been a time- and labor-intensive process. To overcome these limitations, we developed a viral vector-mediated gene knock-out strategy using CRISPR/Cas9. Using this method, we found that a dopamine receptor D1R ablation in the nucleus accumbens (NAc) region effectively increased the active coping behavior in animals under stress, suggesting that the reduced dopamine release in the NAc region initiated an active coping behavior.

(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. Hirayama Takashi, Hiraoka Yuichi, Kitamura Eri, Miyazaki Shinji, Horie Kengo, Fukuda Tomokazu, Hidema Shizu, Koike Masato, Itakura Atsuo, Takeda Satoru, Nishimori Katsuhiko. Oxytocin induced labor causes region and sex-specific transient oligodendrocyte cell death in neonatal mouse brain(和訳中) *The Journal of Obstetrics and Gynaecology Research*. 2020.01; 46(1); 66-78
2. Tomoka Takao, Yuichi Hiraoka, Kenji Kawabe, Daisuke Yamada, Lu Ming, Kohichi Tanaka, Moritoshi Sato, Takeshi Takarada. Establishment of a tTA-dependent photoactivatable Cre recombinase knock-in mouse model for optogenetic genome engineering. *Biochem Biophys Res Commun*. 2020.05; 526(1); 213-217
3. Yoshiko Aihara, Yota Fukuda, Akiyoshi Takizawa, Naomi Osakabe, Tomomi Aida, Kohichi Tanaka, Soichiro Yoshikawa, Hajime Karasuyama, Takahiro Adachi. Visualization of mechanical stress-mediated Ca²⁺ signaling in the gut using intravital imaging *Biosci Microbiota Food Health*. 2020.06; 39(4); 209-218
4. Mariko Sekiguchi, Akira Sobue, Itaru Kushima, Chenyao Wang, Yuko Arioka, Hidekazu Kato, Akiko Kodama, Hisako Kubo, Norimichi Ito, Masahito Sawahata, Kazuhiro Hada, Ryosuke Ikeda, Mio Shinno, Chikara Mizukoshi, Keita Tsujimura, Akira Yoshimi, Kanako Ishizuka, Yuto Takasaki, Hiroki Kimura, Jingrui Xing, Yanjie Yu, Maeri Yamamoto, Takashi Okada, Emiko Shishido, Toshiya Inada, Masahiro Nakatochi, Tetsuya Takano, Keisuke Kuroda, Mutsuki Amano, Branko Aleksic, Takashi Yamamoto,

- Tetsushi Sakuma, Tomomi Aida, Kohichi Tanaka, Ryota Hashimoto, Makoto Arai, Masashi Ikeda, Nakao Iwata, Teppei Shimamura, Taku Nagai, Toshitaka Nabeshima, Kozo Kaibuchi, Kiyofumi Yamada, Daisuke Mori, Norio Ozaki. ARHGAP10, which encodes Rho GTPase-activating protein 10, is a novel gene for schizophrenia risk. *Transl Psychiatry*. 2020.07; 10(1); 247
5. Wanpeng Cui, Tomomi Aida, Hikaru Ito, Kenta Kobayashi, Yusaku Wada, Shigeki Kato, Takashi Nakano, Meina Zhu, Kaoru Isa, Kazuto Kobayashi, Tadashi Isa, Kohichi Tanaka, Hidenori Aizawa. Dopaminergic Signaling in the Nucleus Accumbens Modulates Stress-Coping Strategies during Inescapable Stress. *J Neurosci*. 2020.09; 40(38); 7241-7254
 6. Michiko Yanagisawa, Kazuhiko Namekata, Tomomi Aida, Sayaka Katou, Takuya Takeda, Takayuki Harada, Nobuo Fuse, The Glaucoma Gene Research Group, Kohichi Tanaka. EAAT1 variants associated with glaucoma. *Biochem Biophys Res Commun*. 2020.09; 529(4); 943-949
 7. Hidenori Aizawa, Weinan Sun, Kaori Sugiyama, Yukiko Itou, Tomomi Aida, Wanpeng Cui, Saori Toyoda, Haruhi Terai, Michiko Yanagisawa, Kohichi Tanaka. Glial glutamate transporter GLT-1 determines susceptibility to spreading depression in the mouse cerebral cortex. *Glia*. 2020.12; 68(12); 2631-2642
 8. Yoshifumi Abe, Norio Takata, Yuki Sakai, Hiro Taiyo Hamada, Yuichi Hiraoka, Tomomi Aida, Kohichi Tanaka, Denis Le Bihan, Kenji Doya, Kenji F Tanaka. Diffusion functional MRI reveals global brain network functional abnormalities driven by targeted local activity in a neuropsychiatric disease mouse model. *Neuroimage*. 2020.12; 223; 117318

[Misc]

1. Kohichi Tanaka. The role of glutamate transporters in chronic pain 2020.07; 40(4); 366-374

Neuropathology

Professor: Hitoshi Okazawa
Practical Professor: Kazuhiko Tagawa
Project Lecturer/Part-time Lecturer: Haruhisa Inoue, Masaki Sone
Assistant Professor: Kyota Fujita
Project Assistant Professor: Hidenori Homma
Postdoctoral fellow (JSPS research fellow): Hikari Tanaka
Assistant Administrative Staff: Shigemi Sato
Secretary: Marie Tanaka
Graduate Student : Kanoh Kondo, Yuki Yoshioka, Jin Meihua,
Jin Xiaocen, Huang Yong

(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

[Outline]

Following studies have been intensively carried out in our laboratory with various techniques including molecular biology, cell biology, biochemistry, Drosophila models, and mice models.

- 1)Investigation of molecular pathologies of neurodegenerative disease.
- 2)Development of new therapies for neurodegeneration.
- 3)Development of new seed drug for mental retardation.
- 4)Investigation of molecular function of Oct3/4.

[This year' s progress]

YAP-dependent necrosis occurs in early stages of Alzheimer' s disease and regulates mouse model pathology

The principal pathological hallmark of neurodegenerative disease such as Alzheimer' s disease is accumulation of abnormal protein in intracellular and/or extracellular space. In Alzheimer' s disease, two major hallmarks are well-known; one is extracellular Amyloid-beta plaque, and the other is intracellular neurofibrillary tangle composed by tau protein. Although several therapeutic approaches have been tried, there are still not found any practical and successful candidates. In the current 15 years, clinical therapy using anti-amyloid beta antibody have been performed internationally. However, those therapies brought us the evidence of elimination

of extracellular Amyloid plaque, but not recovery of their symptoms. These results indicate that it is already too late to start treatment after onset, and it is necessary to develop treatments for new molecular targets at the very early (phase 0) stage before extracellular amyloid aggregation.

Previously, we have identified several phosphorylated proteins such as MARCKS whose phosphorylation started prior to extracellular amyloid aggregation (Tagawa et al, Hum Mol Genet 2015) . We also found that phosphorylated MARCKS (pSer46-MARCKS) was located in degenerative neurites along with the extracellular amyloid plaques (Fujita et al, Sci Rep 2016) . The upstream signaling for Ser46-MARCKS phosphorylation appeared to be HMGB1-TLR4 signaling. We have succeeded to prevent the onset of Alzheimer's disease by administration of anti-HMGB1 antibody targeting to extracellular HMGB1 in the mouse model of AD (Fujita et al, Sci Rep 2016) .

HMGB1 is a well-known molecule secreted from cells after necrosis (Scaffidi et al., Nature 2002). So, we have tried to measure the HMGB1 concentration in CSF, and interestingly, the level of HMGB1 was increased more in MCI patient CSF than in post-onset AD patients. This result indicates that the cell death has already occurred prior to clinical symptoms appearance. So, we have developed the novel technique to identify the active necrotic neurons using anti-pSer46-MARCKS antibody, and have found that the active necrosis has been evoked prior to cognitive impairment or extracellular amyloid-beta plaque development.

In addition, we have performed the detailed observations of human Alzheimer's disease-related neurons that have been created from genome edited human iPS cells by introducing Alzheimer's gene mutations. We have found that such necrosis is a new type of necrosis (TRIAD) because of the interaction between intracellular amyloid and YAP which is required neuronal survival.

Furthermore, we performed YAP supplementation by gene therapy on Alzheimer's disease model mice with the aim of normalizing the YAP dysfunction that causes necrosis. As a result, suppression of TRIAD necrosis, improvement of cognitive function, and suppression of extracellular amyloid accumulation were observed.

In this study, it was strongly suggested that the amyloid hypothesis, which considers extracellular amyloid aggregation to be the most upstream, should be corrected. Instead, 1) extracellular amyloid aggregation as a result of necrosis beginning with intracellular amyloid accumulation, 2) (a) necrosis was triggered by intracellular amyloid accumulation, and (b) secondary cell death has occurred in surrounding neurons, 3) Necrosis triggered by intracellular amyloid accumulation is TRIAD by dysfunction of YAP, and 4) it is possible to develop treatments such as gene therapy based on YAP function recovery in the future. In addition, 5) it was shown that the amount of CSF HMGB1 could be developed as a pre-onset molecular marker of Alzheimer's disease.

(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. Tanaka H, Homma H, Fujita K, Kondo K, Yamada S, Jin X, Waragai M, Ohtomo G, Iwata A, Tagawa K, Atsuta N, Katsuno M, Tomita N, Furukawa K, Saito Y, Saito T, Ichise A, Shibata S, Arai H, Saido T, Sudol M, Muramatsu SI, Okano H, Mufson EJ, Sobue G, Murayama S, Okazawa H. YAP-dependent necrosis occurs in early stages of Alzheimer's disease and regulates mouse model pathology. *Nat Commun* . 2020.01; 11(1); 507
2. Yang SS, Ishida T, Fujita K, Nakai Y, Ono T, Okazawa H. PQBP1, an intellectual disability causative gene, affects bone development and growth. *Biochem Biophys Res Commun*. 2020.03; 523(4); 894-899

[Conference Activities & Talks]

1. Hitoshi Okazawa. Development of gene therapies of neurodegenerative diseases targeting new pathological mechanisms. AMED -Gene & Cell Therapy Symposium 2020.02.22 Nihonbashi Life Science Building(Tokyo)
2. Hikari Tanaka, Hidenori Homma, Kyota Fujita, Kanoh Kondo, Jin Xiaocen, Kazuhiko Tagawa, Hitoshi Okazawa. YAP-dependent necrosis regulates early stages of Alzheimer' s disease pathology. The 43rd Annual Meeting of the Japan Neuroscience Society(online) 2020.07.31
3. Hitoshi Okazawa. Discovery of new pathologies and development of new therapeutics based on molecular network analysis against Alzheimer's disease. The 43rd Annual Meeting of the Japan Neuroscience Society(online) 2020.07.31
4. Hikari Tanaka, Kanoh Kondo, Xigui Chen, Hidenori Homma, Kazuhiko Tagawa, Takaomi Saido, Shin-ichi Muramatsu, Kyota Fujita, Hitoshi Okazawa. Phosphorylation of SRRM2 leads to synaptic pathology at ultra-early phase of Alzheimer's disease. 61st Annual Meeting of the Japanese Society of Neurology 2020.09.02 Okayama Convention Center(Okayama)

Ophthalmology and Visual Science

Professor;Kyoko Ohno-Matsui

Specially-appointed professor;Makoto Aihara

Associate Professor;Takeshi Yoshida

Junior Associate Professor;Hiroshi Takase, Koju Kamoi, Shintaro Horie

Assistant Professor; Tae Igarashi, Natsuko Nagaoka, Hiroyuki Takahashi, Yuko Iwasaki, Kengo Uramoto

Graduate student; Hisako Karube, keijia Cao, Yuxin Fang, Ran Du, Xie Shi Qi, Xuejiao Li

(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. Koju Kamoi. HTLV-1 in Ophthalmology. *Front Microbiol.* 2020; 11; 388
2. Hisako Kurozumi-Karube, Koju Kamoi, Naoko Ando, Minami Uchida, Isao Hamaguchi, Ohno-Matsui K. Evaluation of the Safety of Adalimumab for the Eye Under HTLV-1 Infection Status: A Preliminary Study. *Front Microbiol.* 2020; 11; 522579
3. Koju Kamoi, Ohno-Matsui K. Intraocular Infiltration. *Am. J. Trop. Med. Hyg.* 2020.01; 102(1); 7-8
4. Masaru Miyanaga, Hiroshi Takase, Kyoko Ohno-Matsui. Anti-Neutrophil Cytoplasmic Antibody-Associated Ocular Manifestations in Japan: A Review of 18 Patients. *Ocular immunology and inflammation.* 2020.02; 1-6
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10. Tomoka Ishida, Hiroshi Takase, Ayako Arai, Kyoko Ohno-Matsui. Multimodal imaging of secondary vitreoretinal lymphoma with optic neuritis and retinal vasculitis. *Am J Ophthalmol Case Rep*. 2020.06; 18; 100696
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23. Jost B Jonas, Ohno-Matsui K, Leonard Holbach, Songhomitra Panda-Jonas. Histology of myopic posterior scleral staphylomas. *Acta Ophthalmol*. 2020.11; 98(7); e856-e863
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[Misc]

1. Paul N Baird, Seang-Mei Saw, Carla Lanca, Jeremy A Guggenheim, Earl L Smith Iii, Xiangtian Zhou, Ohno-Matsui K, Pei-Chang Wu, Padmaja Sankaridurg, Audrey Chia, Mohamad Rosman, Ecosse L Lamoureux, Ryan Man, Mingguang He. Myopia. *Nat Rev Dis Primers*. 2020.12; 6(1); 99
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[Conference Activities & Talks]

1. Ohno-Matsui K. Dome-shaped macula progressing in parallel with Bruch' s membrane defects. Atlantic Coast Retina Club and Macula 20/20 2020.01.10 NewYork, USA
2. Ohno-Matsui K. Imaging of Pathologic myopia. Atlantic Coast Retina Club and Macula 20/20 2020.01.11
3. Ohno-Matsui K, Takahashi H, Mao Z. En face dynamic observations of posterior vitreous in eyes with and without pathologic myopia. The macula society 43rd Annual meeting 2020.02.19 SanDiego, USA
4. Ohno-Matsui K. Imaging of Pathologic Myopia. Yale eye center grand rounds 2020.08.07 web
5. Ohno-Matsui K. Role of dilated choroidal vein for myopic macular neovascularization. Asia Pacific Retinal Imaging Society 2020.08.20 web
6. Ohno-Matsui K. Management of pathological myopia. COVID-19 impact on lifestyle and myopia progression. IPOSC—IAPB Myopia 2020.08.28 web
7. Ohno-Matsui K. Imaging of pathologic myopia. Daalhouse University Department of Ophthalmology and Visual Sciences 2020.09.23 web
8. Ohno-Matsui K. Myopic macular neovascularization maybe be a unique vascular unit?. China-Japan Forum on macular complications of high myopia 2020.09.26 web
9. Ohno-Matsui K. Ultra wide-field imaging of pathologic myopia. EURETINA 2020 2020.10.02 web
10. Uramoto K, Azuma T, Takahashi H, Igarashi T, Shimada N, Ohno-Matsui K. Characteristics of Pseudo Macular Hole Retinal Detachment in Pathologic Myopia. Japan Myopia Retina Club 3rd Annual Meeting 2020.10.16 web
11. Yana M, Igarashi T, Shinohara K, Watanabe T, Yoshida T, Ohno-Matsui K. Macular Functional Changes evaluated with MP-3 Microperimetry after anti-VEGF therapy for Myopic Macular Neovascularization. Japan Myopia Retina Club 3rd Annual Meeting 2020.10.16 web
12. Watanabe T, Yokoi T, Moriyama M, Tanaka N, Shinohara K, Takahashi H, Yoshida T, Ohno-Matsui K. Comparison of Clinical Features in Highly Myopic Eyes with and without Posterior Staphyloma evaluated with Ultrawide-Field Swept-Source OCT. Japan Myopia Retina Club 3rd Annual Meeting 2020.10.16 web

13. Kanai H, Igarashi T, Mochida S, Nakao N, Saitou R, Ohno-Matsui K. Long-term Prognosis of Visual Development in Children with Congenital High Myopia. Japan Myopia Retina Club 3rd Annual Meeting 2020.10.16
14. Sugisawa K, Takahashi H, Nakao N, Shinohara K, Igarashi-Yokoi T, Yoshida T, Ohno-Matsui K. Premacular Bursa and Surrounding Vitreous Gel investigated by Ultra-widefield OCT. AAO2020 2020.11.13 web
15. Takahashi H, Tanaka N, Shinohara K, Uramoto K, Yokoi T, Yoshida T, Ohno-Matsui K. Vitreous-Retina Interfacial Changes Detected by Ultra-widefield Optical Coherence Tomography in Highly Myopic Children and Young Adults. AAO2020 2020.11.13 web
16. Ohno-Matsui K, Saw SM, Repca M, Grzybowski A, Koffler B. New approaches to the prevention and treatment of myopia: Update 2020. AAO2020 2020.11.13 web
17. Ohno-Matsui K, Moussa M, Sadda S, Fawzi A, Staurenghi G, Papayannis A, Stanga P. Swept-source OCT and OCT angiography in various retinal diseases. AAO2020 2020.11.13
18. Ohno-Matsui K, Cheung G, Lai T, Hiraokata A, Jonas JB. Pathologic Myopia. AAO2020 2020.11.13 web
19. Ohno-Matsui K, Mao Z, Takahashi H. Ultra-widefield Swept Source OCT and AI-predicted 3D structures of Posterior Vitreous. AAO2020 2020.11.13 web
20. Ohno-Matsui K. Pathologic myopia. AAO2020 2020.11.13
21. Ohno-Matsui K. Imaging of myopia. Asia Pacific Ocular Imaging Society 2020.11.21 web
22. Ohno-Matsui K. V for Vitreous. Ocular Imaging360 2020.11.21 web

Otorhinolaryngology

Professor: Takeshi Tsutsumi

Associate Professor: Yoshiyuki Kawashima

Junior Associate Professor: Yasuhiro Suzuki

Assistant Professor: Taku Itou, Tarou Fujikawa, Keiji Honda

Hospital Staff: Hiroki Watanabe, Tomoki Ooka, Natsuko Kurata, Kaori Mori, Shima Isono

Graduate Student: Ayane Makabe, Ayako Maruyama, Bai Jing, Ayame Yamazaki, Yusuke Kiyokawa, Motomu Honjo, Hiroki Watanabe, Natsuki Aoki, Tomoki Ooka

(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. Nakanishi H, Prakash P, Ito T, Kim HJ, Brewer CC, Harrow D, Roux I, Hosokawa S, Griffith AJ. Genetic Hearing Loss Associated With Autoinflammation. *Frontiers in neurology*. 2020; 11; 141
2. Watanabe H, Makabe A, Hirai C, Takeda T, Honda K, Demura S, Tsutsumi T. Frequency analyses of posturography using logarithmic translation. *Acta Oto-Laryngologica*. 2020.01; 140(1); 1-7
3. Maruyama A, Kawashima Y, Fujikawa T, Makabe A, Ito T, Takeda T, Tsutsumi T. Potential Confounding Factors May Influence the Association Between Configurations of the Vertebrobasilar System and the Incidence of Idiopathic Sudden Sensorineural Hearing Loss and Canal Paresis. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2020.03; 41(5); 548-555
4. Makabe A, Kawashima Y, Sakamaki Y, Maruyama A, Fujikawa T, Ito T, Kurima K, Griffith AJ, Tsutsumi T. Systemic Fluorescent Gentamicin Enters Neonatal Mouse Hair Cells Predominantly Through Sensory Mechanoelectrical Transduction Channels. *Journal of the Association for Research in Otolaryngology : JARO*. 2020.03;
5. Takeda T, Ito T, Onishi I, Yokomura M, Kawashima Y, Fujikawa T, Tsutsumi T. Denosumab-induced osteonecrosis of external auditory canal. *Auris, nasus, larynx*. 2020.07;
6. Tomoki Ooka, Jing Bay, Takamori Takeda, Keiji Honda, Takuo Ikeda and Takeshi Tsutsumi. Clinical application of 3D-VOG analysis for quantitative evaluation of Otolith-Ocular reflex in the roll and pitch planes *ACTA OTO-LARYNGOLOGICA*. 2020.10; 140(11); 925-929
7. Fujikawa Taro, Honda Keiji, Ito Taku, Kishino Mitsuhiro, Kimura Naoki, Umezawa Natsuka, Hirano Mana, Aoki Natsuki, Kawashima Yoshiyuki, Tsutsumi Takeshi. Enhanced fallopian canal as a potential marker for temporal bone vasculitis *LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY*. 2020.11;
8. Motomu Honjo, Keiji Honda, Takeshi Tsutsumi. Unusual Vestibulo-Ocular Reflex Responses in Patients With Peripheral Vestibular Disorders Detected by the Caloric Step Stimulus Test. *Frontiers in Neurology*. 2020.11; 11; 597562
9. Kiyokawa Y, Ariizumi Y, Ohno K, Ito T, Kawashima Y, Tsunoda A, Kishimoto S, Asakage T, Tsutsumi T. Indications for and extent of elective neck dissection for lymph node metastasis from external auditory canal carcinoma. *Auris, nasus, larynx*. 2020.12;
10. 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

Neurology and Neurological Science

Professor YOKOTA Takanori
Associate Professor ISHIBASHI Satoru
Junior Associate Professor NISHIDA Yoichiro, KUWAHARA Hiroya, HATTORI Takaaki
Assistant Professor ISHIGURO Taro, YAGI Yohsuke, ONO Daisuke
Project Professor SANJO Nobuo, UCHIHARA Toshiki
Project Junior Associate Professor NAGATA Tetsuya
Project Junior Associate Professor HARA Rintaro
Project Assistant Professor YOSHIOKA Kotaro
Project Assistant Professor HIGASHI Miwa, SAKAUE Fumika,
Project Researcher AMANO Akiko, HIRATA Kosei, SU SU Lei Mon
Research Assistant ASAMI Yutaro
Graduate Student HASEGAWA Jyuri, MIYASHITA Akiko, SANO Tatsuhiko, ISHINOSE Keiko, MARUOKA Hiroyuki,
NISHI Rieko, SUZUKI Motohiro, YAMADA Akane, KINA Satoko, SATO Takefumi,
IIDA Shintaro, TAKAHASHI Yuko, OHARA Masahiro, MIURA Motoki, AOKI Hanako,
YAMADA Hiroki, MATSUDA Sakino, YANAGIDAIRA Mitsugu, OHTANI Tai, SHINYA Akiko,
TOIDE Nozomi, TAMAKI Kana, IWASE Ryo, MATSUBAYASHI Taiki, SHIMANO Kaoru,
AMANO Eiichiro, JIA Chunyan, CHEN Qingmeng, THUNYARUT Bannawongsil, YASUDA Eiji,
MORITO Koji, KATO Tomotaka, YASUDA Kazuma, KATSUYAMA Maho, MOCHIZUKI Erika
Research Student HAMADA Meiko
Resident SUGITA Yoichiro, SUZUKI Masashi, SASO Nasumi, KIM Yangsu, YAMAGATA Naoki, KAWANA Yasuhito,
TAKAHASHI Sunao, SAKAI Sawako, KOBAYASHI Yuki, SATO Ojiro

(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 32 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. Tsuyoshi Hamaguchi, Nobuo Sanjo, Ryusuke Ae, Yosikazu Nakamura, Kenji Sakai, Masaki Takao, Shigeo Murayama, Yasushi Iwasaki, Katsuya Satoh, Hiroyuki Murai, Masafumi Harada, Tadashi Tsukamoto, Hidehiro Mizusawa, Masahito Yamada.. MM2 type sporadic Creutzfeldt-Jakob disease: new diagnostic criteria for MM2-cortical type. *Journal of Neurology, Neurosurgery & Psychiatry* . 2020; in press; in press
2. Kenji Sakai, Tsuyoshi Hamaguchi, Nobuo Sanjo, Hiroyuki Murai, Yasushi Iwasaki, Tadanori Hamano, Mari Honma, Moeko Noguchi-Shinohara, Ichiro Nozaki, Yosikazu Nakamura, Tetsuyuki Kitamoto, Masafumi Harada, Hidehiro Mizusawa, Masahito Yamada. . Diffusion-weighted magnetic resonance imaging in dura mater graft-associated Creutzfeldt-Jakob disease. *Journal of the Neurological Sciences* . 2020; in press;
3. Rintaro Iwata Hara, Kotaro Yoshioka, Takanori Yokota. DNA-RNA Heteroduplex Oligonucleotide for Highly Efficient Gene Silencing. *Methods Mol. Biol.* 2020; 2176; 113-119
4. Nishida Y, Takahashi YK, Kanai T, Nose Y, Ishibashi S, Sanjo N, Uzawa A, Oda F, Ozawa Y, Kuwabara S, Noguchi E, Suzuki S, Nakahara J, Suzuki N, Ogawa T, Yokoyama K, Hattori N, Konno S, Fujioka T, Kawaguchi N, Hatanaka Y, Sonoo M, Kaneko J, Ogino M, Nishiyama K, Nomura K, Yokota T. Safety of tapering tacrolimus dose in patients with well-controlled anti-acetylcholine receptor antibody-positive myasthenia gravis. *European journal of neurology*. 2020.01; 27(1); 100-104
5. Lei Mon SS, Yoshioka K, Jia C, Kunieda T, Asami Y, Yoshida-Tanaka K, Piao W, Kuwahara H, Nishina K, Nagata T, Yokota T. Highly efficient gene silencing in mouse brain by overhanging-duplex oligonucleotides via intraventricular route. *FEBS letters*. 2020.01; 594(9); 1413-1423
6. Okamoto Takumi, Wu Yan, Matsuhisa Koji, Saito Atsushi, Sakaue Fumika, Imaizumi Kazunori, Kaneko Masayuki. Hypertonicity-responsive ubiquitin ligase RNF183 promotes Na⁺, K⁺-ATPase lysosomal degradation through ubiquitination of its β 1 subunit. *Biochem Biophys Res Commun*. 2020.01; 521(4); 1030-1035
7. Matsuhisa Koji, Saito Atsushi, Cai Longjie, Kaneko Masayuki, Okamoto Takumi, Sakaue Fumika, Asada Rie, Urano Fumihiko, Yanagida Kanta, Okochi Masayasu, Kudo Yukitsuka, Matsumoto Masaki, Nakayama Keiichi I, Imaizumi Kazunori. Production of BBF2H7-derived small peptide fragments via endoplasmic reticulum stress-dependent regulated intramembrane proteolysis. *FASEB J*. 2020.01; 34(1); 865-880

8. Teruhiko Sekiguchi, Satoru Ishibashi, Jo Sasame, Jun-Ichi Mukae, Kotaro Noda, Hiroaki Tanaka, Koh Yamamoto, Yasunori Takemoto, Jiro Kumagai, Takanori Yokota. Recurrent stroke due to quasi-moyamoya disease associated with POEMS syndrome: An autopsy case. *J. Neurol. Sci.*. 2020.02; 412; 116738
9. Yamamoto K, Abe S, Honda A, Hashimoto J, Aizawa Y, Ishibashi S, Takemura T, Hanagata N, Yamamoto M, Miura O, Kurata M, Kitagawa M. Fatty acid beta oxidation enzyme HADHA is a novel potential therapeutic target in malignant lymphoma. *Lab Invest.* . 2020.03;
10. Hirata K, Kobayashi M, Miyashita A, Yokota T. Steroid-responsive myositis in a patient with Sjögren's syndrome and refractory peripheral neuropathy. *Neurological sciences* . 2020.05; 41(5); 1303-1305
11. Akihiro Hoshino, Akira Nishimura, Takuya Naruto, Tsubasa Okano, Kazuaki Matsumoto, Keisuke Okamoto, Hiroshi Shintaku, Shown Tokoro, Hiroyuki Okamoto, Taizo Wada, Masatoshi Takagi, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio. High-throughput analysis revealed the unique immunoglobulin gene rearrangements in plasmacytoma-like post-transplant lymphoproliferative disorder. *Br. J. Haematol.*. 2020.05; 189(4); e164-e168
12. Masahiro Ohara, Takaaki Hattori, Takanori Yokota. Progressive supranuclear palsy often develops idiopathic normal pressure hydrocephalus-like MRI features. *Eur. J. Neurol.*. 2020.05; 27; 1930-1936
13. Jinbing Xie, Daniel Gonzalez-Carter, Theofilus A Tockary, Noriko Nakamura, Yonger Xue, Makoto Nakakido, Hiroki Akiba, Anjaneyulu Dirisala, Xueying Liu, Kazuko Toh, Tao Yang, Zengtao Wang, Shigeto Fukushima, Junjie Li, Sabina Quader, Kouhei Tsumoto, Takanori Yokota, Yasutaka Anraku, Kazunori Kataoka. Dual-Sensitive Nanomicelles Enhancing Systemic Delivery of Therapeutically Active Antibodies Specifically into the Brain. *ACS Nano.* 2020.05; 14(6); 6729-6742
14. Tai Otani, Takashi Irioka, Susumu Igarashi, Kimihiko Kaneko, Toshiyuki Takahashi, Takanori Yokota. Self-remitting cerebral cortical encephalitis associated with myelin oligodendrocyte glycoprotein antibody mimicking acute viral encephalitis: A case report. *Mult Scler Relat Disord.* 2020.06; 41; 102033
15. Kosei Hirata, Takaaki Hattori, Satoko Kina, Qingmeng Chen, Masahiro Ohara, Takanori Yokota. Striatal Dopamine Denervation Impairs Gait Automaticity in Drug-Naïve Parkinson's Disease Patients. *Mov. Disord.*. 2020.06; 35(6); 1037-1045
16. Ryo Iwase, Taro Ishiguro, Kyohei Fujita, Satoru Ishibashi, Takanori Yokota. Dupilumab for Atopic Dermatitis, a Possible Risk Factor of Juvenile Ischemic Stroke: A Case Report. *J Stroke Cerebrovasc Dis.* 2020.06; 29(6); 104763
17. Iwase R, Irioka T, Igarashi S, Ayabe J, Yokota T. Intracranial dural arteriovenous fistula mimicking neuromyelitis optica spectrum disorder: A case report. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association.* 2020.08; 29(8); 105007
18. Yuko Yamagishi, Motoi Kuwahara, Hidekazu Suzuki, Masahiro Sonoo, Satoshi Kuwabara, Takanori Yokota, Kyoichi Nomura, Atsuro Chiba, Ryuji Kaji, Takashi Kanda, Ken-Ichi Kaida, Tatsuro Mutoh, Ryo Yamasaki, Hiroshi Takashima, Makoto Matsui, Kazutoshi Nishiyama, Gen Sobue, Susumu Kusunoki. Serum IgG anti-GD1a antibody and mEGOS predict outcome in Guillain-Barré syndrome. *J Neurol Neurosurg Psychiatry.* 2020.10;
19. Kishimoto Y, Nakagawa O, Fujii A, Yoshioka K, Nagata T, Yokota T, Hari Y, Obika S. 2',4'-BNA/LNA with 9-(2-Aminoethoxy)-1,3-diaza-2-oxophenoxazine Efficiently Forms Duplexes and Has Enhanced Enzymatic Resistance*. *Chemistry (Weinheim an der Bergstrasse, Germany).* 2020.10; 2427-2438
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23. Hiroyuki Yokoyama, Takashi Hirai, Tetsuya Nagata, Mitsuhiro Enomoto, Hidetoshi Kaburagi, Li Leiyo, Takayuki Motoyoshi, Toshitaka Yoshii, Atsushi Okawa, Takanori Yokota. DNA Microarray Analysis of Differential Gene Expression in the Dorsal Root Ganglia of Four Different Neuropathic Pain Mouse Models. *J Pain Res.* 2020.11; 13; 3031-3043
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[Misc]

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[Conference Activities & Talks]

1. Shintaku Hiroshi, et al.. A coexistent case of primary gastric choriocarcinoma and alpha fetoprotein-producing gastric cancer. 2020
2. Takanori Yokota. New Stage of DNA/RNA Heteroduplex Oligonucleotide. *Asia TIDES:Oligonucleotide & Peptide Therapeutics* 2020.02.24 kyoto
3. Iwase R, Sanjo N, Ishiguro T, Yokota T. Clinical characteristics and pathophysiology of a rare muscle atrophy in superficial siderosis. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
4. Yokota T, Nagata T, Dwyer C, Yoshida K, Yoshioka K, Seth P, Rigo F, Bennett F. Development of BBB-penetrating heteroduplex oligonucleotides(HDO). 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
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6. Maruoka H, Hattori T, Orimo S, Yokota T. Graph theoretical analysis of structural brain network of Alzheimer's disease patients. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
7. Jia C, Yoshioka K, Lei Mon S, Tanaka K, Nagata T, Yokota T. Heteroduplex Oligonucleotides technology improves therapeutic index for CNS diseases. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31
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9. Aoki H, Higashi M, Okita M, Yokota T, Ishikawa K. Expression of thymidine kinase 2 and mitochondrial proteins in SCA31 human brains. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama

10. Yokote H, Toru S, Nishida Y, Hattori T, Sanjo N, Yokota T. Association between serum amyloid A and cortical volume in patients with multiple sclerosis. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
11. Nishi R, Ohyagi M, Nagata T, Mabuchi Y, Yokota T. DNA/RNA heteroduplex oligonucleotide technology for regulating activated microglia and macrophages. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31
12. Akaza M, Kawabata S, Watanabe T, Miyano Y, Mizuguchi R, Kaminaka S, Iida S, Sasaki T, Adachi Y, Sekihara K, Sumi Y, Okawa A, Yokota . The evaluation of nerve activity using magnetic field measurement and positional information by US. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
13. Sano T, Nagata T, Tanaka K, Ebihara S, Mochizuki H, Hasegawa M, Yokota T. Inhibition of SNCA Propagation by locally injected ASO in wt mice. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31
14. Asami Y, Nagata T, Yoshioka K, Kunieda T, Yoshida-Tanaka K, Yokota T. Efficient gene suppression by DNA/DNA double-stranded oligonucleotide in vivo. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31
15. Irioka T, Motomura M, Igarahi S, Takahahi Y, Iwase R, Otani T, Kitanosono H, Shiraihi H, Iizuka T, Yokota T. Calcium channels antibody-associated paraneoplastic disorders other than Lambert-Eaton syndrome. 61st Annual Meeting of the Japanese Society of Neurology 2020.08.31 Okayama
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19. Tetsuya Nagata. BBB-penetrating heteroduplex oligonucleotide. 61st Annual Meeting of the Japanese Society of Neurology 2020.09.02 Okayama
20. Koki Kosami, Ryusuke Ae, Yosikazu Nakamura, Tsuyoshi Hamaguchi, Tadashi Tsukamoto, Ichiro Takumi, Nobuo Sanjo, Tetsuyuki Kitamoto, Masahito Yamada, Hidehiro Mizusawa. Descriptive epidemiology of prion disease in Japan based on national surveillance (1999-2019).. World Congress of Epidemiology 2020 2020.09.13 Melbourne, Australia
21. Asami Y, Nagata T, Yoshioka K, Kunieda T, Yoshida-Tanaka K, Yokota T. DNA/DNA Double-Stranded Oligonucleotide Suppresses Target RNA Efficiently In Vivo without Evident Innate Immune Responses.. 16th Annual Meeting of the Oligonucleotide Therapeutics Society 2020.09.27 Web

Psychiatry and Behavioral Sciences

Professor, Chair

Hidehiko Takahashi

Professor

Takayuki OKADA

Associate Professor

Genichiro SUGIHARA

Associate Professor

Takashi TAKEUCHI

Junior Associate Professor

Daisuke JITOKU

Assistant Professor

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Junior Assistant Professor

Nanase KOBAYASHI, Masanori ICHIHASHI

Senior Resident

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Clinical Psychologist

Kazunori MURAKAMI, Yukari WAKAYAMA, Hisahi YAMADA, Ryoko NAKAJIMA, Hikaru TANIGUCHI

Psychiatric Social Worker

Yoshifumi KANEKO, Noriko NUMAGUCHI, Sayaka KOJIMA, Sumiko NOGUCHI

Graduate Students

Shigehiro OGATA, Asami ISHIZUYA, Yoshiko NOMURA, Kou FURUTA, Masaki OHYA, Hironobu NAKAMURA, Marino KAWAMOTO, Kazushige HIRAKAKAWA, Takao KANAI, Hidetoshi KINOSHITA, Yosuke SEKIGUCHI, Ikuko ARAKAWA, Takehiro IBARAKI, Marika OKAMURA, Yoshinori SASAKI, Wataru NAKAGAWA, Rie OMOYA, Noriko YOSHIDA, Nami KONDO, Mayo FUHIWARA, Kanako AMANO, Sayaka OZAKA, Shiho MATSUOKA, Kazuhiro KOSUGI, Mayuko IIJIMA, Kensuke KOMTATSU, Hiroyuki TANAKA, Takahiro KAWATA, Yuka BANDO, Takehiro TAMURA (Diagnostic Radiology and Nuclear Medicine)

(1) Outline

The theme of our research is to investigate the pathogenesis of psychiatric disorders such as schizophrenia, mood disorders, and addiction based on brain science, to develop objective diagnostic methods and novel treatments and establish psychosocial therapeutic approaches based on objective and scientific techniques and evidence. Our investigation focuses on the pathophysiology of psychiatric disorders using functional magnetic resonance imaging, nuclear medicine, and other modalities. We are also performing research to investigate the role of neurofeedback as a therapeutic strategy for mental disorders. Brain imaging studies are the most interesting and well-skilled lesion. Our study involves processing a large volume of brain data using machine learning and computational psychiatry to explore prospects for new discoveries and to predict pathological conditions through modeling. We are exploring neurofeedback as a novel therapeutic approach for psychiatric diseases and the role of artificial intelligence (AI) and computational psychiatry. Moreover, we are actively designing studies that can establish evidence-based approaches to address issues observed in routine clinical practice.

(2) Research

1) Studies in biological psychiatry

(i) Molecular and cellular studies to clarify the etiology and conditions of neuropsychiatric diseases We have performed translational and reverse translational research together with molecular, cellular, and behavioral analyses using animal models and clinical samples of DNA, serum, cerebrospinal fluid, and postmortem brain tissue obtained from patients with psychiatric disorders.

(ii) Study of sleep stages and behavior in neuropsychiatric diseases

Using an automatic analysis device (polysomnography), a study is being performed to investigate sleep stages and behavior in patients with various psychiatric disorders.

(iii) Neuroimaging in psychiatric disorders

We are actively incorporating AI technology in our research on brain structure and function and molecular imaging using magnetic resonance imaging and positron emission tomography to elucidate the pathogenesis of mental disorders, identify subtypes, and predict treatment response.

(iv) We are performing an observational study to retrospectively analyze information regarding electroconvulsive therapy (ECT). These data are submitted as performance reports from multi-institutional “ECT Training Facilities” accredited by the Japanese Society of General Hospital Psychiatry. Despite its long history in psychiatric clinical practice, the actual implementation of ECT in daily clinical practice remains unclear. This study will clarify the status of ECT in real-world Japanese medical facilities.

2) Psychopathological studies

Based on a psychotherapeutic approach, we are performing psychological studies of neuropsychiatric diseases with regard to phenomenology, anthropology, and linguistics. Other research activities include a review of fundamental psychiatric concepts and a basic study to establish a diagnostic classification of psychiatric disorders, which are important issues currently being widely recognized in clinical practice. In addition to studies on endogenous psychosis observed in schizophrenia and bipolar disorder, we are involved in psychoanalytical studies to better understand and develop psychotherapeutic modalities for neurosis and borderline personality disorder, which have gained increasing attention in recent times.

3) Research on liaison psychiatry and psycho-oncology

(i) Liaison psychiatry

In collaboration with dental hospitals, we are involved in research on the prevention of postoperative delirium. We are also performing research on delirium prevention in patients admitted to the physical department. We intend to perform research on perinatal mental health in the future.

(ii) Psycho-oncology

The concept of cancer disease is an important factor in the process by which a child accepts and adapts to cancer in his/her family. Therefore, we are analyzing textbooks used in elementary and junior high schools that could affect the development of the concept of cancer. Based on these data, from the perspective of psycho-oncology, we are attempting to prepare user-friendly home-based educational materials for parents to complement educational material available at school. We will verify the effects of these tools once they are operational.

4) Forensic psychiatry research

Our research includes projects for the development of forensic psychiatric evaluation methodology, risk assessment and management in forensic settings, and an investigation of the associations and mechanisms of criminal behavior. Our research encompasses a wide range of topics including the development of a method to assess the capacity to act for appraisal in the adult guardianship system.

(3) Education

Following the 2-year period of mandatory clinical training, during the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists and will undergo practical training at affiliated medical facilities to qualify as psychiatrists. Undergraduate education, which emphasizes clinical clerkship training after a systematic series of lecture courses and seminar-based classes, is designed to develop students’ problem-solving skills and improve their motivation to learn neuropsychiatry, with support from external facilities.

(4) Lectures & Courses

During the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment, laws and regulations related to clinical practice and will acquire other general knowledge, all of which are essential for a comprehensive understanding of the biopsychosocial approaches to neuropsychiatric diseases.

(5) Clinical Services & Other Works

Clinical practice

Among all new outpatients who visit our department, based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10), approximately 30% are diagnosed with “mood disorders” (F3), 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 from other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance, dependence, and neurosis, necessitating intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. This facility is the psychiatric department of a general hospital and is involved with university education and training; therefore, most inpatients are diagnosed as F2, followed by F4 and F3 categories per ICD-10 codes. We also provide care and treatment for patients with sleep rhythm and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided modified ECT for inpatients and individual and group psychotherapy for patients admitted to our psychiatric ward, clinic, and day care center in close collaboration with rehabilitation facilities in the community. The day care team consists of a physician and two nurses, as well as a psychosocial worker or clinical psychologist. Day care (partial hospitalization) is a transitional element between inpatient and outpatient care and is indicated in a wide range of psychiatric disorders, such as schizophrenia, depression, bipolar disorder, adjustment disorder, and personality disorders.

Each member has its own aim, and the team provides care utilizing different types of frameworks. Our day care team places emphasis on the potentiality of the group and in our opinion, the collective efforts of the group could contribute to the therapeutic effect. This experience promotes good communication skills in patients and readaptation to social situations and social reintegration become easier.

(6) Clinical Performances

Per our policy, patients with schizophrenia are treated with clozapine, which is approved for the treatment of refractory schizophrenia. Following effective coordination with the Dental Hospital, we currently treat patients with oral pain or dysesthesia; this collaboration is a characteristic of our university. Our faculty includes board-certified specialists to treat patients who present with sleep disorders and epilepsy. In 2014, we introduced a psychoeducational program for patients with bipolar disorder, which focuses on relapse prevention. Additionally, we ensure close cooperation with the staff for an increasing number of liaison activities implemented for delirium prevention (particularly in surgical wards), interventions for patients with suicide attempts in the emergency room, and mental support for peripartum patients.

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

1. Sasaki Y, Yagihashi T, Kasahara M, Usami M, Kono T, Okada T. Clinical implications of a history of stealing on psychiatric disorders in children and adolescents. *PloS one*. 2020; 15(8); e0237906
2. Koizumi A, Hori T, Maniscalco B, Hayase M, Mishima R, Kawashima T, Miyata J, Aso T, Lau H, Takahashi H, Amano K. Atypical spatial frequency dependence of visual metacognition among schizophrenia patients. *NeuroImage. Clinical*. 2020; 27; 102296
3. Fujii K, Yoshihara Y, Matsumoto Y, Tose K, Takeuchi H, Isobe M, Mizuta H, Maniwa D, Okamura T, Murai T, Kawahara Y, Takahashi H. Cognition and interpersonal coordination of patients with schizophrenia who have sports habits. *PloS one*. 2020; 15(11); e0241863

4. Takagi Shunsuke, Yamashiro Yoshihiro, Sugihara Genichi, Takahashi Hidehiko, Matsuura Masato. Very early-onset of RBD with ADHD: a case report study NEUROCASE. 2020.01; 26(1); 60-63
5. Kosuke Tsurumi, Toshihiko Aso, Ryosaku Kawada, Toshiya Murai, Hidehiko Takahashi. A positive shift in resting-state functional connectivity between the insula and default mode network regions reflects the duration of illness in gambling disorder patients without lifetime substance abuse PSYCHIATRY RESEARCH-NEUROIMAGING. 2020.01; 295; 111018
6. Tei S, Kauppi JP, Jankowski KF, Fujino J, Monti RP, Tohka J, Abe N, Murai T, Takahashi H, Hari R. Brain and behavioral alterations in subjects with social anxiety dominated by empathic embarrassment. Proceedings of the National Academy of Sciences of the United States of America. 2020.02; 117(8); 4385-4391
7. Ichikawa N, Lisi G, Yahata N, Okada G, Takamura M, Hashimoto RI, Yamada T, Yamada M, Suhara T, Moriguchi S, Mimura M, Yoshihara Y, Takahashi H, Kasai K, Kato N, Yamawaki S, Seymour B, Kawato M, Morimoto J, Okamoto Y. Primary functional brain connections associated with melancholic major depressive disorder and modulation by antidepressants. Scientific reports. 2020.02; 10(1); 3542
8. Takeuchi Takashi, Okumura Yasuyuki, Ichikura Kanako. Alcohol Consumption or Excessive Use of Psychotropic Medication Prior to Suicidal Self-injury in Patients with Adjustment Disorder, Depression, and Schizophrenia: A Cross-sectional Study(和訳中) Acta Medica Okayama. 2020.02; 74(1); 49-52
9. Sugihara G, Takei N. Obsolete medical law in Japan harms doctors' health. Lancet (London, England). 2020.04; 395(10230); 1113
10. Tachibana Masumi, Hashimoto Tasuku, Tanaka Mami, Watanabe Hiroyuki, Sato Yasunori, Takeuchi Takashi, Terao Takeshi, Kimura Shou, Koyama Akio, Ebisawa Sachie, Shizu Yuichiro, Nagase Teruyoshi, Hirakawa Junichi, Hatta Kotaro, Nakazato Michiko, Iyo Masaomi. Patterns in Psychiatrists' Prescription of Valproate for Female Patients of Childbearing Age With Bipolar Disorder in Japan: A Questionnaire Survey FRONTIERS IN PSYCHIATRY. 2020.04; 11; 250
11. Aso T, Sugihara G, Murai T, Ubukata S, Urayama SI, Ueno T, Fujimoto G, Thuy DHD, Fukuyama H, Ueda K. A venous mechanism of ventriculomegaly shared between traumatic brain injury and normal ageing. Brain : a journal of neurology. 2020.05;
12. Nakagami Y, Sugihara G, Nakashima N, Hazama M, Son S, Ma S, Matsumoto R, Murai T, Ikeda A, Murakami K. Anti-PDHA1 antibody is detected in a subset of patients with schizophrenia. Scientific reports. 2020.05; 10(1); 7906
13. Takagi Shunsuke, Puhl Matthew D., Anderson Thea, Balu DarrickT, Coyle Joseph T.. Serine Racemase Expression by Striatal Neurons CELLULAR AND MOLECULAR NEUROBIOLOGY. 2020.05;
14. Takashi Itahashi, Junya Fujino, Ryu-Ichiro Hashimoto, Yoshiyuki Tachibana, Taku Sato, Haruhisa Ohta, Motoaki Nakamura, Nobumasa Kato, Simon B Eickhoff, Samuele Cortese, Yuta Y Aoki. Transdiagnostic subtyping of males with developmental disorders using cortical characteristics. Neuroimage Clin. 2020.05; 27; 102288
15. Shiwaku H, Fujita M, Takahashi H. Benzodiazepines Reduce Relapse and Recurrence Rates in Patients with Psychotic Depression. Journal of clinical medicine. 2020.06; 9(6);
16. Yamakawa Toshitaka, Miyajima Miho, Fujiwara Koichi, Kano Manabu, Suzuki Yoko, Watanabe Yutaka, Watanabe Satsuki, Hoshida Tohru, Inaji Motoki, Maehara Taketoshi. Wearable Epileptic Seizure Prediction System with Machine-Learning-Based Anomaly Detection of Heart Rate Variability SENSORS. 2020.07; 20(14);
17. Tamura T, Sugihara G, Takahashi H. Memory Impairment and Hippocampal Volume after Carbon Monoxide Poisoning. Archives of clinical neuropsychology : the official journal of the National Academy of Neuropsychologists. 2020.08;
18. Yoshihara Yujiro, Lisi Giuseppe, Yahata Noriaki, Fujino Junya, Matsumoto Yukiko, Miyata Jun, Sugihara Gen-ichi, Urayama Shin-ichi, Kubota Manabu, Yamashita Masahiro, Hashimoto Ryuichiro, Ichikawa Naho, Cahn Weipke, van Haren Neeltje E. M., Mori Susumu, Okamoto Yasumasa, Kasai Kiyoto, Kato Nobumasa, Imamizu Hiroshi, Kahn Rene S., Sawa Akira, Kawato Mitsuo, Murai Toshiya, Morimoto Jun, Takahashi Hidehiko. Overlapping but Asymmetrical Relationships Between Schizophrenia and Autism Revealed by Brain Connectivity SCHIZOPHRENIA BULLETIN. 2020.09; 46(5); 1210-1218

19. Aso T, Sugihara G, Murai T, Ubukata S, Urayama SI, Ueno T, Fujimoto G, Thuy DHD, Fukuyama H, Ueda K. Reply: A transvenous pressure gradient mechanism behind ventriculomegaly. *Brain : a journal of neurology*. 2020.09; 143(9); e75
20. Omoya Rie, Miyajima Miho, Ohta Katsuya, Suzuki Yoko, Aoki Ai, Fujiwara Mayo, Watanabe Takafumi, Yoshida Noriko, Suwa Hiroshi, Kawara Tokuhiko, Takahashi Hidehiko, Matsushima Eisuke, Takeuchi Takashi. Heart rate response to orthostatic challenge in patients with dementia with Lewy bodies and Alzheimer's disease *PSYCHOGERIATRICS*. 2020.10;
21. Yamasaki S, Aso T, Miyata J, Sugihara G, Hazama M, Nemoto K, Yoshihara Y, Matsumoto Y, Okada T, Togashi K, Murai T, Takahashi H, Suwa T. Early and late effects of electroconvulsive therapy associated with different temporal lobe structures. *Translational psychiatry*. 2020.10; 10(1); 344
22. Ichikawa N, Lisi G, Yahata N, Okada G, Takamura M, Hashimoto RI, Yamada T, Yamada M, Suhara T, Moriguchi S, Mimura M, Yoshihara Y, Takahashi H, Kasai K, Kato N, Yamawaki S, Seymour B, Kawato M, Morimoto J, Okamoto Y. Publisher Correction: Primary functional brain connections associated with melancholic major depressive disorder and modulation by antidepressants. *Scientific reports*. 2020.10; 10(1); 17650
23. Haruhisa Ohta, Yuta Y Aoki, Takashi Itahashi, Chieko Kanai, Junya Fujino, Motoaki Nakamura, Nobumasa Kato, Ryu-Ichiro Hashimoto. White matter alterations in autism spectrum disorder and attention-deficit/hyperactivity disorder in relation to sensory profile. *Mol Autism*. 2020.10; 11(1); 77
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25. Shiwaku H, Doi S, Miyajima M, Matsumoto Y, Fujino J, Hirai N, Jitoku D, Takagi S, Tamura T, Maruo T, Shidei Y, Kobayashi N, Ichihashi M, Noguchi S, Oohashi K, Takeuchi T, Sugihara G, Okada T, Fujiwara T, Takahashi H. Novel brief screening scale, Tokyo Metropolitan Distress Scale for Pandemic (TMDP), for assessing mental and social stress of medical personnel in COVID-19 pandemic. *Psychiatry and clinical neurosciences*. 2020.11;
26. Kubota M, Fujino J, Tei S, Takahata K, Matsuoka K, Tagai K, Sano Y, Yamamoto Y, Shimada H, Takado Y, Seki C, Itahashi T, Aoki YY, Ohta H, Hashimoto RI, Zhang MR, Suhara T, Nakamura M, Takahashi H, Kato N, Higuchi M. Binding of Dopamine D1 Receptor and Noradrenaline Transporter in Individuals with Autism Spectrum Disorder: A PET Study. *Cerebral cortex (New York, N.Y. : 1991)*. 2020.11; 30(12); 6458-6468
27. Takeuchi H, Tsurumi K, Murao T, Mizuta H, Kawada R, Murai T, Takahashi H. Framing effects on financial and health problems in gambling disorder. *Addictive behaviors*. 2020.11; 110; 106502
28. Takashi Itahashi, Junya Fujino, Taku Sato, Haruhisa Ohta, Motoaki Nakamura, Nobumasa Kato, Ryu-Ichiro Hashimoto, Adriana Di Martino, Yuta Y Aoki. Neural correlates of shared sensory symptoms in autism and attention-deficit/hyperactivity disorder. *Brain Commun*. 2020.11; 2(2); fcaa186
29. Yamashita A, Sakai Y, Yamada T, Yahata N, Kunimatsu A, Okada N, Itahashi T, Hashimoto R, Mizuta H, Ichikawa N, Takamura M, Okada G, Yamagata H, Harada K, Matsuo K, Tanaka SC, Kawato M, Kasai K, Kato N, Takahashi H, Okamoto Y, Yamashita O, Imamizu H. Generalizable brain network markers of major depressive disorder across multiple imaging sites. *PLoS biology*. 2020.12; 18(12); e3000966

[Books etc]

1. Takayuki Okada, Alan Felthous (Editor), Henning Sass (Editor). *The Wiley International Handbook on Psychopathic Disorders and the Law*, 2nd Edition. 2020 (ISBN : 978-1-119-15928-5)
2. Kanako Ichikura, Takashi Takeuchi. *Guidebook for healthcare of Gynecologic cancer survivors*. 2020.04 (ISBN : 978-4-7878-2425-7)

[Conference Activities & Talks]

1. Motoaki Nakamura, Junya Fujino, Takashi Itahashi, Yuta Aoki, Haruhisa Ohta, Ryu-ichiro Hashimoto, Nobumasa Kato. Navigation-Guided Repetitive Transcranial Magnetic Stimulation (rTMS) over Ventral Attention Network of Neurodevelopmental Disorders. *INSAR 2020 Annual Meeting* 2020.06

[Awards & Honors]

1. The Japanese Association of Criminology Award, The Japanese Association of Criminology, 2020.11

Neurosurgery

Professor: Taketoshi Maehara

Associate Professor: Tadashi Nariai

Assistant Professors: Yoji Tanaka and Motoki Inaji

Hospital staffs:

Takashi Sugawara, Kaoru Tamura, Jun Karakama, Shoko Hara and Satoka Hashimoto

Graduate Students: Yasuhiro Ueda, Kenji Yamada, Masataka Yoshimura,

Jiro Aoyama, Tomoyuki Nakano, Motoshige Yamashina, Asumi Orihara, Satoru Takahashi,

Yusuke Ebiko and Daisu Abe

(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. Hasegawa Mitsuhiro, Hatayama Toru, Kondo Akinori, Nagahiro Shinji, Fujimaki Takamitsu, Amagasaki Kenichi, Arita Kazunori, Date Isao, Fujii Yukihiko, Goto Takeo, Hanaya Ryosuke, Higuchi Yoshinori, Hongo Kazuhiro, Inoue Toru, Kasuya Hidetoshi, Kayama Takamasa, Kawashima Masatou, Kohmura Eiji, Maehara Taketoshi, Matsushima Toshio, Mizobuchi Yoshihumi, Morita Akio, Nishizawa Shigeru, Noro Shusaku, Saito Shinjiro, Shimano Hirofumi, Shirane Reizo, Takeshima Hideo, Tanaka Yuichiro, Tanabe Hidenori, Toda Hiroki, Yamakami Iwao, Nishiyama Yuya, Ohba Shigeo, Hirose Yuichi, Suzuki Takeya. Prosthesis Used in Microvascular Decompressions: A Multicenter Survey in Japan Focusing on Adverse Events (vol 130, pg e251, 2019) WORLD NEUROSURGERY. 2020.02; 134; 685
2. Shimizu K, Hara S, Hori M, Tanaka Y, Maehara T, Aoki S, Tazawa T, Nariai T. Transient Global Amnesia: A Diffusion and Perfusion MRI study. *Journal of neuroimaging : official journal of the American Society of Neuroimaging.* 2020.06;
3. Egawa M, Hara K, Ikeda M, Kono E, Miyashita S, Miyasaka N, Inaji M, Maehara T, Yoshida M. Role of obstetricians in promoting pregnancy-related knowledge among women with epilepsy in Japan. *Epilepsy & behavior : E&B.* 2020.06; 111; 107176
4. Hara S, Kudo T, Hayashi S, Inaji M, Tanaka Y, Maehara T, Ishii K, Nariai T. Improvement in cognitive decline after indirect bypass surgery in adult moyamoya disease: implication of ^{15}O -gas positron emission tomography. *Annals of nuclear medicine.* 2020.07; 34(7); 467-475
5. Yamakawa Toshitaka, Miyajima Miho, Fujiwara Koichi, Kano Manabu, Suzuki Yoko, Watanabe Yutaka, Watanabe Satsuki, Hoshida Tohru, Inaji Motoki, Maehara Taketoshi. Wearable Epileptic Seizure Prediction System with Machine-Learning-Based Anomaly Detection of Heart Rate Variability *SENSORS.* 2020.07; 20(14);
6. Hara Shoko, Kudo Takumi, Hayashi Shihori, Inaji Motoki, Tanaka Yoji, Maehara Taketoshi, Ishii Kenji, Nariai Tadashi. Improvement in cognitive decline after indirect bypass surgery in adult moyamoya disease: implication of ^{15}O -gas positron emission tomography(和訳中) *Annals of Nuclear Medicine.* 2020.07; 34(7); 467-475
7. Hara S, Shimizu K, Nariai T, Kishino M, Kudo T, Umemoto T, Inaji M, Maehara T. De Novo Renal Artery Stenosis Developed in Initially Normal Renal Arteries during the Long-Term Follow-Up of Patients with Moyamoya Disease. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association.* 2020.08; 29(8); 104786
8. Aoyama J, Nariai T, Moriyama K, Hara S, Mukawa M, Inaji M, Tanaka Y, Miyasaka N, Taketoshi Maehara. Clinical characteristics of the pregnancies and deliveries of patients with moyamoya disease: A single-center analysis over three decades. *International journal of stroke : official journal of the International Stroke Society.* 2020.10; 1747493020963806
9. Takahashi Satoshi, Takahashi Masamichi, Kinoshita Manabu, Miyake Mototaka, Kawaguchi Risa, Shinojima Naoki, Mukasa Akitake, Saito Kuniaki, Nagane Motoo, Otani Ryohei, Ueki Keisuke, Tanaka Shota, Hata Nobuhiro, Nishikawa Ryo, Arita Hideyuki, Nonaka Masahiro, Tamura Kaoru, Tateishi Kensuke, Uda Takehiro, Fukai Junya, Okita Yoshiko, Tsuyuguchi Naohiro, Kanemura Yonehiro, Kobayashi

- Kazuma, Sese Jun, Ichimura Kouichi, Narita Yoshitaka, Hamamoto Ryuji. DEVELOPING AUTOMATIC SEGMENTATION METHOD FOR BRAIN TUMOR MR IMAGES THAT CAN BE USED AT MULTIPLE FACILITIES NEURO-ONCOLOGY. 2020.11; 22; 153-154
10. Orihara Asumi, Hara Keiko, Hara Shoko, Shimizu Kazuhide, Inaji Motoki, Hashimoto Satoka, Maehara Taketoshi. Effects of sevoflurane anesthesia on intraoperative high-frequency oscillations in patients with temporal lobe epilepsy SEIZURE-EUROPEAN JOURNAL OF EPILEPSY. 2020.11; 82; 44-49
 11. Sano Takashi, Tamura Kaoru, Kuroha Masae, Sumita Kazutaka, Arai Yukika, Sugawara Takashi, Inaji Motoki, Tanaka Yoji, Nariai Tadashi, Maehara Taketoshi. ANALYSIS OF BRAIN TUMOR INDUCED BY IRRADIATION IN CHILDHOOD - A SINGLE INSTITUTIONAL ANALYSIS NEURO-ONCOLOGY. 2020.12; 22; 458-459
 12. Takami Hirokazu, Elzawahry Asmaa, Kato Mamoru, Fukuoka Kohei, Mamatjan Yasin, Suzuki Tomonari, Yanagisawa Takaaki, Matsushita Yuko, Nakamura Taishi, Yamasaki Kai, Mukasa Akitake, Saito Nobuhito, Kanamori Masayuki, Kumabe Toshihiro, Tominaga Teiji, Kobayashi Keiichi, Nagane Motoo, Iuchi Toshihiko, Tamura Kaoru, Maehara Taketoshi, Sugiyama Kazuhiko, Nakada Mitsutoshi, Kanemura Yonehiro, Nonaka Masahiro, Asai Akio, Yokogami Kiyotaka, Takeshima Hideo, Narita Yoshitaka, Shibui Soichiro, Nakazato Yoichi, Totoki Yasushi, Shibata Tatsuihiro, Nishikawa Ryo, Matsutani Masao, Ichimura Koichi. TRANSCRIPTOME OF CENTRAL NERVOUS SYSTEM GERM CELL TUMOR REVEALS ITS PATHOGENESIS AND CONTRASTS WITH TESTICULAR COUNTERPARTS IN INTEGRATED OMICS ANALYSIS NEURO-ONCOLOGY. 2020.12; 22; 338-339
 13. Kuroha Masae, Tamura Kaoru, Inaji Motoki, Hashimoto Satoka, Kobayashi Daisuke, Tanaka Yoji, Nariai Tadashi, Maehara Taketoshi. TWO CASES OF H3 K27M-MUTANT DIFFUSE MIDLINE GLIOMA OF CERVICAL SPINAL CORD NEURO-ONCOLOGY. 2020.12; 22; 353
 14. Satomi Kaishi, Takami Hirokazu, Fukushima Shintaro, Nakazato Yoichi, Tanaka Shota, Saito Nobuhito, Kanamori Masayuki, Kumabe Toshihiro, Kobayashi Keiichi, Nagane Motoo, Iuchi Toshihiko, Yoshimoto Koji, Mizoguchi Masahiro, Tamura Kaoru, Maehara Taketoshi, Sakai Keiichi, Sugiyama Kazuhiko, Yokogami Kiyotaka, Takeshima Hideo, Nonaka Masahiro, Asai Akio, Nishikawa Ryo, Matsutani Masao, Ichimura Koichi. GAIN OF SHORT ARM OF CHROMOSOME 12 IS A MOLECULAR MARKER TO PREDICT PROGNOSIS AND REPRESENTS AN EARLY EVENT IN TUMORIGENESIS IN INTRACRANIAL GERM CELL TUMORS NEURO-ONCOLOGY. 2020.12; 22; 336
 15. Arita Hideyuki, Matsushita Yuko, Machida Ryunosuke, Yamasaki Kai, Hata Nobuhiro, Ohno Makoto, Yamaguchi Shigeru, Sasayama Takashi, Tanaka Shota, Higuchi Fumi, Iuchi Toshihiko, Saito Kuniaki, Kanamori Masayuki, Matsuda Ken-ichiro, Miyake Yohei, Tamura Kaoru, Tamai Sho, Nakamura Taishi, Uda Takehiro, Okita Yoshiko, Fukai Junya, Sakamoto Daisuke, Hattori Yasuhiko, Pareira Eriel Sandika, Hatae Ryusuke, Ishi Yukitomo, Miyakita Yasuji, Tanaka Kazuhiro, Takayanagi Shunsaku, Otani Ryohei, Sakaida Tsukasa, Kobayashi Keiichi, Saito Ryuta, Kurozumi Kazuhiko, Shofuda Tomoko, Nonaka Masahiro, Suzuki Hiroyoshi, Shibuya Makoto, Komori Takashi, Sasaki Hikaru, Mizoguchi Masahiro, Kishima Haruhiko, Nakada Mitsutoshi, Sonoda Yukihiko, Tominaga Teiji, Nagane Motoo, Nishikawa Ryo, Kanemura Yonehiro, Kuchiba Aya, Narita Yoshitaka, Ichimura Koichi. TERT promoter mutation confers favorable prognosis regardless of 1p/19q status in adult diffuse gliomas with IDH1/2 mutations ACTA NEUROPATHOLOGICA COMMUNICATIONS. 2020.12; 8(1); 201
 16. Satomi Kaishi, Takami Hirokazu, Fukushima Shintaro, Nakazato Yoichi, Tanaka Shota, Saito Nobuhito, Kanamori Masayuki, Kumabe Toshihiro, Kobayashi Keiichi, Nagane Motoo, Iuchi Toshihiko, Yoshimoto Koji, Mizoguchi Masahiro, Tamura Kaoru, Maehara Taketoshi, Sakai Keiichi, Sugiyama Kazuhiko, Yokogami Kiyotaka, Takeshima Hideo, Nonaka Masahiro, Asai Akio, Nishikawa Ryo, Matsutani Masao, Ichimura Koichi. GAIN OF SHORT ARM OF CHROMOSOME 12 IS A MOLECULAR MARKER TO PREDICT PROGNOSIS AND REPRESENTS AN EARLY EVENT IN TUMORIGENESIS IN INTRACRANIAL GERM CELL TUMORS NEURO-ONCOLOGY. 2020.12; 22; 336
 17. Takami Hirokazu, Elzawahry Asmaa, Kato Mamoru, Fukuoka Kohei, Mamatjan Yasin, Suzuki Tomonari, Yanagisawa Takaaki, Matsushita Yuko, Nakamura Taishi, Yamasaki Kai, Mukasa Akitake, Saito Nobuhito, Kanamori Masayuki, Kumabe Toshihiro, Tominaga Teiji, Kobayashi Keiichi, Nagane Motoo, Iuchi Toshihiko, Tamura Kaoru, Maehara Taketoshi, Sugiyama Kazuhiko, Nakada Mitsutoshi, Kanemura Yonehiro, Nonaka Masahiro, Asai Akio, Yokogami Kiyotaka, Takeshima Hideo, Narita Yoshitaka, Shibui Soichiro, Nakazato Yoichi, Totoki Yasushi, Shibata Tatsuihiro, Nishikawa Ryo, Matsutani Masao, Ichimura

Koichi. TRANSCRIPTOME OF CENTRAL NERVOUS SYSTEM GERM CELL TUMOR REVEALS ITS PATHOGENESIS AND CONTRASTS WITH TESTICULAR COUNTERPARTS IN INTEGRATED OMICS ANALYSIS NEURO-ONCOLOGY. 2020.12; 22; 338-339

18. Sano Takashi, Tamura Kaoru, Kuroha Masae, Sumita Kazutaka, Arai Yukika, Sugawara Takashi, Inaji Motoki, Tanaka Yoji, Nariai Tadashi, Maehara Taketoshi. ANALYSIS OF BRAIN TUMOR INDUCED BY IRRADIATION IN CHILDHOOD - A SINGLE INSTITUTIONAL ANALYSIS NEURO-ONCOLOGY. 2020.12; 22; 458-459
19. Kuroha Masae, Tamura Kaoru, Inaji Motoki, Hashimoto Satoka, Kobayashi Daisuke, Tanaka Yoji, Nariai Tadashi, Maehara Taketoshi. TWO CASES OF H3 K27M-MUTANT DIFFUSE MIDLINE GLIOMA OF CERVICAL SPINAL CORD NEURO-ONCOLOGY. 2020.12; 22; 353
20. 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. Takashi Sugawara, Yoji Tanaka, Taketoshi Maehara. Treatment strategy and clinical outcome of cavernous sinus lesion. North America Skull Base Society 30th annual meeting 2020.02.07 San Antonio, TX, USA

Endovascular Surgery

Professor Shigeru Nemoto
Professor Kazutaka Sumita
Assistant Professor Kazunori Miki, Kyohei Fujita
Clinical Fellow Shoko Fujii, Yuki Aizawa, Hiroto Yamaoka
Secretary 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

[Conference Activities & Talks]

1. Significance of P2Y₁₂ reaction unit to predict the perioperative complications of endovascular treatment.
2020.11.19

NCNP Brain Physiology and Pathology

1. Staffs

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Takashi HANAKAWA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Professor	Yoshitsugu AOKI
Collaborative Associate Professor	Yuichi YAMASHITA

(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 published papers on molecular machinery for delamination of newborn neurons (Science Advances 2020), synapse formation in the cerebral cortex (iScience, 2020a) and the cerebellum (iScience, 2020b), and identification of new epilepsy-related gene (Acta Neuropathol Commun, 2020).

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. Since 2013, we investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and diseases with cortical and white matter dysplasia. We detected pathogenic mutations in NFIX gene in Malan syndrome (Tabata K, et al. J Neurol Sci. 2020), and studied a molecule that improve the activity of cytochrome c oxidase in the patient-derived fibroblasts (Nagao T, et al. FASEB J. 2020).

3) 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 2020, we discovered the neural substrates underlying the “grit” (Hosoda et al. *Commun Biol* 2020). We contributed to the technical understanding of neural mechanisms of transcranial direct current stimulation (Tanaka et al. *Front Neurosci* 2020) and to comparing brain connectivity measures proposed for magnetoencephalography (Yoshinaga et al. *Front Neurosci* 2020).

4) Autism research using a primate model marmoset

(Noritaka Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, NCNP)

Autism is a neurodevelopmental disorder that begins before birth. There have been numerous reports in recent years that early treatment is effective in autism. In order to devise strategies for this early treatment, knowledge of the early biological abnormalities of autistic individuals is necessary, but this knowledge is currently scarce because autism is not diagnosed until childhood. Therefore, we examined developmental changes in synapses and gene expression in model marmosets during neonatal, childhood, and adolescence. The results showed that abnormalities in synapses and gene expression during the neonatal period were considerably different from those during the post-childhood period. The dysregulated genes were enriched by genes involved in synapse formation. This result is consistent with the synaptic underdevelopment revealed by synaptic analysis in this model marmoset. In addition, abnormal expression of synaptic plasticity and abnormalities in critical period-related genes were observed in the model marmosets during childhood, suggesting the existence of abnormalities in neural circuit formation. In addition, synapses in adolescence are overproduced, which is consistent with findings in human autism. The abnormalities in gene expression were very similar to those in human autism, indicating the usefulness of this model marmoset for translational research. These results indicate

that different treatment strategies are needed in infancy and childhood than in adults, and that the abnormally expressed genes found in this study may provide seeds for the treatment of autism in early development.

5) Development of state-of-the-art genetic therapies for neuromuscular diseases

(Yoshitsugu Aoki, Department of Molecular Therapy, National, National Institute of Neuroscience, NCNP)

Our research group integrates molecular, pharmacologic, proteomic, and genomic methodologies to clarify the molecular mechanisms of disease pathogenesis and develop novel genetic or stem cell-based therapies for the diseases. Primarily, our research focuses on novel genetic therapies targeting messenger RNA and DNA. We also investigate RNA interference-based and genome editing therapies for several neuromuscular disorders. We have successfully shown the proof of concept of exon skipping in our unique animal models, such as canine X-linked muscular dystrophy in Japan and mdx52 mice with an exon 52 deletion of the Dmd gene. Recently, we have successfully developed an exon 53-skipping drug (viltolarsen: NS-065/NCNP-01) in collaboration with a Japanese pharmaceutical company (conditional approval in Japan and the US FDA). Additionally, our department has drawn on research worldwide to create a picture of the current state of urine-derived stem cells and induced pluripotent stem cell (iPSC) research in this area. Furthermore, to elucidate the complex molecular mechanisms of muscular dystrophy, we focus on the functional analysis of intracellular calcium regulation and mechanosensing in muscle cells, entailing several promising discoveries and offering hope to patients afflicted with the potentially life-limiting condition of DMD.

6) Computational approach for psychiatric disorders

(Yuchi Yamashita, Department of Information Medicine, National, National Institute of Neuroscience, NCNP)

Computational approach for psychiatric disorders, referred to as “Computational psychiatry (CPSY)”, is a new research field which seeks to understand mental disorders as aberrant computation by using mathematical modeling of information processing in the brain. Our laboratory conducted series of experiments in which behavioral control mechanisms with hierarchical predictive process were implemented by the physical actions of a humanoid robot driven by a hierarchical recurrent neural network. These experimental results provided a mechanistic explanation that unifies the various levels of observations in ASD, including behavioral level (hyper-sensitivity, motor clumsiness,

reduced generalization, and cognitive inflexibility), neurophysiological level (altered E/I balance, over-developed synapses) and computational level (hyper precision in predictive processing) (Idei et al. *Front Psych*, 2020). In addition, we proposed a novel interpretation of action selection via free energy principle (FEP), by introducing a computational component referred to as the 'retrospective (or residual) surprise' (Katahira et al. *J. Math Psych*, 2020). Finally, in order to promote research in the area of CPSY, we developed a new database for visualizing CPSY papers from the aspects of neuroscience, psychiatry, and computational methods: Computational Psychiatry Research Map (CPSYMAP): (Kato et al. *Front Psych*, 2020).

(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. Yamashiro K, Hori K, Esther L, Aoki R, Shimaoka K, Arimura N, Egusa SF, Sakamoto A, Abe M, Sakimura K, Watanabe T, Uesaka N, Kano M, Hoshino M: AUTS2 governs cerebellar development Purkinje cell maturation, motor function and social communication. *iScience*, 23(12), 101820, 2020b
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3. Hiraga K, Inoue YU, Asami J, Hotta M, Morimoto Y, Tatsumoto S, Hoshino M, Go Y, * Inoue T: Redundant type II cadherins define neuroepithelial cell states for cytoarchitectonic robustness. *Commun Biol*, 3(1), 574, 2020
4. Yamashita M, Owa T, Shiraishi R, Adachi T, Ichijo K, Taya S, Miyashita S, Hoshino M: The role of SCFSkp2 and SCF β -TrCP1/2 in the cerebellar granule cell precursors. *Genes Cells*, 25(12):796-810, 2020
5. Kutscher LM, Okonechnikov K, Batora NV, Clark J, Silva PBG, Vouri M, van Rijn S, Sieber L, Statz B, Gearhart MD, Shiraishi R, Mack N, Orr BA, Korshunov A, Gudenbas BL, Smith KS, Mercier AL, Ayrault O, Hoshino M, Kool M, von Hoff K, Graf N, Fleischhack G, Bardwell VJ, Pfister SM, Northcott PA, Kawauchi D: Functional loss of a noncanonical BCOR-PRC1.1 complex accelerates SHH-driven medulloblastoma formation. *Genes Dev*, 34(17-18), 1161-1176. 2020
6. Arimura N, Okada M, Taya S, Dewa KI, Tsuzuki A, Uetake H, Miyashita S, Hashizume K,

- Shimaoka K, Egusa S, Nishioka T, Yanagawa Y, Yamakawa K, Inoue YU, Inoue T, Kaibuchi K, Hoshino M: DSCAM regulates delamination of neurons in the developing midbrain. *Science Advances*, 6(36), eaba1693. 2020
7. Hori K, Yamashiro K, Nagai T, Shan W, Egusa SF, Shimaoka K, Kuniishi H, Sekiguchi M, Go Y, Tatsumoto S, Yamada M, Shiraishi R, Kanno K, Miyashita S, Sakamoto A, Abe M, Sakimura K, Sone M, Sohya K, Kunugi H, Wada K, Yamada M, Yamada K, Hoshino M: AUTS2 Regulation of Synapses for Proper Synaptic Inputs and Social Communication. *iScience*, 23(6), 101183. 2020a
 8. Nagao T, Shintani Y, Hayashi T, Koika H, Kato H, Nishida Y, Yamazaki S, Tsukamoto O, Yashirogi S, Yazawa I, Asano Y, Shinzawa-Itoh K, Imamura H, Suzuki T, Goto Y, Takashima S. Higd1a improves respiratory function in the modes of mitochondrial disorder. *FASEB J*, 34:1859-1871, 2020
 9. Tabata K, Iida A, Takeshita E, Nakagawa E, Sato N, Sasaki M, Inoue K, Goto Y. A novel pathogenic *NFIX* variant in a Malan syndrome patient associated with hindbrain overcrowding. *J Neurolo Sci*, 412:116758, 2020
 10. Yokota Y, Hara M, Akimoto T, Mizoguchi T, Goto Y, Nishino I, Kamei S, Nakajima H. Late-onset MELAS syndrome with mtDNA 14453G→A mutation masquerading as an acute encephalitis: a case report *BMC Neurol*, 20:247, 2020
 11. Tanaka T, Isomura Y, Kobayashi K, Hanakawa T, Tanaka S, Honda M: Electrophysiological effects of transcranial direct current stimulation on neural activity in the rat cortex. *Front Neurosci* 14:495, 2020.
 12. Yoshinaga K, Matsushashi M, Mima T, Fukuyama H, Takahshi R, Hanakawa T, Ikeda A: Comparison of different phase synchronization measures for identifying event-related functional connectivity in human magnetoencephalographic and simulated data. *Front Neurosci* 14:648, 2020.
 13. Hosoda C, Tsujimoto S, Tatekawa M, Honda M, Osu R, Hanakawa T: Plastic frontal pole cortex structure related to individual persistence for goal achievement. *Commun Biol* 3, 194, 2020.
 14. Ohki T, Matsuda T, Gunji A, Takei Y, Sakuma R, Kaneko Y, Inagaki M, Hanakawa T, Ueda K, Fukuda M, Hiraki K: Timing of phase-amplitude coupling is essential for neuronal and functional maturation in adolescents. *Brain Behav* e01635, 2020.
 15. Honda T, Mitoma H, Yoshida H, Bando K, Terashi H, Taguchi T, Miyata Y, S, Hanakawa T, Aizawa H, Kondo T, Mizusawa H, Manto M, Kakei S: Assessment and rating of motor cerebellar ataxias with Kinect v2 depth sensor: Extending our appraisal. *Front Neurol* 11:179, 2020.
 16. Kurashige H, Yamashita Y, Osu R, Otaka Y, Hanakawa T, Honda M, Kawabata H: Revealing relationship among cognitive functions using functional connectivity and large-scale meta-analysis database. *Front Human Neurosci* 13:457, 2020.
 17. Tsoumpra MK, Sawatsubashi S, Imamura M, Fukumoto S, Takeda S, Matsumoto T, Aoki Y: Dystrobrevin alpha gene is a direct target of the vitamin D receptor in muscle. *J Mol Endocrinol*. 2020 Apr;64(3):195-208.
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21. van Westering TLE, Johansson HJ, Hanson B, Coenen-Stass AML, Lomonosova Y, Tanihata J, Motohashi N, Yokota T, Takeda S, Lehtiö J, Wood MJA, El Andaloussi S, Aoki Y, Roberts TC: Mutation-independent Proteomic Signatures of Pathological Progression in Murine Models of Duchenne Muscular Dystrophy. *Mol Cell Proteomics*. 2020 Dec;19(12):2047-2068.
22. Nakada S, Yamashita Y, Machida S, Miyagoe-Suzuki Y, Arikawa-Hirasawa E: Perlecan facilitates neuronal nitric oxide synthase delocalization in denervation-induced muscle atrophy. *Cells*. 2020 Nov 23;9(11):2524.
23. Matsuzaka Y, Tanihata J, Ooshima Y, Yamada D, Sekiguchi M, Miyatake S, Aoki Y, Terumitsu M, Yashiro R, Komaki H, Ishiyama A, Oya Y, Inoue YU, Inoue T, Takeda S, Hashido K: The nSMase2/Smpd3 gene modulates the severity of muscular dystrophy and the emotional stress response in mdx mice. *BMC Med*. 2020 Nov 19;18(1):343.
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26. Takizawa H, Takeshita E, Sato M, Shimizu-Motohashi Y, Ishiyama A, Mori-Yoshimura M, Takahashi Y, Komaki H, Aoki Y: Highly sensitive screening of antisense sequences for different types of DMD mutations in patients' urine-derived cells. *J Neurol Sci*. 2021 Feb 15;423:117337.
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[Review Articles • Books]

1. Sathyaprakash C, Manzano R, Varela MA, Hashimoto Y, Wood MJA, Talbot K, Aoki Y: Development of LNA Gapmer Oligonucleotide-Based Therapy for ALS/FTD Caused by the C9orf72 Repeat Expansion. *Methods Mol Biol*. 2020;2176:185-208.
2. Takizawa H, Sato M, Aoki Y: Exon Skipping in Directly Reprogrammed Myotubes Obtained from Human Urine-Derived Cells. *J Vis Exp*. 2020 May 7;(159).
3. Nordin JZ, Mizobe Y, Nakamura H, Komaki H, Takeda S, Aoki Y: Characterizing Exon Skipping Efficiency in DMD Patient Samples in Clinical Trials of Antisense Oligonucleotides. *J Vis Exp*. 2020 May 7;(159).
4. Katahira K, Kunisato Y, Yamashita Y and Suzuki S (2020) Commentary: A robust

data-driven approach identifies four personality types across four large data sets. *Front. Big Data* 3:8. doi: 10.3389/fdata.2020.00008

Molecular Virology

Professor : Shoji YAMAOKA
Junior Associate Professor : Hiroaki TAKEUCHI
Project Junior Associate Professor: Takaya HAYASHI
Assistant Professor: Takeshi YOSHIDA
sayaka SUKEGAWA
Medical Technologist : Yoshio INAGAKI
Secretary : Kumiko THORPE-MATSUI

-Students-

Ph.D. course: SELEASE DELETSU, ADIZA ABASS, Haruki KITAMURA,
Kei SEKIGUCHI

Master course: Yuuki HONDA, Kazuya TSUKITANI, Hiroki YOSHINO, Kazuho TAKAHASHI, Yuuya ABE,
Saki ECHIGOYA

(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.
- Virological approaches for robust increase in lentiviral titer.

(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. Yao W, Yoshida T, Hashimoto S, Takeuchi H, Strebel K, Yamaoka S. Vpu of a simian immunodeficiency virus isolated from greater spot-nosed monkey antagonizes human BST-2 via two AxxxxxxxW motifs. *Journal of virology*. 2020.01; 94(2); e01669-19
2. Yoshino J, Akiyama Y, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Loss of ARID1A induces a stemness gene ALDH1A1 expression with histone acetylation in the malignant subtype of cholangiocarcinoma. *Carcinogenesis*. 2020.07; 41(6); 734-742
3. Lotfi S, Nasser H, Noyori O, Hiyoshi M, Takeuchi H, Koyanagi Y, Suzu S. M-Sec facilitates intercellular transmission of HIV-1 through multiple mechanisms. *Retrovirology*. 2020.07; 17(1); 20
4. Prah I, Ayibieke A, Huong NTT, Iguchi A, Mahazu S, Sato W, Hayashi T, Yamaoka S, Suzuki T, Iwanaga S, Ablordey A, Saito R. Virulence profile of diarrhoeagenic *Escherichia coli* from the Western region of Ghana. *Japanese journal of infectious diseases*. 2020.08;
5. Amoa-Bosompem M, Kobayashi D, Itokawa K, Faizah AN, Kuwata R, Dadzie S, Hayashi T, Yamaoka S, Sawabe K, Iwanaga S, Isawa H. Establishment and characterization of a cell line from Ghanaian *Aedes aegypti* (Diptera: Culicidae) focusing on *Aedes*-borne flavivirus susceptibility. *In vitro cellular & developmental biology. Animal*. 2020.10; 56(9); 792-798

[Conference Activities & Talks]

1. Prah Isaac, Ayibieke Alafate, 井口 純, Mahazu Samiratu, 佐藤 和佳菜, 鈴木 敏彦, 山岡 昇司, 岩永 史朗, Ablordey Anthony, 齋藤 良一. Virulence Profile of Diarrheagenic *E. coli* from the Western region of Ghana(和訳中). *日本細菌学雑誌* 2020.01.01

Immunotherapeutics

Professor: Mari Kannagi
Associate Professor: Takao Masuda
Assistant Professor: Atsuhiko Hasegawa (Lecturer)
Assistant Professor: Yoshiko Nagano
Visiting Researcher: Sayaka Ito
Research Assistant: Kumiko Katagiri
Graduate Student: Undrakh Ganbaatar, Yu-Lun HUANG, Tomokma Fujikawa, Atsushi Otsuka, Jianchun Zhang, Takeru Yoneda, Nobuyo Kondo, Miku Ishizawa

(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. *Br J Haematol*, 2015) (Kannagi, M., et al. *Cancer Sci*, 2019).

② Involvement of innate immune response in HTLV-1 pathogenesis.

There are several enigmas in HTLV-1 pathogenesis. The level of HTLV-1 expression in infected cells is very low *in vivo* but rapidly induced *in vitro*. Despite the low viral expression, NF κ B is constitutively activated, which plays an important role in leukemogenesis of adult T-cell leukemia/lymphoma (ATL). In addition, the combination therapy of AZT/IFN- α used for ATL outside Japan, while its transient anti-ATL mechanism has been unclear because HTLV-1-infected cells are resistant to this therapy *in vitro*. We found that host innate immune responses against HTLV-1 are involved in these long-puzzling phenomena. (Kinpara, et al. *J Virol.* 2009, *Retrovirol.* 2013, *Leukemia*, 2015). Furthermore, our findings elucidated that IL-10-dominant microenvironment is critical for HTLV-1 leukemogenesis partly explaining how HTLV-1 induces totally different lymphoproliferative or inflammatory diseases without differences in viral strains (Sawada, et al. *PLOS Pathog.* 2017). These findings indicate that both innate and acquired immune response against HTLV-1 are deeply involved in HTLV-1 pathogenesis (Kannagi, et al. *Retrovirology.* 2019).

③ Novel molecular basis to regulate HIV-1 replication.

Reverse transcription of viral genomic RNAs into DNA forms followed by integration of the viral DNA into host cell chromosome is an essential step for retroviral replication including human immunodeficiency virus type 1 (HIV-1). We have proposed that essential roles of integrase (IN) during reverse transcription step which could be the next target for novel anti-HIV drug development (Masuda. *Front Microbiol.* 2011). Recently we found that critical contribution of HIV-1 IN in facilitating reverse transcription is exerted through the IN precursor fusion form with reverse transcriptase (RT) (Takahata et al., *J. Virol.* 2017). Furthermore, we established *in vitro* cell-free HIV-1 reverse transcription assay to delineate the contribution of other cis- and trans-acting candidate factors in regulating HIV-1 reverse transcription. We revealed unprecedented roles of the 5' -end nucleotide of HIV-1 genomic RNA for reverse transcription (Masuda et al, *Sci. Rep.* 2015, Huang et al, *BBRC.* 2019). These studies have provided novel molecular basis and concept to regulate HIV-1 replication.

(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 held the 5th Annual Meeting of Japanese Society of HTLV-1 Associated Diseases in Tokyo on Aug 31 through Sept 2, 2018.

(6) Clinical Performances

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.

(7) Publications

[Original Articles]

1. 永野 佳子, チョウ・カンシュン, 長谷川 温彦, 片桐 邦子, 近藤 伸世, 増田 貴夫, 神奈木 真理. HTLV-1 感染細胞の細胞増殖シグナル伝達の調節における IRF4 の役割 (Roles of IRF4 in the regulation of cell growth signaling in HTLV-1-infected cells) 日本生化学会大会プログラム・講演要旨集. 2020.09; 93 回; [P-522]
2. 長谷川 温彦, 村田 めぐみ, 富士川 朋夏, 永野 佳子, 明里 宏文, 増田 貴夫, 神奈木 真理. STLV-1 感染ニホンザルを用いた CTL 誘導型ワクチンによる STLV-1 特異的 CTL 低応答の改善 日本癌学会総会記事. 2020.10; 79 回; PE3-1

[Conference Activities & Talks]

1. 永野佳子, チョウカンシュン, 長谷川温彦, 片桐邦子, 近藤伸世, 増田貴夫, 神奈木真理. HTLV-1 感染細胞の増殖シグナル制御における IRF4 の役割. 第 93 回日本生化学会大会 2020.09
2. Hasegawa A, Murata M, Fujikawa T, Nagano Y, Akari H, Masuda T, Kannagi M. Restoration of impaired STLV-1-specific CTL response in STLV-1-infected Japanese macaques by a CTL-based vaccine. The 79th Annual Meeting of the Japanese Cancer Association 2020.10
3. Nagano Y, Suehiro Y, Ando S, Koga R, Ganbaater U, Katagiri K, Kannagi M, Hasegawa A. Analysis of PD-1 expression on the Tax-specific CTL in ATL patients treated with Tax- targeted dendritic cell therapy. The 79th Annual Meeting of the Japanese Cancer Association 2020.10

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. MATSUOKA Chiyomi, AZUMA Rikako, TSUNOKUNI Hiroyuki, MATSUNAMI Keiichi, HARA Masayuki, KATOH Shinsuke, IIZUKA Hiroyuki. Creation of the user's guides about Safety handling of radioisotope reagents and Fundamental method of life-science experiment using radioisotope, by customer surveys. 53th Annual Meeting of Japan Health Physics Society 2020.06.29
2. MATSUOKA Chiyomi, TSUNOKUNI Hiroyuki, MATSUNAMI Keiichi, HARA Masayuki, KATOH Shinsuke, IIZUKA Hiroyuki. Content development efforts aimed at appropriate matching between experiment applicants and RI facilities -Report on the activities of the RI facility list creation subcommittee nationwide-. Radiation Safety Handling Subcommittee Annual Meeting 2020 2020.11.02
3. Chiyomi MATSUOKA, Hiroyuki TSUNOKUNI, Keiichi MATSUNAMI, Masayuki HARA, Shinsuke KATOH, Hiroyuki IIZUKA. Efforts to provide information for promotion of use of radioactive reagents - Safe Handling Guide for Radioactive Reagents-. The 19th Annual Meeting of the Japanese Society for Radiation Safety Management 2020.12.09

4. Kiyoshi NOMURA, Masayuki HARA, Yuya KOIKE, Toshiou FUJIBUTI, Shogo HIGAKI, Tugumi MASTUURA, Ikuo KOBAYASHI. Application of Flexible Liquid Scintillation Light Guide (LSLG) Detector to Radiation Dose Meter. The 19th Annual Meeting of the Japanese Society for Radiation Safety Management 2020.12.09

Biodefense Research

Professor Toshiaki Ohteki
 Associate Professor Taku Sato
 Adjunct Lecturer Nobuyuki Onai
 Assistant Professor Masashi Kanayama
 Project Assistant Professor Mihoko Kajita
 Graduate Student Kana Minamide
 Graduate Student Miwako Sase
 Graduate Student Shun Ishikawa
 Graduate Student Yuta Izumi
 Research Technician Shoko Kuroda
 Research Technician Kisho Shiseki
 Research Technician Tomiki Hayashi
 Staff 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 myeloid cells (dendritic cells and macrophages), tissue stem cells, and their functional interplay in the immunological and non-immunological organs. 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 myeloid cells

1) Identification of novel sources of mononuclear phagocytes

Mononuclear phagocytes contain monocytes, macrophages and dendritic cells (DCs). In a recent decade, it has been continuing epoch-making discoveries in the field of mononuclear phagocytes and their functions are now beyond classical Immunology and extend to broad life phenomenon, e.g. tissue development/regeneration, wound-healing, and establishment of tumor environments and 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 (*Immunity* 2017; *Int Immunol* 2018). 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. Collaborations with pharmaceutical company and Department of Hematology of TMDU toward the development of therapeutic agents targeting cMoP and monocyte lineage and with Department of Pediatrics of TMDU for the pathology clarification of congenital pulmonary alveolar proteinosis (PAP) are currently in progress.

2) Mechanism of brain function impairment by spatiotemporal transformation of microglial enhancer

The decline in tissue regeneration and homeostasis associated with life-stage progression is closely related to the functional alteration of macrophages. Microglia, a macrophage in the brain, is actively contributing to the brain development and maintenance during young age (regenerative microglia). However, with age, microglial inflammatory trait becomes prominent with impaired phagocytosis and brain-derived neurotrophic factor (BDNF) production etc (inflammatory microglia). As a result, functional neurons and synapses are decreased and destroyed. However, the overall picture and entire process of the microglial functional alteration and causative epigenomic transformation have not been clarified.

In this study, using a novel technology that can detect the active enhancer region and its activity with high sensitivity, we will identify the super enhancers (hereafter, SEs) responsible for the microglial transformation during life-stage progression, and elucidate the entire process of transformation dynamics. As SEs are activated in a cell-type specific manner, one can expect that it will lead to the development of novel technology to specifically control the age-related functional alteration of microglia. To date, we have identified 36,320 new microglial enhancers including 937 regions that become different with age (unpublished).

3) Mechanism of emergency myelopoiesis

Unlike steady-state hematopoiesis, hematopoiesis triggered at infection, irradiation and anti-cancer therapy is biased toward myeloid cell differentiation and production, that is “emergency myelopoiesis”. However, due to the fluctuation of cell-surface marker(s) on hematopoietic stem progenitor cells (HSPCs), it has long been difficult to understand bona-fide emergency myelopoiesis. Recently, our laboratory succeeded in identifying a novel marker with less fluctuation during emergency myelopoiesis. Using this unique marker, we will elucidate the mechanism of emergency myelopoiesis.

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 (submitted).

2) Establishment of biobank for human tongue cancer

Oral cancer has an increasing trend of 270,000 new cases per year worldwide. Two-thirds of them are tongue cancers, and in advanced cases, they become refractory to treatment and have a poor prognosis, and causal genes have not been identified. Under these backgrounds, we succeeded in establishing a human tongue cancer organoid culture system. In the future, we aim to develop fundamental technologies that lead to personalized treatment.

(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. Jumpei Asano, Taku Sato, Toshiaki Ohteki. Autophagy Detection in Intestinal Stem Cells. *Methods Mol Biol.* 2020; 2171; 115-125

2. 泉 湧太, 金山 剛士, 秋山 めぐみ, 甲斐 正之, 沈 鐘楚子, 川又 紀彦, 樗木 俊聡. Targeting monocyte lineage-restricted antigen as a novel therapeutic strategy for monocytic leukemia(和訳中) 日本病理学会会誌. 2020.03; 109(1); 304
3. Kanayama M, Izumi Y, Yamauchi Y, Kuroda S, Shin T, Ishikawa S, Sato T, Kajita M, Ohteki T. CD86-based analysis enables observation of bona fide hematopoietic responses. *Blood*. 2020.05;
4. Taku Sato, Miwako Sase, Shun Ishikawa, Mihoko Kajita, Jumpei Asano, Toshiro Sato, Yoshiyuki Mori, Toshiaki Ohteki. Characterization of radioresistant epithelial stem cell heterogeneity in the damaged mouse intestine. *Sci Rep*. 2020.05; 10(1); 8308
5. Liang J, Zhang JJ, Huang HI, Kanayama M, Youssef N, Jin YJ, Reyes EY, Abram CL, Yang S, Lowell CA, Wang D, Shao L, Shinohara ML, Zhang JY, Hammer GE. The ubiquitin-modifying enzyme A20 terminates C-type lectin receptor signals and is a suppressor of host defense against systemic fungal infection. *Infection and immunity*. 2020.06;
6. Taku Sato, Shun Ishikawa, Jumpei Asano, Hirona Yamamoto, Masayuki Fujii, Toshiro Sato, Kouhei Yamamoto, Keisuke Kitagaki, Takumi Akashi, Ryuichi Okamoto, Toshiaki Ohteki. Regulated IFN signalling preserves the stemness of intestinal stem cells by restricting differentiation into secretory-cell lineages. *Nat Cell Biol*. 2020.08; 22(8); 919-926
7. Kana Minamide, Taku Sato, Yusuke Nakanishi, Hiroshi Ohno, Tamotsu Kato, Jumpei Asano, Toshiaki Ohteki. IRF2 maintains the stemness of colonic stem cells by limiting physiological stress from interferon. *Sci Rep*. 2020.09; 10(1); 14639

[Conference Activities & Talks]

1. Miwako Sase, Taku Sato, Mihoko Kajita, Toshiaki Ohteki. Establishment of human tongue cancer organoid biobank. The 79th annual meeting of the Japanese cancer association 2020.10.01 Hiroshima
2. Miwako Sase, Taku Sato, Tadahide Noguchi, Yoshiyuki Mori, Toshiaki Ohteki. Establishment of human tongue cancer organoid biobank. The 58th annual meeting of Japanese society of clinical oncology 2020.10.22 kyoto
3. Masashi Kanayama. CD86-based analysis enables identification of hematopoietic progenitors under biological stresses which upregulate interferon. 8th Annual Meeting of the International Cytokine & Interferon Society 2020.11.02

Pathological Cell Biology

Professor : Shigeomi SHIMIZU

Associate Professor : Norio SHIMIZU

Junior Associate Professor : Satoko ARAKAWA

Project Associate Professor : Masatsune TSUJIOKA, Satoshi TORII, Shinya HONDA

Assistant Professor : Hirofumi YAMAGUCHI

Project Assistant Professor : Michiko MUROHASHI, Hajime SAKURAI, Minkyon SHIN, Saori NOGUCHI, Hatuki ENDO

Graduate Student : Toyokazu SEKI, Tomoyo YOSHIDA, Kazuma OHSHIMA,

Chinami OGAWA, Mizuki KATOH

Research Assistant : Ikuyo YOSHINO, Naomi KOJIMA, Hikari SHIMADA

Secretary : Hitomi Fukabori, Setsu TAMAI

(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

[Original Articles]

1. Kana Otsubo, Chiaki Maeyashiki, Yoichi Nibe, Akiko Tamura, Emi Aonuma, Hiroki Matsuda, Masanori Kobayashi, Michio Onizawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Satoru Torii, Eisuke Itakura, Mamoru Watanabe, Shigeru Oshima. Receptor-Interacting Protein Kinase 3 (RIPK3) inhibits autophagic flux during necroptosis in intestinal epithelial cells. *FEBS Letters*. 2020.01; 594; 1586-1595
2. Hironori Kato, Kohki Okabe, Masato Miyake, Kazuki Hattori, Tomohiro Fukaya, Kousuke Tanimoto, Shi Beini, Mariko Mizuguchi, Satoru Torii, Satoko Arakawa, Masaya Ono, Yusuke Saito, Takashi Sugiyama, Takashi Funatsu, Katsuaki Sato, Shigeomi Shimizu, Seiichi Oyadomari, Hidenori Ichijo, Hisae Kadowaki, Hideki Nishitoh. ER-resident sensor PERK is essential for mitochondrial thermogenesis in brown adipose tissue. *Life Science Alliance*. 2020.03; 3(3);
3. Satoru Torii, Hirofumi Yamaguchi, Akira Nakanishi, Satoko Arakawa, Shinya Honda, Kenta Moriwaki, Hiroyasu Nakano, Shigeomi Shimizu . Identification of a phosphorylation site on Ulk1 required for genotoxic stress-induced alternative autophagy *Nature Communications*. 2020.03;
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[Books etc]

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[Conference Activities & Talks]

1. Yuji Kato, Satoko Arakawa, Kazue Terasawa, Jin-ichi Inokuchi, Takanori Iwata, Shigeomi Shimizu, Tetsuro Watabe, and Miki Hara-Yokoyama. The ceramide analogue N-(1-hydroxy-3-morpholino-1-phenylpropan-2-yl)decanamide induces large lipid droplet accumulation and highlights the effect of LAMP-2 deficiency on lipid droplet degradation. The 62nd Japan Lipid Chemistry Society 2020.05.14 Funabori
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Lipid Biology

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 Associate Professor Junko Sasaki
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 JSPS Research Fellow Emi Tokuda
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 Graduate student (master) Takumi Ikeda
 Graduate student (master) Daichi Sato
 Graduate student (master) Kouichiro Takehashi
 Graduate research student Yixin Zhang
 Graduate research student Wang Tian
 Secretary Kaori Kofuji

(1) Outline

Lipids are biological molecules essential for the integrity of cell membranes, energy storage, and intra/extracellular signal transduction. What our group is mostly focused on now is the roles of phosphoinositide metabolism in health and disease. Phosphoinositides (PIPs) are bipolar lipids that contain a phosphatidylinositol (PI). PI has a glycerol backbone, an inositol head group linked to the glycerol through a phosphate group, and two long-chain fatty acids linked to the glycerol through ester bonds. Phosphorylation patterns of the hydroxyls of the inositol moiety give rise to seven other PIPs classes. In humans and mice, there are 18 interconversion reactions involving all eight PIPs classes, and these reactions are orchestrated by as many as 48 genes encoding 19 lipid kinases and 29 phosphatases. Three acyltransferases that modify the acyl moiety of phosphoinositides have also been identified.

Our goal is to achieve a comprehensive understanding of this whole metabolic system to propose new strategies for the treatment and diagnosis of incurable diseases. To this end, we have been systematically generating and characterizing knockout mouse mutants for each PIPs metabolizing enzyme. Another unique strength of the group is our original methods for lipid profiling based on LC-MS/MS technique, which will help explore novel therapeutic targets as well as biomarkers.

(2) Research

We are proposing the **"Department of Lipid Biology's Four Postulates"** to find out the relationship between lipids and diseases, and proceed with basic research to prove it scientifically.

1. Find specific lipid changes (deficiency/accumulation) in certain human pathological conditions.
2. Identify the lipid metabolizing (production/degradation) enzyme.
3. Cause the same disease state by deleting/expressing the metabolizing enzyme in mice.
4. Find the same lipid changes as in 1.

Based on this basic concept, we are trying to elucidate the true nature of the following various pathologies and to develop medical applications based on these new findings.

- Stratification method of lymphomas based on lipid acyl group composition
- Prediction method for the sensitivity of cancers (breast cancer, pancreatic cancer, lymphoma) to molecular target drugs by lipid profile.

- Identification of phospholipids involved in the pathogenesis of inflammatory diseases (pneumonia, colitis, and non-alcoholic steatohepatitis).
- Identification of phospholipids involved in basal ganglia neurodegeneration.
- Discovery of new phospholipids, their metabolic enzymes, and target proteins.
- Elucidation of target protein activation mechanism by phospholipid (MD simulation, Shotgun proteomics)

(3) Education

Topics of research for graduate student

1. Exploring bioactive lipids that cause disease conditions
2. Exploring bioactive lipids that reflect disease conditions
3. Elucidation of the true nature of cancer, inflammatory diseases, and neurodegenerative diseases by lipid profiling
4. Development of lipid analysis technology based on mass spectrometry
5. Pathological analysis of mice lacking lipid metabolizing enzymes (PI3K, PTEN, etc.)

(4) Lectures & Courses

Each student has an independent research theme.

Systematically teach experimental science knowledge and skills through research and practice, including cell culture, genome editing, and how to use knockout mice, multivariate analysis, chromatography, and mass spectrometer technology.

It is aiming for scientifically original discovery that is useful for medical progress.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

(5) Publications

[Original Articles]

1. Nishio M, To Y, Maehama T, Aono Y, Otani J, Hikasa H, Kitagawa A, Mimori K, Sasaki T, Nishina H, Toyokuni S, Lydon JP, Nakao K, Wah Mak T, Kiyono T, Katabuchi H, Tashiro H, Suzuki A. Endogenous YAP1 activation drives immediate onset of cervical carcinoma in situ in mice. *Cancer science*. 2020.07;
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Pediatrics and Developmental Biology

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(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 research spans 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. Development of innovative techniques for ex vivo cell therapy after hematopoietic stem cell transplantation.

5. Multicenter Registry, Pediatric Idiopathic/heritable pulmonary arterial hypertension
6. Multicenter Registry, Congenital Heart Disease related pulmonary arterial hypertension
7. Effectiveness evaluation of live attenuated vaccines for patients using immunosuppressants
8. Multicenter Registry study on Kawasaki Disease with coronary aneurysm
9. Multicenter study for risk factors associated with disease severity of human metapneumovirus (hMPV) infection
10. Identifying the pathological mechanisms of periventricular leukomalacia and pulmonary damage using model rats
11. Elucidating the molecular mechanisms of gonadal development
12. Molecular pathology of congenital adrenal diseases and disorder of sex development
13. Molecular pathology of diabetes mellitus caused by mutations of the insulin receptor
14. Identifying pathological mechanisms of neurological diseases caused by defective DNA damage response
15. Investigation of molecule marker determine the prognosis of infant leukemia
16. Development of therapeutic strategy targeting homologous recombination repair
17. Genetic background of leukemia development
18. Genetic analysis and development of therapeutic approach for epilepsy syndrome
19. Developing data base of JIA (juvenile inflammatory arthritis), CoNinJa (Children's version of National Database of Rheumatic Diseases by iR-net in Japan)
20. Clarifying immunological profiles of the patients with autoimmune diseases
21. Developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker
22. Development of newborn screening for treatable childhood diseases including spinal muscular atrophy
23. Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease
24. Clarifying prognostic predictor of nephritis /nephrotic syndrome

We are collaborating with Medical Research Institute at TMDU, Tokyo University, Institute of Medical Science, Hiroshima University, 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, Kyoto University, Tokyo University and many other laboratories.

● Hematology/Oncology/Immunology Group (Basic Research)

Immunology

We have explored inborn error of immunity (IEI) candidate genes using the whole-exome analysis (WES) method using next-generation sequencers and have identified several candidate mutations. Molecular characterization of these candidates has also been conducted parallelly. To date, we have performed WES for 136 cases of IEI and identified candidate genes in 36 cases (27%) (Okano). Imai et al reported novel disease concepts caused by APRIL mutation exhibiting attenuated plasmacyte differentiation. The etiology of OAS1 deficiency that exhibits pulmonary proteinosis has been revealed by the assay using iPS cells (Okano and Morio). Yamashita and Morio are analyzing the case with B cell deficiency and lymphoma using the Knock-in mouse model. Nishimura and Imai reported the summary of 42 IEI cases that underwent hematopoietic stem cell transplantation in our department. Also, we are working with domestic and overseas researchers to analyze the pathogenesis of IEI and to develop therapeutic methods. Imai is conducting a nationwide newborn screening for IEI using the TREC/KREC test. As adoptive immunotherapy to promote immunological reconstitution after transplantation, we have developed virus-specific T cell therapy for refractory viral infections and are pursuing the clinical trial (Kamiya and Morio).

Oncology

In the research for the diseases related to DNA damage response pathways, we have elucidated the usefulness of PARP inhibitors for neuroblastoma by targeting homologous recombination repair and launched phase I physician-led clinical trials for refractory pediatric solid tumors. We have also developed a simple method to measure genomic copy number aberrations in neuroblastoma using digital PCR to classify the risk. We analyzed the cases of acute lymphocytic leukemia and submandibular adenocarcinoma caused by germline abnormalities of ETV6 and found that mutant ETV6 was located at cytoplasmic fraction and accelerated degradation of ETV6 led to a loss of function. (Takagi)

● Cardiology Group

We have three graduate school students. Yamaguchi is struggling to elucidate the mechanism of pulmonary

arterial hypertension as a basic research, his current project is to examine the effect of dexmedetomidine for monocrotaline-induced pulmonary hypertension in rats. Ishii is engaged in a clinical research, he has two projects which are “Effect of Automated External Defibrillator (AED) for sudden cardiac death in young people” and “Effectiveness evaluation of live attenuated vaccines for patients using immunosuppressants”. In addition, Watanabe is a principal investigator of the project of “Multicenter study for risk factors associated with disease severity of human metapneumovirus (hMPV) infection”.

● Neurology Group

< Basic research >

We are trying to establish the gene therapy using viral vectors for ataxia telangiectasia (AT), one of the major neurodegenerative diseases. Our another project is to establish diagnostic tools for early detection and early treatment of spinal muscular atrophy (SMA). We are also investigating the pathological mechanism of Moyamoya syndrome.

To Elucidate cytoprotective effect of astrocyte in oxygen-glucose deprivation condition, we have investigated the role of Nuclear Receptor 4A (NR4A) subfamily and another cytoprotective transcription factor associated with hypoxia-induced factor 1 alpha (HIF-1 α). Another study is to establish a rat neonatal white matter injury model. (collaborative project with Hiroshi Sakuma, Tokyo Metropolitan Institute of Medical Science).

< Clinical research >

“Genetic analysis and development of therapeutic approach for epilepsy syndrome” (collaboration with Showa University)

“Research for rare epilepsy syndrome” (collaboration with Institute of Epilepsy and Neurological Disorders)

“Systematic measurement and functional analysis of autoantibody in immunologic neurological diseases” (collaboration with Tokyo Metropolitan Institute of Medical Science)

“Evaluation of adrenocortical function in the patients with West syndrome treated with ACTH therapy”

“Development of newborn screening for treatable childhood diseases including spinal muscular atrophy”

● Endocrinology Group

Molecular mechanisms of gonadal development

To understand the pathophysiology of DSD, our current research is focusing on elucidating the molecular mechanisms of sex determination and gonadal development, especially in the aspect of the transcriptional network of sex determination and gonadal development. Another our target is to identify the precise functions of transcription factors, such as NR5A1 (SF1), FOXL2, and SOX9, in gonadal development.

Molecular analysis of pathological mechanisms in congenital adrenal hyperplasia (CAH)

One of our major tasks is supervising the CAH neonatal mass-screening in Tokyo. Currently, large number of CAH patients we treat, and clarifying the clinical details and we are focusing on clarifying the long term prognosis of the disease. In addition to adrenal insufficiency and androgen excess, metabolic syndrome during adulthood is reported to be another major concern of CAH. The precise pathophysiology is not known. We are looking at elucidating the molecular mechanisms of the metabolic syndrome in CAH patients by using mice model.

Identifying novel molecules of congenital endocrinological diseases

We aim to identify novel molecules responsible for development of congenital endocrine disorders such as insulin resistance. 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.

● Rheumatology 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, developing a methodology for the diagnosis of atypical Kawasaki Disease by exploiting a novel biomarker, and Kinetic and functional analysis of novel T and B cell subsets in patients with autoimmune disease are other our current projects. In addition, in joint research with the department of rheumatology, we are analyzing the current status and effectiveness of treatment for childhood and adult onset of collagen disease.

● Neonatology group

We are examining changes of profile in umbilical cord-derived mesenchymal stem cells due to the intrauterine environment in humans through joint clinical research with related hospitals.

We are trying to elucidate the mechanism and effect of umbilical cord-derived mesenchymal stem cell therapy for diseases in preterm infant and the involvement of mesenchymal stem cells in the establishment of diseases. We aim to identify predictive biomarkers for preterm complications by intrauterine environment using umbilical cord-derived mesenchymal stem cells.

As a preliminary step before starting clinical trials of dental pulp stem cell administration for chronic phase of cerebral palsy, we are establishing the chronic phase of cerebral palsy in rat and examining the therapeutic effect of dental pulp stem cell administration on the chronic phase of cerebral palsy as a four-party joint research with Nagoya University Pediatrics, Tokyo Metropolitan Institute of Medical Sciences, and Gene Technoscience.

● 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 addition, we carry out immunological and epidemiological studies on therapeutic effects of oral immunotherapy against food allergy.

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.

● Nephrology Group

We aim to clarifying predictor of nephritic and/or idiopathic nephrotic syndrome for improving the therapeutic protocols of them through joint clinical research with related hospitals.

(3) Education

Block Lecture

The systematic lecture was performed for M4 students. One third of lectures “were performed using an active-learning” style. The number of frames of the active-learning from nine frames in the previous fiscal year to 12 frames. Two frames of team-based learning (TBL) were also provided. Although one frame of active-learning alone cannot cover the whole area of pediatrics, about 85% of students reach the passing point in the final test covering the whole area of pediatrics by student self-study. At this point, we believe that the usefulness of active learning has been demonstrated.

Project semester

This provides the opportunities of basic research for the 4th grade students for half a year. This year, one student was committed to the research of our department and presented at a scientific meeting.

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)

Clinical clerkship (CC) for 5th-year medical students in pediatrics was shortened from 1 month (4 weeks) to 2 weeks due to the pandemic of COVID-19. Each student spent two weeks in one of the two groups (hematology, immunology, cardiology, neurology, endocrinology, nephrology, Rheumatology, neonatology).

Lectures were given to all students on Mondays and Fridays (diagnostics, congenital heart disease, neonates, infusion, EEG, endocrinology, leukemia, immunodeficiency infections, and the role of the Child Life Specialist in pediatrics), and student conferences were held every Friday for further understanding of the clinical practice program.

During the period when ward practice was interrupted due to COVID-19, miniCEX based problem-solving lectures were performed to each assigned medical group every day using web conferencing tools to promote their self-study, and two to three lectures were given to all students per week.

The number of 6th-year medical students accepted for clinical training in pediatrics was increased by one student to two this year, and they will continue to practice for two weeks in a medical group of their choice as an advanced program.

In terms of post-graduate education, at least one month of basic clinical education was provided to the first and second year of clinical residents at on-campus or off-campus facilities (Soka Municipal Hospital, Tokyo North

Medical Center, Tsuchiura Kyodo General Hospital). On the other hand, for early clinical residents who chose pediatrics for at least two months, specialized clinical education was mainly provided on TMDU campus. For the second semester clinical residents at the university, we provided a wide range of more specialized clinical education to prepare them to become pediatric specialists.

(4) Lectures & Courses

Primary care of pediatrics covers a wide spectrum of health care and clinical problems in children, and all pediatricians should be well trained in those subjects. Further, Tokyo Medical and Dental University is one of the top ranked national medical universities 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 pediatrics 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 FY2020, we performed HCT for 13 (12 allo-HCT and 1 auto-HCT), and 9 cases were for PID patients. For IEI (9 cases), 1 Related bone marrow cell transplantation, 1 related peripheral blood stem cell transplantation, 2 unrelated bone marrow transplantations, 1 cord blood transplantation, and 5 HLA haplo-matched transplantations were performed.

For malignancies (4 cases), 3 HLA haplo-matched transplantations were performed. Autologous peripheral blood stem cell transplantation was performed for advanced malignancy (1 case).

Our experience of HCT exceeds 230 cases including more than 100 cases with primary immunodeficiency diseases, so far.

Clinical trial

Three doctor-initiated clinical trials led by the pediatric department of Tokyo Medical and Dental University are ongoing.

” 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 center hospitals providing medical care of pediatric pulmonary hypertension.

In 2019, the number of inpatients was 97, which consisted of 56 congenital heart disease, 17 pulmonary hypertension, 10 Kawasaki Disease, 8 arrhythmia, 2 cardiomyopathy and 4 others. Cardiac catheterizations were performed in 48 patients and cardiac surgery was performed in 18 patients (16 open-heart surgery), which consisted of 8 VSDs, 5 ASDs, 1 TOF+PA+MAPCA reRastelli, 1 DORV, 1 PDA. The number of outpatients was 1,793, echocardiogram was performed in 612, Treadmill exercise-induced electrocardiogram was performed

in 63, and Holter 24hr electrocardiogram was performed in 58 patients.

● 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. We also provide nucleic acid drug and gene therapy for patients with spinal muscular atrophy. We focus on diagnosis, genetic analysis and treatment for rare neurologic diseases.

● Endocrinology Group

We provide comprehensive diagnostic and treatment services for children with endocrinological abnormality and diabetes, such as disorders of growth, pubertal development, Ca/P metabolism (including skeletal dysplasia), gonadal development and adrenal cortex function. Especially, we are focusing on providing advanced medical service for congenital adrenal hyperplasia (CAH) and disorders of sex development (DSD). Our institute is one of the DSD central facilities approved by the Japanese Society for Pediatric Endocrinology (JSPE). For social contribution, we supervise the neonatal screening system for CAH in Tokyo metropolitan city and peer support group of type 1 diabetes, "Tokyo Wakamatsu-kai" .

● 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.

● Rheumatology group

Medical treatment and treatment of children with collagen disease and rheumatic diseases in general, but not limited to these cases, undiagnosed cases such as unknown fever and joint pain, and autoinflammatory syndrome represented by periodic fever. Is going. In addition, the current status of pediatric rheumatic diseases. The emphasis is on the issues and challenges of transitional care in adulthood for pediatric rheumatic diseases, depending on the situation and the actual situation.

The medical treatment started in July 2015, and the number of outpatients in 2019 exceeded 1600 mainly for referrals. The total number of hospitalized patients in one year is 157, all of which are increasing year by year.

● Neonatology group

Collaborating with other medical departments or special care groups in pediatrics, we are treating preterm infants (≥ 27 weeks gestation, birth weight ≥ 800 g), neonates with complications and babies born from mothers with complication.

● Allergy Group

The qualified allergists of the group attend both inpatient and outpatient care units for allergic diseases in the allergy medical center of our university and extramural, affiliated hospitals, 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 transplantation for refractory diseases. Specifically, 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 the approval of industry-based clinical trials for drugs (such as anticancer drugs).

● Cardiology Group

Cardiology group performs diagnosis, evaluation of treatment and decision of treatment strategy for pediatric pulmonary hypertension patients. We actively treat severe idiopathic/hereditary pulmonary arterial hypertension (IPAH/HPAH) patients by upfront combination therapy (uCT) with two or three kinds of disease targeted drugs including continuous venous infusion of epoprostenol. We made considerable achievements of treatment in severe IPAH/HPAH patients with epoprostenol/treprostinil.

● Neurology Group

Neurology group provide highly specialized diagnostic approach and medical care for neurological disorders such as intractable epilepsy, cerebellar ataxia, immune-mediated neurological disease, spinal muscular atrophy, involuntary movement, perinatal brain damage, infection of nervous system, acute encephalopathy/encephalitis, neurodegenerative disease.

● Endocrinology Group

The leader of our endocrinology group is a supervisor of congenital adrenal hyperplasia (CAH) newborn screening in Tokyo. We treat substantial number of 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 organizing a Type 1 DM patients' association (Wakamatsu-kai) and have the summer camp for diabetic children 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.

● Rheumatology 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. We are also actively involved in the expansion and standardization of treatment indications through participation in clinical trials and formulation of guidelines. 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 provides intensive care for preterm infants and critically ill newborns. As a designated perinatal medical center in Tokyo, we accept maternal and neonatal transfer from various areas in Tokyo and contribute to perinatal medicine in Tokyo.

● 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. We introduce new biological medicines to the long-term management for severe persistent asthma patients.

(7) Publications

[Original Articles]

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[Misc]

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2. Kenji Okada, Mihoko Mizuno, Hiroyuki Moriuchi, Satoshi Kusuda, Ichiro Morioka, Masaaki Mori, Keisuke Okamoto, Kuniyuki Okada, Shigemi Yoshihara, Hiroyuki Yamagishi, Utako Yokoyama, Tomohiro Kubota, Kazuko Kudo, Masatoshi Takagi, Shuichi Ito, Yutaka Kanamori, Yoji Sasahara. The Working Group for Revision of "Guidelines for the Use of Palivizumab in Japan": A Committee Report. *Pediatr Int.* 2020.11; 62(11); 1223-1229

[Conference Activities & Talks]

1. Imai K. How I Approach A Patient With Combined Immunodeficiency?. APSID2020 2020.02.06 India
2. Takahiro Tomoda, Tsubasa Okano, Kento Inoue, Motoi Yamashita, Takahiro Kamiya, Takeshi Isoda, Masakatsu Yanagimachi, Hirokazu Kanegane, Masatoshi Takagi, Tomohiro Morio, Kohsuke Imai. An intractable case of hyper IgE syndrome. APSID (Asia Pacific Society for Immunodeficiencies) School cum Workshop 2020.02.06 Chandigarh, India.
3. Miko Okamura, Kay Tanita, Hidetoshi Takada, Tetsuo Mitsui, Yoshiyuki Minegishi, Kohsuke Imai, Tomohiro Morio, Hirokazu Kanegane. Somatically reverted T cells in dedicator of cytokinesis 8 deficiency modify cellular immunity. 3rd Scientific Congress of Asia Pacific Society for Immunodeficiencies 2020.02.09 Chandigarh, India
4. Takahiro Tomoda, Tsubasa Okano, Kento Inoue, Motoi Yamashita, Takahiro Kamiya, Takeshi Isoda, Masakatsu Yanagimachi, Hirokazu Kanegane, Masatoshi Takagi, Tomohiro Morio, Kohsuke Imai. Second transplantation rescued the graft failure after hematopoietic stem cell transplantation. 3rd Scientific Congress of Asia Pacific Society for Immunodeficiencies 2020.02.09 Chandigarh, India.
5. Imai K. Viral infections in patients with hypogammaglobulinemia - What is our current understanding. 3rd Scientific Congress of Asia Pacific Society for Immunodeficiencies 2020.02.09 Chandigarh, India.
6. A PHASE 3 STUDY OF SAFETY AND TOLERABILITY OF IgPro10(PRIVIGEN®) IN JAPANESE PATIENTS WITH PRIMARY IMMUNODEFICIENCY. 2020.02.15
7. Mikhail A.Rojavin, Tomohiro Morio, Dandan Luo, Gautam Baheti, Jutta Hofmann, Michael A. Tortorici. INDIVIDUAL AND POPULATION-LEVEL PHARMACOKINETIC PROPERTIES OF PRIVIGEN® IN JAPANESE PATIENTS WITH PRIMARY IMMUNODEFICIENCY (PID). The 3rd Annual Scientific Meeting of the Japanese Society for Immunodeficiency and Autoinflammatory Diseases (JSIAD) 2020.02.15 Tokyo
8. An adult case of A20 haploinsufficiency diagnosed by the development of myocardial infarction due to coronary arteritis. 2020.02.15
9. Two cases identified CARD11 mutation with atopic dermatitis and susceptibility to infection. 2020.02.15
10. Genomics analysis of leukemia predisposition in X-linked agammaglobulinemia. 2020.02.16
11. A case of rheumatoid arthritis associated with IKAROS deficiency treated with abatacept. 2020.02.16
12. 175 cases of genetic testing by health insurance for primary immunodeficiency in Japan. 2020.02.16
13. Yoonsun Yoon, Ji-man Kang, Junsik Choi, Kangmo Ahn, Keon Hee Yoo, Eun-Suk Kang, Kyoung-Mee Kim, Jung Eun Lee, Geum-Youn gawk, Kihyun Kim, Kosuke Imai, Hirokazu Kanegane, Yae-jean Kim. Cancer development in a Korean family with CTLA-4 haploinsufficiency. The 3rd Annual Scientific Meeting of the Japanese Society for Immunodeficiency and Autoinflammatory Diseases (JSIAD) 2020.02.16 東京

14. Satoshi Miyamoto , Masakatsu Yanagimachi , Katsutsugu Umeda , Akihiro Iguchi , Yoji Sasahara , Hidetoshi Takada , Masafumi Yamada , Masataka Ishimura , Takashi Koike , Masahiro Yasui , Yoshiyuki Takahashi , Hiroshi Kawaguchi , Michiko Kajiwara , Masami Inoue , Koji Kato, Yoshiko Hashii, Yoshiko Atsuta , Hiromasa Yabe , Kohsuke Imai , Tomohiro Morio. Hematopoietic stem cell transplantation for inborn errors of immunity in Japan: overview of a nationwide retrospective analysis. 46th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2020 Virtual) 2020.08.29 WEB
15. Satoshi Miyamoto, Masakatsu Yanagimachi, Katsutsugu Umeda, Akihiro Iguchi, Yoji Sasahara, Hidetoshi Takada, Yoshiyuki Takahashi, Michiko Kajiwara, Masami Inoue, Koji Kato, Yoshiko Hashii, Yoshiko Atsuta, Hiromasa Yabe, Kohsuke Imai, Tomohiro Morio. Hematopoietic stem cell transplantation for severe combined immunodeficiency in Japan: a nationwide retrospective analysis. 46th Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT 2020 Virtual) 2020.08.29 WEB
16. Analysis of viral antigen-specific T memory stem cells induced by HTLV-I infection. Japanese Society of Immunotherapy for Hematological Disorders (JSIHD) 2020.09.12
17. Y. Imanaka, M. Taniguchi, T. Doi, M. Shimomura, M. Tsumura, S. Karakawa, K. Imai, T. Morio, A. Puel, J.-L. Casanova, O. Ohara, K. Kamei, M. Kobayashi, S. Okada. CARD9 DEFICIENCY IN A PATIENT WITH INVASIVE INFECTION DUE TO EXOPHIALA DERMATITIDIS AND THE ASYMPTOMATIC SIBLINGS. 19th Biennial Meeting of The European Society of immunodeficiencies (ESID 2020) 2020.10.14 web
18. P. Vignesh, A. Rawat, A. Singh, R. Kumrah, A. Gummadi, A. Kaur, S. Bhattad, A. Mehta, D. Suri, A. Jinda, D. Leung, S. Ramprakash, R. Cp, K.W. Chan, Y. Ogura, K. Imai, O. Ohara, S. Nonoyama, M. Hershfield, Y. Lau, S. Singh. CLINICAL, IMMUNOLOGICAL, AND MOLECULAR FEATURES OF SEVERE COMBINED IMMUNE DEFICIENCY: A REPORT OF 87 PATIENTS FROM 3 TERTIARY CARE CENTRES IN INDIA. 19th Biennial Meeting of The European Society of immunodeficiencies (ESID 2020) 2020.10.14 web
19. K. Tanita, F. Sakura, M. Tsumura, H. Ohnishi, A. Hoshino, K. Suzuki, S. Okada, R. Nambu, S. Umetsu, K. Imai, T. Morio, H. Kanegane. PATIENTS WITH THE GAIN-OF-FUNCTION MUTATIONS IN STAT3 PRESENT WITH A VARIETY OF AUTOIMMUNE DISEASES. 19th Biennial Meeting of The European Society of immunodeficiencies (ESID 2020) 2020.10.14 web
20. Akihiro Hoshino, Yuya Koda, Jun Kato, Kay Tanita, Hirokazu Kanegane . A plastic anemia as an initial manifestation in a patient with SAP deficiency. The 27th Annual Meeting of the Japan Childhood Aplastic Anemia Study Group 2020.11.08 Web 開催
21. CAR-T Therapy Practice: Through experience under various situations. 2020.11.21
22. A case of relapsed infant ALL with MLL rearrangement who underwent CAR-T cell therapy. 2020.11.21
23. A case of Autoimmune Lymphoproliferative Syndrome diagnosed by lymphadenopathy and autoantibody positivity. 2020.11.21
24. Non-coding RNA ThymoD transcription specifies T-cell fate and inhibits T-cell malignancies. 2020.11.21
25. Development of phase I clinical study of oral olaparib in pediatric patients with refractory solid tumors. 2020.11.21
26. Genomic analysis of B-lymphoblastic lymphoma with TCF3-PBX1. 2020.11.21
27. Preexisting conditions in ALL patients: A Nationwide Survey in Japan (JPLSG Scientific Committee). 2020.11.21
28. Clinical utility of comprehensive genomic profiling for pediatric and AYA solid tumor patients. 2020.11.21
29. Clinical feature and genetic alteration of Myeloid/Natural killer cell precursor acute leukemia (MNKPL). 2020.11.21
30. Allogeneic hematopoietic stem cell transplantation from haploidentical donors for non-malignant diseases with post-transplantation cyclophosphamide and anti-thymoglobulin. 2020.11.22
31. Inflammatory bowel disease associated with XIAP deficiency can be cured by allogeneic hematopoietic cell transplantation. 2020.11.22

Bio-Environmental Response

32. Salvage haploidentical bone marrow transplant using post-transplant cyclophosphamide for graft failure in a patient with EDA-ID due to NEMO deficiency. 2020.11.22
33. Pediatric Hodgkin's lymphoma subsequently diagnosed as common variable immunodeficiency with FAS mutation. 2020.11.22
34. Ruxolitinib administration for two cases with steroid-refractory lung GVHD. 2020.11.22
35. A retrospective study of six cases of HLA haplo-identical hematopoietic stem cell transplantation with Post-Transplant Cyclophosphamide. 2020.11.22
36. Challenges and Opportunities in Processing of Raw Materials and Cellular and Tissue-based Products at Hospitals. 5th DIA Cell and Gene Therapy Products Symposium in Japan(DIA) 2020.12.11

[Others]

1. Human Lifelong Immunity Depends on APRIL(Kohsuke Imai), 2020.06
AAAS EurekAlert! The Global Source for Science News

Rheumatology

Professor	Shinsuke YASUDA (2) Tetsuo KUBOTA (2) Kazuki TAKADA (3)
Associate Professor	Takahiko SUGIHARA
Junior Associate Professor	Hideyuki IWAI
Assistant Professor	Fumitaka MIZOGUCHI, Tadashi HOSOYA, Naoki KIMURA, Hisanori HASEGAWA, Natsuka UMEZAWA, Hirokazu SASAKI, Mari KAMIYA
Visiting Lecturer	Kimito KAWAHATA, Kenji NAGASAKA, Akito TAKAMURA, Makoto SOEJIMA, Hiroyuki HAGIYAMA, Yusuke MATSUO, Fumihito SUZUKI, Reiko TSUBATA, Kaori WATANABE, Jyunko NISHIO, Mari KIHARA, Toshihiro MATSUI, Tokishige MIYABE, Yasuo HIRANO
Affiliated Hospital Fumiaki	KONDO, Takeshi KUSUDA, Wakako KAWSAKI, Marina TSUCHIDA, Takuji ITAKURA, Masami TOKURA, Seiya OBA, Yuriko YAGYU, Motohiko SATO, Takahiro NAKAHARA
Resident	Tomoko NIWANO, Daisuke KAWADA, Riku YOSHITUKA, Yasuo YAMAGUCHI
Graduate Student	Akiou YAMAMOTO, Yasuhiro TAGAWA, Takumi MATSUMOTO, Fumiaki KONDO, Youji KOMIYA, Seiji NODA, Nao TANAKA, Hiroyuki BABA Seiya OBA, Marina TSUCHIDA
Office Administrator	Kaori KONNO, Yumiko KAWAKAMI, Yukako NAKAMURA, Tomoko TAKAHASHI (1)
Technical Staff	Kazuko YAMAZAKI, Naoko FUJITA

(1) Department of Lifetime Clinical Immunology, (2) Medical Innovation Promotion Center,
(3) Institute of global affairs

(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, Hagiyama H, Hirata S, Matsui K, Nonomura Y, Kondo M, Suzuki F, Nawata Y, Tomita M, Kihara M, Yokoyama-Kokuryo W, Hirano F, Yamazaki H, Sakai R, Nanki T, Koike R, Miyasaka N, Harigai M. An open-label, randomized controlled trial of sulfamethoxazole-trimethoprim for *Pneumocystis* prophylaxis: results of 52-week follow-up. *Rheumatology advances in practice*. 2020; 4(2); rkaa029
2. Kohei Karino, Michihiro Kono, Michihito Kono, Keita Sakamoto, Yuichiro Fujieda, Masaru Kato, Olga Amengual, Kenji Oku, Shinsuke Yasuda, Tatsuya Atsumi. Myofascia-dominant involvement on whole-body MRI as a risk factor for rapidly progressive interstitial lung disease in dermatomyositis. *Rheumatology (Oxford, England)*. 2020.01;
3. Slowikowski K, Nguyen HN, Noss EH, Simmons DP, Mizoguchi F, Watts GFM, Gurish MF, Brenner MB, Raychaudhuri S. CUX1 and I κ B ζ (NFKBIZ) mediate the synergistic inflammatory response to TNF and IL-17A in stromal fibroblasts. *Proceedings of the National Academy of Sciences of the United States of America*. 2020.02;
4. Yuichiro Fujieda, Mototsugu Doi, Takuya Asaka, Masahiro Ota, Ryo Hisada, Naoki Ohnishi, Michihiro Kono, Hiraku Kameda, Daigo Nakazawa, Masaru Kato, Olga Amengual, Masahiko Takahata, Shinsuke Yasuda, Yoshimasa Kitagawa, Tatsuya Atsumi. Incidence and risk of antiresorptive agent-related osteonecrosis of the jaw (ARONJ) after tooth extraction in patients with autoimmune disease. *Journal of bone and mineral metabolism*. 2020.02;
5. Noda S, Hasegawa H, Tokura M, Mizoguchi F, Kohsaka H. A Case of Systemic Lupus Erythematosus Presenting With Thrombotic Microangiopathy-Induced Cardiomyopathy. *Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases*. 2020.02;
6. Sae Ochi, Kazuyoshi Saito, Fumitaka Mizoguchi, Shigeaki Kato, Yoshiya Tanaka. Insensitivity versus poor response to tumour necrosis factor inhibitors in rheumatoid arthritis: a retrospective cohort study. *Arthritis Research & Therapy*. 2020.03; 22(1); 41
7. Yokoyama-Kokuryo Waka, Yamazaki Hayato, Takeuchi Tsutomu, Amano Koichi, Kikuchi Jun, Kondo Tsuneo, Nakamura Seiji, Sakai Ryoko, Hirano Fumio, Nanki Toshihiro, Koike Ryuji, Harigai Masayoshi. Identification of molecules associated with response to abatacept in patients with rheumatoid arthritis. *ARTHRITIS RESEARCH & THERAPY*. 2020.03; 22(1); 46
8. Wen Shi Lee, Shinsuke Yasuda, Michihiro Kono, Yuki Kudo, Sanae Shimamura, Michihito Kono, Yuichiro Fujieda, Masaru Kato, Kenji Oku, Tomohiro Shimizu, Tomohiro Onodera, Norimasa Iwasaki, Tatsuya Atsumi. MicroRNA-9 ameliorates destructive arthritis through down-regulation of NF- κ B1-RANKL pathway in fibroblast-like synoviocytes. *Clinical immunology (Orlando, Fla.)*. 2020.03; 212; 108348

9. Nobuya Abe, Masaru Kato, Michihito Kono, Yuichiro Fujieda, Hiroshi Ohira, Ichizo Tsujino, Noriko Oyama-Manabe, Kenji Oku, Toshiyuki Bohgaki, Shinsuke Yasuda, Tatsuya Atsumi. Right ventricular dimension index by cardiac magnetic resonance for prognostication in connective tissue diseases and pulmonary hypertension. *Rheumatology (Oxford, England)*. 2020.03; 59(3); 622-633
10. Yukino Usui, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Draft Genome Sequence of a *Clostridioides difficile* Sequence Type 97 Strain Belonging to Hypervirulent Clade 2. *Microbiol Resour Announc*. 2020.04; 9(14); e00245-20
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12. Protective Role of Optineurin Against Joint Destruction in Rheumatoid Arthritis Synovial Fibroblasts Arthritis and Rheumatology. 2020.09;
13. Tanaka N, Terao C, Nakayama Y, Sasai T, Umezawa N, Yagyu Y, Ito K, Koike R, Nakashima R, Hatta K, Mizoguchi F. Anti-MDA5 antibody-positive dermatomyositis with rapidly progressive interstitial lung disease disguising as anti-synthetase syndrome. *Rheumatology (Oxford, England)*. 2020.10;
14. Fujikawa Taro, Honda Keiji, Ito Taku, Kishino Mitsuhiro, Kimura Naoki, Umezawa Natsuka, Hirano Mana, Aoki Natsuki, Kawashima Yoshiyuki, Tsutsumi Takeshi. Enhanced fallopian canal as a potential marker for temporal bone vasculitis LARYNGOSCOPE INVESTIGATIVE OTOLARYNGOLOGY. 2020.11;
15. Hosoya T, Shukla NM, Fujita Y, Yao S, Lao FS, Baba H, Yasuda S, Cottam HB, Carson DA, Hayashi T, Corr M. Identification of Compounds With Glucocorticoid Sparing Effects on Suppression of Chemokine and Cytokine Production by Rheumatoid Arthritis Fibroblast-Like Synoviocytes. *Frontiers in pharmacology*. 2020.11; 11; 607713
16. Hosoya T, Sugihara T, Miyasaka N, Yasuda S. Novel treatment strategy of polymyalgia rheumatica targeting drug-free remission. *Clinical and experimental rheumatology*. 2020.11;

[Misc]

1. B cells targeting therapy in the management of systemic lupus erythematosus *Immunological Medicine*. 2020.01;
2. Natsuka Umezawa. Novel Therapeutic targets for inflammatory myopathies *Rheumatology*. 2020.04; 63(4); 433-437
3. Fumitaka Mizoguchi. The molecular mechanism to drive synovial inflammation and joint destruction in rheumatoid arthritis synovial fibroblasts *BIO Clinica*. 2020.08; 9(1); 61-65

[Conference Activities & Talks]

1. Fumitaka Mizoguchi. Gene expression profiling of synovial fibroblast subsets revealed novel transcription factors driving their pathogenic functions in rheumatoid arthritis. Keystone Symposia, Stromal Cells in Immunity and Disease 2020.02.23 Victoria, Canada
2. Mari Kamiya, Seon Uk Kim, Jeong Yeon Kim, Yeong Wook Song, Eun Young Lee, Fumitaka Mizoguchi. Glucagon-like peptide-1 receptor agonist ameliorated muscle weakness and inflammation in experimental polymyositis. European Congress of Rheumatology (EULAR) 2020 2020.06.06
3. Yamaguchi Ayako, Hirata Shintaro, Miyamoto Toshiaki, Tanimura Kazuhide, Iwai Hideyuki, Kaneko Yuko, Takeuchi Tsutomu, Amano Koichi, Iwamoto Naoki, Kawakami Atsushi, Murakami Miho, Nishimoto Norihiro, Atsumi Tatsuya, Sumida Takayuki, Mimori Tsuneyo, Yamanaka Hisashi, Fujio Keishi, Nakano Kazuhisa, Tanaka Yoshiya.. Treatment strategy of RA Possibility of drug free remission after sustained remission in patients with RA - The two-year results of the FREE-J study, a real world prospective

observational cohort study. 64th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2020.08

4. Mari Kamiya, Kimito Kawahata, Hitoshi Kohsaka , Fumitaka Mizoguchi. Targeting necroptosis in muscle cells ameliorates inflammatory myopathies. 64th Annual General Assembly and Scientific Meeting of the Japan College of Rheumatology 2020.08.17
5. Mari Kamiya, Seon Uk Kim, Jeong Yeon Kim, Shinsuke Yasuda, Eun Young Lee, Fumitaka Mizoguchi. Glucagon-like Peptide-1 Receptor Agonist Suppresses Muscle Inflammation and Muscle Fiber Death, and Ameliorates Muscle Weakness in Experimental Polymyositis. ACR Convergence 2020 2020.11.09 Online

Dermatology

Professor: Hiroo YOKOZEKI

Associate Professor: Takeshi NAMIKI

Junior Associate Professor: Tsukasa UGAJIN, Takichi MUNETSUGU

Project Associate Professor: Kaoru TAKAYAMA

Project Junior Associate Professor: Makiko NISHIDA

Assistant Professor: Shown TOKORO, Kohei KATO, Tadatsune IIDA

Senior Resident: Masahiro KATAGIRI, Rina Otake, Shogo WADA

Resident: Masato FUNAZUMI, Misaki KITAHARA

Student: Minako INAZAWA, Aiko FURUI, Michiko NAKAMURA, Kohei NOJIMA, Kohei KATO, Sally ESHIBA, Atushi SHIRANE, Daiki FUKAE

Technical Assistant: Chiyako MIYAGISHI

Staff Assistant: Masae SAKATA, Mayuko HAYASHI,

(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 theories (STAT6 decoy ODN) for

severe atopic dermatitis in the clinic.

(4) Publications

[Original Articles]

1. Kumazawa T, Kotake K, Nishimura A, Asai N, Ugajin T, Yokozeki H, Adachi T. Isolation of food-derived bacteria inducing interleukin-22 in B cells. *Bioscience of microbiota, food and health*. 2020; 39(1); 1-9
2. Kumazawa Toshihiko, Kotake Kunihiko, Nishimura Atsuhisa, Asai Noriyuki, Ugajin Tsukasa, Yokozeki Hiroo, Adachi Takahiro. Isolation of food-derived bacteria inducing interleukin-22 in B cells(和訳中) *Bioscience of Microbiota, Food and Health*. 2020.01; 39(1); 1-9
3. Al-Busani H, Al-Sobaihi S, Nojima K, Tanemura A, Yaguchi T, Kawakami Y, Matsumura H, Nishimura EK, Yokozeki H, Namiki T. NUA2 localization in normal skin and its expression in a variety of skin tumors with YAP. *Journal of dermatological science*. 2020.02; 97(2); 143-151
4. Al-Busani Hind, Al-Sobaihi Saber, Nojima Kohei, Tanemura Atsushi, Yaguchi Tomonori, Kawakami Yutaka, Matsumura Hiroyuki, Nishimura Emi K., Yokozeki Hiroo, Namiki Takeshi. NUA2 localization in normal skin and its expression in a variety of skin tumors with YAP(和訳中) *Journal of Dermatological Science*. 2020.02; 97(2); 143-151
5. Inui Keiko, Ugajin Tsukasa, Namiki Takeshi, Yokozeki Hiroo. Chronic prurigo: A retrospective study of 168 cases *JOURNAL OF DERMATOLOGY*. 2020.03; 47(3); 283-289
6. Inui Keiko, Ugajin Tsukasa, Namiki Takeshi, Yokozeki Hiroo. Chronic prurigo: A retrospective study of 168 cases(和訳中) *The Journal of Dermatology*. 2020.03; 47(3); 283-289
7. Chinuki Yuko, Yagami Akiko, Adachi Atsuko, Matsunaga Kayoko, Ugajin Tsukasa, Yokozeki Hiroo, Hayashi Misa, Katayama Ichiro, Kohno Kunie, Shiwaku Kuninori, Morita Eishin. 加水分解コムギ蛋白質アレルギーにおいてオマリズマブ短期投与により in vitro 好塩基球活性化が低下する (In vitro basophil activation is reduced by short-term omalizumab treatment in hydrolyzed wheat protein allergy) *Allergology International*. 2020.04; 69(2); 284-286
8. Dobashi K, Usami A, Yokozeki H, Tsurikisawa N, Nakamura Y, Sato K, Okumura J, Yamaguchi M, Committee for Japanese Guideline for Diagnosis and Management of Occupational Allergic Disease., Japanese Society of Allergology.. Japanese guidelines for occupational allergic diseases 2020. *Allergology international : official journal of the Japanese Society of Allergology*. 2020.05;
9. Al-Busani Hind, Namiki Takeshi, Miura Keiko, Yokozeki Hiroo. Mixed-pattern syphilitic alopecia of the scalp associated with uveitis and asymptomatic neurosyphilis *JOURNAL OF DERMATOLOGY*. 2020.05;
10. Wataya-Kaneda Mari, Nagai Hiroshi, Ohno Yuuki, Yokozeki Hiroo, Fujita Yasuyuki, Niizeki Hironori, Yoshida Kazue, Ogai Masaaki, Yoshida Yuichi, Asahina Akihiko, Fukai Kazuyoshi, Tateishi Chiharu, Hamada Izumi, Takahata Tatsuro, Shimizu Kenji, Shimasaki Shigeki, Murota Hiroyuki. Safety and Efficacy of the Sirolimus Gel for TSC Patients With Facial Skin Lesions in a Long-Term, Open-Label, Extension, Uncontrolled Clinical Trial *DERMATOLOGY AND THERAPY*. 2020.05;
11. Hind Al-Busani, Takeshi Namiki, Shown Tokoro, Tsukasa Ugajin, Keiko Miura, Hiroo Yokozeki. Bilateral juvenile temporal arteritis mimicking clinical features of classic giant cell arteritis. *Int. J. Dermatol.*. 2020.06;
12. Al-Busani Hind, Namiki Takeshi, Yoshioka Yusuke, Ugajin Tsukasa, Miura Keiko, Yokozeki Hiroo. Basal cell carcinoma in a patient with Wiskott-Aldrich syndrome: an immunohistochemical analysis of infiltrating cells around the tumour *EUROPEAN JOURNAL OF DERMATOLOGY*. 2020.07; 30(4); 421-422
13. Dobashi Kunio, Usami Atsushi, Yokozeki Hiroo, Tsurikisawa Naomi, Nakamura Yoichi, Sato Kazuhiro, Okumura Jiro, Yamaguchi Masao, Akiyama Kazuo, Ikezawa Zenro, Takayama Kaoru, Matsunaga Kayoko, Naito Kensei, Nakazawa Tsugio, Ohta Ken, Okano Mitsuhiko, Tohda Yuji, Watanabe Masanari, Committee for Japanese Guideline for Diagnosis and Management of Occupational Allergic Disease, The Japanese Society of Allergology. Japanese guidelines for occupational allergic diseases 2020(和訳中) *Allergology International*. 2020.07; 69(3); 387-404

14. Al-Busani Hind, Namiki Takeshi, Miura Keiko, Yokozeki Hiroo. ブドウ膜炎および無症候性神経梅毒を伴う頭皮の混合パターン梅毒脱毛症 (Mixed-pattern syphilitic alopecia of the scalp associated with uveitis and asymptomatic neurosyphilis) *The Journal of Dermatology*. 2020.08; 47(8); e311-e313
15. Ugajin Tsukasa, Kobayashi Yukihiro, Takayama Kaoru, Yokozeki Hiroo. A case of fish allergy to parvalbumin successfully treated with oral immunotherapy using cooked, hypoallergenic fish(和訳中) *アレルギー*. 2020.10; 69(臨時増刊号); 164
16. Mori Yukari, Ugajin Tsukasa, Okada Kouhei, Handa Yutaro, Umemoto Naoshi, Iijima Hazuki, Igawa Ken, Yokozeki Hiroo. Epicutaneously sensitized food-induced anaphylaxis is ameliorated with "oral tolerance" to antigen *EXPERIMENTAL DERMATOLOGY*. 2020.11;
17. Ugajin Tsukasa, Mori Yukari, Okada Kohei, Umemoto Naoshi, Igawa Ken, Yokozeki Hiroo. Food-induced anaphylaxis caused by epicutaneous sensitization is prevented with prior oral exposure to antigen(和訳中) *日本研究皮膚科学会年次学術大会・総会プログラム*. 2020.11; 45 回; 152
18. Hashimoto Takashi, Yamazaki Yuki, Yokozeki Hiroo, Satoh Takahiro. Macrophages are the major cellular sources of IL-31 in atopic dermatitis: a novel network of itch comprising TSLP, periostin, and basophils(和訳中) *日本研究皮膚科学会年次学術大会・総会プログラム*. 2020.11; 45 回; 161
19. Iida Tadatsune, Fukae Daiki, Yokozeki Hiroo. Multicolor three-dimensional reconstruction of whole murine sweat glands using optical clearing and twophoton excitation microscopy(和訳中) *日本研究皮膚科学会年次学術大会・総会プログラム*. 2020.11; 45 回; 180

NCCHD Child Health and Development

1. Staffs and Students

Collaborative Professor	Akutsu, Hidenori
Collaborative Professor	Onodera, Masashi
Collaborative Professor	Fukami, Maki
Collaborative Professor	Hata, Kenichiro
Collaborative Professor	Takada, Shuji
Collaborative Professor	Matsumoto, Kenji

2. Purpose of Education

The goal of this course is to learn the developmental process of human life from the viewpoints of latest molecular biology and genetics. Medical science for child health and development is the study to comprehensively grasp various health problems related to “human life cycle” to begin with the fertilization and to continue to the next generation through generation and development. Students of this course are required to understand a role and a function of medical care for child health and development, to acquire ability to handle such health problems and support relevant person with specialized theory and technique.

3. Research Subjects

1) Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells Application studies for reproductive medicine and regenerative medicine (Akutsu, Hidenori; Center for Regenerative Medicine, National Institute for Child Health and Development)

Exploring molecular mechanism for acquisition of zygote totipotency, epigenetic reprogramming and pluripotency in stem cells. Application studies for reproductive medicine and regenerative medicine.

2) Studying for cellular model in human severe disease by advancing flow cytometry (Onodera, Masashi; Dept. of Human Genetics, National Institute for Child Health and Development)

We aim to identify causative genes for child intractable hereditary diseases and analyze their functions to develop new gene-based therapeutic options. We also establish iPS cells from peripheral blood or skin fibroblasts obtained from patients with intractable hereditary diseases such as primary immunodeficiencies and congenital metabolic disorders.

3) Elucidation of genetic abnormality in congenital severe metabolic diseases using advanced genetic analysis

(Fukami, Maki; Dept. of Molecular Endocrinology, National Institute for Child Health and Development)

Our objective is to clarify the molecular basis of congenital endocrine-related disorders and apply our findings to new innovations in clinical medicine. We investigate the molecular basis of single gene disorders, epigenetic/inprinting disorders, and multifactorial disorder.

4) Elucidating for molecular mechanism of perinatal abnormality using system biology

(Hata, Kenichiro; Dept. of Maternal-Fetal Biology, National Institute for Child Health and Development)

We aim to clarify mechanisms underlying abnormalities in fetal development and placentation, and/or perinatal diseases with developmental defects. To identify the underlying mechanisms of perinatal diseases, we take advantage of post-genomic technologies and investigate etiologies using an integrated genomic and epigenomic approach.

5) Identification of target molecules in severe diseases and establishment of disease model mice by studying molecular mechanisms of genomic imprinting, gametogenesis and sexual differentiation

(Takada, Shuji; Dept. of Systems Biomedicine, National Institute for Child Health and Development)

Our aim is to reveal the molecular mechanisms underlying embryonic development, cell differentiation and tissue formation and apply our findings to understand the causes of developmental diseases.

6) Elucidation for allergic disease mechanism and target molecules using molecular biology and 'omics' technology

(Matsumoto, Kenji; Dept. of Allergy and Clinical Immunology, National Institute for Child Health and Development)

Our mission is to clarify the precise pathogenic mechanisms of various immunological and allergic diseases, such as Kawasaki disease, various allergic diseases, allogenic immune tolerance, congenital viral infections and severe infectious diseases. To achieve this, we employ various experimental approaches, including epidemiology, clinical and basic research. Our ultimate aim is to develop better means of preventing, diagnosing and treating allergic and immunological and infectious diseases based on our research findings and cumulative knowledge.

4. Publications

[OriginalArticles]

1. Isono W, Kawasaki T, Ichida JK, Ayabe T, Hiraike O, Umezawa A, Akutsu H*. The combination of dibenzazepine and a DOT1L inhibitor enables a stable maintenance of human naïve-state

- pluripotency in non-hypoxic conditions. *Regen Ther* 2020; 15: 161-168.
2. Tsuruta S, Uchida H, Akutsu H*. Intestinal Organoids Generated from Human Pluripotent Stem Cells. *JMA J* 2020; 3: 9-19.
 3. Umezawa A, Sato Y, Kusakawa S, Amagase R, Akutsu H, Nakamura K, Kasahara M, Matsubara Y, and Igarashi T. Research and Development Strategy for Future Embryonic Stem Cell-Based Therapy in Japan. *JMA Journal*. 2020; 3: 287-294.
 4. Nishino K, Takasawa K, Okamura K, Arai Y, Sekiya A, Akutsu H, Umezawa A. Identification of an epigenetic signature in human induced pluripotent stem cells using a linear machine learning model. *Hum Cell*. 2021; 34: 99-110.
 5. Sugawara T, Miura T, Kawasaki T, Umezawa A, Akutsu H*. The hsa-miR-302 cluster controls ectodermal differentiation of human pluripotent stem cell via repression of DAZAP2. *Regen Ther*. 2020; 15: 1-9.
 6. Nakatake Y, Ko SBH, Sharov AA, Wakabayashi S, Murakami M, Sakota M, Chikazawa N, Ookura C, Sato S, Ito N, Ishikawa-Hirayama M, Mak SS, Jakt LM, Ueno T, Hiratsuka K, Matsushita M, Goparaju SK, Akiyama T, Ishiguro KI, Oda M, Gouda N, Umezawa A, Akutsu H, Nishimura K, Matoba R, Ohara O, Ko MSH. Generation and Profiling of 2,135 Human ESC Lines for the Systematic Analyses of Cell States Perturbed by Inducing Single Transcription Factors. *Cell Rep*. 2020; 31(7):107655.
 7. Tsuchida N, Kojima J, Fukuda A, Oda M, Kawasaki T, Ito H, Kuji N, Isaka K, Nishi H, Umezawa A, Akutsu H*. Transcriptomic features of trophoblast lineage cells derived from human induced pluripotent stem cells treated with BMP 4. *Placenta*. 2020; 89: 20-32.
 8. Tomikawa J, Takada S, Okamura K, Terao M, Ogata-Kawata H, Akutsu H, Tanaka S, Hata K, Nakabayashi K. Exploring trophoblast-specific Tead4 enhancers through chromatin conformation capture assays followed by functional screening. *Nucleic Acids Research*. 2020;48(1):278-289.
 9. Fujitani K, Otomo A, Nagayama Y, Tachibana T, Kato R, Kawashima Y, Kodera Y, Kato T, Takada S, Tamura K, Takamatsu N, Ito M. PACT/PRKRA and p53 regulate transcriptional activity of DMRT1. *Genetics and Molecular Biology*. 2020;43(2):e20190017.
 10. Sato T, Kataoka K, Ito Y, Yokoyama S, Inui M, Mori M, Takahashi S, Akita K, Takada S, Ueno-Kudoh H, Asahara H. Lin28a/let-7 Pathway Modulates the Hox Code via Polycomb Regulation during Axial Patterning in Vertebrates. *Elife*. 2020;9:e53608.
 11. Akiba K, Narumi S, Nishimura R, Kato-Fukui Y, Takada S, Hasegawa Y, Fukami M. SOX9 is colocalized with paraspeckle protein NONO in cultured murine sertoli cells and features structural characteristics of intrinsically disordered proteins. *Molecular Reproduction and Development*. 2020;87(11):1124-1125.
 12. Akino R, Matsui D, Kawahara-Miki R, Amita M, Tatsumi K, Ishida E, Kang W, Takada S, Miyado K, Sekizawa A, Saito T, Kono T, Saito H. Next-generation sequencing reveals downregulation of the Wnt signaling pathway in human dysmature cumulus cells as a hallmark for evaluating oocyte quality. *Reproductive Medicine*, 2020;1(3):205-215.
 13. Yamamoto-Hanada K, Pak K, Saito-Abe M, Yang L, Sato M, Mezawa H, Sasaki H, Nishizato M, Konishi M, Ishitsuka K, Matsumoto K, Saito H, Ohya Y. Cumulative inactivated vaccine exposure and allergy development among children: a birth cohort from Japan. *Environ Health Prev Med* 2020;25:27.
 14. Yamamoto-Hanada K, Kawakami E, Saito-Abe M, Sato M, Mitsubuchi H, Oda M, Katoh T, Sanefuji M, Ohga S, Kuwajima M, Mise N, Ikegami A, Kayama F, Senju A, Shimono M, Kusuhara K, Yamazaki S, Nakayama SF, Matsumoto K, Saito H, Ohya Y. Exploratory analysis

- of plasma cytokine/chemokine levels in 6-year-old children from a birth cohort study. *Cytokine* 2020;130:155051.
15. Unno H, Arae K, Matsuda A, Ikutani M, Tamari M, Motomura K, Toyama S, Suto H, Okumura K, Morita H, Sudo K, Saito H, Matsumoto K, Nakae S. Critical role of IL-33, but not IL-25 or TSLP, in silica crystal-mediated exacerbation of allergic airway eosinophilia. *Biochem Biophys Res Commun* 2020;533:493-500.
 16. Tanaka K, Nakabayashi K, Kawai T, Tanigaki S, Matsumoto K, Hata K, Kobayashi Y. Gene expression and DNA methylation changes in BeWo cells dependent on tumor necrosis factor-alpha and insulin-like growth factor-I. *Hum Cell* 2020;33:37-46.
 17. Sato M, Yamamoto-Hanada K, Tada H, Irahara M, Saito-Abe M, Matsumoto K, Pak K, Kido H, Ohya Y. Diagnostic performance of IgE avidity for hen's egg allergy in young infants. *J Allergy Clin Immunol Pract* 2020;8:2417-20 e6.
 18. Okada N, Sasaki A, Saito J, Mitani Y, Yachie A, Takahashi H, Matsubara S, Tenkumo C, Tanaka H, Hata T, Motomura K, Nagasawa J, Wada Y, Sako M, Yamaguchi K, Matsumoto K, Nakamura H, Sago H, Mizuta K. The Japanese experience and pharmacokinetics of antenatal maternal high-dose immunoglobulin treatment as a prophylaxis for neonatal hemochromatosis in siblings. *J Matern Fetal Neonatal Med* 2020;33:142-8.
 19. Ohno T, Nakamura T, Nakae S, Morita H, Matsumoto K, Saito H, Takeda K, Okumura K, Azuma T. TSLP is a negative regulator of RANKL-induced osteoclastogenesis. *Biochem Biophys Res Commun* 2020;530:508-12.
 20. Kobari S, Kusakabe T, Momota M, Shibahara T, Hayashi T, Ozasa K, Morita H, Matsumoto K, Saito H, Ito S, Kuroda E, Ishii KJ. IL-33 Is Essential for Adjuvant Effect of Hydroxypropyl- β -Cyclodextrin on the Protective Intranasal Influenza Vaccination. *Front Immunol* 2020;11:360.
 21. Iwata W, Unoki-Kubota H, Kato H, Shimizu A, Matsumoto M, Imasawa T, Igarashi A, Matsumoto K, Noda T, Terauchi Y, Nangaku M, Kasuga M, Kaburagi Y. Podocyte-specific deletion of tubular sclerosis complex 2 promotes focal segmental glomerulosclerosis and progressive renal failure. *PLoS One* 2020;15:e0229397.
 22. Inoue T, Murakami S, Matsumoto K, Matsuda A. Functional benefits of corticosteroid and IVIG combination therapy in a coronary artery endothelial cell model of Kawasaki disease. *Pediatr Rheumatol Online J* 2020;18:76.
 23. Inoue T, Miyashita M, Murakami S, Igarashi A, Motomura K, Abe J, Matsumoto K, Matsuda A. IL-1 β and IL-17A are involved in IVIG resistance through activation of C/EBP β and δ in a coronary artery model of Kawasaki disease. *Allergy* 2020;75:2102-5.
 24. Fujishima H, Okada N, Matsumoto K, Shimizu E, Fukuda S, Tomita M. Conjunctival Injection Reduction in Patients with Atopic Keratoconjunctivitis Due to Synergic Effect of Bovine Enteric-Coated Lactoferrin in 0.1% Tacrolimus Ophthalmic Suspension. *J Clin Med* 2020;9:3093.
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 26. Sutani A, Shima H, Hijikata A, Hosokawa S, Katoh-Fukui Y, Takasawa K, Suzuki E, Doi S, Shirai T, Morio T, Fukami M, Kashimada K. WDR11 is another causative gene for coloboma, cardiac anomaly and growth retardation in 10q26 deletion syndrome. *Eur J Med Genet.* 63(1),

- 103626, 2020
27. Kinjo K, Yoshida T, Kobori Y, Okada H, Suzuki E, Ogata T, Miyado M, Fukami M. Random X chromosome inactivation in patients with Klinefelter syndrome. *Mol Cell Pediatr* 7(1):1, 2020
 28. Saito-Abe M, Yamamoto-Hanada K, Nakayama SF, Hashimoto Y, Natsume O, Fukami M, Hasegawa T, Ohya Y. Reference values for salivary cortisol in healthy young infants by LC-MS/MS. *Pediatr Int.* 62(7):785-788, 2020
 29. Suzuki E, Kobori Y, Katsumi M, Ushijima K, Uchiyama T, Okada H, Miyado M, Fukami M. Copy-number analysis of Y chromosomal loci in young men with non-obstructive azoospermia: Implications for the rarity of early onset mosaic loss of chromosome Y. *Reprod Med Biol.* 19(2):178-181, 2020
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 31. Inoue T, Nakamura A, Iwahashi-Odano M, Tanase-Nakao K, Matsubara K, Nishioka J, Maruo Y, Hasegawa Y, Suzumura H, Sato S, Kobayashi Y, Murakami N, Nakabayashi K, Yamazawa K, Fuke T, Narumi S, Oka A, Ogata T, Fukami M, Kagami M. Contribution of gene mutations to Silver-Russell syndrome phenotype: multigene sequencing analysis in 92 etiology-unknown patients. *Clin Epigenet.* 12(1):86, 2020
 32. Yamoto K, Saitsu H, Fujisawa Y, Kato F, Matsubara K, Fukami M, Kagami M, Ogata T. Coffin-Lowry syndrome in a girl with 46,XX,t(X;11)(p22;p15)dn: Identification of RPS6KA3 disruption by whole genome sequencing. *Clin Case Rep.* 8(6):1076-1080, 2020
 33. Kinjo K, Nagasaki K, Muroya K, Suzuki E, Ishiwata K, Nakabayashi K, Hattori A, Nagao K, Nozawa RS, Obuse C, Miyado K, Ogata T, Fukami M, Miyado M. Rare variant of the epigenetic regulator SMCHD1 in a patient with pituitary hormone deficiency. *Sci Rep.* 10(1):10985. 2020
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Human Pathology

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(1) Outline

Pathology is the studies in which one theorizes and understands disease, as the language implies disease (pathos hardship) + theory (logos logic). Later, as research subjects that caused diseases were subdivided and research methods advanced, bacteriology (microbiology), parasitology (medical zoology), immunology, and molecular biology became independent from the category of pathology. In recent years, academic fields have been restructured beyond the framework of conventional academic fields, and there is a tendency for them to be further subdivided according to purposes, research subjects, and research methods. At present, pathology, based on morphology, is the study of understanding and organizing the causes of diseases (etiology), the formation of lesions (histogenesis), and disease status (pathogenesis). In the recent pathology, the fields of experimental pathology, in which hypotheses are experimentally proven using laboratory animals and cultured cells, and the fields of surgical pathology and diagnostic pathology, which are closely related to the clinical medicine, tend to be separated, and the number of pathologists engaged in the latter, which deals with human tissues, is increasing.

In the field of Human Pathology of TMDU, we aim to train pathologists who can accurately make pathological diagnosis of various human diseases, and at the same time, to develop pathologists who have a research mind capable of carrying out research that leads to improvement of pathological diagnosis, with the aim of elucidating the etiology, histogenesis and mechanism of human diseases.

(2) Research

About human cancer:

There are three main purposes.

(1) Carcinogenesis and histogenesis of cancers: For the understanding of G-I tract cancers, such as esophageal cancers, gastric cancers, colorectal cancers, and colitic cancers, and lung cancers, premalignant lesions will be clarified by histopathological analyses, clinicopathological analyses, and genetic analyses, and the process and molecular basis of carcinogenesis from premalignant lesions will be clarified.

(2) Objective diagnosis of pathological diagnosis related to cancer: Cancer originating from any organ is difficult to differentiate from benign tumors originating from that organ, and there are also borderline tumors of benign and malignant tumors. In addition, many of the pathological findings with clinical significance are based on subjective judgment, and the objectivity, reproducibility, and agreement rate among observers of the findings are problematic. In pathological diagnosis, it is important to apply computer, Ai, and image analysis technology, and

establishment of new pathological diagnosis which integrates genome information and various marker expression information of which the advance is remarkable recently is required.

(3) Malignant tumor progression and mechanism of metastasis: In human esophageal cancer, gastric cancer, colorectal cancer, and lung cancer, early cancer is often found, and reduced operations and treatments such as endoscopic resection are often performed. However, there are some high-grade cases showing metastasis from the early stage, and it is necessary to diagnose them in the early stage and select an appropriate therapy. In the process of invasion of early cancers, it is important to clarify the pathological findings related to metastasis and recurrence and to clarify the molecular basis closely related to them. By establishing markers that can be applied to pathological diagnosis, more accurate pathological diagnosis will become possible.

About chronic inflammatory diseases:

To clarify the etiology and origin of a chronic inflammatory disease of unknown origin by thoroughly analyzing the lesion site from a pathological standpoint. In addition, markers useful for diagnosis will be developed and applied to actual pathological diagnosis.

1) The possibility that intracellular latent infection in the deep organ of *Propionibacterium acnes* and rapid activation of autophagy and induction of Th1 immune response with the endogenous activation are causes of granuloma formation is studied on the sarcoidosis from the immunopathology viewpoint. Acne infection has been reported to be associated with diseases other than sarcoidosis, and its relationship to other diseases is also being studied.

2) Regarding the pathogenetic mechanism of chronic gastritis caused by infection of *Helicobacter pylori* on the surface of gastric mucosa, we found that *Helicobacter pylori* invades the lamina propria and translocates to regional lymph nodes of the stomach due to injury of the surface epithelium of the mucosa. Therefore, we investigated the possibility that *Helicobacter pylori* contributes to chronic inflammation of the gastric mucosa by directly stimulating immunocompetent cells in the mucosa and chronically stimulates the immune system in the paracortical region after influx to the lymph nodes. It is also known that the risk of developing gastric cancer varies depending on the structure of *Helicobacter pylori*. We are also developing test kits that can clarify the relationship between the structure of *H. pylori* and the risk of carcinogenesis and evaluate the risk of carcinogenesis by *H. pylori*.

3) Characteristic pathological findings observed in inflammatory colitis such as ulcerative colitis and Crohn's disease are analyzed, and their occurrence mechanism and significance are verified. In addition, evaluation of the activity of inflammation using biopsy materials and expression of molecular markers are studied.

4) Diagnosis of the type of systemic amyloidosis is very important for deciding the treatment plan of patients, but useful antibodies for diagnosis are not sufficiently available. Research is being conducted on the development and application of diagnostic antibodies that can improve the accuracy of pathological diagnosis.

(3) Education

In the graduate school doctoral program, the acquisition of the pathology medical specialist qualification is also made to be a goal with the doctor degree acquisition. First of all, training in autopsy, biopsy tissue diagnosis, rapid tissue diagnosis, tissue diagnosis of surgical specimens, etc., will be conducted, and training in the department of Diagnostic Pathology, TMDU hospital, as well as in the department of pathological diagnosis of the related hospitals will be conducted, with the aim of forming the basis for a "pathologist". During the training, participants will participate in various conferences or meetings in joint with clinical departments to announce pathological diagnoses, identify current problems in each clinical field, and discuss or collaborate with clinicians. While forming a basis as a pathologist, we will conduct research using clinicopathological, immunohistologic, and molecular pathological methods on issues directly related to the causes, diagnosis, and treatment of human diseases. The results will be published in academic meetings and academic journals in Japan and overseas.

(4) Lectures & Courses

What society calls for in medical care is proper diagnosis and treatment. Therefore, in the field of Human Pathology, the aim is to study the etiology, histogenesis, diagnosis, and treatment of human diseases with a strong awareness of problems and deep thought, while focusing on the study of clinical pathology, including histopathological diagnosis of autopsy, biopsy and surgically resected specimens. The results of the research should not only deepen the understanding of diseases, but also be useful for medical care and pathological diagnosis.

(5) Clinical Services & Other Works

As a general rule, all graduate students with a medical doctor's license are concurrently engaged in the Diagnostic Pathology department, TMDU hospital, where they are trained in pathological diagnosis and autopsy, with the aim of acquiring a qualification as a pathology specialist. In addition, staff and graduate students are working as part-time physicians at affiliated hospitals of TMDU in Tokyo, Kanagawa, Saitama, Chiba, and Ibaraki prefectures, which play a central role in supporting local medical care, to support pathological diagnosis and conduct joint research. In the field of Human Pathology, we hope to contribute to community medicine and society by improving the accuracy of pathological diagnosis. We are also actively cooperating in various academic activities, such as lecture presentations and conference participation in local hospitals. We also actively participate in and cooperate with the activities of various academic societies, including the Japanese Society of Pathology. In particular, we are involved in the management of the Japanese Society of Pathology and play a core role. Staff members also participate in and cooperate with various committees of ministries and agencies, including the Ministry of Health, Labour and Welfare.

(6) 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."

(7) Publications

[Original Articles]

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32. Koga-Kobori S, Sawa N, Kido R, Sekine A, Mizuno H, Yamanouchi M, Hayami N, Suwabe T, Hoshino J, Kinowaki K, Ohashi K, Fujii T, Ubara Y. Fabry Disease on Peritoneal Dialysis with Cardiac Involvement. *Internal medicine (Tokyo, Japan)*. 2020.12;

33. Koike C, Okudela K, Matsumura M, Mitsui H, Suzuki T, Arai H, Kataoka T, Ishikawa Y, Umeda S, Tateishi Y, Ohashi K. Frequent DYRK2 gene amplification in micropapillary element of lung adenocarcinoma - an implication in progression in EGFR-mutated lung adenocarcinoma. *Histology and histopathology*. 2020.12; 18294
34. Kuroha Masae, Tamura Kaoru, Inaji Motoki, Hashimoto Satoka, Kobayashi Daisuke, Tanaka Yoji, Nariai Tadashi, Maehara Taketoshi. TWO CASES OF H3 K27M-MUTANT DIFFUSE MIDLINE GLIOMA OF CERVICAL SPINAL CORD NEURO-ONCOLOGY. 2020.12; 22; 353

Physiology and Cell Biology

Professor: Yoshikazu Isomura
 Associate professor: Riichiro Hira
 Assistant professor: Alain Rios
 Assistant professor: Tomohiko Yoshizawa (until Sept 2020)
 Specially appoint researcher: Masanori Kawabata

(1) Outline

One of the major goals of the Department of Physiology and Cell Biology is to elucidate the basic principles of the brain networks that are responsible for behavioral expression in rodents. Our neurophysiological research focuses mainly on the neural networks of the cerebral cortex, hippocampus, basal ganglia and thalamus that regulate particular behavioral tasks in rats; this research utilizes multichannel electrode-based multineuronal recording technology, optogenetics involving genetically modified animals and adeno-associated virus vectors, and theoretical analysis technologies.

(2) Research

Research Agenda – What do we want to know?

In the sensory, association and motor cortices in the cerebral cortex, the excitatory pyramidal cells and inhibitory interneurons form an intracortical circuit. These brain areas, which play important roles in appropriate behavioral expression, are connected with each other and form the interareal circuit that consists of complex intercortical and subcortical connections through the hippocampus, striatum, substantia nigra and thalamus.

In the 20th century, the spike (unit) activity of single neurons in the brain that are related to behavior was actively studied using the single-unit recording technique. From a technical point of view, however, it was extremely difficult to investigate neuron subtypes and axonal connections by this method. Therefore, we developed a new experimental technique and used it to initiate a study of the basic principles whereby neural networks, particularly those in the cerebral cortex, encode behavioral information.

Research Techniques – How do we find answers?

1. Operant Learning Task

With the conventional technique of operant conditioning, it took weeks to months to train rats to obtain rewards by pushing a lever with their forelimb. Therefore, we developed a “spout-lever” by integrating a lever and a spout, and this enabled us to train rats to perform the forelimb movement task in a short period of time. This method allows for more rapid generation of rats to perform particular behavioral tasks in physiological experiments.

2. Multineuronal Recording

Multineuronal recording is a physiological technique in which spike activities of a large number of neurons are simultaneously recorded using silicon probes (multichannel electrodes). Signals recorded with electrode are distinguished by spike sorting, an analysis technique, to separate the spike (unit) activity produced by each neuron. Multineuronal recording also makes it possible to simultaneously record local field potentials and spike activities to permit the analysis of functional synchronous oscillation activities such as gamma and ripple waves.

3. Optogenetics

To understand the mechanism of information processing in neuronal networks, it is useful to demonstrate causality by optogenetically manipulating signals flowing in the networks. We are conducting experiments using gene-expressing virus vectors as well as transgenic rats that express channelrhodopsin-2, which uses blue light to depolarize membrane potentials. In addition, we are conducting research to establish a multi-line analysis technique that identifies axonal projections of recorded neurons by combining multineuronal recording technology with optogenetics.

4. Theoretical Analysis – Simulation Modeling

In collaboration with computational neuroscientists, we are conducting sophisticated and efficient theoretical analyses of multineuronal recording data. Our goal is to fuse experiment and theory by utilizing simulation and modeling techniques.

Research Methodologies – Pursuing Originality

Our research targets the brain networks in rats that are responsible for behavioral expression in order to understand essential brain mechanisms. Conventional neuroscience has often explored the functional localization in the brain by “averaging” brain activities. However, brain activities dynamically change every second, and there is no doubt that it is not just single areas that play a role in information processing, but rather the whole network, which consists of multiple areas. Therefore, we aim to perform truly original research by increasing the sophistication of our methods and extending our interests to multidisciplinary research without fear of failure, from the viewpoints of “from static to dynamic states” and “from points to lines.”

see

<https://researchmap.jp/yoshikazuisomura/>

(3) Education

The Department of Physiology and Cell Biology supports excellent next-generation researchers such as post-doctoral research fellows and graduate students through research activities that aim to elucidate the basic principles of brain networks. In principle, students define their research topics based on their future goals. One experimental setup is provided per one or two students/researchers. They receive curricula to learn a series of experimental techniques, join discussions that develop their logical thinking ability rather than simply increasing their knowledge, and receive opportunities to effectively conduct collaborative research in and out of the laboratory.

The Department is responsible for a lecture and laboratory practice on General Physiology for medical school students. It also provides research training for students during the project semester and MD-PhD courses that aim to foster basic researchers in the early stages of their education. The field of physiology is essential for comprehensively understanding body functions and providing the foundation for doctors to treat patients. We hope that you will voluntarily and actively participate in the activities of the department to immerse yourself in physiology.

(4) Lectures & Courses

We respect each one’s independence and positive attitude, and foster a sense of social cooperation and responsibility.

(5) Publications

[Original Articles]

1. Daisuke Kato, Hiroaki Wake, Philip R Lee, Yoshihisa Tachibana, Riho Ono, Shouta Sugio, Yukio Tsuji, Yasuyo H Tanaka, Yasuhiro R Tanaka, Yoshito Masamizu, Riichiro Hira, Andrew J Moorhouse, Nobuaki Tamamaki, Kazuhiro Ikenaka, Noriyuki Matsukawa, R Douglas Fields, Junichi Nabekura, Masanori

- Matsuzaki. Motor learning requires myelination to reduce asynchrony and spontaneity in neural activity. *Glia*. 2020.01; 68(1); 193-210
2. Tomoko Tanaka, Yoshikazu Isomura, Kazuto Kobayashi, Takashi Hanakawa, Satoshi Tanaka, Manabu Honda. Electrophysiological effects of transcranial direct current stimulation on neural activity in the rat motor cortex *Frontiers in Neuroscience*. 2020.06; 14; article 495
 3. Yoshizawa T, Funahashi M. Effects of methyl methacrylate on the excitability of the area postrema neurons in rats. *Journal of oral biosciences*. 2020.09;
 4. CH Yu, JN Stirman, Y Yu, R Hira, SL Smith. Diesel2p mesoscope with dual independent scan engines for flexible capture of dynamics in distributed neural circuitry *bioRxiv*. 2020.09;
 5. Masanori Kawabata, Shogo Soma, Akiko Saiki-Ishikawa, Satoshi Nonomura, Junichi Yoshida, Alain Ríos, Yutaka Sakai, Yoshikazu Isomura. A spike analysis method for characterizing neurons based on phase locking and scaling to the interval between two behavioral events. *J Neurophysiol*. 2020.12; 124(6); 1923-1941

[Conference Activities & Talks]

1. Tomohiko Yoshizawa, Satoshi Nonomura, Alain Rios, Masanori Kawabata, Tomomi Sakairi, Yutaka Sakai, Yoshikazu Isomura. VTA neuronal activity represents trial- and block-based reward prediction errors. The 4th Research Area Meeting of Development and application of optical technology for spatiotemporal control of biological functions 2020.01.17
2. Yoshikazu Isomura. Functional spike activity of cortical and striatal neuron subtypes in behaving rats. Seminar (Albert Einstein College of Medicine) 2020.01.22 New York, USA
3. Tomohiko Yoshizawa. Reinforcement learning model of the basal ganglia for reward prediction. 2020.02.12
4. 吉澤 知彦 他. 腹側被蓋野の神経活動に対する交互報酬の影響. 第12回 CBIR/ONSA/大学院セミナー共催 若手インスパイアシンポジウム 2020.02.12
5. Kawabata M, Nonomura S, Yoshizawa T, Rios A, Sakairi T, Sakai Y, Isomura Y. Establishment and demonstration of a novel spike analysis for neuronal activity during sensorimotor transformation . FENS Forum 2020 2020.07.12 Virtual: SEC Centre, Glasgow, UK
6. Kawabata M , Nonomura S , Yoshizawa T , Rios A , Sakairi T , Sakai Y , Isomura Y. Establishment and demonstration of an analytical method to evaluate neuronal activity during sensorimotor transformation.. The 43rd Annual Meeting of the Japan Neuroscience Society (Neuroscience 2020) 2020.07.30 Virtual: Kobe International Conference Center, Kobe, Hyogo

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. Tabu K, Liu W, Kosaku A, Terashima K, Murota Y, Aimaitijiang A, Nobuhisa I, Hide T, Taga T. Glioma stem cell (GSC)-derived autoschizis-like products confer GSC niche properties involving M1-like tumor-associated macrophages. *Stem cells (Dayton, Ohio)*. 2020.08; 38(8); 921-935
2. Takahashi S, Nobuhisa I, Saito K, Melig G, Itabashi A, Harada K, Osawa M, Endo AT, Iwama A, Taga T. Sox17-mediated expression of adherent molecules is required for the maintenance of undifferentiated hematopoietic cluster formation in midgestation mouse embryos *Differentiation*. 2020.09; 115; 53-61

[Misc]

1. Tabu K and Taga T. Polymer-based chemical approach for cancer stem cell regulation *Journal of Clinical and Experimental Medicine*. 2020.05; 273(5); 474-479
2. Tabu K and Taga T. Eradication of cancer stem cells by targeting niche in glioblastomas *Medical Science Digest*. 2020.05; 46(8); 77-79
3. Taga T and Tabu K. Glioma progression and recurrence involving maintenance and expansion strategies of glioma stem cells by organizing self-advantageous niche microenvironments. *Inflammation and Regeneration*. 2020.09; 40; 33
4. Tabu K and Taga T. Exploring therapeutic targets against glioblastoma stem cell niche *Precision Medicine*. 2020.09; 3(11); 70-73
5. Anani M, Nobuhisa I, Taga T. Sry-related High Mobility Group Box 17 Functions as a Tumor Suppressor by Antagonizing the Wingless-related Integration Site Pathway. *Journal of cancer prevention*. 2020.12; 25(4); 204-212

[Conference Activities & Talks]

1. Taga T and Tabu K. Cancer stem cell niche construction involving inflammatory cells. Symposium on Frontiers in inflammation-associated tumorigenesis and metastasis. The 41st Annual Meeting of the Japanese Society of Inflammation and Regeneration 2020.07.08
2. Aimaitijiang A, Tabu K, Wang W, Nobuhisa I, Taga T. Glioma stem cells promote erythroid differentiation in mouse bone marrow. The 41st Annual Meeting of the Japanese Society of Inflammation and Regeneration 2020.07.08
3. Nobuhisa I, Tsukahara R, Saito S, Kanai Y, Kanai M, Taga T. Contribution of GIMAP6 expression mediated by transcription factor Sox17 to hematopoietic ability in the aortic lumen of midgestation mouse embryos. The 41st Annual Meeting of the Japanese Society of Inflammation and Regeneration 2020.07.08
4. Melig G, Nobuhisa I, Kiyoka S, Tsukahara R, Itabashi A, Kanai Y, Kanai M, Taga T. Role of the Rasip1 in the hematopoiesis of HSC-containing hematopoietic cluster cells in midgestation of mouse embryos. The 41st Annual Meeting of the Japanese Society of Inflammation and Regeneration 2020.07.08
5. Itabashi A, Nobuhisa I, Yokoi Y, Saito K, Tsukahara R, Melig G, Taga T. Formation of hematopoietic cell clusters and maintenance of undifferentiated state by forced expression of transcription factor Sox17 in a cell population containing hematopoietic stem cells of mouse fetal liver and adult bone marrow. The 41st Annual Meeting of the Japanese Society of Inflammation and Regeneration 2020.07.08
6. Tabu K and Taga T. Chemical fabrication of bio-functional polymer-hydrogels that mimic cancer stem cell niche. The 79th Annual Meeting of the Japanese Cancer Association 2020.10.01
7. Kosaku A, Tabu K, Kohsaka S, Taga T. A new stratification method for predicting chemosensitivities of soft tissue sarcomas using synthetic polymer microarray. The 79th Annual Meeting of the Japanese Cancer Association 2020.10.01
8. Nagane M, Tabu K, Murota Y, Tanaka S, Taga T. Fabrication of niche-mimicking polymer hydrogels to characterize human pancreatic cancer stem cells. The 43rd Annual Meeting of the Molecular Biology Society of Japan 2020.12.02

9. Melig G, Nobuhisa I, Kiyoka S, Tsukahara R, Itabashi A, Kanai Y, Kanai M, Taga T. Contribution of Rasip1 to the maintenance of hematopoietic activity of cluster-forming cells in midgestation mouse embryos. The 43rd Annual Meeting of the Molecular Biology Society of Japan 2020.12.02
10. Itabashi A, Nobuhisa I, Yokoi Y, Kiyoka S, Tsukahara R, Melig G, Taga T. Ability to form the cell cluster of Sox17-transduced HSPCs weakens along with the development. The 43rd Annual Meeting of the Molecular Biology Society of Japan 2020.12.02
11. Tabu K, Zhang S, Kosaku A, Venkateswaran S, Kohsaka S, Bradley M, Taga T. Synthetic polymer-based stratification of soft tissue sarcomas with different gene alterations and cells of origin. 11th World Biomaterials Congress (WBC Virtual 2020) 2020.12.11

Respiratory Medicine

Professor: Yasunari Miyazaki

Professor, Department of Respiratory and Nervous System Science: Yuki Sumi

Professor, Health Administration Center: Ryushi Tazawa

Associate Professor, Department of Respiratory Physiology and Sleep Medicine: Meiyo Tamaoka

Associate Professor, Department of Pulmonary Immunotherapeutics: Tsukasa Okamoto

Junior Associate Professor: Tomoya Tateishi

Assistant Professor: Masahiro Ishizuka, Tuyoshi Shirai, Takayuki Honda, Sho Shibata

Project Assistant Professor: Takahiro Mitsumura, Rie Sakakibara, Yuki Iijima

Assistant Professor, Health Administration Center: Keiko Komatsuzaki

Clinical Fellow: Kei Aoyagi, Makoto Izumi, Satoshi Chonabayashi, Mizuho Tosaka, Sutsu Ryu

Resident: Takumi Murakami

Ph.D. student; Sho Shimada, Takashi Yamana, Shinji Katayanagi, Masaru Ejima, Takafumi Suzuki, Tatuo Kawahara,

Yuri Tasaka, Hidetaka Majima, Rei Sagawa, Seiko Takazawa, Hikaru Aoki, Shohei Yamashita

Specialty-appointed Professor: Yasuhiro Setoguchi

(1) Outline

Respiratory Medicine deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders. The aim of our department is to understand the pathophysiology of a variety of lung diseases and to discover the development of the diseases.

(2) Research

1. Pathogenesis of hypersensitivity pneumonitis and identification of environmental causative antigens
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
6. Pathophysiology of sleep apnea
7. Treatment of drug-resistance bacteria

(3) Education

Main objective in the graduate course is to provide our 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. Iijima Y, Sakakibara R, Ishizuka M, Honda T, Shirai T, Okamoto T, Tateishi T, Sakashita H, Tamaoka M, Takemoto A, Kumaki Y, Ikeda S, Miyazaki Y. Notable response to nivolumab during the treatment of SMARCA4-deficient thoracic sarcoma: a case report. *Immunotherapy*. 2020.01; 12(8); 563-569
2. Hirose S, Murakami N, Takahashi K, Kuno I, Takayanagi D, Asami Y, Matsuda M, Shimada Y, Yamano S, Sunami K, Yoshida K, Honda T, Nakahara T, Watanabe T, Komatsu M, Hamamoto R, Kobayashi Kato M, Matsumoto K, Okuma K, Kuroda T, Okamoto A, Itami J, Kohno T, Kato T, Shiraishi K, Yoshida H. Genomic Alterations in STK11 Can Predict Clinical Outcomes in Cervical Cancer Patients. *Gynecologic Oncology*. 2020.01; 156(1); 203-210
3. Tateishi T, Johkoh T, Sakai F, Miyazaki Y, Ogura T, Ichikado K, Suda T, Taguchi Y, Inoue Y, Takemura T, Colby TV, Sumikawa H, Fujimoto K, Arakawa H, Raouf S, Inase N. High-resolution CT features distinguishing usual interstitial pneumonia pattern in chronic hypersensitivity pneumonitis from those with idiopathic pulmonary fibrosis. *Japanese Journal of Radiology*. 2020.01; 38(6); 524-532
4. Sakakibara R, Kobayashi M, Takahashi N, Inamura K, Ninomiya H, Wakejima R, Kitazono S, Yanagitani N, Horiike A, Ichinose J, Matsuura Y, Nakao M, Mun M, Nishio M, Okumura S, Motoi N, Ito T, Miyazaki Y, Inase N, Ishikawa Y. Insulinoma-associated Protein 1 (INSM1) Is a Better Marker for the Diagnosis and Prognosis Estimation of Small Cell Lung Carcinoma Than Neuroendocrine Phenotype Markers Such as Chromogranin A, Synaptophysin, and CD56. *The American Journal of Surgical Pathology*. 2020.02; 44(6); 757-764
5. Hayashi S, Tamaoka M, Tateishi T, Murota Y, Handa I, Miyazaki Y. A New Feature with the Potential to Detect the Severity of Obstructive Sleep Apnoea via Snoring Sound Analysis. *International Journal of Environmental Research and Public Health*. 2020.04; 17(8); 2951
6. Shimada S, Nakai R, Aoki K, Shimoeda N, Ohno G, Miyazaki Y, Kudoh S, Imura S, Watanabe K, Ishii Y, Tateda K. Complete Genome Sequence of Novel Psychrotolerant Legionella Strain TUM19329, Isolated from Antarctic Lake Sediment. *Microbiology Resource Announcements*. 2020.04; 9(16); e00253-20
7. Hanzawa S, Tateishi T, Ishizuka M, Inoue Y, Honda T, Kawahara T, Tomita M, Miyazaki Y. Changes in serum KL-6 levels during short-term strict antigen avoidance are associated with the prognosis of patients with fibrotic hypersensitivity pneumonitis caused by avian antigens. *Respiratory Investigation*. 2020.07; S2212-5345(20); 30092-7
8. Watanabe T, Honda T, Totsuka H, Yoshida M, Tanioka M, Shiraishi K, Shimada Y, Arai E, Ushiyama M, Tamura K, Yoshida T, Kanai Y, Kohno T. Simple prediction model for homologous recombination deficiency in breast cancers in adolescents and young adults. *Breast Cancer Research and Treatment*. 2020.07; 182(2); 491-502

9. Tanioka M, Watanabe T, Honda T, Totsuka H, Arai , Kanai Y, Shiraishi K, Tamura K, Kohno T. Simple vs. comprehensive prediction models of homologous recombination deficiency based on mutational and clinical features in three independent breast cancer datasets. *Cancer Research*. 2020.08; 80(16); 3551
10. Shirai T, Mitsumura T, Aoyagi K, Okamoto T, Kimura M, Gemma T, Shigematsu T, Takahashi J, Azuma S, Yoshizuka R, Sasaki H, Urushibata N, Ochiai K, Hondo K, Morishita K, Aiboshi J, Otomo Y, Miyazaki Y. COVID-19 pneumonia complicated by bilateral pneumothorax: A case report. *Respiratory Medicine Case Reports*. 2020.09; 31; 101230
11. Nishiyama N, Masuo M, Nukui Y, Tateishi T, Kishino M, Tateishi U, Morota K, Ohbo K, Miyazaki Y. Human epididymis protein 4 is a new biomarker to predict the prognosis of progressive fibrosing interstitial lung disease. *Respiratory Investigation*. 2020.09; 59(1); 90-98
12. Inoue Y, Okamoto T, Honda T, Nukui Y, Akashi T, Takemura T, Tozuka M, Miyazaki Y. Disruption in the balance between apolipoprotein A-I and mast cell chymase in chronic hypersensitivity pneumonitis. *Immunity Inflammation and Disease*. 2020.10; 8(4); 659-671
13. Shirai T, Tanino Y, Nikaido T, Takaku Y, Hashimoto S, Taguchi Y, Baba T, Ogura T, Kataoka K, Nakayama M, Yamada Y, Matsushima S, Nakayama S, Miyazaki Y. Screening and diagnosis of acute and chronic bird-related hypersensitivity pneumonitis by serum IgG and IgA antibodies to bird antigens with ImmunoCAP®. *Allergology International*. 2020.10; S1323-8930(20); 30128-3
14. Furusawa H, Cardwell JH, Okamoto T, Walts AD, Konigsberg IR, Kurche JS, Bang TJ, Schwarz MI, Brown KK, Kropski JA, Rojas M, Cool CD, Lee JS, Wolters PJ, Yang IV, Schwartz DA. Chronic Hypersensitivity Pneumonitis, an Interstitial Lung Disease with Distinct Molecular Signatures. *American Journal of Respiratory and Critical Care Medicine*. 2020.11; 202(10); 1430-1444
15. Johansson KA, Barnes H, Bellanger AP, Dalphin JC, Fernández Pérez ER, Flaherty KR, Huang YT, Jones KD, Kawano-Dourado L, Kennedy K, Millerick-May M, Miyazaki Y, Morisset J, Morell F, Raghu GR, Robbins C, Sack CS, Salisbury ML, Selman M, Vasakova M, Walsh SLF, Rose CS. Exposure Assessment Tools for Hypersensitivity Pneumonitis. An Official American Thoracic Society Workshop Report. *Annals of the American Thoracic Society*. 2020.12; 17(12); 1501-1509
16. Yamana T, Okamoto T, Ishizuka M, Hanzawa S, Ejima M, Shibata S, Miyazaki Y. IL-17A-Secreting Memory γ δ T Cells Play a Pivotal Role in Sensitization and Development of Hypersensitivity Pneumonitis. *Journal of Immunology*. 2020.12; 206(2); 355-356
17. Okamoto Y, Ghosh T, Okamoto T, Schuyler RP, Seifert J, Charry LL, Visser A, Feser M, Fleischer C, Pedrick C, August J, Moss L, Bemis EA, Norris JM, Kuhn KA, Demoruelle MK, Deane KD, Ghosh D, Holers VM, Hsieh EWY. Subjects at-risk for future development of rheumatoid arthritis demonstrate a PAD4-and TLR-dependent enhanced histone H3 citrullination and proinflammatory cytokine production in CD14hi monocytes. *Journal of Autoimmunity*. 2020.12; 117; 102581
18. Gally F, Sasse SK, Kurche J, Gruca MA, Cardwell JH, Okamoto T, Chu HW, Hou X, Poirion O, Buchanan J, Preissl S, Ren B, Colgan SP, Dowell RD, Yang IV, Schwartz DA, Gerber AN. The MUC5B-associated variant, rs35705950, resides within an enhancer subject to lineage- and disease-dependent epigenetic remodeling. *JCI Insight*. 2020.12; 6(2); e144294

[Misc]

1. Costabel U, Miyazaki Y, Pardo A, Koschel D, Bonella F, Spagnolo P, Guzman J, Ryerson CJ, Selman M. Hypersensitivity pneumonitis. *Nature Reviews Disease Primers*. 2020.08; 6(1); 65

[Conference Activities & Talks]

1. Majima H, Arai T, Watanabe A, Miyazaki Y, Yaguchi T, Kamei K.. Analysis of cyp51A polymorphisms of *Aspergillus fumigatus* in Japan. 9th Advances Against Aspergillosis and Mucormycosis. 2020.02.27
2. Ejima M, Okamoto T, Miyazaki Y. Therapeutic Efficacy of Corticosteroid and Predictors of Survival in Patients with Chronic Hypersensitivity Pneumonitis: A Single Center Cohort. American Thoracic Society 2020.05.15

3. Tateishi T, Okamoto T, Miyazaki Y. Long-Term Tolerability of Antifibrotic Therapy for the Patients with Pulmonary Fibrosis After Acute Exacerbation. American Thoracic Society 2020.05.15
4. Okamoto T, Takasawa S, Mitsumura T, Suhara K, Ejima M, Miyazaki Y. Clinical Characteristics in Patients with Asymmetric Chronic Hypersensitivity Pneumonitis. American Thoracic Society 2020.05.15

Gastroenterology and Hepatology

Professor

Ryuichi OKAMOTO(Department of Gastroenterology and Hepatology)

Professor

Yasuhiro ASAHINA(Department of Liver Disease Control)

Kazuo OHTSUKA(Endoscopy)

Sei KAKINUMA(Department of Clinical and Diagnostic Laboratory Science)

Distinguished Professor

Mamoru WATANABE

Associate Professor

Seishin AZUMA(Department of Collaborative Medicine for Gastroenterology and Hepatology)

Kiichiro TSUCHIYA(Gastroenterology and Hepatology)

Mina NAKAGAWA(Curricular Management Division)

Takashi NAGAISHI(Department of Advanced Therapeutics for GI Diseases)

Masakazu NAGAHORI(Clinical Research Center)

Shiro YUI(Center for Stem Cell and Regenerative Medicine)

Junior Associate Professor

Yasuhiro ITSUI(Professional Development Center)

Shigeru OSHIMA(Gastroenterology and Hepatology)

Eriko OKADA(Department of Medical Education Research and Development)

Assistant Professor

Toshimitsu FUJII, Eiko SAITO(Gastroenterology and Hepatology)

Yasuhiro NEMOTO (Department of Gastroenterology and Hepatology)

Michio ONIZAWA(Department of Advanced Therapeutics for GI Diseases)

Miyako MURAKAWA(Clinical Laboratory)

Masayohi FUKUDA(Endoscopy)

Kento TAKENAKA(Department of Collaborative Medicine for Gastroenterology and Hepatology)

Hiromichi SHIMIZU(Center for Stem Cell and Regenerative Medicine)

Project Assistant Professor

Masato MIYOSHI(Department of Gastroenterology and Hepatology)

Specially Appointed Assistant Professor

Sayuri NITTA, Fukiko KITAHATA, Ami KAWAMOTO
(Gastroenterology and Hepatology)

Masanori KOBAYASHI, Shuji HIBIYA (Endoscopy)

Yoshihito KANO(Department of Clinical Oncology)

Go ITO(Inflammatory Bowel Disease Laboratory)

Senior Resident

Miyuki KANESHIRO, Hiromune KATSUDA, Shohei TANAKA, Masamichi KURIHARA, Ryouusuke ISHII,
Eri Oshina(Department of Gastroenterology and Hepatology)

Sho WATANABE(Endoscopy)

Resident

Sho KAWASAKI(Gastroenterology and Hepatology)

Graduate Student

Yuria TAKEI, Sho ANZAI, Tomoyuki SHIRASKI, Ayako WATANABE,
Kana OTSUBO, Nobuhiro KATSUKURA, Hiroki MATSUDA, Takehito ASAKAWA,
Reiko KUNO, Ai MASUMOTO, Emi AONUMA, Mao KAWAI, Ryo MORIKAWA,
Junichi TAKAHASHI, Naoya TSUGAWA, Akiko TAMURA, Jun TSUCHIYA,
Taro SHIMIZU, Sakurako KOBAYASHI, Eiko TAKEICHI, Daiki YAMADA,
Satoshi WATANABE, Yuki YONEMOTO, Nobuhiko OGASAWARA,
Keiya WATAKABE

(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 diseasespecific 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 assisted 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 enterography).
- 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. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient *Hepatol Res.* 2020; 50(4); 524-531
2. Naoya Tsugawa, Daiki Yamada, Taro Watabe, Michio Onizawa, Shuang Wang, Yasuhiro Nemoto, Shigeru Oshima, Takeshi Tsubata, Takahiro Adachi, Yohei Kawano, Mamoru Watanabe, Richard S. Blumberg, Ryuichi Okamoto, Takashi Nagaishi. CEACAM1 specifically suppresses B cell receptor signaling-mediated activation. *Biochemical and Biophysical Research Communications.* 2020;
3. Nobuhiro Katsukura, Sho Watanabe, Tomoaki Shirasaki, Shuji Hibiya, Yoshihito Kano, Keiichi Akahoshi, Minoru Tanabe, Susumu Kirimura, Takumi Akashi, Masanobu Kitagawa, Ryuichi Okamoto, Mamoru Watanabe, Kiichiro Tsuchiya. Intestinal phenotype is maintained by *Atoh1* in the cancer region of intraductal papillary mucinous neoplasm. *Cancer Science.* 2020;
4. Kana Otsubo, Chiaki Maeyashiki, Yoichi Nibe, Akiko Tamura, Emi Aonuma, Hiroki Matsuda, Masanori Kobayashi, Michio Onizawa, Yasuhiro Nemoto, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Satoru Torii, Eisuke Itakura, Mamoru Watanabe, Shigeru Oshima. Receptor-Interacting Protein Kinase 3 (RIPK3) inhibits autophagic flux during necroptosis in intestinal epithelial cells. *FEBS Letters.* 2020.01; 594; 1586-1595
5. Toshifumi Hibi, Makoto Naganuma, Eisei Oda, Yoji Yamada, Yoshitomo Chujoh, Ryoichi Yoshihara, Mamoru Watanabe. Predictive factors for achievement of mucosal healing by budesonide 2-mg foam in ulcerative colitis: a pooled analysis of data from two clinical trials. *Intest Res.* 2020.01; 18(1); 56-68
6. Masayuki Saruta, Dong Il Park, Young-Ho Kim, Suk-Kyun Yang, Byung-Ik Jang, Jae Hee Cheon, Jong Pil Im, Takanori Kanai, Tatsuro Katsuno, Yoh Ishiguro, Makoto Nagaoka, Naoki Isogawa, Yinhua Li, Anindita Banerjee, Alaa Ahmad, Mina Hassan-Zahraee, Robert Clare, Kenneth J Gorelick, Fabio Cataldi, Mamoru Watanabe, Toshifumi Hibi. Anti-MAdCAM-1 antibody (PF-00547659) for active refractory Crohn's disease in Japanese and Korean patients: the OPERA study. *Intest Res.* 2020.01; 18(1); 45-55
7. Shohei Tanaka, Yasuhiro Nemoto, Yuria Takei, Ryo Morikawa, Shigeru Oshima, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Susanne Stutte, Mamoru Watanabe. High-fat diet-derived free fatty acids impair the intestinal immune system and increase sensitivity to intestinal epithelial damage. *Biochem Biophys Res Commun.* 2020.02; 522(4); 971-977
8. Kento Takenaka, Kazuo Ohtsuka, Toshimitsu Fujii, Mariko Negi, Kohei Suzuki, Hiromichi Shimizu, Shiori Oshima, Shintaro Akiyama, Maiko Motobayashi, Masakazu Nagahori, Eiko Saito, Katsuyoshi Matsuoka, Mamoru Watanabe. Development and Validation of a Deep Neural Network for Accurate Evaluation of Endoscopic Images From Patients With Ulcerative Colitis. *Gastroenterology.* 2020.02;
9. Ryuichi Okamoto, Hiromichi Shimizu, Kohei Suzuki, Ami Kawamoto, Junichi Takahashi, Mao Kawai, Sayaka Nagata, Yui Hiraguri, Sayaka Takeoka, Hady Yuki Sugihara, Shiro Yui, Mamoru Watanabe. Organoid-based regenerative medicine for inflammatory bowel disease. *Regen Ther.* 2020.03; 13; 1-6

10. Yuria Takei, Yasuhiro Nemoto, Ryo Morikawa, Shohei Tanaka, Shigeru Oshima, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. T cells show amoeboid shape and frequent morphological change in vitro, and localize to small intestinal intraepithelial region in vivo. *Biochem Biophys Res Commun.* 2020.03; 523(2); 328-335
11. Takenaka K, Kitazume Y, Fujii T, Tsuchiya K, Watanabe M, Ohtsuka K. Objective evaluation for treat to target in Crohn's disease. *Journal of gastroenterology.* 2020.03;
12. Kenji Watanabe, Satoshi Motoya, Haruhiko Ogata, Takanori Kanai, Toshiyuki Matsui, Yasuo Suzuki, Mitsuhiro Shikamura, Kenkichi Sugiura, Kazunori Oda, Tetsuharu Hori, Takahiro Araki, Mamoru Watanabe, Toshifumi Hibi. Effects of vedolizumab in Japanese patients with Crohn's disease: a prospective, multicenter, randomized, placebo-controlled Phase 3 trial with exploratory analyses. *J Gastroenterol.* 2020.03; 55(3); 291-306
13. Kento Takenaka, Yoshio Kitazume, Toshimitsu Fujii, Kiichiro Tsuchiya, Mamoru Watanabe, Kazuo Ohtsuka. Objective evaluation for treat to target in Crohn's disease. *J Gastroenterol.* 2020.03; 55(3); 579-587
14. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient. *Hepatol Res.* 2020.04; 50(4); 524-531
15. Sho Anzai, Ami Kawamoto, Sayaka Nagata, Junichi Takahashi, Mao Kawai, Reiko Kuno, Sakurako Kobayashi, Satoshi Watanabe, Kohei Suzuki, Hiromichi Shimizu, Yui Hiraguri, Sayaka Takeoka, Hady Yuki Sugihara, Shiro Yui, Shigeru Oshima, Mamoru Watanabe, Ryuichi Okamoto. TGF- β promotes fetal gene expression and cell migration velocity in a wound repair model of untransformed intestinal epithelial cells. *Biochem Biophys Res Commun.* 2020.04; 524(3); 533-541
16. Cayetano Pleguezuelos-Manzano, Jens Puschhof, Axel Rosendahl Huber, Arne van Hoeck, Henry M Wood, Jason Nomburg, Carino Gurjao, Freek Manders, Guillaume Dalmasso, Paul B Stege, Fernanda L Paganelli, Maarten H Geurts, Joep Beumer, Tomohiro Mizutani, Yi Miao, Reinier van der Linden, Stefan van der Elst, K Christopher Garcia, Janetta Top, Rob JL Willems, Marios Giannakis, Richard Bonnet, Phil Quirke, Matthew Meyerson, Edwin Cuppen, Ruben van Boxtel, Hans Clevers. Mutational signature in colorectal cancer caused by genotoxic pks+ E. coli. *Nature.* 2020.04; 580; 269-273
17. Chikako Watanabe, Masakazu Nagahori, Toshimitsu Fujii, Kaoru Yokoyama, Naoki Yoshimura, Taku Kobayashi, Hirokazu Yamagami, Kazuya Kitamura, Kagaya Takashi, Shiro Nakamura, Makoto Naganuma, Shunji Ishihara, Motohiro Esaki, Maria Yonezawa, Reiko Kunisaki, Atsushi Sakuraba, Naoaki Kuji, Soichiro Miura, Toshifumi Hibi, Yasuo Suzuki, Ryota Hokari. Non-adherence to medications in pregnant ulcerative colitis patients contributes to disease flares and adverse pregnancy outcomes. *Dig Dis Sci.* 2020.04; Epub ahead of print
18. Ryoichi Ando, Yasuhiro Asahina, Kazuaki Chayama, Naoki Hiramatsu, Toru Ikegami, Namiki Izumi, Kan Kikuchi, Kazuhiko Koike, Masayuki Kurosaki, Satoshi Mochida, Fumitaka Suzuki, Tetsuo Takehara, Hajime Takikawa, Atsushi Tanaka, Eiji Tanaka, Yasuhito Tanaka, Hiroshi Yotsuyanagi; Drafting Committee for Hepatitis Management Guidelines, the Japan Society of Hepatology. JSH guidelines for the management of hepatitis B virus infection: 2019 Update. *Hepatol Res.* 2020.04;
19. Sakura Kirino, Kaoru Tsuchiya, Masayuki Kurosaki, Shun Kaneko, Kento Inada, Koji Yamashita, Leona Osawa, Yuka Hayakawa, Shuhei Sekiguchi, Mao Okada, Wan Wang, Mayu Higuchi, Kenta Takaura, Chiaki Maeyashiki, Nobuharu Tamaki, Yutaka Yasui, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Namiki Izumi. Relative dose intensity over the first four weeks of lenvatinib therapy is a factor of favorable response and overall survival in patients with unresectable hepatocellular carcinoma. *PLoS One.* 2020.04; 15(4); e0231828
20. Masayuki Kato, Kiyohito Tanaka, Mitsuhiro Kida, Shomei Ryozaawa, Koji Matsuda, Mitsuhiro Fujishiro, Yutaka Saito, Kazuo Ohtsuka, Ichiro Oda, Chikatashi Katada, Kiyonori Kobayashi, Shu Hoteya, Takahiro Horimatsu, Shinya Kodashima, Takahisa Matsuda, Manabu Muto, Hironori Yamamoto, Ryuichi Iwakiri, Hiromu Kutsumi, Hiroaki Miyata, Mototsugu Kato, Ken Haruma, Kazuma Fujimoto, Naomi Uemura, Michio Kaminishi, Hisao Tajiri. Multicenter database registry for endoscopic retrograde cholangiopancreatography: Japan Endoscopic Database Project. *Dig Endosc.* 2020.05; 32(4); 494-502

21. Kento Takenaka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe, Kazuo Ohtsuka. Small bowel healing detected by endoscopy in patients with Crohn's disease after treatment with antibodies against tumor necrosis factor. *Clin Gastroenterol Hepatol.* 2020.06; 18(7); 1545-1552
22. Shigeki Bamba, Ryosuke Sakemi, Toshimitsu Fujii, Teruyuki Takeda, Shin Fujioka, Kento Takenaka, Hiroki Kitamoto, Shotaro Umezawa, Hirotake Sakuraba, Toshihiro Inokuchi, Norimasa Fukata, Shinta Mizuno, Masaki Yamashita, Shinichiro Shinzaki, Hiroki Tanaka, Hidetoshi Takedatsu, Ryo Ozaki, Kei Moriya, Manabu Ishii, Tetsu Kinjo, Keiji Ozeki, Makoto Ooi, Ryohei Hayashi, Kazuki Kakimoto, Yuichi Shimodate, Kazuya Kitamura, Akihiro Yamada, Akira Sonoda, Yu Nishida, Kyouko Yoshioka, Shinya Ashizuka, Fumiaki Takahashi, Toshio Shimokawa, Taku Kobayashi, Akira Andoh, Toshifumi Hibi. A nationwide, multi-center, retrospective study of symptomatic small bowel stricture in patients with Crohn's disease. *J Gastroenterol.* 2020.06; 55(6); 615-626
23. Nobuyuki Tanaka, Shigeaki Kanatani, Dagmara Kaczynska, Keishiro Fukumoto, Lauri Louhivuori, Tomohiro Mizutani, Oded Kopper, Pauliina Kronqvist, Stephanie Robertson, Claes Lindh, Lorand Kis, Robin Pronk, Naoya Niwa, Kazuhiro Matsumoto, Mototsugu Oya, Ayako Miyakawa, Anna Falk, Johan Hartman, Cecilia Sahlgren, Hans Clevers, Per Uhlén. Three-dimensional single-cell imaging for the analysis of RNA and protein expression in intact tumour biopsies. *Nat Biomed Eng.* 2020.06; 4; 875-888
24. Tomohiro Mizutani, Hans Clevers. Primary intestinal epithelial organoid culture. *Methods Mol Biol.* 2020.06; 2171; 185-200
25. Hideki Iijima, Taku Kobayashi, Mitsuo Nagasaka, Shinichiro Shinzaki, Kazuya Kitamura, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi. Management of primary nonresponders and partial responders to tumor necrosis factor- α inhibitor induction therapy among patients with Crohn's disease. *Inflamm Intest Dis.* 2020.06; 5(2); 78-83
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27. Hiromichi Shimizu, Toshimitsu Fujii, Shuji Hibiya, Maiko Motobayashi, Kohei Suzuki, Kento Takenaka, Eiko Saito, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Rapid prediction of 1-year efficacy of tofacitinib for treating refractory ulcerative colitis. *Intest Res.* 2020.06; Online ahead of print.
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29. Shin-Ei Kudo, Masashi Misawa, Yuichi Mori, Kinichi Hotta, Kazuo Ohtsuka, Hiroaki Ikematsu, Yutaka Saito, Kenichi Takeda, Hiroki Nakamura, Katsuro Ichimasa, Tomoyuki Ishigaki, Naoya Toyoshima, Toyoki Kudo, Takemasa Hayashi, Kunihiko Wakamura, Toshiyuki Baba, Fumio Ishida, Haruhiro Inoue, Hayato Itoh, Masahiro Oda, Kensaku Mori. Artificial intelligence-assisted system improves endoscopic identification of colorectal neoplasms. *Clin Gastroenterol Hepatol.* 2020.07; 18(8); 1874-1881.e2
30. Masashi Misawa, Shin-Ei Kudo, Yuichi Mori, Kinichi Hotta, Kazuo Ohtsuka, Takahisa Matsuda, Shoichi Saito, Toyoki Kudo, Toshiyuki Baba, Fumio Ishida, Hayato Itoh, Masahiro Oda, Kensaku Mori. Development of a computer-aided detection system for colonoscopy and a publicly accessible large colonoscopy video database (with video). *Gastrointest Endosc.* 2020.07; Online ahead of print
31. Zhihua Ran, Kaichun Wu, Katsuyoshi Matsuoka, Yoon Tae Jeon, Shu Chen Wei, Vineet Ahuja, Minhu Chen, Pin-Jin Hu, Akira Andoh, Hyo Jong Kim, Suk-Kyun Yang, Mamoru Watanabe, Siew Chien Ng, Toshifumi Hibi, Ida Normiha Hilmi, Yasuo Suzuki, Dong Soo Han, Wai Keung Leung, Jose Sollano, Choon Jin Ooi, Jiaming Qian. Asian Organization for Crohn's and Colitis and Asia Pacific Association of Gastroenterology practice recommendations for medical management and monitoring of inflammatory bowel disease in Asia. *J Gastroenterol Hepatol.* 2020.07; Online ahead of print

32. Keisuke Hata, Soichiro Ishihara, Yoichi Ajioka, Keiichi Mitsuyama, Kenji Watanabe, Hiroyuki Hanai, Reiko Kunisaki, Hiroshi Nakase, Keiji Matsuda, Ryuichi Iwakiri, Nobuyuki Hida, Shinji Tanaka, Yoshiaki Takeuchi, Masaru Shinozaki, Noriyuki Ogata, Kentaro Moriichi, Fumihito Hirai, Kenichi Sugihara, Tadakazu Hisamatsu, Yasuo Suzuki, Mamoru Watanabe, Toshifumi Hibi. Long-term follow-up of targeted biopsy yield (LOFTY Study) in ulcerative colitis surveillance colonoscopy. *J Clin Med.* 2020.07; 9(7); 2286
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35. Taku Sato, Shun Ishikawa, Jumpei Asano, Hirona Yamamoto, Masayuki Fujii, Toshiro Sato, Kouhei Yamamoto, Keisuke Kitagaki, Takumi Akashi, Ryuichi Okamoto, Toshiaki Ohteki. Regulated IFN signalling preserves the stemness of intestinal stem cells by restricting differentiation into secretory-cell lineages. *Nat Cell Biol.* 2020.08; 22(8); 919-926
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37. Taku Kobayashi, Hiroaki Ito, Toshifumi Ashida, Tadashi Yokoyama, Masakazu Nagahori, Tomoki Inaba, Mitsuhiro Shikamura, Takayoshi Yamaguchi, Tetsuharu Hori, Philippe Pinton, Mamoru Watanabe, Toshifumi Hibi. Efficacy and safety of a new vedolizumab subcutaneous formulation in Japanese patients with moderately to severely active ulcerative colitis. *Intest Res.* 2020.08; Online ahead of print
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40. Shin-Ei Kudo, Katsuro Ichimasa, Benjamin Villard, Yuichi Mori, Masashi Misawa, Shoichi Saito, Kinichi Hotta, Yutaka Saito, Takahisa Matsuda, Kazutaka Yamada, Toshifumi Mitani, Kazuo Ohtsuka, Akiko Chino, Daisuke Ide, Kenichiro Imai, Yoshihiro Kishida, Keiko Nakamura, Yasumitsu Saiki, Masafumi Tanaka, Shu Hoteya, Satoshi Yamashita, Yusuke Kinugasa, Masayoshi Fukuda, Toyoki Kudo, Hideyuki Miyachi, Fumio Ishida, Hayato Itoh, Masahiro Oda, Kensaku Mori. Artificial intelligence system to determine risk of T1 colorectal cancer metastasis to lymph node. *Gastroenterology.* 2020.09; Online ahead of print.
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42. Kento Takenaka, Kazuo Ohtsuka, Kohei Suzuki, Mamoru Watanabe. Reply to GASTRO-D- 20-00591 *Gastroenterology.* 2020.10; 159(4); 1626-1627

43. Yong-Hee Cho, Eun Ji Ro, Jeong-Su Yoon, Tomohiro Mizutani, Dong-Woo Kang, Jong-Chan Park, Tae Il Kim, Hans Clevers, Kang-Yell Choi. 5-FU promotes stemness of colorectal cancer via p53-mediated WNT/ β -catenin pathway activation. *Nat Commun.* 2020.10; 11; 5321
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45. Yoshio Kitazume, Junichi Tsuchiya, Kento Takenaka, Kazuo Ohtsuka, Koichiro Kimura, Ryosuke Watanabe, Tomoyuki Fujioka, Toshimitsu Fujii, Mamoru Watanabe, Ukihide Tateisi. High b-value computed diffusion-weighted imaging for differentiating bowel inflammation in Crohn's disease. *Eur J Radiol.* 2020.10; 133; 109362
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48. Yasuharu Maeda, Shin-Ei Kudo, Noriyuki Ogata, Yuichi Mori, Masashi Misawa, Mayumi Homma, Tetsuo Nemoto, Masataka Ogawa, Seiko Sasanuma, Yuta Sato, Shinichi Kataoka, Yuta Kouyama, Tatsuya Sakurai, Kenta Igarashi, Yushi Ogawa, Kazuki Kato, Katsuro Ichimasa, Hiroki Nakamura, Toyoki Kudo, Takemasa Hayashi, Kunihiko Wakamura, Toshiyuki Baba, Haruhiro Inoue, Kazuo Ohtsuka. Endocytoscopic intramucosal capillary network changes and crypt architecture abnormalities can predict relapse in patients with an ulcerative colitis Mayo endoscopic score of 1. *Dig Endosc.* 2020.11; 32(7); 1082-1091

[Conference Activities & Talks]

1. Sakurako Kobayashi, Satoshi Watanabe, Yosuke Yoneyama, Kousuke Tanimoto, Ryu Nishimura, Sayaka Nagata, Masami Inoue, Kouhei Suzuki, Sei Kakinuma, Kiichiro Tsuchiya, Ryuichi Okamoto, Mamoru Watanabe, Takanori Takebe, Shiro Yui. Conceptual basis of lineage shift between intestinal epithelium and hepatocytes. Keystone Symposia, Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease 2020.01.22 Vancouver (Canada)
2. Real world experience with tofacitinib in refractory ulcerative colitis.. 2020.02.07
3. Toshimitsu Fujii, Shuji Hibiya, Chiaki Maeyashiki, Eiko Saito, Kento Takenaka, Maiko Motobayashi, Hiromichi Shimizu, Masakazu Nagahori, Kazuo Ohtsuka, Masayuki Kurosaki, Tsunehito Yauchi, Mamoru Watanabe. Intolerance to 5-aminosalicylate is a risk of poor prognosis in Ulcerative colitis patients.. ECCO2020 2020.02.14 Vienna (Austria)
4. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Taro Watabe, Michio Onizawa, Mamoru Watanabe. B cell receptor signaling in lymphoid tissues may be regulated by CEACAM1.. ECCO2020 2020.02.14 Vienna (Austria)
5. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Taro Watabe, Michio Onizawa, Yudai Kojima, Richard S. Blumberg, Mamoru Watanabe. BCR signaling in lymphoid tissues is regulated by the long isoform of Ceacam1.. MICS2020 2020.07.20 Web 開催

6. Fukiko Kawai-Kitahata, Yasuhiro Asahina , Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka , Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Online
7. Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka, Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and aav/hepatitis b virus integration into genome on development of hepatocellular carcinoma in patients with prior hepatitis b virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Web 開催
8. 勝倉暢洋、日比谷秀爾、土屋輝一郎. The role of intestinal differentiation system in carcinogenesis of IPMN. 第 79 回日本癌学会学術総会 2020.10.01 Web 開催
9. Takashi Nagaishi, Daiki Yamada, Naoya Tsugawa, Taro Watabe, Eiko Saito, Masayoshi Fukuda, Ayako Arai, Kazuo Ohtsuka, Mamoru Watanabe. A case of villous atrophy with CCR4+ T cell infiltration in the small intestine.. UEGW2020 2020.10.10 Web 開催
10. Mamoru Watanabe. Organoid medicine in human GI diseases.. EMBO EMBL SYMPOSIUM 2020.10.22 オンライン
11. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Yudai Kojima, Michio Onizawa, Taro Watabe, Richard S. Blumberg, Mamoru Watanabe. BCR signaling in lymphoid tissues regulated by the long isoform of Ceacam1.. FOCIS2020 2020.10.28 Web 開催
12. Mamoru Watanabe. Clinical Application of Organoids for Tissue Regeneration.. KDDW2020 2020.11.20 オンライン

Anesthesiology

Professor: Tokujiro Uchida

Associate Professor: Satoshi Toyama

Senior Assistant Professor: Hiroto Yamamoto

Assistant Professor: Megumi Ohata, Yudai Yamamoto, Kunio Suzuki, Takafumi Omori, Aya Takemoto, Myumi Suzuki

Staff: Moeko Hori, Shoko Kumada, Tatsuya Tanifuji, Eri Mizuno

Resident: Yasunori Kato, Taiga Nagase, Makoto Yoshiga, Mario Noguchi, Arisa Tamura, Jaewon Park

Graduate School Student: Yudai Yamamoto, Ayumi Maeda, Kenta Takeishi, Yulin Zeng

(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) Perioperative monitoring of coagulation system
- 2) Perioperative acute lung injury
- 3) Perioperative acute kidney injury
- 4) Factors associated with outcome of patients undergoing major surgeries.

(3) Publications

[Original Articles]

1. Yamamoto H, Uchida Y, Chiba T, Kurimoto R, Matsushima T, Inotsume M, Ishikawa C, Li H, Shiga T, Muratani M, Uchida T, Asahara H. Transcriptome analysis of sevoflurane exposure effects at the different brain regions. *PloS one*. 2020; 15(12); e0236771
2. Takayama W, Endo A, Yoshii J, Arai H, Oi K, Nagaoka E, Toyama S, Yamamoto H, Uchida T, Otomo Y. Severe COVID-19 Pneumonia in a 30-Year-Old Woman in the 36th Week of Pregnancy Treated with Postpartum Extracorporeal Membrane Oxygenation. *The American journal of case reports*. 2020.10; 21; e927521

[Conference Activities & Talks]

1. Uchida Y, Yamamoto H, Chiba T, Kurimoto R, Matsushima T, Shiga T, Muratani M, Asahara H, Uchida T. Identification of Klf4 as a potential transcriptional regulator of brain exposed to sevoflurane by RNA-seq analysis. *Anesthesiology* 2020 2020.10.05 WEB
2. Uchida T, Yamamoto Y. Estimation of plasma fibrinogen levels and platelet count using dielectric blood coagulometer in patients undergoing cardiovascular surgery using cardiopulmonary bypass; single center prospective observational study. *Euroanaesthesia* 2020 2020.11.30 WEB

3. Uchida T, Yamamoto Y. Evaluation of dielectric blood coagulometer as a point of care test for measurement of anticoagulation potential caused by direct oral anticoagulants. *Euroanaesthesia*. *Euroanaesthesia* 2020 2020.11.30 WEB

Cardiovascular Surgery

Professor: Hirokuni ARAI
 Associate Professor: Tomohiro MIZUNO
 Junior Associate Professor: Keiji OI, Eiki NAGAOKA
 Assistant Professor:
 Masafumi YASHIMA, Tatsuki FUJIWARA, Kiyotoshi OISHI, Masashi TAKESHITA
 Graduate Student:
 Dai TASAKI, Kenji SAKAI, Ryoji KINOSHITA, Kiyotoshi OISHI, Kenji YOKOYAMA
 Masashi TAKESHITA, Hironobu SAKURAI, Haruna SEKI, Tomoki TAHARA
 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. Taichi Sakaguchi, Tomohiro Mizuno, Masaaki Ryomoto, Naosumi Sekiya, Toshinori Totsugawa, Kentaro Tamura, Arudo Hiraoka, Hirokuni Arai. A New MultiSuction Heart Positioner for Minimally Invasive Coronary Artery Bypass Grafting. *Ann. Thorac. Surg.*. 2020.01; 109(1); e63-e65
2. Eiki Nagaoka, Jill Gelinias, Marco Vola, Bob Kiaii. Early Clinical Experiences of Robotic Assisted Aortic Valve Replacement for Aortic Valve Stenosis with Sutureless Aortic Valve. *Innovations*. 2020.01; 15(1); 88-92
3. Kuroki H, Arai H, Srisont S, Oi K, Tomita M, Mizuno T. Corrugated Sheet of Unsintered Hydroxyapatite Poly-L-Lactide for Sternal Fixation: A Preclinical Study. *Ann Thorac Cardiovasc Surg*. 2020.02; 26(1); 40-46
4. Koichiro Kinugawa, Takashi Nishimura, Koichi Toda, Yoshikatsu Saiki, Hiroshi Niinami, Shinichi Nunoda, Goro Matsumiya, Motonobu Nishimura, Hirokuni Arai, Shigeki Morita, Masanobu Yanase, Norihide Fukushima, Takeshi Nakatani, Yasushi Sakata, Minoru Ono, . The second official report from Japanese registry for mechanical assisted circulatory support (J-MACS): first results of bridge to bridge strategy. *Gen Thorac Cardiovasc Surg*. 2020.02; 68(2); 102-111
5. Teruhiko Imamura, Minoru Ono, Koichiro Kinugawa, Norihide Fukushima, Akira Shiose, Yoshiro Matsui, Kenji Yamazaki, Yoshikatsu Saiki, Akihiko Usui, Hiroshi Niinami, Goro Matsumiya, Hirokuni Arai, Yoshiki Sawa, Nir Uriel. Hemocompatibility-related Adverse Events Following HeartMate II Left Ventricular Assist Device Implantation between Japan and United States. *Medicina (Kaunas)*. 2020.03; 56(3);
6. Nakajima Y, Suzuki R, Suzuki Y, Sugino T, Kawase T, Onogi S, Seki H, Fujiwara T, Ouchi K.. Suction-fixing surgical device for assisting liver manipulation with laparoscopic forceps. *International Journal of Computer Assisted Radiology and Surgery*. 2020.07;
7. TakeshitaM, Arai H, Nagaoka E, Mizuno T. Papillary muscle relocation and annular repositioning for functional tricuspid regurgitation JTCVS techniques. 2020.09; 3; 162-165
8. Hirasawa Kensuke, Izumo Masaki, Umemoto Tomoyuki, Suzuki Kengo, Kitanaka Yosuke, Oi Keiji, Mizuno Tomohiro, Harada Tomoo, Ashikaga Takashi, Miyairi Takeshi, Arai Hirokuni, Hirao Kenzo, Akashi Yoshihiro J.. Geometry of Tricuspid Valve Apparatus in Patients with Mitral Regurgitation due to Fibroelastic Deficiency versus Barlow Disease: A Real-Time Three-dimensional Transesophageal Echocardiography Study *JOURNAL OF THE AMERICAN SOCIETY OF ECHOCARDIOGRAPHY*. 2020.09; 33(9); 1095-1105
9. Haruna Seki, Tatsuki Fujiwara, Wataru Hijikata, Tomotaka Murashige, Takuro Maruyama, Sachie Yokota, Asato Ogata, Katsuhiro Ouchi, Tomohiro Mizuno, Hirokuni Arai. Verification of a thrombus induction method at the target point inside the blood pump using a fibrinogen coating for a thrombus detection study. *Artif Organs*. 2020.09; 44(9); 968-975
10. Oishi K, Arai H, Yoshida T.. Coronary ostial plasty using femoral artery patch in Takayasu aortitis: A 15-year follow-up study *JTCVS Techniques*. 2020.09; 1(3); 176-178
11. Takayama W, Endo A, Yoshii J, Arai H, Oi K, Nagaoka E, Toyama S, Yamamoto H, Uchida T, Otomo Y. Severe COVID-19 Pneumonia in a 30-Year-Old Woman in the 36th Week of Pregnancy Treated with Postpartum Extracorporeal Membrane Oxygenation. *The American journal of case reports*. 2020.10; 21; e927521
12. Yasunori Cho, Satoru Wakasa, Akihiko Usui, Kenji Minatoya, Hirokuni Arai, Hitoshi Yaku, Atsushi Yamaguchi, Tatsuhiko Komiya, Goro Matsumiya, Kimikazu Hamano, Yoshikatsu Saiki, Yoshiro Matsui. Non-heart transplant surgical approaches with mitral valve operation and surgical ventricular reconstruction for non-ischaeic dilated cardiomyopathy: a Japanese multicenter study. *Gen Thorac Cardiovasc Surg*. 2020.10;
13. Mizuno T, Ohuchi K, Fujiwara T, Oi K, Nagaoka E, Oishi K, Yashima M, Takeshita M, Arai H. Development of a novel heart positioner for minimally invasive coronary surgery. *The Annals of thoracic surgery*. 2020.11; 110(5); 1746-1750

14. Teruhiko Imamura, Koichiro Kinugawa, Minoru Ono, Norihide Fukushima, Akira Shiose, Yoshiro Matsui, Kenji Yamazaki, Yoshikatsu Saiki, Goro Matsumiya, Hirokuni Arai, Yoshiki Sawa. Bridge-to-Bridge Left Ventricular Assist Device Implantation Strategy vs. Primary Left Ventricular Assist Device Implantation Strategy. *Circ J.* 2020.11; 84(12); 2198-2204
15. Kiyotoshi Oishi, Hirokuni Arai, Tetsuya Yoshida, Keiji Oi, Eiki Nagaoka, Masafumi Yashima, Tatsuki Fujiwara, Masashi Takeshita, Yushi Okumura, Tomohiro Mizuno. Coronary Ostial Patch Angioplasty With Femoral Artery in Takayasu Arteritis. *Ann Thorac Surg.* 2020.11; 110(5); e427-e430
16. Nakatsutsumi K, Sekiya K, Urushibata N, Hosoi M, Arai H, Nagaoka E, Fujiwara T, Morishita K, Aiboshi J, Otomo Y. A successful case of extracorporeal membrane oxygenation treatment for intractable pneumothorax in a patient with COVID-19. *Acute medicine & surgery.* 2020.12; 7(1); e612

[Conference Activities & Talks]

1. Arai H.. Recent Evidence for OPCAB.. 1st Philippine Heart Center Advanced Coronary Artery Surgery Workshop 2020.01.10 Quezon City, Philippine
2. Arai H.. Choice of Grafts in Multi-arterial CABG.. 1st Philippine Heart Center Advanced Coronary Artery Surgery Workshop 2020.01.10 Quezon City, Philippine
3. Arai H. Techniques and Strategies in Multi-Arterial CABG.. 1st Philippine Heart Center Advanced Coronary Artery Surgery Workshop 2020.01.10 Quezon City, Philippine
4. Arai H. Anatomical - Epiaortic and Epicardial – Assessment.. 1st Philippine Heart Center Advanced Coronary Artery Surgery Workshop 2020.01.10 Quezon City, Philippine
5. Arai H. FFR Guided CABG.. 1st Philippine Heart Center Advanced Coronary Artery Surgery Workshop 2020.01.10 Quezon City, Philippine
6. Arai H. Coronary Ostial Patch Angioplasty with Femoral Artery in Takayasu Aortitis . The Society of Thoracic Surgeons 56th Annual Meeting 2020.01.25 New Orleans, USA
7. Arai H. Innovative Surgical Approach for Coronary Ostial Stenosis.. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.07 Chiang Mai, Thailand
8. Arai H. Subvalvular Repair for Functional TR.. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.07 Chiang Mai, Thailand
9. Arai H. Intraoperative Ultrasonic Quality Assessment and Surgical Guidance to Improve CABG Outcomes.. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.07 Chiang Mai, Thailand
10. Arai H. Mt.Fuji Technique for Complex Valve Prolapse.. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.07 Chiang Mai, Thailand
11. Arai H. Breakout Session : Reducing risk in CABG (Moderator) . 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.08 Chiang Mai, Thailand
12. Mizuno T, Oishi K, Okumura Y, Sai Y, Takeshita M, Yashima M, Nagaoka E, Oi K, Arai H.. One-stage hybrid total aortic arch repair involving descending thoracic aortic disease: a comparison to conventional procedures.. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.10 Chiang Mai, Thailand
13. Okumura Y, Mizuno T, Oi K, Nagaoka E, Yashima M, Fujiwara T, Oishi K, Takeshita M, Sai Y, Seki H, Arai H.. Efficacy of perioperative blood transfusion therapy using Thromboelastography. 28th Congress of the Asian Society for Cardiovascular and Thoracic Surgery 2020.02.10 Chiang Mai, Thailand
14. Arai H. Intraoperative Assessment of Coronary Artery Bypass Graft Patency.. Webinar The Society of Thoracic Surgeons of Thailand Coronary Artery Bypass Graft Surgery 2020.07.05 Thailand
15. E. Nagaoka, T. Mizuno, K. Oi, M. Yashima, T. Fujiwara, K Oishi, M. Takeshita, Y. Okumura, Y Sai, H. Seki, and H. Arai. Long-term Results of Mitral Valve Repair for Multi-Regional Complex Mitral Regurgitation. The 50th Annual Meeting of the Japanese Society for Cardiovascular Surgery 2020.08

16. Arai H. Tricuspid valve surgery: going beyond the common scenarios' -'Subvalvular Procedures For Massive Functional TR'. The 34th 34th Annual Meeting of European Association for Cardio-Thoracic Surgery 2020.10.08 virtual
17. Masashi Takeshita Hirokuni Arai, Tomohiro Mizuno, Keiji Oi, Eiki Nagaoka, Masafumi Yashima, Tatsuki Fujiwara, Kiyotoshi Oishi . Surgical strategy and midterm results of tricuspid valve repair for tricuspid regurgitation concomitant with mitral valve surgery . The 34th Annual Meeting of European Association for Cardio-Thoracic Surgery 2020.10.09 Barcelona, Spain
18. Arai H. Adjunctive Techniques for Repair of Ischemic Mitral Regurgitation. America Heart Association 2020 Annul Meeting 2020.11.13 virtual

Nephrology

Professor:

Shinichi UCHIDA
Tatemitsu RAI (Dept. of Nephrology and Regional Medicine (Ibaraki))

Associate Professor:

Eisei SOHARA
Shotaro NAITO (Dept. of Blood Purification)

Junior Associate Professor:

Soichiro IIMORI

Assistant Professor:

Takayasu MORI (Dept. of Blood Purification)
Koichiro SUSA
Fumiaki ANDO (Dept. of Nephrology and Regional Medicine (Ibaraki))
Shintaro MANDAI (Dept. of Blood Purification)
(second half) Yu NANAMATSU

Graduate Student:

Naohiro TAKAHASHI, Tamami FUJIKI, Azuma NANAMATSU
Yu HARA, Soichiro SUZUKI, Tomoki YANAGI, Takaaki KOIDE
Hisazumi MATSUKI, Ryosuke KAWAMOTO, Yuta NAKANO, Hideki YANAGAWA

Hospital Staff:

Chisato YAMAMURA (Project Assistant Professor)
Yuichiro AKAGI (Project Assistant Professor)
Taku GENMA, Kaho IKESHITA, Kazuki KOJIMA
Yurika HIROSE, Motoki HOSHINO
(first half) Jun TAKAMI, (second half) Yuta SEKIGUCHI

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 pioneering institutes that introduced 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 2020, Participation in the Annual Meeting of American Society of Nephrology was postponed this year due to the COVID-19 pandemic. At the Annual Meeting of Japanese Society of Nephrology, which was held on the web, a total of 9 presentations of 8 oral and 1 poster including the Oshima Award commemorative lecture by Assistant Professor Fumiaki Ando and the YIA (Young Investigator Award) award commemorative lecture by Dr. Taisuke Furusho was adopted. Moreover, our research manuscripts were published in *Kidney International* (IF: 8.3), *Bone* (IF: 4.4), *Human Mutation* (IF: 4.1), and *Scientific Reports* (IF: 4.0). We published 19 reports in English and one of them were presented as "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.

(3) Education

"Undergraduate education"

(Systematic lectures)

For third grade medical students, we are conducting lectures organized in a three-week 'block form' in collaboration with the Urology and Pathology sections. Under the name of "Body Fluid Regulation and Urology" Block, students can learn intensively about kidney and urologic diseases during this period. In this lecture, we incorporate PBL (Problem-Based Learning) lectures so that the students will be able to study independently and bi-directionally. This year (2020), due to the COVID-19 pandemic, all the lectures were conducted in remote form.

(Project semester)

We accept several students every year in the project semester, in which the students are expected to participate in the forefront research with the assistance of graduate students.

(Clinical clerkship)

For the last three months of fourth grade following the project semester, we provide the Pre-Clinical Clerkship (PCC) lectures for ten weeks (two weeks of large-class comprehensive lectures and eight weeks of small-class lectures), which are more practical and interactive than the previous lectures held in the classroom. This year, all lectures were conducted in remote form. After PCC, fifth grade 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. Although limitations were set for the frequency and time of actual access to the ward, the students were assigned to be in charge of one new inpatient each week and make a presentation about their patient at the regular ward conference. They 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. 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 very active, and by carrying out the state-of-the-art research, we are training doctors to be able to excel in both basic and clinical works.

(4) Clinical Services & Other Works

We are one of the first groups that introduced the hemodialysis therapy in Japan, and thus, have a long experience of clinical practice of kidney diseases. We have close coordination with our 20 affiliated hospitals. 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 kidney disease patients, vascular access surgery, peritoneal dialysis-related surgery, and induction of dialysis are consistently carried out in our department. In 2020, among hemopurification centers in 42 hospitals belonging to national universities, the number of plasma exchange was in 1st place, the number of newly started dialysis patients was in 3rd 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. Shoda W, Nomura N, Ando F, Tagashira H, Iwamoto T, Ohta A, Isobe K, Mori T, Susa K, Sohara E, Rai T, Uchida S. Sodium-calcium exchanger 1 is the key molecule for urinary potassium excretion against acute hyperkalemia. *PLoS one*. 2020; 15(6); e0235360
2. Fujimaru T, Shimada K, Hamada T, Watanabe K, Ito Y, Nagahama M, Taki F, Isokawa S, Hifumi T, Otani N, Nakayama M. Development of acute kidney injury with massive granular casts and microscopic hematuria in patients with COVID-19: two case presentations with literature review. *Renal replacement therapy*. 2020; 6(1); 59
3. Mandai S, Sato H, Iimori S, Naito S, Tanaka H, Ando F, Susa K, Isobe K, Mori T, Nomura N, Sohara E, Okado T, Uchida S, Fushimi K, Rai T. Nationwide in-hospital mortality following major fractures among hemodialysis patients and the general population: An observational cohort study. *Bone*. 2020.01; 130; 115122
4. Saito D, Fujimaru T, Inoue Y, Hirayama T, Ezaki I, Kin H, Shuo T, Nakayama M, Komatsu Y. Serial measurement of electrolyte and citrate concentrations in blood-primed continuous hemodialysis circuits during closed-circuit dialysis. *Pediatric nephrology (Berlin, Germany)*. 2020.01; 35(1); 127-133
5. Furusho T, Sohara E, Mandai S, Kikuchi H, Takahashi N, Fujimaru T, Hashimoto H, Arai Y, Ando F, Zeniya M, Mori T, Susa K, Isobe K, Nomura N, Yamamoto K, Okado T, Rai T, Uchida S. Renal TNF α activates the WNK phosphorylation cascade and contributes to salt-sensitive hypertension in chronic kidney disease. *Kidney international*. 2020.02;
6. Mishima E, Mori T, Nakajima Y, Toyohara T, Kikuchi K, Oikawa Y, Matsushashi T, Maeda Y, Suzuki T, Kudo M, Ito S, Sohara E, Uchida S, Abe T. HPRT-related hyperuricemia with a novel p.V35M mutation in HPRT1 presenting familial juvenile gout. *CEN case reports*. 2020.03;
7. Nakamura Y, Yokoyama M, Yoshida S, Tanaka H, Kijima T, Ishioka J, Matsuoka Y, Saito K, Minami I, Yoshimoto T, Naito S, Ogawa Y, Yamada T, Uchida S, Fujii Y. Postoperative renal impairment and longitudinal change in renal function after adrenalectomy in patients with Cushing's syndrome. *International journal of urology : official journal of the Japanese Urological Association*. 2020.03;
8. Saran Sinha Adya, Wang Tianying, Hosoi Yasushi, Sohara Eisei, Akita Tenpei, Uchida Shinichi, Fukuda Atsuo. WNK3 kinase maintains basal excitability by regulating inward rectification and intracellular chloride in layer V pyramidal neurons of mouse medial prefrontal cortex *The Journal of Physiological Sciences*. 2020.03; 70(Suppl.1); S157
9. Nakamura Yuki, Yokoyama Minato, Yoshida Soichiro, Tanaka Hajime, Kijima Toshiki, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Minami Isao, Yoshimoto Takanobu, Naito Shotaro, Ogawa Yoshihiro, Yamada Tetsuya, Uchida Shinichi, Fujii Yasuhisa. Postoperative renal impairment and longitudinal change in renal function after adrenalectomy in patients with Cushing's syndrome(和訳中) *International Journal of Urology*. 2020.05; 27(5); 395-400
10. Fujimaru Takuya, Sohara Eisei. Copy Number Variation: A New Genetic Form of Polycystic Kidney and Liver Disease *KIDNEY INTERNATIONAL REPORTS*. 2020.05; 5(5); 575-576
11. Shohei Noda, Shintaro Mandai, Takashi Oda, Tomoko Shinoto, Hidehiko Sato, Keiko Sato, Katsui Hirokawa, Yumi Noda, Shinichi Uchida. Asymptomatic sinusitis as an origin of infection-related glomerulonephritis manifesting steroid-resistant nephrotic syndrome: A case report. *Medicine (Baltimore)*. 2020.06; 99(25); e20572
12. Umene R, Kitamura M, Arai H, Matsumura K, Ishimaru Y, Maeda K, Uramatsu T, Obata Y, Mori T, Sohara E, Uchida S, Nishino T. Bartter syndrome representing digenic-based salt-losing tubulopathies presumably accelerated by renal insufficiency. *CEN case reports*. 2020.06;

13. Nakano K, Kubota Y, Mori T, Chiga M, Mori T, Sonoda S, Ueda D, Asakura I, Ikegaya T, Kagawa J, Uchida S, Kubota A. Familial cases of pseudohypoaldosteronism type II harboring a novel mutation in the Cullin 3 gene. *Nephrology (Carlton, Vic.)*. 2020.07; e13752
14. Tsuji Kiyokazu, Kitamura Mineaki, Muta Kumiko, Mochizuki Yasushi, Mori Takayasu, Sohara Eisei, Uchida Shinichi, Sakai Hideki, Mukae Hiroshi, Nishino Tomoya. Transplantation of a kidney with a heterozygous mutation in the SLC22A12 (URAT1) gene causing renal hypouricemia: a case report *BMC NEPHROLOGY*. 2020.07; 21(1); 282
15. Moena Ishikawa, Yumi Tada, Hiromu Tanaka, Wataru Morii, Masako Inaba, Hidetoshi Takada, Takayasu Mori, Emiko Noguchi. A Family with Gitelman Syndrome with Asymptomatic Phenotypes while Carrying Reported SLC12A3 Mutations. *Case Rep Nephrol Dial*. 2020.07; 10(2); 71-78
16. Yang L, Frindt G, Xu Y, Uchida S, Palmer LG. Aldosterone-dependent and -independent regulation of Na and K excretion and ENaC in mouse kidneys. *American journal of physiology. Renal physiology*. 2020.08; 319(2); F323-F334
17. Sekine A, Hoshino J, Fujimaru T, Suwabe T, Mizuno H, Kawada M, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Mandai S, Chiga M, Kikuchi H, Ando F, Mori T, Sohara E, Uchida S, Sawa N, Takaichi K, Ubara Y. Genetics May Predict Effectiveness of Tolvaptan in Autosomal Dominant Polycystic Kidney Disease. *American journal of nephrology*. 2020.08; 1-7
18. Kosaka S, Ohara Y, Naito S, Iimori S, Kado H, Hatta T, Yanishi M, Uchida S, Tanaka M. Association among kidney function, frailty, and oral function in patients with chronic kidney disease: a cross-sectional study. *BMC nephrology*. 2020.08; 21(1); 357
19. Mishima Eikan, Mori Takayasu, Nakajima Yoko, Toyohara Takafumi, Kikuchi Koichi, Oikawa Yoshitsugu, Matsushashi Tetsuro, Maeda Yasuhiro, Suzuki Takehiro, Kudo Masataka, Ito Sadayoshi, Sohara Eisei, Uchida Shinichi, Abe Takaaki. HPRT-related hyperuricemia with a novel p.V35M mutation in HPRT1 presenting familial juvenile gout *CEN Case Reports*. 2020.08; 9(3); 210-214
20. Fujii Shinya, Kikuchi Eriko, Watanabe Yuko, Suzuyama Honoka, Ishigami-Yuasa Mari, Mori Takayasu, Isobe Kiyoshi, Uchida Shinichi, Kagechika Hiroyuki. Structural development of N-(4-phenoxyphenyl)benzamide derivatives as novel SPAK inhibitors blocking WNK kinase signaling *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS*. 2020.09; 30(17); 127408
21. Ishii T, Fujimaru T, Nakano E, Takahashi O, Nakayama M, Yamauchi T, Komatsu Y. Association between chronic kidney disease and mortality in stage IV cancer. *International journal of clinical oncology*. 2020.09; 25(9); 1587-1595
22. Takashi Iijima, Takayasu Mori, Eisei Sohara, Tatsuya Suwabe, Junichi Hoshino, Yoshifumi Ubara. A patient with congenital nephrogenic diabetes insipidus due to AVPR2 mutation complicated by persisting polydipsia under hemodialysis treatment. *CEN Case Rep*. 2020.10;
23. Takayasu Mori, Motoko Chiga, Takuya Fujimaru, Ryosuke Kawamoto, Shintaro Mandai, Azuma Nanamatsu, Naohiro Nomura, Fumiaki Ando, Koichiro Susa, Eisei Sohara, Tatemitsu Rai, Shinichi Uchida. Phenotypic differences of mutation-negative cases in Gitelman syndrome clinically diagnosed in adulthood. *Hum Mutat*. 2020.12;
24. Yohei Arai, Kenichi Asano, Shintaro Mandai, Fumiaki Ando, Koichiro Susa, Takayasu Mori, Naohiro Nomura, Tatemitsu Rai, Masato Tanaka, Shinichi Uchida, Eisei Sohara. WNK1-TAK1 signaling suppresses lipopolysaccharide-induced cytokine production and classical activation in macrophages. *Biochem Biophys Res Commun*. 2020.12; 533(4); 1290-1297

[Misc]

1. Taisuke Furusho, Shinichi Uchida. Monogenic Hypertension *Nihon Rinsho*. 2020.03;
2. Furusho Taisuke, Uchida Shinichi, Sohara Eisei. The WNK signaling pathway and salt-sensitive hypertension *Hypertension Research*. 2020.08; 43(8); 733-743

[Conference Activities & Talks]

1. Sohara Eisei. WNK signal in salt-sensitive hypertension. The 9th CKD Frontier Meetings 2020.02.15 Nagoya, Japan
2. Genetic background in clinically diagnosed Gitelman syndrome in adulthood and phenotypic characteristics of the mutation-negative cases. 2020.08
3. Ando F. 【大島賞受賞記念講演】Identification of Therapeutic Targets for Congenital Nephrogenic Diabetes Insipidus. 第 63 回日本腎臓学会学術総会 2020.08.18 横浜, web
4. Shintaro Mandai. WNK1 kinase: a novel potential player in skeletal muscle hypertrophy and sarcopenia induced by chronic kidney disease. The 43th Annual Meeting of the Molecular Biology Society of Japan (MBSJ2020) 2020.12.03 web
5. Ando F, Uchida S. Development of Novel Therapeutic Strategies for Congenital NDI and Other PKA-Related Diseases. The 43th Annual Meeting of the Molecular Biology Society of Japan (MBSJ2020) 2020.12.03 web

[Awards & Honors]

1. CKD Frontier Award, The CKD Frontier Meeting, 2020.02

Comprehensive Reproductive Medicine

Professor : Naoyuki MIYASAKA
Associate Professor : Naoyuki YOSHIKI
Project Professor : Masakazu TERAUCHI
Junior Associate Professor : Kimio WAKANA
Project Associate Professor : Tomonori ISHIKAWA
Assistant Professor : Noriko OSHIMA, Yuki IWAHARA, Masaki SEKIGUCHI, Shiro HIRAMITSU,
Takafumi TUKADA, Asuka HIROSE, Reiko NAKAMURA, Haruko OHNO
Project Assistant Professor : Kazuki SAITO, Takayuki TATSUMI, Tamami ODAI
Hospital Staff : Rinko IBI, Tatuya SATOU, Shouko KATUMATA
Graduate Student : Takuto MATSUURA, Mayumi KATOU, Shiho HIDAKA, Misako IWATA, Nobuyuki
KIDERA, Ayako FUDONO, Kotoi TSURANE, Atsushi FUSEGI, Hiroshi YOMOGIDA, Junichiro MITSUI

(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 staffs, 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. Yamada Ichiro, Oshima Noriko, Wakabayashi Akira, Miyasaka Naoyuki, Wakana Kimio, Saida Yukihisa, Tateishi Ukihide, Kobayashi Daisuke. Diffusion-Tensor Imaging of Uterine Cervical Carcinoma: Correlation With Histopathologic Findings JOURNAL OF COMPUTER ASSISTED TOMOGRAPHY. 2020; 44(3); 426-435
2. Fujii M, Yamashita S, Fudono A, Yanai S, Tashiro J, Takenaka Y, Yamasaki K, Ito E, Masaki Y. Splenic artery aneurysm rupture during pregnancy: A case report of maternal and fetal survival. International journal of surgery case reports. 2020; 76; 94-97
3. Yoshino Y, Yoshiki N, Nakamura R, Iwahara Y, Ishikawa T, Miyasaka N. Large leiomyomatosis peritonealis disseminata after laparoscopic myomectomy: A case report with literature review. International journal of surgery case reports. 2020; 77; 866-869
4. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Mihoko Akiyoshi, Naoyuki Miyasaka. Muscle and joint pains in middle-aged women are associated with insomnia and low grip strength: a cross-sectional study Journal of Psychosomatic Obstetrics & Gynecology. 2020.01; 41(1); 15-21
5. Hirose A, Terauchi M, Odai T, Kato K, Miyasaka N. Depressive symptoms at postpartum are associated with those at the second trimester of pregnancy and the antioxidant activity immediately after delivery. J Psychosom Obstet Gynaecol. 2020.01; 6; 1-7
6. Hirose Asuka, Terauchi Masakazu, Odai Tamami, Kato Kiyoko, Miyasaka Naoyuki. Depressive symptoms at postpartum are associated with those at the second trimester of pregnancy and the antioxidant activity immediately after delivery JOURNAL OF PSYCHOSOMATIC OBSTETRICS & GYNECOLOGY. 2020.01; 1-7
7. Masakazu Terauchi, Tamami Odai, Asuka Hirose, Kiyoko Kato, Naoyuki Miyasaka. Chilliness in Japanese middle-aged women is associated with anxiety and low n-3 fatty acid intake. Climacteric. 2020.02; 23(2); 178-183
8. Toshimitsu Okamura, Satoshi Tsukamoto, Kotaro Nagatsu, Maki Okada, Katsuyuki Minegishi, Takayuki Tatsumi, Aya Sugyo, Tatsuya Kikuchi, Hidekatsu Wakizaka, Hideki Ishii, Atsushi B Tsuji, and Ming-Rong Zhang. 6-[124I] Iodo-9-pentylpurine for imaging the activity of the sodium iodide symporter in the brain Journal of Medical Chemistry. 2020.02;
9. Fukumoto Seiji, Soen Satoshi, Taguchi Tetsuya, Ishikawa Takashi, Matsushima Hisashi, Terauchi Masakazu, Horie Shigeo, Yoneda Toshiyuki, Sugimoto Toshitsugu, Matsumoto Toshio. Management manual for cancer treatment-induced bone loss (CTIBL): position statement of the JSBMR JOURNAL OF BONE AND MINERAL METABOLISM. 2020.02;

10. 寺内公一. 更年期診療 UPDATE はじめに 別冊・医学のあゆみ. 2020.02; 1
11. Yuka Yonekura, Masakazu Terauchi, Asuka Hirose, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. Daily coffee and green tea consumption is inversely associated with body mass index, body fat percentage, and cardio-ankle vascular index in middle-aged Japanese women: a cross-sectional study *Nutrients*. 2020.05; 12(5); 1370
12. Yonekura Y, Terauchi M, Hirose A, Odai T, Kato K, Miyasaka N. Daily Coffee and Green Tea Consumption Is Inversely Associated with Body Mass Index, Body Fat Percentage, and Cardio-Ankle Vascular Index in Middle-Aged Japanese Women: A Cross-Sectional Study. *Nutrients*. 2020.05; 12(5);
13. Mayumi Kobayashi Kato, Mayu Yunokawa, Seiko Bun, Tatsunori Shimoi, Kan Yonemori, Naoyuki Miyasaka, Tomoyasu Kato, Kenji Tamura. Treatment strategies for recurrent ovarian cancer in older adult patients in Japan: a study based on real-world data *Journal of Cancer Research and Clinical Oncology*. 2020.05; 146(5); 1335-1341
14. Mayumi Kobayashi Kato, Satoru Muro, Tomoyasu Kato, Naoyuki Miyasaka, Keiichi Akita. Spatial distribution of smooth muscle tissue in the female pelvic floor and surrounding the urethra and vagina *Anatomical Science International*. 2020.05;
15. Kato MK, Yunokawa M, Bun S, Shimoi T, Yonemori K, Miyasaka N, Kato T, Tamura K.. Treatment strategies for recurrent ovarian cancer in older adult patients in Japan: a study based on real-world data. *J Cancer Res Clin Oncol.* 2020.05; 146(5); 1335-1341
16. Takahashi Kenta, Gen Yasuyuki, Tanimoto Kousuke, Kudo Atsushi, Oshima Noriko, Ban Daisuke, Takemoto Akira, Onishi Ichiro, Kumaki Yuichi, Yokobori Junko, Takamine Eriko, Kano Yoshihito, Miyake Satoshi, Miyasaka Naoyuki, Tanabe Minoru, Inazawa Johji, Ikeda Sadakatsu. Clinical impact of hemizygous deletion detection and panel-size in comprehensive genomic profiling. *JOURNAL OF CLINICAL ONCOLOGY*. 2020.05; 38(15);
17. Yamada I, Oshima N, Wakana K, Miyasaka N, Wakabayashi A, Sakamoto J, Saida Y, Tateishi U, Kobayashi D. Uterine Cervical Carcinoma: Evaluation Using Non-Gaussian Diffusion Kurtosis Imaging and Its Correlation With Histopathological Findings. *Journal of computer assisted tomography*. 2020.06;
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19. Mayumi Kobayashi Kato, Dai Shida, Yutaka Yoneoka, Hiroshi Yoshida, Naoyuki Miyasaka, Yukihide Kanemitsu, Tomoyasu Kato. Novel classification of ovarian metastases originating from colorectal cancer by radiological imaging and macroscopic appearance *International Journal of Clinical Oncology*. 2020.06;
20. Odai Tamami, Terauchi Masakazu, Suzuki Risa, Kato Kiyoko, Hirose Asuka, Miyasaka Naoyuki. Severity of subjective forgetfulness is associated with high dietary intake of copper in Japanese senior women: A cross-sectional study *FOOD SCIENCE & NUTRITION*. 2020.07;
21. Terui-Kohbata Hiroko, Egawa Makiko, Yura Kei, Yoshida Masayuki. Knowledge and attitude of hereditary breast cancer among Japanese university female students *Journal of Human Genetics*. 2020.07; 65(7); 591-599
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29. Yoshioka W, Miyasaka N, Okubo R, Shimizu R, Takahashi Y, Oda Y, Nishino I, Nakamura H, Mori-Yoshimura M.. Pregnancy in GNE myopathy patients: a nationwide repository survey in Japan. Orphanet J Rare Dis.. 2020.09; 15(1); 245
30. Kato MK, Shida D, Yoneoka Y, Yoshida H, Miyasaka N, Kanemitsu Y, Kato T.. Novel classification of ovarian metastases originating from colorectal cancer by radiological imaging and macroscopic appearance. Int J Clin Oncol.. 2020.09; 25(9); 1663-1671
31. Suto EG, Mabuchi Y, Toyota S, Taguchi M, Naraoka Y, Itakura N, Matsuoka Y, Fujii Y, Miyasaka N, Akazawa C.. Advantage of fat-derived CD73 positive cells from multiple human tissues, prospective isolated mesenchymal stromal cells. Sci Rep.. 2020.09; 10(1); 15073
32. Kato K, Terauchi M. Annual report of the Women's Health Care Committee, Japan Society of Obstetrics and Gynecology, 2020. The journal of obstetrics and gynaecology research. 2020.10;
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34. Aizawa R, Ibayashi M, Hatakeyama T, Tatsumi T, Tsukamoto S. Impact of short-term high-fat feeding on lipid droplet content in mouse oocytes. The Journal of reproduction and development. 2020.10;
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38. Tamami Odai, Masakazu Terauchi, Risa Suzuki, Kiyoko Kato, Asuka Hirose, Naoyuki Miyasaka. Depressive symptoms in middle-aged and elderly women are associated with a low intake of vitamin B6: a cross-sectional study NUTRIENTS. 2020.11; 12(11); 3437
39. Odai Tamami, Terauchi Masakazu, Suzuki Risa, Kato Kiyoko, Hirose Asuka, Miyasaka Naoyuki. Depressive Symptoms in Middle-Aged and Elderly Women Are Associated with a Low Intake of Vitamin B6: A Cross-Sectional Study NUTRIENTS. 2020.11; 12(11);
40. Yamamoto A, Kurata M, Yamamoto K, Nogawa D, Inoue M, Ishibashi S, Ikeda M, Miyasaka N, Kitagawa M.. High amplification of PVT1 and MYC predict favorable prognosis in early ovarian carcinoma. Pathol Res Pract.. 2020.11; 216(11); 153175

41. Yuka Enokuchi, Atsushi Suzuki, Tohru Yamaguchi, Ryuji Ochiai, Masakazu Terauchi, Kiyoshi Kataoka. Effects of Chlorogenic Acids on Menopausal Symptoms in Healthy Women: A Randomized, Placebo-Controlled, Double-Blind, Parallel-Group Trial Nutrients. 2020.12; 12(11); 3757
42. Terauchi Masakazu, Odai Tamami, Kato Kiyoko, Miyasaka Naoyuki. Body Mass Index and Percentage Body Fat Are Negatively Associated with Severe Dyspareunia in Japanese Post-menopausal Women MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY. 2020.12; 27(12); 1474
43. Ye C, Katagiri S, Miyasaka N, Kobayashi H, Khemwong T, Nagasawa T, Izumi Y.. The periodontopathic bacteria in placenta, saliva and subgingival plaque of threatened preterm labor and preterm low birth weight cases: a longitudinal study in Japanese pregnant women. Clin Oral Investig.. 2020.12; 24(12); 4261-4270

[Misc]

1. Masakazu Terauchi. Menopausal hormone therapy does not prevent age-related muscle loss in postmenopausal women Menopause Live. 2020.02; 2/20;
2. Masakazu Terauchi. Maintaining muscle mass may protect from hot flushes Menopause Live. 2020.12; 12/7;
3. Toru Izumi, Masakazu Terauchi. The Diverse Efficacy of Food-Derived Proanthocyanidins for Middle-Aged and Elderly Women Nutrients. 2020.12; 12(11); 3833

[Conference Activities & Talks]

1. Odai Tamami, Terauchi Masakazu, Hirose Asuka, Miyasaka Naoyuki. Chronic stress disorients stress response and induces depression-like behavior in ovariectomized mice(和訳中). 日本産科婦人科学会雑誌 2020.03.01
2. Mai Inagaki, Takayuki Tatsumi, Hiroshi Yomogita, Asuka Hirose, Masaki Sekiguchi, Naoyuki Miyasaka. Obstetrical management of a patient with Andersen-Tawil syndrome. 第72回日本産科婦人科学会 学術講演会 2020.04.23
3. Tomonori Ishikawa. Personalized Embryo Transfer improves implantation rate in patients with RIF. 1st Igenomix APAC Online Symposium 2020.09.27 web
4. Masakazu Terauchi, Tamami Odai, Kiyoko Kato, Naoyuki Miyasaka. Body Mass Index and Percentage Body Fat Are Negatively Associated with Severe Dyspareunia in Japanese Post-menopausal Women. North American Menopause Society 2020 Virtual Annual Meeting 2020.09.28 web

Urology

Professor and Chairman: Yasuhisa Fujii

Associate Professor: Yoh Matsuoka

Junior Associate Professor: Minato Yokoyama (Department of Insured Medical Care Management),
Soichiro Yoshida, Hajime Tanaka

Assistant Professor: Yosuke Yasuda, Sho Uehara, Hiroshi Fukushima, Shohei Fukuda

Hospital Staff: Masahiro Toide, Yusuke Uchida, Yuki Nakamura, Madoka Kataoka, Yoshitomo Yamaguchi,
Wataru Shimada

Graduate Student: Bo Fan

(1) Outline

Urology is the branch of medicine that focuses on surgical and medical diseases of the male and female urinary-tract system and the male reproductive organs. 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” .

(2) Research

Clinical Research

1. A minimally invasive surgery, minimum-incision endoscopic urological surgery
2. Optimal MRI-ultrasonography fusion prostate needle biopsy
3. Curative and minimally invasive bladder preservation using transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy
4. Minimum-incision endoscopic clampless partial nephrectomy against kidney cancer
5. Focal brachytherapy against localized prostate cancer
6. Diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
7. Whole body MRI using DWIBS technique
8. Imaging diagnosis for prostate and kidney cancers using deep learning
9. Serum C-reactive protein as a prognostic biomarker of urological malignancies
10. Prognostic prediction model for non-muscle-invasive bladder cancer
11. Renal function after kidney cancer surgery
12. Prevention of postoperative inguinal hernia after robot assisted radical prostatectomy

Translational Research

1. Biomarker in bladder preservation therapy using chemoradiotherapy
2. Overcoming therapeutic resistance to immune-check point inhibitors for urological cancers
3. Mechanisms of abscopal effect of immune-check point inhibitors and radiation in urothelial cancer

(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 including robot-assisted surgery and laparoscopic sacrocolpopexy, we are making a continuous effort to improve daily practices. To realize the mission, we have been developing various procedures with high quality and affordable cost.

1. Minimum-incision endoscopic urological surgery which can be applied to most of patients with urological tumors
2. Tetra-modal bladder sparing treatment consisting of transurethral resection of bladder tumor, low-dose chemoradiotherapy and partial cystectomy with pelvic lymph node dissection
3. Clampless partial nephrectomy
4. Focal brachytherapy
5. Prediction model of non-muscle invasive bladder cancer
6. Diagnostic model for small renal masses
7. Clinical implication of diffusion-weighted MRI

(5) Publications

[Original Articles]

1. Yoshida S, Takahara T, Arita Y, Toda K, Yoshimura R, Fujii Y. . Patterns of failure after progressive site-directed therapy in oligo-progressive castration-resistant prostate cancer. *Int J Urol.* 2020; 27: 634-635. doi: 10.1111/iju.14249.. 2020;
2. Yoshida S, Taniguchi N, Moriyama S, Matsuoka Y, Saito K, Fujii Y. . Application of virtual reality in patient explanation of magnetic resonance imaging-ultrasound fusion prostate biopsy. *Int J Urol.* 2020; 27: 471-472. doi: 10.1111/iju.14204.. 2020;
3. Kaneko K, Yoshida S, Yamamoto K, Arita Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. . Renal epithelioid angiomyolipoma: Incidence in a Japanese cohort and diagnostic utility of diffusion-weighted magnetic resonance imaging. *Int J Urol.* 2020 Jul;27(7):599-604. doi: 10.1111/iju.14251.. 2020;
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6. Tanaka H, Fukushima H, Kijima T, Nakamura Y, Yajima S, Uehara S, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Kihara K, Fujii Y. Feasibility and outcomes of selective tetramodal bladder-preservation therapy in elderly patients with muscle-invasive bladder cancer *Int J Urol.* 2020; 27: 236-243. *Equal contribution. 2020;
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8. Tanaka H, Fujii Y. Editorial Comment to Lymph node dissection for bladder cancer: Current standards and the latest evidence *Int J Urol.* 2020. doi: 10.1111/iju.14419. 2020;
9. Ye Y*, Tanaka H*, Wang Y, Campbell RA, Aguilar Palacios D, Dewitt-Foy ME, Mahmood FA, Eltemamy M, Remer EM, Li J, Campbell SC. Split Renal Function in Patients with Renal Masses: Utility of

- Parenchymal Volume Analysis versus Nuclear Renal Scans *BJU International*. 2020; 125: 686-694. *Equal contribution. 2020;
10. Tanaka H. Editorial Comment to Clinical Practice Guidelines for Bladder Cancer 2019 update by the Japanese Urological Association -Summary of the Revision *Int J Urol*. 2020. doi: 10.1111/iju.14314. 2020;
 11. Tanaka H. Editorial Comment to Retroperitoneal tumors: review of diagnosis and management *Int J Urol*. 2020; 27: 1071. 2020;
 12. Fukushima H, Fukuda S, Moriyama S, Uehara S, Yasuda Y, Tanaka H, Yoshida S, Yokoyama M, Matsuoka Y, Fujii Y. Impact of sarcopenia on the efficacy of pembrolizumab in patients with advanced urothelial carcinoma: a preliminary report *Anticancer Drugs*. 2020; 31: 866-871. doi: 10.1097/CAD.0000000000000982.. 2020;
 13. Fukushima H, Kijima T, Fukuda S, Moriyama S, Uehara S, Yasuda Y, Tanaka H, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Matsubara N, Numao N, Sakai Y, Yuasa T, Masuda H, Yonese J, Kageyama Y, Fujii Y. Impact of radiotherapy to the primary tumor on the efficacy of pembrolizumab for patients with advanced urothelial cancer: a preliminary study *Cancer Med*. 2020; 9: 8355-8363. doi: 10.1002/cam4.3445. 2020;
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 15. Fukushima H, Moriyama S, Waseda Y, Fukuda S, Uehara S, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Significance of Bladder Neck Involvement in Risk Substratification of Intermediate-Risk Non-muscle-invasive Bladder Cancer *Eur Urol Focus*. 2020;
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 17. Fukushima H, Fujii Y. Editorial Comment to Does asymptomatic bacteriuria affect the response to intravesical bacillus Calmette-Guerin? *Int J Urol*. 2020;
 18. Ishii A, Yokoyama M, Tsuji H, Fujii Y, Tamaoka A. Pembrolizumab treatment of metastatic urothelial cancer without exacerbating myasthenia gravis *eNeurologicalSci*. 2020;
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[Conference Activities & Talks]

1. Rie Kato, Hiroshi Fukushima, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Ishioka Junichiro, Yoh Matsuoka, Kazutaka Saito, Yukihiro Otsuka, Fumitaka Koga, Masataka Yano, Tetsuro Tsukamoto, Hitoshi Masuda, Tetsuo Okuno, Junji Yonese, Katsushi Nagahama, Shigeyoshi Kamata, Akira Noro, Yukio Kageyama, Toshihiko Tsujii, Shinji Morimoto, Yasuhisa Fujii.. Predictive performance of the qSOFA score for in-hospital mortality of obstructive pyelonephritis patients: a multi-institutional study.. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam Netherlands.
2. Rie Kato, Hiroshi Fukushima, Toshiki Kijima, Soichiro Yoshida, Minato Yokoyama, Ishioka Junichiro, Yoh Matsuoka, Kazutaka Saito, Yukihiro Otsuka, Fumitaka Koga, Masataka Yano, Tetsuro Tsukamoto, Hitoshi Masuda, Tetsuo Okuno, Junji Yonese, Katsushi Nagahama, Shigeyoshi Kamata, Akira Noro, Yukio Kageyama, Toshihiko Tsujii, Shinji Morimoto, Yasuhisa Fujii.. The qSOFA score outperforms the SIRS score in predicting in-hospital mortality of obstructive pyelonephritis patients: results from a multi-institutional study.. 114th annual meeting of the American Urological Association, 2020 2020 Washington DC, USA
3. Matsumoto S, Yoshida S, Yamada I, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Tateishi U, Fujii Y. Utility of diffusion-weighted MRI radiomics features in differentiation of fat-poor angiomyolipoma from clear cell renal cell carcinoma.. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam Netherlands.
4. Yoshida S, Taniguchi N, Moriyama S, Uehara S, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. . Application of virtual reality in patient education about MRI-ultrasound fusion prostate biopsy.. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam, Netherlands
5. Yoshida S., Takahara T., Ishii C., Nakagawa K., Toda K., Arita Y., Kijima T., Yokoyama M., Ishioka J., Matsuoka Y., Saito K., Yoshimura R., Fujii Y. Treatment outcomes of progressive site-directed therapy for oligoprogressive castration-resistant prostate cancer. . The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam, Netherlands
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8. Moriyama S, Yokoyama M, Nakamura Y, Fukuda S, Fukushima H, Uehara S, Tanaka H, Kijima T, Yoshida S, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Impact of nocturia on deteriorated renal function after adrenalectomy in patients with primary aldosteronism. 114th annual meeting of the American Urological Association, 2020 2020 Washington DC, USA
9. Nakamura Y, Yokoyama M, Yoshida S, Tanaka H, Kijima T, Ishioka J, Matsuoka Y, Saito K, Minami I, Yoshimoto T, Naito S, Ogawa Y, Yamada T, Uchida S, Fujii Y. Postoperative renal impairment and longitudinal change in renal function after adrenalectomy in patients with Cushing' s syndrome. The 35th Annual European Association of Urology Congress Virtual, July 2020 2020
10. Tanaka H, Shimada W, Fukuda S, Fukushima H, Moriyama S, Uehara S, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Campbell SC, Fujii Y. Novel classification model of tumour shape irregularity: significance for predicting potential oncologic risks in clinically localised renal cell carcinoma. The 35th Annual Congress of the European Association of Urology, 2020 (Virtual) 2020
11. Tanaka H, Shimada W, Fukuda S, Fukushima H, Moriyama S, Uehara S, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Campbell SC, Fujii Y. Significance of tumor shape irregularity for predicting potential oncologic risks in clinically localized renal cell carcinoma. The 114th Annual Meeting of the American Urological Association, 2020 (Virtual) 2020

12. Fukushima H, Kijima T, Uehara S, Tanaka H, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Matsubara N, Yuasa T, Masuda H, Yonese J, Kageyama Y, Fujii Y. Previous chemoradiotherapy may enhance the efficacy of pembrolizumab in advanced urothelial carcinoma patients. The 35th Annual Congress of the European Association of Urology 2020 Amsterdam, Netherlands
13. Kato R, Fukushima H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Otsuka Y, Koga F, Yano M, Tsukamoto T, Masuda H, Okuno T, Yonese J, Nagahama K, Kamata S, Noro A, Kageyama Y, Tsujii T, Morimoto S, Fujii Y. Predictive performance of the qSOFA score for in-hospital mortality of obstructive pyelonephritis patients: A multi-institutional study. The 35th Annual Congress of the European Association of Urology 2020 Amsterdam, Netherlands
14. Maruyama R, Fukushima H, Fukuda S, Moriyama S, Uehara S, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Feasibility of non-use of antimicrobial prophylaxis in clean urologic surgeries for adrenal and renal tumors: A prospective single-institutional study of 1339 patients. The 35th Annual Congress of the European Association of Urology 2020 Amsterdam Netherlands
15. Fukushima H, Fukuda S, Moriyama S, Uehara S, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Matsuoka Y, Saito K, Abe Y, Takemura Y, Fujii Y. Relationship between nocturia and whole-body fluid distribution assessed by bioelectrical impedance. The 115th annual meeting of the American Urological Association 2020
16. Kato R, Fukushima H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Otsuka Y, Koga F, Yano M, Tsukamoto T, Masuda H, Okuno T, Yonese J, Nagahama K, Kamata S, Noro A, Kageyama Y, Tsujii T, Morimoto S, Fujii Y. The qSOFA score outperforms the SIRS score in predicting in-hospital mortality of obstructive pyelonephritis patients: results from a multi-institutional study. The 115th annual meeting of the American Urological Association 2020 Washington DC, USA
17. Maruyama R, Fukushima H, Fukuda S, Moriyama S, Uehara S, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Low incidence of perioperative infections without antimicrobial prophylaxis in clean surgeries for adrenal and renal tumors: a prospective single-institutional study of 1339 patients. The 115th annual meeting of the American Urological Association 2020 Washington DC, USA
18. Yokoyama M, Masuda H, Ito M, Waseda Y, Moriyama S, Toide M, Uchida Y, Uehara S, Tanaka H, Kijima T, Yoshida S, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Longitudinal change in urinary incontinence, lower urinary tract symptoms and quality of life after artificial urinary sphincter implantation. 114th annual meeting of the American Urological Association 2020 Washington DC, USA
19. Uehara S, Matsuoka Y, Tanaka H, Moriyama S, Tanaka H, Kijima T, Yoshida Y, Yokoyama M, Ishioka J, Saito K, Fujii Y. Systematic biopsy cores near targets are of value for the detection of significant cancer: Analysis of prostate biopsy mapping using multiplanar MRI reconstruction.. The 12th international symposium on focal therapy and imaging in prostate and kidney cancer, 2020 2020 Washington DC, USA
20. Uehara S, Matsuoka Y, Tanaka H, Moriyama S, Tanaka H, Kijima T, Yoshida Y, Yokoyama M, Ishioka J, Saito K, Fujii Y. Systematic biopsy cores away from targets are of limited value for the detection of significant cancer: Analysis of 3D prostate biopsy mapping using multiplanar MRI reconstruction.. 114th annual meeting of the American Urological Association, 2020 2020 Washington DC, USA
21. Uehara S, Matsuoka Y, Tanaka H, Moriyama S, Tanaka H, Kijima T, Yoshida Y, Yokoyama M, Ishioka J, Saito K, Fujii Y. Systematic biopsy cores apart from targets are of limited value for the detection of significant cancer: Analysis of prostate biopsy mapping using multiplanar MRI reconstruction. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam, Netherlands
22. Toide M, Tanaka H, Uchida Y, Fukuda S, Fukushima H, Moriyama S, Uehara S, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Stepwise diagnostic algorithm using CT and MRI for diagnosis of fat-poor angiomyolipoma in small renal masses: Prospective validation study. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam, Netherlands
23. Toide M, Tanaka H, Uchida Y, Fukuda S, Fukushima H, Moriyama S, Uehara S, Kijima T, Yoshida S, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Stepwise algorithm using CT and MRI for differential diagnosis of fat-poor angiomyolipoma in small renal masses: Prospective validation study. 114th annual meeting of the American Urological Association, 2020 2020 Washington DC, USA

24. Yoshida S, Taniguchi N, Moriyama S, Uehara S, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Application of virtual reality in patient education about MRI-ultrasound fusion prostate biopsy. The 35th Annual Congress of the European Association of Urology, 2020 2020 Amsterdam, Netherlands
25. Matsuoka Y, Uehara S, Yoshida S, Tanaka H, Fukuda S, Fukushima H, Moriyama S, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Saito K, Fujii Y. Value of extra-target sampling in addition to intra-target sampling for the detection of prostate cancer upgrading according to PIRADS scores. 12th International Symposium on Focal Therapy and Imaging in Prostate & Kidney Cancer 2020.02.09 Washington DC, USA
26. Matsuoka Y, Uehara S, Yoshida S, Tanaka H, Fukuda S, Fukushima H, Moriyama S, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Saito K, Fujii Y. Who needs extra-target sampling in addition to intra-target sampling for the detection of adverse prostate pathology?: Spatial analysis of biopsy-proven cancer sites. The 115th annual meeting of the American Urological Association 2020.05.15 Washington DC, USA
27. Matsuoka Y, Ishioka J, Tanaka H, Fukuda S, Fukushima H, Moriyama S, Uehara S, Tanaka H, Kijima T, Yoshida S, Yokoyama M, Saito K, Fujii Y. Apparent diffusion coefficient ratio as a quantitative imaging marker: Utility in a nomogram for predicting biochemical recurrence after radical prostatectomy. The 115th annual meeting of the American Urological Association 2020.05.15 Washington DC, USA
28. Matsuoka Y, Uehara S, Yoshida S, Tanaka H, Fukuda S, Fukushima H, Moriyama S, Tanaka H, Kijima T, Yokoyama M, Ishioka J, Saito K, Fujii Y. Who benefits from extra-target sampling in addition to intra-target sampling for the detection of adverse prostate pathology?: Stereological analysis of biopsy-proven cancer sites. The 35th Annual Congress of the European Association of Urology 2020.07.17 Amsterdam Netherlands.

Gastrointestinal Surgery

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(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. Yojiro Hashiguchi, Kei Muro, Yutaka Saito, Yoshinori Ito, Yoichi Ajioka, Tetsuya Hamaguchi, Kiyoshi Hasegawa, Kinichi Hotta, Hideyuki Ishida, Megumi Ishiguro, Soichiro Ishihara, Yukihide Kanemitsu, Yusuke Kinugasa, Keiko Murofushi, Takako Eguchi Nakajima, Shiro Oka, Toshiaki Tanaka, Hiroya Taniguchi, Akihito Tsuji, Keisuke Uehara, Hideki Ueno, Takeharu Yamanaka, Kentaro Yamazaki, Masahiro Yoshida, Takayuki Yoshino, Michio Itabashi, Kentaro Sakamaki, Keiji Sano, Yasuhiro Shimada, Shinji Tanaka, Hiroyuki Uetake, Shigeki Yamaguchi, Naohiko Yamaguchi, Hiroto Kobayashi, Keiji Matsuda, Kenjiro Kotake, Kenichi Sugihara, Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer *International Journal of Clinical Oncology*. 2020.01; 25(1); 1-42
2. Kazuya Takahashi, Takaki Yoshikawa, Shinji Morita, Takahiro Kinoshita, Masahiro Yura, Sho Otsuki, Masanori Tokunaga, Yukinori Yamagata, Akio Kaito, Hitoshi Katai. Different risks of nodal metastasis by tumor location in remnant gastric cancer after curative gastrectomy for gastric cancer *Gastric Cancer*. 2020.01; 23(1); 195-201
3. Masanori Tokunaga, Yuya Sato, Masatoshi Nakagawa, Tomoki Aburatani, Takatoshi Matsuyama, Yasuaki Nakajima, Yusuke Kinugasa. Perioperative chemotherapy for locally advanced gastric cancer in Japan: current and future perspectives *Surgery Today*. 2020.01; 50(1); 30-37
4. Toshiro Tanioka, Rawat Waratchanont, Ryosuke Fukuyo, Toshifumi Saito, Yuya Umebayashi, Emi Kanemoto, Kenta Kobayashi, Masatoshi Nakagawa, Mikito Inokuchi. Surgical and nutritional outcomes of laparoscopic proximal gastrectomy versus total gastrectomy: a meta-analysis *Surgical Endoscopy*. 2020.01; 34(3); 1061-1069
5. Tomiyuki Miura, Megumi Ishiguro, Toshiaki Ishikawa, Satoshi Okazaki, Hironobu Baba, Akifumi Kikuchi, Shinichi Yamauchi, Takatoshi Matsuyama, Hiroyuki Uetake, Yusuke Kinugasa. Methylation of bone morphogenetic protein 2 is associated with poor prognosis in colorectal cancer *Oncology letters*. 2020.01; 19(1); 229-238
6. Tomonori Akagi, Masafumi Inomata, Takao Hara, Junki Mizusawa, Hiroshi Katayama, Dai Shida, Masayuki Ohue, Masaaki Ito, Yusuke Kinugasa, Yoshihisa Saida, Tadahiko Masaki, Seiichiro Yamamoto, Tsunekazu Hanai, Shigeki Yamaguchi, Masahiko Watanabe, Kenichi Sugihara, Haruhiko Fukuda, Yukihide Kanemitsu, Seigo Kitano. Clinical impact of D3 lymph node dissection with left colic artery (LCA) preservation compared to D3 without LCA preservation: Exploratory subgroup analysis of data from JCOG0404. *Annals of Gastroenterological Surgery*. 2020.03; 4(2); 163-169
7. Yujiro Nakayama, Hiroshi Kobayashi, Hidetaka Kawamura, Rie Matsunaga, Yukitoshi Todate, Yoshinao Takano, Keiichi Takahashi, Shinichi Yamauchi, Kenichi Sugihara, Michitaka Honda. The long-term outcomes in adolescent and young adult patients with colorectal cancer -A multicenter large-scale cohort study *Journal of Cancer*. 2020.03; 11(11); 3180-3185
8. Yusuke Yamaoka, Hiroyasu Kagawa, Akio Shiomi, Yushi Yamakawa, Hitoshi Hino, Shoichi Manabe, Yusuke Kinugasa. Robotic-assisted surgery may be a useful approach to protect urinary function in the modern era of diverse surgical approaches for rectal cancer *Surgical endoscopy*. 2020.03; Online ahead of print;
9. Masanori Terashima, Takaki Yoshikawa, Narikazu Boku, Seiji Ito, Akira Tsuburaya, Yoshiaki Iwasaki, Takeo Fukagawa, Masanori Tokunaga, Takeshi Sano, Mitsuru Sasako, Stomach Cancer Study Group, Japan Clinical Oncology Group. Current status of perioperative chemotherapy for locally advanced gastric cancer and JCOG perspectives *Japanese journal of clinical oncology*. 2020.05; 50(5); 528-534
10. Shizuki Sugita, Takahiro Kinoshita, Takeshi Kuwata, Masanori Tokunaga, Akio Kaito, Masahiro Watanabe, Akiko Tonouchi, Reo Sato, Masato Nagino. Intramucosal-lymphatic invasion has a slight impact on lymph node metastasis in patients with early gastric cancer *Surgery today*. 2020.05; 50(5); 484-489
11. Yutaka Tokairin, Yasuaki Nakajima, Kenro Kawad, Akihiro Hoshino, Takuya Okada, Toshihiro, Matsui, Kazuya Yamaguchi, Kagami Nagai, Yusuke Kinugasa. Mediastinoscopic esophagectomy with lymph node dissection using a bilateral transcervical and transhiatal pneumomediastinal approach Mini-invasive Surgery. 2020.05; 4(32);

12. Nozomu Nakai, Tomohiro Yamaguchi, Yusuke Kinugasa, Akio Shiomi, Hiroyasu Kagawa, Yushi Yamakawa, Masakatsu Numata, Akinobu Furutani, Yusuke Yamaoka, Shoichi Manabe, Akihiro Sawada. Diagnostic value of computed tomography (CT) and positron emission tomography (PET) for paraaortic lymph node metastasis from left-sided colon and rectal cancer *Asian Journal of Surgery*. 2020.06; 43(6); 676-682
13. Yutaka Tokairin, Yasuaki Nakajima, Kagami Nagai, Kumiko Yamaguchi, Keiichi Akita&Yusuke Kinugasa. Aortic inflation with agar injection is a useful method of cadaveric preparation which creates a mediastinal anatomy that better mimics the living body for surgical training. *General Thoracic and Cardiovascular Surgery*. 2020.06; 68(6); 652-654
14. Tomoki Yamano, Shinichi Yamauchi, Masataka Igeta, Yuya Takenaka, Jihyung Song, Kei Kimura, Michiko Yasuhara, Akihito Babaya, Kozo Kataoka, Naohito Beppu, Masataka Ikeda, Naohiro Tomita, Kenichi Sugihara. Combination of preoperative tumour markers and lymphovascular invasion with TNM staging as a cost and labour efficient subtyping of colorectal cancer *Scientific reports*. 2020.06; 10(1); 10238
15. S Matsui, K Okabayashi, H Hasegawa, M Tsuruta, K Shigeta, T Ishida, T Yamada, T Kondo, S Yamauchi, K Sugihara, Y Kitagawa . Prognostic impact of primary tumor location in Stage III colorectal cancer-right-sided colon versus left-sided colon versus rectum: a nationwide multicenter retrospective study *BJS open*. 2020.06; 4(3); 508-515
16. Marie Hanaoka, Hitoshi Hino, Akio Shiomi, Hiroyasu Kagawa, Shoichi Manabe, Yusuke Yamaoka, Shunichiro Kato, Yusuke Kinugasa . Minimally invasive surgery for colorectal cancer with persistent descending mesocolon: radiological findings and short-term outcomes *Surgical endoscopy*. 2020.06; Online ahead of print;
17. Akihiro Hoshino, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Takuya Okada, Toshihiro Matsui, Kazuya Yamaguchi, Tatsuyuki Kawano, Yusuke Kinugasa. The Impact of Hybrid Minimally Invasive Esophagectomy with Neck-Abdominal First Approach on the Short- and Long-Term Outcomes for Esophageal Squamous Cell Carcinoma *World journal of surgery*. 2020.06; Online ahead of print;
18. Yuya Sato, Junki Mizusawa, Hiroshi Katayama, Kenichi Nakamura, Takeo Fukagawa, Hitoshi Katai, Shusuke Haruta, Makoto Yamada, Masakazu Takagi, Shigeyuki Tamura, Tsunehiro Yoshimura, Masanori Tokunaga, Takaki Yoshikawa, Narikazu Boku, Takeshi Sano, Mitsuru Sasako, Masanori Terashima . Diagnosis of invasion depth in resectable advanced gastric cancer for neoadjuvant chemotherapy: An exploratory analysis of Japan clinical oncology group study: JCOG1302A *European journal of surgical oncology*. 2020.06; 46(6); 1074-1079
19. Dai Shida, Manabu Inoue, Taro Tanabe, Konosuke Moritani, Shunsuke Tsukamoto, Shinichi Yamauchi, Kenichi Sugihara, Yukihide Kanemitsu. Prognostic impact of primary tumor location in Stage III colorectal cancer-right-sided colon versus left-sided colon versus rectum: a nationwide multicenter retrospective study *Journal of gastroenterology*. 2020.07; Online ahead of print;
20. Yasuhiro Nakashima, Masashi Kobayashi, Kuniyo Sueyoshi, Erika Mori, Ayaka Asakawa, Hironori Ishibashi, Tetsuro Sugishita, Kazuya Yamaguchi, Akihiro Hoshino, Kenichi Okubo. Intrathoracic omental herniation mimics posterior mediastinal lipomatous tumor *General Thoracic and Cardiovascular Surgery*. 2020.07; Online ahead of print;
21. Takatoshi Matsuyama, Raju Kandimalla, Toshiaki Ishikawa, Naoki Takahashi, Yasuhide Yamada, Masamichi Yasuno, Yusuke Kinugasa, Torben Frøstrup Hansen, Marwan Fakih, Hiroyuki Uetake, Balázs Győrffy, Ajay Goel . A novel mesenchymal-associated transcriptomic signature for risk-stratification and therapeutic response prediction in colorectal cancer *International journal of cancer*. 2020.07; Online ahead of print;
22. Heita Ozawa, Shinichi Yamauchi, Hiroki Nakanishi, Junichi Sakamoto, Shin Fujita, Kenichi Sugihara . Clinical impact of non-predominant histopathological subtypes on the long-term prognosis of colorectal cancer patients in Japan *International journal of colorectal disease*. 2020.08; Online ahead of print;
23. Ichiro Yamada, Shinichi Yamauchi, Hiroyuki Uetake, Masamichi Yasuno, Yusuke Kinugasa, Yukihisa Saida, Ukihide Tateishi, Daisuke Kobayashi . Diffusion tensor imaging of rectal carcinoma: Clinical evaluation and its correlation with histopathological findings *Clinical imaging*. 2020.08; 13(67); 177-188

24. Tsuyoshi Ozawa, Yojiro Hashiguchi, Soichiro Ishihara, Tamuro Hayama, Takeshi Tsuchiya, Keiji Nozawa, Shinichi Yamauchi, Kenichi Sugihara, Keiji Matsuda. Proposal for a post-operative surveillance strategy for stage I colorectal cancer patients based on a novel recurrence risk stratification: a multicenter retrospective study *International journal of colorectal disease*. 2020.08; Online ahead of print;
25. Baoqing Chen, Mihnea P Dragomir, Linda Fabris, Recep Bayraktar, Erik Knutsen, Xu Liu, Changyan Tang, Yongfeng Li, Tadanobu Shimura, Tina Catela Ivkovic, Mireia Cruz De Los Santos, Simone Anfossi, Masayoshi Shimizu, Maitri Y Shah, Hui Ling, Peng Shen, Asha S Multani, Barbara Pardini, Jared K Burks, Hiroyuki Katayama, Lucas C Reineke, Longfei Huo , Muddassir Syed, Shumei Song, Manuela Ferracin, Eiji Oki, Bastian Fromm, Cristina Ivan, Krithika Bhuvaneshwar, Yuriy Gusev, Koshi Mimori, David Menter, Subrata Sen, Takatoshi Matsuyama, Hiroyuki Uetake, Catalin Vasilescu, Scott Kopetz, Jan Parker-Thornburg, Ayumu Taguchi, Samir M Hanash, Leonard Girnita, Ondrej Slaby, Ajay Goel, Gabriele Varani, Mihai Gagea, Chunlai Li, Jaffer A Ajani, George A Calin. The Long Noncoding RNA CCAT2 induces chromosomal instability through BOP1 - AURKB signaling *Gastroenterology*. 2020.08; Online ahead of print;
26. Sanae Kaji, Tomoyuki Irino, Masatoshi Kusuhara, Rie Makuuchi, Yushi Yamakawa, Masanori Tokunaga, Yutaka Tanizawa, Etsuro Bando, Taiichi Kawamura, Kenjiro Kami, Yoshiaki Ohashi, Shun Zhang, Hajime Orita, Hyeon-Cheol Lee-Okada, Tetsu Fukunaga, Masanori Terashima. Metabolomic profiling of gastric cancer tissues identified potential biomarkers for predicting peritoneal recurrence *Gastric Cancer*. 2020.09; 23(5); 874-883
27. Shizuki Sugita, Takeshi Kuwata, Masanori Tokunaga, Akio Kaito, Masahiro Watanabe, Akiko Tonouchi, Takahiro Kinoshita, Masato Nagino. Clinical significance of lymphatic invasion in the esophageal region in patients with adenocarcinoma of the esophagogastric junction *Journal of surgical oncology*. 2020.09; 122(3); 433-441
28. Yuya Sato, Takanobu Yamada, Takaki Yoshikawa, Ryunosuke Machida, Junki Mizusawa, Hiroshi Katayama, Masanori Tokunaga, Narikazu Boku, Masanori Terashima, Stomach Cancer Study Group/Japan Clinical Oncology Group. Randomized controlled Phase III trial to evaluate omentum preserving gastrectomy for patients with advanced gastric cancer (JCOG1711, ROAD-GC) *Japanese journal of clinical oncology*. 2020.10; 50(11); 1321-1324
29. Shinsaku Honda, Kenichiro Furukawa, Rie Makuuchi, Tomoyuki Irino, Masanori Tokunaga, Yutaka Tanizawa, Etsuro Bando, Taiichi Kawamura, Kaori Shinsato, Teruaki Matsumoto, Masanori Terashima . A phase II study of ramelteon for the prevention of postoperative delirium in elderly patients undergoing gastrectomy *Surgery today*. 2020.12; 50(12); 1681-1686
30. Inokuhi 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*.
31. Nishikawaji t,Akiyama Y,Shimada s,Kojima K,Kawano T,Eishi Y,Yusa Y,Tanaka S. Onco-genic roles of the SETDB2 histone methyltransferase in gastric cancer. *Oncotarget*.
32. 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*.
33. 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*.
34. 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*.
35. 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*.
36. Kobayashi k,Inokuchi M, Takagi Y,Otsuki S,Fujimori Y,Sato Y,Yanaka Y,Higuchi K,Aburatani T,Tomii C,Uketake H,Kojima K,Kawano T. Prognostic significance of PAK4 expression in gastric cancer. *J Clin Pathol*.

[Conference Activities & Talks]

1. Yutaka Tokairin, Akihiro Hoshino, Kagami Nagai, Yusuke Kinugasa. The usefulness of mediastinoscopic esophagectomy under pneumomediastinum for high-risk patients. The 33rd Annual Meeting of the Japanese Society for Endoscopic Surgery 2020.03.12 WEB
2. Yusuke Kinugasa. Lateral lymph node dissection for low rectal cancer. 13th Annual Meeting of Chinese College of Surgeons 2020.05.22 WEB
3. Yukihide Kanemitsu, Yasuhiro Shimizu, Junki Mizusawa, Yoshitaka Inaba, Tetsuya Hamaguchi, Dai Shida, Masayuki Ohue, Koji Komori, Akio Shiomi, Manabu Shiozawa, Jun Watanabe, Takeshi Suto, Yusuke Kinugasa, Yasumasa Takii, Hiroyuki Bando, Takaya Kobatake, Tomoyuki Kato, Yasuhiro Shimada, Hiroshi Katayama, Haruhiko Fukuda. A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study.. ASCO20Virtual 2020.05.29 WEB
4. Yusuke Kinugasa. Robotic surgery for rectal cancer, its technique and pitfall. China National Telemedicine and Connected Health Center 2020 年度大腸癌外科治療国際会議 2020.08.28 WEB
5. Yusuke Kinugasa. Robotic Approach to Rectal Cancer Resection. Endoscopic and Laparoscopic Surgeons of Asia (ELSA)2020 2020.09.11 WEB
6. Yusuke Kinugasa. Robotic LPND. ARCCS 2020 The 9th Asian Robotic Camp for Colorectal Surgeons 2020.10.17 WEB
7. 山口和哉、熊谷洋一、齋藤賢将、山崎繁、松井俊大、岡田卓也、星野明弘、東海林裕、川田研郎、中島康晃、絹笠祐介. 食道癌切除胃管再建術における ICG 蛍光法での胃管血流評価と「90 秒ルール」の有用性 (他施設共同前向き研究) . Japan Digestive Disease Week 2020 (JDDW2020) 2020.11.05 WEB
8. Yusuke Kinugasa, Takatoshi Matsuyama, Masanori Tokunaga. Current status of Robotic surgery for rectal cancer. Japan Digestive Disease Week 2020 (JDDW2020) 2020.11.06 WEB
9. Yusuke Kinugasa, Takatoshi Matsuyama, Shinichi Ymauchi, Akifumi Kikuchi, Taiki Masuda, Yuriko Matsumiya, Yuudai Yamamoto, Yamato Yamashita, Masako Mizoguchi, Kei Nakajima, Tetsutoshi Nankaku, Hiroki Yonezawa, Masayoshi Sakano. The surgical technique and outcome of robotic colorectal cancer surgery in high volume center in Japan. The International Society of University Colon and Rectal Surgeons 30th Biennial Congress(ISUCRS 2020) 2020.11.12 WEB
10. Yuriko Matsumiya, Shinichin Yamauchi, Hiroki Yonezawa, Sono Ito, Masayoshi Sakano, Takashi Shigeno, Kei Nakajima, Ryuta Kakuta, Sodai Arai, Masako Mizoguchi, Akitoshi Nankaku, Yudai Yamamoto, Taiki Masuda, Akifumi Kikuchi, Takatoshi Matsuyama, Masanori Tokunaga, Yusuke Kinugasa. The risk factors of postoperative outcomes for elderly colorectal cancer patients. The International Society of University Colon and Rectal Surgeons 30th Biennial Congress(ISUCRS 2020) 2020.11.13 WEB
11. Yudai Yamamoto, Shinichi Yamauchi, Sodai Arai, Sono Ito, Ryuta Kakuta, Takashi Shigeno, Akitoshi Nankaku, Kei Nakajima, Masako Mizoguchi, Yuriko Matsumiya, Taiki Masuda, Akifumi Kikuchi, Takatoshi Matsuyama, Masanori Tokunaga, Yusuke Kinugasa. Short-term outcomes of robotic-assisted abdominoperineal resection in our hospital. The International Society of University Colon and Rectal Surgeons 30th Biennial Congress(ISUCRS 2020) 2020.11.13 WEB
12. Hisashi Fujiwara, Yasuaki Nakajima, Kenro Kawada, Yutaka Tokairin, Masafumi Okuda, Taichi Ogo, Katsumasa Saito, Naoto Fujiwara, Tairou Ryoutokuji, 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

Thoracic Surgery

Professor Kenichi Okubo
 Junior Associate Professor Hironori Ishibashi
 Hospital assistant professor Ryo Wakejima
 Hospital assistant professor Katsutoshi Seto
 Hospital assistant professor Yasuhiro Nakashima
 Graduate Student Akiko Sugawara
 Graduate Student Syunichi Baba
 Graduate Student Ayaka Asakawa
 Graduate Student Yuya Ishikawa
 Graduate Student Mariko Takemura
 Graduate Student Yasuyuki Kurihara
 Graduate Student Yusuke Sugita

(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, 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. Ayaka Asakawa, Hirotoshi Horio, Takashi Yamamichi, Masayuki Okui, Masahiko Harada. Clinical features of HIV-infected patients with non-small-cell lung cancer after lung resection *General Thoracic and Cardiovascular Surgery*. 2020.01; 68(1); 38-42
2. Masayuki Okui, Hirotoshi Horio, Ayaka Asakawa, Takashi Yamamichi, Masahiko Harada. The prognostic nutritional index in resected high-grade pulmonary neuroendocrine carcinoma *General Thoracic and Cardiovascular Surgery*. 2020.01; 68(1); 43-48
3. Mikubo M, Seto K, Kitamura A, Nakaguro M, Hattori Y, Maeda N, Miyazaki T, Watanabe K, Murakami H, Tsukamoto T, Yamada T, Fujita S, Masago K, Ramkissoon S, Ross JS, Elvin J, Yatabe Y. Calculating the Tumor Nuclei Content for Comprehensive Cancer Panel Testing *Journal of Thoracic Oncology*. 2020.01; 15(1); 130-137
4. Ryo Wakejima, Kentaro Inamura, Hironori Ninomiya, Hiroko Nagano, Mingyon Mun, Sakae Okumura, Kenichi Okubo, Yuichi Ishikawa. Mucinous lung adenocarcinoma, articularly referring to EGFR-mutated mucinous adenocarcinoma. *Pathology international*. 2020.02; 70(2); 72-83
5. Ken Takahashi , Yosuke Seto , Koutaroh Okada , Shinya Uematsu , Ken Uchibori , Mika Tsukahara , Tomoko Oh-Hara , Naoya Fujita , Noriko Yanagitani , Makoto Nishio , Kenichi Okubo , Ryohei Katayama. Overcoming resistance by ALK compound mutation (I1171S + G1269A) after sequential treatment of multiple ALK inhibitors in non-small cell lung cancer *Thorac Cancer*. 2020.03; 11(3); 581-587
6. Masashi Kobayashi, Sachiko Imai, Hironori Ishibashi, Kenichi Okubo . “Selective bronchus-blowing” method for effective inflate-deflate line identification in lung segmentectomy. *Journal of Thoracic Disease* *Journal of Thoracic Disease*. 2020.05; 12(5); 2146-2152
7. Seto K, Haneda M, Masago K, Fujita S, Kato S, Sasaki E, Hosoda W, Murakami Y, Kuroda H, Horio Y, Hida T, Okubo K, Yatabe Y. Negative reactions of BRAF mutation-specific immunohistochemistry to non-V600E mutations of BRAF *Pathology International*. 2020.05; 70(5); 253-261
8. Seto K, Masago K, Fujita S, Haneda M, Horio Y, Hida T, Kuroda H, Hosoda W, Okubo K. Targeted RNA sequencing with touch imprint cytology samples for non-small cell lung cancer patients *Thorac Cancer*. 2020.07; 11(7); 1827-1834
9. Hirohisa Horinouchi , Fumihiro Asano , Kenichi Okubo, Yoshinori Okada, Yoshinobu Ohsaki , Yuko Komase, Toshinori Hashizume, Mitsutomo Kohno , Motoi Aoe . Safety Management Committee of Japan Society for Respiratory Endoscopy, The 2016 National Survey Working Group. The Incidence of Hemorrhagic Complications Was Lower With the Guide Sheath Than With the Conventional Forceps Biopsy Method: Results of Bronchoscopy in the 2016 Nationwide Survey by the Japan Society for Respiratory Endoscopy *Journal of Bronchology & Interventional Pulmonology*. 2020.10; 27(4); 253-258
10. Yasuhiro Nakashima, Kentaro Inamura, Hironori Ninomiya, Sakae Okumura, Mingyon Mun, Susumu Kirimura, Masashi Kobayashi , Kenichi Okubo, Yuichi Ishikawa. Frequent expression of conventional endothelial markers in pleural mesothelioma: usefulness of claudin-5 as well as combined traditional markers to distinguish mesothelioma from angiosarcoma *Lung Cancer*. 2020.10; 148; 20-27

11. Hironori Ishibashi, Ryo Wakejima, Ayaka Asakawa, Shunichi Baba, Yasuhiro Nakashima, Katsutoshi Seto, Masashi Kobayashi, Kenichi Okubo. Postoperative Atrial Fibrillation in Lung Cancer Lobectomy—Analysis of Risk Factors and Prognosis *World Journal of Surgery*. 2020.11; 44(11); 3952-3959

[Others]

1. Successful excision of epithelioid hemangioendothelioma of the superior vena cava, 2020.04
The Annals of Thoracic Surgery. Vol.109(4) e271-e273, April 2020
Hironori Ishibashi, Chihiro Takasaki, Takumi Akashi, Kenichi Okubo.
2. Successful treatment of combined thymic epithelial tumor with hepatic metastasis: a long disease-free survival case, 2020.12
General Thoracic and Cardiovascular Surgery. 2020;68:1551-1554. Hironori Ishibashi, Masahide Hirose, Shinichiro Ohta.

Igakuken Disease-oriented Molecular Biology

Visiting Professor Takahiko Hara
 Visiting Professor Makoto Arai
 Visiting Professor Masato Hasegawa
 Visiting Professor Haruo Okado
 Associate Visiting Professor Takashi Shichita
 Associate Visiting Professor Yuichiro Mitaoka
 Graduate Student Chihiro Nakata, Miho
 Nakagawa, Miyu Tanikawa, Kaho Ishige, Mai
 Asakura, Akari Nakamura, Satoko Takagi
 (April~), Kyoka Iino (April~), Daiki Kondo
 (April~), Ittetsu Nakajima (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.

[Takashi Shichita] To develop the therapeutic method for stroke and dementia, we will clarify the cellular and molecular mechanisms underlying sterile inflammation and tissue repair after brain tissue injury. In addition to the classical method of molecular biology and biochemistry, the latest analysis methods of immunology, neuroscience, and epigenetics are applied to our research.

[Yuichiro Miyaoka] Our goal is to develop new therapeutic approaches for genetic disorders by using genome editing in human iPS cells. We introduce causative mutations of heart and liver diseases into human iPS cells to study the pathogenic mechanism by analyzing these cells with cellular and molecular biology techniques such as PCR and immuno-staining. We also seek for ways to improve genome editing technologies including CRISPR/Cas9 to achieve precise genome editing.

(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. Sato, M. Maeda, E. Kamata, S. Ishii, K. Yanagisawa, K. Kitajima, and T. Hara. Nitric oxide and a conditioned medium affect the hematopoietic development in a microfluidic mouse embryonic stem cell/OP9 co-cultivation system. *Micromachines*, 11: 305, 2020.
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- transplantation: a possible approach to treat human X-linked disorders. *Mol. Ther. Methods Clin. Dev.*, 17: 369-377, 2020.
3. Y. Torii, S. Iritani, H. Sekiguchi, C. Habuchi, H. Fujishiro, I. Kushima, I. Kawakami, M. Itokawa, M. Arai, S. Hayashida, K. Masaki, JI. Kira, K. Kawashima, and N. Ozaki. The accumulation of advanced glycation end-products in a schizophrenic patient with a glyoxalase 1 frameshift mutation: An autopsy study. *Schizophr. Res.*, 223: 356-358, 2020.
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 6. M. Sekiguchi, A. Sobue, I. Kushima, C. Wang, Y. Arioka, H. Kato, A. Kodama, H. Kubo, N. Ito, M. Sawahata, K. Hada, R. Ikeda, M. Shinno, C. Mizukoshi, K. Tsujimura, A. Yoshimi, K. Ishizuka, Y. Takasaki, H. Kimura, J. Xing, Y. Yu, M. Yamamoto, T. Okada, E. Shishido, T. Inada, M. Nakatochi, T. Takano, K. Kuroda, M. Amano, B. Aleksic, T. Yamamoto, T. Sakuma, T. Aida, K. Tanaka, R. Hashimoto, M. Arai, M. Ikeda, N. Iwata, T. Shimamura, T. Nagai, T. Nabeshima, K. Kaibuchi, K. Yamada, D. Mori, and N. Ozaki. ARHGAP10, which encodes Rho GTPase-activating protein 10, is a novel gene for schizophrenia risk. *Transl. Psychiatry*, 10: 247, 2020.
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 8. W. Zhang, A. Tarutani, K. Newell, A. Murzin, T. Matsubara, B. Falcon, R. Vidal, H. Garringer, Y. Shi, T. Ikeuchi, S. Murayama, B. Ghetti, M. Hasegawa, M. Goedert, and S. H.W. Scheres. Novel tau filament fold in corticobasal degeneration. *Nature*, 580(7802): 283-287, 2020.
 9. M. Masuda-Suzukake, G. Suzuki, M. Hosokawa, T. Nonaka, M. Goedert, and M. Hasegawa. Dextran sulphate-induced tau assemblies cause endogenous tau aggregation and propagation in wild-type mice. *Brain Communications*, 2(2): fcaa091, 2020.

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12. T. Tanaka, S. Hirai, M. Hosokawa, T. Saito, H. Sakuma, T. Saido, M. Hasegawa, and H. Okado. Early-life stress induces the development of Alzheimer's disease pathology via angiopathy. *Exp. Neurol.*, 337: 113552, 2020.
13. H. L. Watry, C. M. Feliciano, K. Gjoni, G. Takahashi, Y. Miyaoka, B. R. Conklin, and L. M. Judge. Rapid, precise quantification of large DNA excisions and inversions by ddPCR. *Sci. Rep.*, 10: 14896, 2020.

[Review Articles]

1. T. Suzuki, Y. Kazuki, T. Hara, and M. Oshimura. Current advances in microcell-mediated chromosome transfer technology and its applications. *Exp. Cell Res.*, 390: 111915, 2020.
2. M. Itokawa, K. Oshima, M. Arai, Y. Torii, I. Kushima, S. Iritani, N. Ozaki, R. Saiga, and R. Mizutani. Cutting-edge morphological studies of post-mortem brains of patients with schizophrenia and potential applications of X-ray nanotomography (nano-CT). *Psychiatry Clin. Neurosci.*, 74: 176-182, 2020.
3. K. Toriumi, M. Miyashita, K. Suzuki, Y. Horiuchi, A. Yoshikawa, M. Itokawa, and M. Arai. Vitamin B6 in schizophrenia. *IMARS HIGHLIGHTS*, 15(2): 7-10, 2020.
4. Y. Horiuchi, M. Miyashita, K. Toriumi, M. Itokawa, and M. Arai. Modeling schizophrenia using induced pluripotent stem cells. *IMARS HIGHLIGHTS*, 15(1): 10-14, 2020.
5. M. Hasegawa. Experimental models of prion-like protein propagation. *Neuropathology*, doi: 10.1111/neup.12656, 2020.
6. H. Okado. Nervous system regulated by POZ domain Krüppel-like zinc finger (POK) family transcription repressor RP58. *Br. J. Pharmacol.*, 178(4): 813-826, 2021.
7. K. Otani, and T. Shichita. Cerebral sterile inflammation in neurodegenerative diseases. *Inflammation and Regeneration*, 40(1): 28, 2020.
8. A. Nakamura, K. Otani, and T. Shichita. Lipid mediators and sterile inflammation in ischemic stroke. *Int. Immunol.*, 32(11): 719-725, 2020.

[Books]

[Conference Activities & Talks]

Clinical Anatomy

Professor : Keiichi AKITA

Professor : Akimoto NIMURA (Department of Functional Joint Anatomy)

Junior Associate Professor : Kumiko YAMAGUCHI (Institute of Education Curricular Management Division)

Junior Associate Professor : Kouji FUJITA (Department of Functional Joint Anatomy)(April ~)

Assistant Professor : Masayo HARADA

Assistant Professor : Hisayo NASU (~ March)

Assistant Professor : Satoru MURO (April ~)

Research Technician : Masahiro TSUTSUMI

Staff Assistant : Kaoru SUZUKI

Parttime Lecturer : Kenji IBUKURO, Itsuko OKUDA, Sachiyuki TSUKADA, Masataka NAKAZAWA, Kaoru KITSUKAWA, Tomoyuki YANO, Kenro CHIKAZAWA, Shirou SUZUKI (April ~)

Graduate Student : Janyaruk SURİYUT (~ March), Eiichirou KAGAWA,

Kohtaro EGUCHI, Saya HORIUCHI, Yusuke UEDA, Atsuhiko OCHI (~ Sept.), Souichi HATTORI,

Koh MIWA, Syuusaku HOSONO, Haruka EISHI, Wachirawit SIRIRAT, Shouko MOUE,

Ming Yan HE, Areeya JIAMJUNYASIRI, Atsuhiko FUKAI, Tharnmanularp SUTHASINEE,

Ryo KARAKAWA (April ~), Hidehiko YOSHIMATU (April ~)

Research student : Mamiko SUZUKI (~ March)

(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. Hattori S, Nimura A, Koyama M, Tsutsumi M, Amaha K, Ohuchi H, Akita K. Dorsiflexion is more feasible than plantar flexion in ultrasound evaluation of the calcaneofibular ligament: a combination study of ultrasound and cadaver Knee Surgery Sports Traumatology Arthroscopy. 2020.01; 28(1); 262-269
2. Phichaya Baramee, Satoru Muro, Janyaruk Suriyut, Masayo Harada, Keiichi Akita. Three muscle slings of the pelvic floor in women: an anatomic study. Anat Sci Int. 2020.01; 95(1); 47-53
3. Lu Zhao, Koji Makino, Koji Fujita, Toru Sasaki, Nobutaka Sato, Kazuki Yamada, Kensuke Koyama, Hirotaka Haro, Hidetsugu Terada. High-Accuracy Finger Force Distribution Measurement System with Precision Calibration Function 2020 IEEE/SICE International Symposium on System Integration. 2020.01;
4. Kohtaro Eguchi, Shigeo Kawai, Masayoshi Mukai, Hiroaki Nagashima, Satoshi Shirakura, Taro Sugimoto, Takahiro Asakage. Medial lingual lymph node metastasis in carcinoma of the tongue. Auris Nasus Larynx. 2020.02; 47(1); 158-162
5. Hoshika S, Nimura A, Takahashi N, Sugaya H, Akita K. Valgus stability is enhanced by flexor digitorum superficialis muscle contraction of the index and middle fingers. J Orthop Surg Res. 2020.03; 15(1); 121
6. Kenro Chikazawa, Ken Imai, Takaki Ito, Azusa Kimura, K O Hiroyoshi, Yokota Miho, Tomoyuki Kuwata, Ryo Konno. Pegfilgrastim Maintains Relative Dose Intensity and Decreases Hospitalisations in Patients With Endometrial Cancer. In Vivo. 2020.03; 34(6); 3669-3673
7. Kawabata A, Nimura A, Fujita K, Ishii S, Okawa A. Locking of the Distal Radioulnar Joint Caused by Dorsal Tear of the Triangular Fibrocartilage Complex A Case Report JBJS Case Connector. 2020.04; 10(2); e0143
8. Harada Masayo, Akita Keiichi. Mouse fibroblast growth factor 9 N143T mutation leads to wide chondrogenic condensation of long bones HISTOCHEMISTRY AND CELL BIOLOGY. 2020.04; 153(4); 215-223
9. Yuki Tsuruta, Ryo Karakawa, Koya Majima, Satoru Yamamoto, Tomoyoshi Shibata, Hidehiko Yoshimatsu, Hiroki Miyashita, Kenta Tanakura, Tomoyuki Yano. The Reconstruction after a Giant Phyllodes Tumor Resection Using a DIEP Flap. Plast Reconstr Surg Glob Open. 2020.04; 8(4); e2760
10. Tsutsumi M, Nimura A, Akita K. New insight into the iliofemoral ligament based on the anatomical study of the hip joint capsule. Journal of anatomy. 2020.05; 236(5); 946-953

11. Satoru Muro, Ryuzaburo Kagawa, Maika Habu, Hiromasa Ka, Masayo Harada, Keiichi Akita. Coexistence of Dense and Sparse Areas in the Longitudinal Smooth Muscle of the Anal Canal: Anatomical and Histological Analyses Inspired by Magnetic Resonance Images. *Clin Anat.* 2020.05; 33(4); 619-626
12. Tempei Sato, Kensuke Kataoka, Yoshiaki Ito, Shigetoshi Yokoyama, Masafumi Inui, Masaki Mori, Satoru Takahashi, Keiichi Akita, Shuji Takada, Hiroe Ueno-Kudoh, Hiroshi Asahara. Lin28a/let-7 pathway modulates the Hox code via Polycomb regulation during axial patterning in vertebrates *Elife.* 2020.05; 9;
13. Yoko Ohishi, Aki Mitsuda, Kozue Ejima, Hidetomo Morizono, Tomoyuki Yano, Masahiro Yokoyama, Kengo Takeuchi, Mutsunori Fujiwara, Tetsuo Nemoto, Toshiharu Minabe. Breast implant-associated anaplastic large-cell lymphoma: first case detected in a Japanese breast cancer patient. *Breast Cancer.* 2020.05; 27(3); 499-504
14. Ryo Karakawa, Tomoyuki Yano, Hidehiko Yoshimatsu, Hideyuki Katsuta, Yukiomi Kushihashi, Toshikazu Shimane. Computer-aided Design and Syringe-aided Manufacturing for Mandibular Reconstruction Using a Vascularized Fibula Flap. *Plast Reconstr Surg Glob Open.* 2020.05; 8(5); e2819
15. Janyaruk Suriyut, Satoru Muro, Phichaya Baramee, Masayo Harada, Keiichi Akita. Various significant connections of the male pelvic floor muscles with special reference to the anal and urethral sphincter muscles. *Anat Sci Int.* 2020.06; 95(3); 305-312
16. Kohtaro Eguchi, Satoru Muro, Koh Miwa, Kumiko Yamaguchi, Keiichi Akita. Deep cervical fascia as an anatomical landmark of lingual lymph nodes: An anatomic and histologic study. *Auris Nasus Larynx.* 2020.06; 47(3); 464-471
17. Yutaka Tokairin, Yasuaki Nakajima, Kagami Nagai, Kumiko Yamaguchi, Keiichi Akita, Yusuke Kinugasa. Aortic inflation with agar injection is a useful method of cadaveric preparation which creates a mediastinal anatomy that better mimics the living body for surgical training. *Gen Thorac Cardiovasc Surg.* 2020.06; 68(6); 652-654
18. Hosono S, Fujita K, Nimura A, Akita K. Release of cervical muscular tension improved severe pruritus in moderate-to-severe atopic dermatitis: A case series. *JAAD case reports.* 2020.06; 6(6); 510-513
19. Satoru Yamamoto, Tomoyuki Yano, Gen Furubayashi, Masayuki Sawaizumi. A Labia Majora Sharing Perforator Flap for Labial Defect Reconstruction. *Plast Reconstr Surg Glob Open.* 2020.06; 8(6); e2931
20. Toshikazu Kimura, Tomoyuki Yano, Atsuya Akabane. Temporo-parietal muscle pedicle flap for reconstruction of the anterior skull base after resection of recurrent olfactory groove meningioma: a technical note. *Br J Neurosurg.* 2020.06; 1-4
21. Kenro Chikazawa, Ken Imai, Liangcheng Wang, Tomoyuki Kuwata, Ryo Konno. A cystectomic technique with low risk of rupture for women with benign ovarian cyst. *J Obstet Gynaecol.* 2020.06; 1-3
22. Shin Takenaka, Kenro Chikazawa, Eri Yoshiizumi, Yusuke Hirose, Masato Tamate, Ken Nakayama, Miki Morioka, Akihiko Sekizawa, Koji Matsumoto. Three-Dimensional Peripheral Bloodstream Model of the Uterus for Laparoscopic Radical Hysterectomy. *J Minim Invasive Gynecol.* 2020.07; 27(5); 1196-1202
23. Sasaki T, Makino K, Nimura A, Suzuki S, Kuroiwa T, Koyama T, Okawa A, Terada H, Fujita K. Assessment of grip-motion characteristics in carpal tunnel syndrome patients using a novel finger grip dynamometer system. *Journal of orthopaedic surgery and research.* 2020.07; 15(1); 245
24. Kuroiwa T, Nimura A, Takahashi Y, Sasaki T, Koyama T, Okawa A, Fujita K. Device Development for Detecting Thumb Opposition Impairment Using Carbon Nanotube-Based Strain Sensors. *Sensors (Basel, Switzerland).* 2020.07; 20(14);
25. Fujita Koji, Iijima Hirotaka, Eguchi Ryo, Kuroiwa Tomoyuki, Sasaki Toru, Yokoyama Yukihiro, Koyama Takafumi, Nimura Akimoto, Kato Ryuichi, Okawa Atsushi, Takahashi Masaki. Gait analysis of patients with distal radius fracture by using a novel laser Timed Up-and-Go system GAIT & POSTURE. 2020.07; 80; 223-227
26. Ochi A, Muro S, Adachi T, Akita K. Zoning inside the renal fascia: The anatomical relationship between the urinary system and perirenal fat. *International journal of urology : official journal of the Japanese Urological Association.* 2020.07; 27(7); 625-633

27. Kenya Kobayashi, Fumihiko Matsumoto, Yasuji Miyakita, Masaki Arikawa, Go Omura, Satoko Matsumura, Atsuo Ikeda, Azusa Sakai, Kohtaro Eguchi, Yoshitaka Narita, Satoshi Akazawa, Shimpei Miyamoto, Seiichi Yoshimoto. Risk Factors for Delayed Surgical Recovery and Massive Bleeding in Skull Base Surgery. *Biomed Hub*. 2020.07; 5(2); 87-100
28. Kenro Chikazawa, Sachiko Netsu, Ken Imai, Aya Ishiguro, Azusa Kimura, Liangcheng Wang, Tomoyuki Kuwata, Ryo Konno. Nedaplatin use in patients with hypersensitivity reaction episodes to carboplatin. *Taiwan J Obstet Gynecol*. 2020.07; 59(4); 546-550
29. Oh Yoto, Yamamoto Kouhei, Hashimoto Jun, Fujita Koji, Yoshii Toshitaka, Fukushima Kazuyuki, Kurosa Yoshiro, Wakabayashi Yoshiaki, Kitagawa Masanobu, Okawa Atsushi. Biological activity is not suppressed in mid-shaft stress fracture of the bowed femoral shaft unlike in "typical" atypical subtrochanteric femoral fracture: A proposed theory of atypical femoral fracture subtypes BONE. 2020.08; 137; 115453
30. Bird AD, Croft BM, Harada M, Tang L, Zhao L, Ming Z, Bagheri-Fam S, Koopman P, Wang Z, Akita K, Harley VR. Ovocentric disorders of sex development in FGF9 mouse models of human synostosis syndromes. *Human molecular genetics*. 2020.08; 29(13); 2148-2161
31. Keiichi Akita. Abstracts presented at the meeting of the 23rd Congress of the Japanese Research Society of Clinical Anatomy. *Surg Radiol Anat*. 2020.08; 1517-1525
32. Kato MK, Muro S, Kato T, Miyasaka N, Akita K. Spatial distribution of smooth muscle tissue in the female pelvic floor and surrounding the urethra and vagina. *Anatomical science international*. 2020.09; 95(4); 516-522
33. Nasu H, Nimura A, Yamaguchi K, Akita K. Morphology of the anterolateral ligament: a complex of fibrous tissues spread to the anterolateral aspect of the knee joint. *Anatomical science international*. 2020.09; 95(4); 470-477
34. Koh-Ichi Yamaki, Keiichi Akita. Abstracts presented at the Joint meeting of the 22nd Congress of the Japanese Research Society of Clinical Anatomy and the 3rd Congress of Kurume Research Society of Clinical Anatomy. *Surg Radiol Anat*. 2020.09; 1393-1403
35. Itsuko Okuda, Yumika Yamakawa, Nobu Mitani, Naoko Ota, Marie Kawabata, Naoki Yoshioka. Objective evaluation of the relationship between facial expression analysis by the facial action coding system (FACS) and CT/MRI analyses of the facial expression muscles. *Skin Res Technol*. 2020.09; 26(5); 727-733
36. Ryo Karakawa, Hidehiko Yoshimatsu, Kenta Tanakura, Hiroki Miyashita, Tomoyoshi Shibata, Yukiko Kuramoto, Tomoyuki Yano. An anatomical study of the lymph-collecting vessels of the medial thigh and clinical applications of lymphatic vessels preserving profunda femoris artery perforator (LpPAP) flap using pre- and intraoperative indocyanine green (ICG) lymphography. *J Plast Reconstr Aesthet Surg*. 2020.09; 73(9); 1768-1774
37. Miwa K, Tsutsumi M, Fukino K, Eguchi K, Okada R, Akita K. An anatomical study of the anterior wall of the hypopharyngeal and the cervical esophageal junction. *Auris, nasus, larynx*. 2020.10; 47(5); 849-855
38. Tomoyuki Yano, Ryo Karakawa, Hidehiko Yoshimatsu, Yuma Fuse, Tomoyoshi Shibata, Yukiko Kuramoto, Nobuko Suesada, Hiroki Miyashita. The Feasibility of Harvesting an Innervated Profunda Artery Perforator Flap for Breast Reconstruction. *Plast Reconstr Surg Glob Open*. 2020.10; 8(10); e3160
39. Akiko Ito, Kenya Kobayashi, Mika Shiotsuka, Tetsufumi Sato, Go Omura, Yoshifumi Matsumoto, Atsuo Ikeda, Azusa Sakai, Kohtaro Eguchi, Tomonari Takano, Fumihiko Matsumoto, Osamu Kobayashi, Satoshi Iwata, Seiichi Yoshimoto. Uniform infection screening allowed safe head and neck surgery during the coronavirus disease 2019 pandemic in Japan. *Jpn J Clin Oncol*. 2020.10;
40. Masanori Isobe, Yuki Kataoka, Kenro Chikazawa, Hiroshi Nishigori, Toshifumi Takahashi, Takayuki Enomoto. The number of overall hysterectomies per population with the perimenopausal status is increasing in Japan: A national representative cohort study. *J Obstet Gynaecol Res*. 2020.10; 46(12); 2651-2661
41. Sritara S, Tsutsumi M, Fukino K, Matsumoto Y, Ono T, Akita K. Evaluating the morphological features of the lateral pterygoid insertion into the medial surface of the condylar process. *Clinical and experimental dental research*. 2020.11;

42. Ienaga N, Fujita K, Koyama T, Sasaki T, Sugiura Y, Saito H. Development and User Evaluation of a Smartphone-Based System to Assess Range of Motion of Wrist Joint. *Journal of hand surgery global online*. 2020.11; 2(6); 339-342
43. Kenya Kobayashi, Seiichi Yoshimoto, Mizuo Ando, Fumihiko Matsumoto, Naoya Murakami, Go Omura, Yoshitaka Honma, Yoshifumi Matsumoto, Atsuo Ikeda, Azusa Sakai, Kohtaro Eguchi, Akiko Ito, Eigitsu Ryo, Yasushi Yatabe, Taisuke Mori. Full-coverage TP53 deep sequencing of recurrent head and neck squamous cell carcinoma facilitates prognostic assessment after recurrence. *Oral Oncol*. 2020.11; 113; 105091
44. Kenro Chikazawa, Kuwata Tomoyuki. Why not use "Twitter" of core clinical journals for rapid dissemination of medical information during the COVID-19 pandemic? *Arch Gynecol Obstet*. 2020.11; 302(5); 1047-1048
45. Saya Horiuchi, Akimoto Nimura, Masahiro Tsutsumi, Shiro Suzuki, Koji Fujita, Taiki Nozaki, Keiichi Akita. Anatomical relationship between the morphology of the styloid process of the ulna and the attachment of the radioulnar ligaments. *J Anat*. 2020.12; 237(6); 1032-1039
46. Eiichiro Kagawa, Akimoto Nimura, Hisayo Nasu, Ryuichi Kato, Keiichi Akita. Fibrous Connection Between Cervical Nerve and Zygapophysial Joint and Implication of the Cervical Spondylotic Radiculopathy: An Anatomic Cadaveric Study. *Spine (Phila Pa 1976)*. 2020.12; Publish Ahead of Print;
47. Ryo Karakawa, Hidehiko Yoshimatsu, Erisa Maeda, Tomoyoshi Shibata, Kenta Tanakura, Yukiko Kuramoto, Hiroki Miyashita, Tomoyuki Yano. Use of the Profunda Femoris Artery Perforator Flap for Reconstruction after Sarcoma Resection. *Plast Reconstr Surg Glob Open*. 2020.12; 8(12); e3289
48. Soichi Hattori, Kentaro Onishi, Yuji Yano, Yuki Kato, Hiroshi Ohuchi, MaCalus V Hogan, Tsukasa Kumai. Sonographically Guided Anchor Placement in Anterior Talofibular Ligament Repair Is Anatomic and Accurate. *Orthop J Sports Med*. 2020.12; 8(12); 2325967120967322
49. Yusuke Kimura, Tsuneo Yamashiro, Yuki Saito, Kaoru Kitsukawa, Hisateru Niki, Hidefumi Mimura. MRI findings of spring ligament injury: association with surgical findings and flatfoot deformity. *Acta Radiol Open*. 2020.12; 9(12); 2058460120980145

[Books etc]

1. Soichi Hattori. Ultrasound guided minimally invasive surgery for chronic lateral ligament injury of the ankle. 2020.05 (ISBN : 978-4-88117-788-4 C3047)
2. Soichi Hattori. Future of ultrasound guided surgery. 2020.05 (ISBN : 0557-0433)
3. Soichi Hattori. Lateral ligament injury of the ankle. 2020.10 (ISBN : 978-4-7849-5813-9)

[Conference Activities & Talks]

1. Masahiro Tsutsumi, Akimoto Nimura, Keiichi Akita. Anatomy of the hip joint capsule for a better understanding of the hip stabilization. The 2nd Annual Congress of Asia Society of Hip Arthroscopy & Preservation 2020.04.05 Web
2. Kenji Ibukiro, Kenichiro Tago, Kazu Shibutani, Mariko Mizuno, Takahiro Miyauchi, Misaki. Shoji, Naohiro Sudo, Yusuke Toda, Jitsuro Tsukada, Masahiro Okada. The relationship between the clinical outcomes and the clinical and radiological findings in patients with pneumatosis intestinalis. ESGAR2020 2020.06.19 Web
3. Yusuke Ueda, Hiroyuki Sugaya, Norimasa Takahashi, Morihito Tokai, Takeshi Morioka, Shota Hoshika. Clinical and Radiographic Outcomes after Arthroscopic Iliac Bone Grafting for Traumatic Anterior Shoulder Instability with Significant Glenoid Bone Loss – A Minimum of Five-year Follow-up. AOSSM 2020 Annual Meeting 2020.07.13 Web
4. Ryo Karakawa. Profunda femoris Artery Perforator (PAP) flap: An anatomical study of the correlation of the perforators, the accessory saphenous vein, and the lymph collecting vessels and clinical applications of Lymphatic Vessels Preserving PAP (LpPAP) flap. JSPRS award of excellence 2020.08.26 Nagoya, Aichi

5. Naohiro Sudo, Jitsuro Tsukada, Kenji Ibukuro, Misaki Shoji, Takahiro Miyauchi, Kazu Shibutani, Kenichiro Tago, Mariko Mizuno, Takayuki Matsumoto, Yusuke Toda, Masahiro Okada. A successful embolization of closest upstream lymph-node using isocenter puncture (ISOP) technique under fluoroscopy for a patient with intractable postoperative lymphorrhea. . Cardiovascular and Interventional Radiological Society of Europe 2020 2020.09.12 Web
6. Tomoyuki Yano. Combined SIEA and SCIP double pedicle flap (SaS flap) for breast reconstruction. PRS Korea 2020 2020.11.13 Web
7. Ryo Karakawa. Profunda femoris Artery Perforator (PAP) flap: An anatomical study of the correlation of the perforators, the accessory saphenous vein, and the lymph collecting vessels and clinical applications of Lymphatic Vessels Preserving PAP (LpPAP) flap. PRS KOREA 2020 2020.11.13 Web
8. Masayo Harada, Keiichi Akita. Mouse fibroblast growth factor 9 N143T mutation leads to wide chondrogenic condensation of long bones. The 43rd Annual Meeting of the Molecular Biology Society of Japan MBSJ 2020 Online 2020.12.02 Web
9. Tomoyuki Yano. New idea and concept of iPAP flap and SaS flap for breast reconstruction. TSPS 2020 2020.12.05 Web
10. Shimano S., Ohkawa R., Nambu M., Sasaoka M., Yamazaki A., Fujii Y., Igarashi K., Horiuchi Y., Lai SJ., Kameda T., Ichimura N., Fujita K., Tohda S. and Tozuka M. Dramatic change of high-density lipoprotein structure and serum amyloid A distribution after orthopedic surgery. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
11. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line

Systems BioMedicine

Professor Hiroshi ASAHARA

Assistant Professor Tomoki CHIBA, Takahide MATSUSHIMA, Ryouta KURIMOTO

Graduate Students Hiroki TSUTSUMI, Maiko INOTSUME, Lin LIU, Takayuki MIYAZAKI, Kaho TAKADA, Risa YAGASAKI, Haruka HOSOGAI, Mari MATSUNAGA, Yutaro UCHIDA, Mayu KOIKE, Risa SANADA, Nao WATANABE

(1) Research

Screening with an RNA binding protein library identified new regulators of microRNA.

We identified novel regulators of tumor suppressor microRNAs.

The function of the epigenome on bone morphogenesis was analyzed using micro-CT.

We have been shown that the tendons/ligaments specific transcription factor Mohawk is essential for the development and homeostasis processes in tendons and ligaments.

We have been developed completely automated ChIP system using LabDroid “Maholo” .

Search for novel regulator of microRNA by high throughput screening.

Revealed the molecular mechanism by which osteocytes regulate bone homeostasis.

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.

In research education for undergraduate students, as part of the research practice program, a new research training system was established as the “Meister Training Course,” covering basic and applied research from molecular biology to experiments using individual mice, in order to enhance their basic research skills.

(3) Publications

[Original Articles]

1. Yuki Yano, Tomoki Chiba, Hiroshi Asahara. Analysis of the Mouse Y Chromosome by Single-Molecule Sequencing With Y Chromosome Enrichment. *Front Genet.* 2020; 11; 406
2. Kensuke Kataoka, Ryota Kurimoto, Hiroki Tsutsumi, Tomoki Chiba, Tomomi Kato, Kana Shishido, Mariko Kato, Yoshiaki Ito, Yuichiro Cho, Osamu Hoshi, Ayako Mimata, Yuriko Sakamaki, Ryo Nakamichi, Martin K Lotz, Keiji Naruse, Hiroshi Asahara. In vitro Neo-Genesis of Tendon/Ligament-Like Tissue by Combination of Mohawk and a Three-Dimensional Cyclic Mechanical Stretch Culture System *Front Cell Dev Biol.* 2020; 8; 307
3. Yamamoto H, Uchida Y, Chiba T, Kurimoto R, Matsushima T, Inotsume M, Ishikawa C, Li H, Shiga T, Muratani M, Uchida T, Asahara H. Transcriptome analysis of sevoflurane exposure effects at the different brain regions. *PloS one.* 2020; 15(12); e0236771
4. Eric Gracey, Arne Burssens, Isabelle Cambré, Georg Schett, Rik Lories, Iain B McInnes, Hiroshi Asahara, Dirk Elewaut. Tendon and ligament mechanical loading in the pathogenesis of inflammatory arthritis. *Nat Rev Rheumatol.* 2020.02; 16(4); 193-207
5. Tempei Sato, Kensuke Kataoka, Yoshiaki Ito, Shigetoshi Yokoyama, Masafumi Inui, Masaki Mori, Satoru Takahashi, Keiichi Akita, Shuji Takada, Hiroe Ueno-Kudoh, Hiroshi Asahara. Lin28a/let-7 pathway modulates the Hox code via Polycomb regulation during axial patterning in vertebrates *Elife.* 2020.05; 9;
6. Kurimoto R, Chiba T, Ito Y, Matsushima T, Yano Y, Miyata K, Yashiro Y, Suzuki T, Tomita K, Asahara H. The tRNA pseudouridine synthase TruB1 regulates the maturation of let-7 miRNA. *The EMBO journal.* 2020.09; e104708
7. Kwang Il Lee, Ramya Gamini, Merissa Olmer, Yasunari Ikuta, Joe Hasei, Jihye Baek, Oscar Alvarez-Garcia, Shawn P Grogan, Darryl D D'Lima, Hiroshi Asahara, Andrew I Su, Martin K Lotz. Mohawk is a transcription factor that promotes meniscus cell phenotype and tissue repair and reduces osteoarthritis severity. *Sci Transl Med.* 2020.10; 12(567);

[Misc]

1. Gracey E, Burssens A, Cambre I, Schett G, Lories R, McInnes I, Asahara H, Elewaut D. . From molecular mechanobiology to structural macroanatomy: the role of mechanical loading in tendon and ligament associated disease. *Nat Rev Rheumatol.* 2020.02;
2. Ryo Nakamichi, Hiroshi Asahara. The transcription factors regulating intervertebral disc development. *JOR Spine.* 2020.03; 3(1); e1081
3. Mokuda S, Nakamichi R, Ito Y, Asahara H. Genetic, Epigenetic, and MicroRNA Regulation of Osteoarthritis *Encyclopedia of Bone Biology*, vol.[1] . 2020.06; 1; 641-651
4. Kurimoto R, Sakurai K, Motoori K, Suda A. A case of COVID-19 with the atypical CT finding. *Clinical case reports.* 2020.07;
5. Ryo Nakamichi, Ryota Kurimoto, Yusuke Tabata, Hiroshi Asahara. Transcriptional, epigenetic and microRNA regulation of growth plate. *Bone.* 2020.08; 137; 115434
6. Ryo Nakamichi, Hiroshi Asahara. Regulation of tendon and ligament differentiation. *Bone.* 2020.08; 115609

[Conference Activities & Talks]

1. Hiroshi Asahara. Mechano-signal Pathway Regulating Tendon and Ligament Via Mxk. AMED 革新的先端研究開発支援事業 (AMED-CREST,PRIME) 「メカノバイオ」領域 令和元年度 領域会議 2020.02.06
2. Hiroshi Asahara. Mechano-signal on tendon and ligament homeostasis via Mxk. International Symposium on AMED “Mechanobiology” Project 2020.02.08
3. Ryota Kurimoto, Hiroshi Asahara. The tRNA pseudouridine synthase TruB1 regulates the maturation of let-7 miRNA.. 第2回 RNAJ オンラインミーティング 2020.08.27 Tokyo

4. Ryota KURIMOTO, Hiroshi ASAHARA. The tRNA pseudouridine synthase TruB1 regulates the maturation of let-7 miRNA. 2nd RNAJ Online Meeting mRNA/miRNA Metabolism 2020.08.27 web
5. 松島隆英、浅原弘嗣、. Localizatome Project:タンパク質の網羅的細胞内ダイナミクス解析. 第43回日本分子生物学会 2020.12.02 web

[Awards & Honors]

1. Catalyst Award, Healthy Longevity Global Competition, 2020.10

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
Ryoko KATO, Naoko YAMADA, Keisuke Sugita, Towako TAGUCHI,
Yuta TSUGENO, Jyunko KUNIEDA, Yuko MATSUKI, Genji KAWADE,
Yuki WATARI, Jyunichiro SATO, Masahiro KAWADA,
Noriaki FUKUHARA, Tomohiro YOKOUCHI, Shigeo TODA,
Jyunnosuke HAYASAKA, Jyunpei KAWAMURA, Azusa TERAOKA

(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

In vivo and in vitro using mice as experimental models, immunohistological, virological, biochemical and molecular biological analyzes of cells of the blood system are performed.

1. Analysis of the mechanism of retrovirus-induced leukemia and development of its therapeutic model
The function of host T cells plays an important role in the onset of tumors by Friend Leukemia Virus. We are analyzing what signaling mechanisms are activated by virus infection and how T cell functions are controlled.
2. Apoptosis induction using retrovirus-derived proteins and its application to gene therapy. Gp70 from Friend Leukemia Virus activates the pro-apoptotic pathway for DNA damage signals, highlighting host-derived genes. Using this system, we are applying it to treatments including gene therapy.
3. Molecular and pathological study on the mechanism of Myelodysplastic syndromes (MDS) onset. MDS is a disease that occurs in relatively elderly people, and causes peripheral blood cytopenias due to the frequent apoptosis in the bone marrow. We are analyzing the expression and regulation of molecules that cause apoptosis in MDS bone marrow cells from both hematopoietic cells and stromal cells.
4. Study on drug resistance of various hematopoietic diseases

Analysis of drug resistance genes of various hematopoietic diseases and the movement of related molecules.

5. Comprehensive study on the mechanism of immune system formation and its breakdown with age. The formation of the immune system progresses rapidly after birth, reaches a peak during puberty, and then declines with age. As a result, it is not uncommon for elderly people after the age of 70 to have markedly reduced immune function, and are susceptible to infectious diseases, similar to AIDS. In order to elucidate the mechanism of such age-related changes in the immune system, the age-related changes in the thymus, T cells, and the neuroendocrine immune system are analyzed at the molecular level.

6. Molecular pathological study on cancer growth and progression.

We mainly use human pathological tissue of the digestive system to analyze various substances related to the growth and progression of cancer using molecular pathological techniques.

(3) Education

Undergraduate education: Education is provided throughout the four years from the first grade to the fourth grade of specialized courses through the general pathology, each theory practice, PBL, block type learning, comprehensive diagnostics practice, BSL, and the like. The program is implemented in cooperation with the human pathology department, hospital pathology department, molecular pathology department, difficult research neuropathology department, and dentistry oral pathology course. At the case study meeting, CPE, which is held at the end of each discussion practice, a small number of students are in charge of one case, give presentations, and promote understanding of pathology through case experience.

(4) Lectures & Courses

Post-graduate education: Training of pathological, anatomy and surgical pathology for the purpose of acquiring the qualification of a pathological society-certified physician, as well as training in related hospitals. Through CPC and case study meetings with clinical departments, the aim is to deepen their understanding of clinical medicine. Regarding research, in addition to the usual pathological methods, we will use them according to the theme of each person such as immunopathology, virology, biochemistry and molecular biology methods, so that we can conduct advanced research.

(5) Clinical Services & Other Works

In the university hospital, surgical materials, biopsy materials, and various organs obtained by pathological dissection are subjected to immunohistological technic in addition to the usual morphological methods.

(6) Clinical Performances

To improve diagnostic accuracy, the methods of molecular pathology are also applied.

(7) Publications

[Original Articles]

1. Fukuhara N, Iwata T, Yoshimoto K, Kitagawa M, Fukuhara H, Tatsushima K, N, Iwata T, Yoshimoto K, Kitagawa M, Fukuhara H, Tatsushima K, Yamaguchi-Okada M, Takeshita A, Ito J, Takeuchi Y, Tamada S, Nishioka H, Inoshita N. . Immunohistochemistry or Molecular Analysis: Which method is better for subtyping craniopharyngioma? *Endocrine Pathology* . 2020;
2. Tsugeno Y, Nakano K, Nakajima T, Namikawa K, Takamatsu M, Yamamoto N, Fujisaki J, Nunobe S, Kitagawa M, Takeuchi K, Kawachi H.. Histopathologic analysis of signet-ring cell carcinoma in situ in patients with hereditary diffuse gastric cancer. *Am J Surg Pathol* . 2020;

3. Yamaguchi N, Tomaru U, Kiuchi T, Ishizu A, Deguchi T, Otsuka N, Tanaka S, Marukawa K, Matsuno Y, Kitagawa M, Kasahara M. . Expression of cathepsins B, D, and K in thymic epithelial tumors. *J Clin Pathol* . 2020;
4. Toru S, Ishida S, Uchihara T, Hirokawa K, Kitagawa M, Ishikawa K.. Comorbid argyrophilic grain disease in an 87-year-old male patient of spinocerebellar ataxia type 31 with dementia: a case report. *BMC Neurology*. 2020;
5. Matsuda M, Ninomiya H, Wakejima R, Inamura K, Okumura S, Mun M, Kitagawa M, Ishikawa Y. . Calretinin-expressing lung adenocarcinoma: distinct characteristics of advanced stages, smoker-type features, and rare expression of other mesothelial markers are useful to differentiate epithelioid mesothelioma. *Pathology Res Practice*. 2020;
6. Takeda T, Uchihara T, Endo T, Kitagawa M, Hirokawa K, Kobayashi T, Toru S. . Numerous ballooned neurons in a 94-year-old man with dementia with Lewy bodies. *J Neurol Sci* . 2020;
7. Yanai M, Kurata M, Muto Y, Iha H, Kanao T, Ishibashi S, Ikeda M, Kitagawa M, Yamamoto K.. Clinicopathological and molecular analysis of SIRT7 in hepatocellular carcinoma. *Pathology*. 2020;
8. Umemori M, Kurata M, Yamamoto A, Yamamoto K, Ishibashi S, Ikeda M, Tashiro K, Kimura T, Sato S, Takahashi H, Kitagawa M. The expression of MYC is strongly dependent on the circular PVT1 expression in pure Gleason pattern 4 of prostatic cancer. *Medical molecular morphology*. 2020.01;
9. Furusho T, Sohara E, Mandai S, Kikuchi H, Takahashi N, Fujimaru T, Hashimoto H, Arai Y, Ando F, Zeniya M, Mori T, Susa K, Isobe K, Nomura N, Yamamoto K, Okado T, Rai T, Uchida S. Renal TNF α activates the WNK phosphorylation cascade and contributes to salt-sensitive hypertension in chronic kidney disease. *Kidney Int*. 2020.02;
10. Kitagawa Masanobu, Kurata Morito, Onishi Iichiroh, Yamamoto Kouhei. Bone marrow niches in myeloid neoplasms(和訳中) *Pathology International*. 2020.02; 70(2); 63-71
11. Yamamoto K, Abe S, Honda A, Hashimoto J, Aizawa Y, Ishibashi S, Takemura T, Hanagata N, Yamamoto M, Miura O, Kurata M, Kitagawa M.. Fatty acid beta oxidation enzyme HADHA is a novel potential therapeutic target in malignant lymphoma. *Lab Invest*. . 2020.03;
12. Ayako Arai, Hiroshi Takase, Mayumi Yoshimori, Kouhei Yamamoto, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. *Cancer science*. 2020.04; 111(4); 1417-1421
13. Yamamoto Akiko, Kurata Morito, Onishi Iichiroh, Sugita Keisuke, Matsumura Miwa, Ishibashi Sachiko, Ikeda Masumi, Yamamoto Kouhei, Kitagawa Masanobu. CRISPR screening identifies M1AP as a new MYC regulator with a promoter-reporter system *PEERJ*. 2020.05; 8; e9046
14. Takahashi Kenta, Gen Yasuyuki, Tanimoto Kousuke, Kudo Atsushi, Oshima Noriko, Ban Daisuke, Takemoto Akira, Onishi Iichiro, Kumaki Yuichi, Yokobori Junko, Takamine Eriko, Kano Yoshihito, Miyake Satoshi, Miyasaka Naoyuki, Tanabe Minoru, Inazawa Johji, Ikeda Sadakatsu. Clinical impact of hemizygous deletion detection and panel-size in comprehensive genomic profiling. *JOURNAL OF CLINICAL ONCOLOGY*. 2020.05; 38(15);
15. Keiko Miura, Takumi Akashi, Takeshi Namiki, Tsunekazu Hishima, Yuan Bae, Urara Sakurai, Keimei Murano, Junichi Shiraishi, Masahiro Warabi, Toru Tanizawa, Michio Tanaka, Ekapot Bhunchet, Jiro Kumagai, Shinya Ayabe, Takahiro Sekiya, Noboru Ando, Hiroshi Shintaku, Yuko Kinowaki, Shohei Tomii, Susumu Kirimura, Kou Kayamori, Kurara Yamamoto, Takashi Ito, Yoshinobu Eishi. Engrailed Homeobox 1 and Cytokeratin 19 Are Independent Diagnostic Markers of Eccrine Porocarcinoma and Distinguish It From Squamous Cell Carcinoma. *Am. J. Clin. Pathol.*. 2020.06;
16. Takeda T, Ito T, Onishi I, Yokomura M, Kawashima Y, Fujikawa T, Tsutsumi T. Denosumab-induced osteonecrosis of external auditory canal. *Auris, nasus, larynx*. 2020.07;
17. Kaneko K, Yoshida S, Yamamoto K, Arita Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Saito K, Fujii Y. Renal epithelioid angiomyolipoma: Incidence in a Japanese cohort and diagnostic utility of diffusion-weighted magnetic resonance imaging. *International journal of urology : official journal of the Japanese Urological Association*. 2020.07; 27(7); 599-604

18. Oda G, Nakagawa T, Ogawa A, Kumaki Y, Hosoya T, Sugimoto H, Ishiba T, Mio M, Fujioka T, Kubota K, Onishi I, Uetake H. Predictors for upstaging of ductal carcinoma *in situ* (DCIS) to invasive carcinoma in non-mass-type DCIS. *Molecular and clinical oncology*. 2020.07; 13(1); 67-72
19. Kaneko Kasumi, Yoshida Soichiro, Yamamoto Kouhei, Arita Yuki, Kijima Toshiki, Yokoyama Minato, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Fujii Yasuhisa. Renal epithelioid angiomyolipoma: Incidence in a Japanese cohort and diagnostic utility of diffusion-weighted magnetic resonance imaging(和訳中) *International Journal of Urology*. 2020.07; 27(7); 599-604
20. Oh Yoto, Yamamoto Kouhei, Hashimoto Jun, Fujita Koji, Yoshii Toshitaka, Fukushima Kazuyuki, Kurosa Yoshiro, Wakabayashi Yoshiaki, Kitagawa Masanobu, Okawa Atsushi. Biological activity is not suppressed in mid-shaft stress fracture of the bowed femoral shaft unlike in "typical" atypical subtrochanteric femoral fracture: A proposed theory of atypical femoral fracture subtypes *BONE*. 2020.08; 137; 115453
21. Taku Sato, Shun Ishikawa, Jumpei Asano, Hirona Yamamoto, Masayuki Fujii, Toshiro Sato, Kouhei Yamamoto, Keisuke Kitagaki, Takumi Akashi, Ryuichi Okamoto, Toshiaki Ohteki. Regulated IFN signalling preserves the stemness of intestinal stem cells by restricting differentiation into secretory-cell lineages. *Nat Cell Biol*. 2020.08; 22(8); 919-926
22. Yanai Masae, Kurata Morito, Muto Yutaka, Iha Hiroto, Kanao Toshinori, Tatsuzawa Anna, Ishibashi Sachiko, Ikeda Masumi, Kitagawa Masanobu, Yamamoto Kouhei. Clinicopathological and molecular analysis of SIRT7 in hepatocellular carcinoma *PATHOLOGY*. 2020.08; 52(5); 529-537
23. Yamamoto A, Kurata M, Yamamoto K, Nogawa D, Inoue M, Ishibashi S, Ikeda M, Miyasaka N, Kitagawa M. High amplification of PVT1 and MYC predict favorable prognosis in early ovarian carcinoma. *Pathology, research and practice*. 2020.08; 216(11); 153175
24. Kurata Morito, Antony Marie L., Noble Klara E., Rathe Susan K., Hirakouchi Haruka, Yamamoto Kouhei, Kitagawa Masanobu, Sachs Zohar, Largaespada David A.. Dose-dependent NRAS(G12V)-mediated signaling controls cell cycle progression and leukemogenic signaling in a CRISPR/Cas9-modified human AML cell line *CANCER RESEARCH*. 2020.08; 80(16);
25. Yokoyama Kota, Manabe Osamu, Tsuchiya Jyunichi, Oyama Jun, Kawabe Hiroaki, Tateishi Yumiko, Asakage Takahiro, Yamamoto Kouhei, Tateishi Ukihide. A rare case of cranial and spinal leptomeningeal dissemination of recurrent ethmoid carcinoma detected by [18F]-FDG PET/CT *EUROPEAN JOURNAL OF NUCLEAR MEDICINE AND MOLECULAR IMAGING*. 2020.09;
26. Umemori Miyaka, Kurata Morito, Yamamoto Akiko, Yamamoto Kouhei, Ishibashi Sachiko, Ikeda Masumi, Tashiro Kojiro, Kimura Takahiro, Sato Shun, Takahashi Hiroyuki, Kitagawa Masanobu. The expression of MYC is strongly dependent on the circular PVT1 expression in pure Gleason pattern 4 of prostatic cancer(和訳中) *Medical Molecular Morphology*. 2020.09; 53(3); 156-167
27. Towako Taguchi, Morito Kurata, Iichiroh Onishi, Yuko Kinowako, Yunosuke Sato, Sayuri Shiono, Sachiko Ishibashi, Masumi Ikeda, Masahide Yamamoto, Masanobu Kitagawa, Kouhei Yamamoto. SECISBP2 is a novel prognostic predictor that regulates selenoproteins in diffuse large B-cell lymphoma. *Lab Invest*. 2020.10;
28. Sanjo N, Nose Y, Miyamoto S, Shishido-Hara Y, Saito T, Fukuda T, Yamamoto K, Kobayashi D, Yokota T. Early Pathological JC Virus Lesions in a Patient without any MRI-based Indications. *Intern Med*. 2020.11; 60(8); 1279-1282
29. Iwayam K, Ogawa A, Tanaka Y, Yajima K, Park I, Ando A, Ogata H, Kayaba M, Zhang S, Tanji F, Nabekura Y, Yamamoto K, Tokuyama K. Effects of exercise before breakfast on plasma free fatty acid profile and 24-h fat oxidation. *Metabolism open*. 2020.12; 8; 100067

[Conference Activities & Talks]

1. 倉田 盛人, 大西 威一郎, 山本 浩平, 北川 昌伸. CRISPR library を用いた NRAS 発現調整可能 THP-1 細胞株によるシグナル解析. *日本癌学会総会記事* 2020.10.01
2. 田口 登和子, 山本 浩平, 木脇 祐子, 大西 威一郎, 倉田 盛人, 山本 正英, 北川 昌伸. びまん性大細胞性リンパ腫において SECISBP2 はセレノプロテインを調整する新規の予後予測因子になりうる. *日本癌学会総会記事* 2020.10.01

3. 川出 玄二, 山本 浩平, 立澤 杏奈, 矢内 雅恵, 倉田 盛人, 北川 昌伸. 肝細胞癌における GPX4 発現の臨床病理学的検討. 日本癌学会総会記事 2020.10.01
4. 大西 威一郎, 倉田 盛人, 山本 浩平, 木村 剛, 岸田 晶夫, 北川 昌伸. 脱細胞化骨を用いた、ヒト骨髄微小環境再構築の試み. 日本癌学会総会記事 2020.10.01
5. 倉田 盛人, 大西 威一郎, 山本 浩平, 北川 昌伸. CRISPR library を用いた NRAS 発現調整可能 THP-1 細胞株によるシグナル解析. 日本癌学会総会記事 2020.10.01
6. 松寺 翔太郎, 加納 嘉人, 青柳 康子, 遠山 皓基, 木村 浩一朗, 大西 威一郎, 竹本 暁, 荻野 恵, 岡本 健太郎, 植竹 宏之, 田邊 稔, 三宅 智, 土岡 丘, 小嶋 一幸, 池田 貞勝. Liquid biopsy が変えるがん治療 がんゲノム医療におけるリキッドバイオプシーの臨床的有用性の検討. 日本癌治療学会学術集会抄録集 2020.10.01
7. 田口 登和子, 山本 浩平, 木脇 祐子, 大西 威一郎, 倉田 盛人, 山本 正英, 北川 昌伸. びまん性大細胞性リンパ腫において SECISBP2 はセレノプロテインを調整する新規の予後予測因子になりうる. 日本癌学会総会記事 2020.10.01
8. 大西 威一郎, 倉田 盛人, 山本 浩平, 木村 剛, 岸田 晶夫, 北川 昌伸. 脱細胞化骨を用いた、ヒト骨髄微小環境再構築の試み. 日本癌学会総会記事 2020.10.01

[Social Contribution]

1. Journal of Cancer Research and Clinical Oncology, Springer Nature, Journal of Cancer Research and Clinical Oncology, 2017.04.01 - Now

Molecular Oncology

Professor: Shinji TANAKA
 Associate Professor: Yoshimitsu AKIYAMA
 Assistant Professor: Shu SHIMADA
 Assistant Professor: Ayano NIIBE
 Laboratory Technician: Hiromi NAGASAKI
 Graduate Student: Yuna TAKAGI
 Graduate Student: Ayumi KONO

(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. Fujita M, Yamaguchi R, Hasegawa T, Shimada S, Arihiro K, Hayashi S, Maejima K, Nakano K, Fujimoto A, Ono A, Aikata H, Ueno M, Hayami S, Tanaka H, Miyano S, Yamaue H, Chayama K, Kakimi K, Tanaka

- S, Imoto S, Nakagawa H. Classification of primary liver cancer with immunosuppression mechanisms and correlation with genomic alterations. *EBioMedicine*. 2020.03; 53; 102659
2. Hiroaki Ono, Atsushi Kudo, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. Combination of weekly streptozocin and oral S-1 treatment for patients of unresectable or metastatic pancreatic neuroendocrine neoplasms *Journal of Cancer Research and Clinical Oncology*. 2020.03; 146(3); 793-799
 3. Yoshino J, Akiyama Y, Shimada S, Ogura T, Ogawa K, Ono H, Mitsunori Y, Ban D, Kudo A, Yamaoka S, Tanabe M, Tanaka S. Loss of ARID1A induces a stemness gene ALDH1A1 expression with histone acetylation in the malignant subtype of cholangiocarcinoma. *Carcinogenesis*. 2020.07; 41(6); 734-742
 4. EeeLN H Buckarma, Nathan W Werneburg, Caitlin B Conboy, Ayano Kabashima, Daniel R O'Brien, Chen Wang, Sumera Rizvi, Rory L Smoot. The YAP-Interacting Phosphatase SHP2 can Regulate Transcriptional Coactivity and Modulate Sensitivity to Chemotherapy in Cholangiocarcinoma. *Mol. Cancer Res.*. 2020.07;
 5. Yoshiki Murase, Daisuke Ban, Aya Maekawa, Shuichi Watanabe, Yoshiya Ishikawa, Keiichi Akahoshi, Kosuke Ogawa, Hiroaki Ono, Atsushi Kudo, Toshifumi Kudo, Shinji Tanaka, Minoru Tanabe. Successful conversion surgery of distal pancreatectomy with celiac axis resection(DP-CAR) with double arterial reconstruction using saphenous vein grafting for locally advanced pancreatic cancer: a case report *Surgical Case Reports*. 2020.12;
 6. Seol HS, Akiyama Y, Lee SE, Shimada S, Jang SJ.. Loss of miR-100 and miR-125b results in cancer stem cell properties through IGF2 upregulation in hepatocellular carcinoma. *Scientific Reports*.. 2020.12; 10(1); 21412

[Conference Activities & Talks]

1. Fukiko Kawai-Kitahata, Yasuhiro Asahina , Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka , Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe.. Comprehensive analysis of cancer-related genes and aav/hepatitis b virus integration into genome on development of hepatocellular carcinoma in patients with prior hepatitis b virus infection.. *EASL The Digital International Liver Congress 2020* 2020.08.28 Online
2. Shimada S, Akiyama Y, Tanaka S. Loss of KDM6A characterizes a poor prognostic subtype of pancreatic cancer and potentiates HDAC inhibitor lethality . *The 23rd Frontier Scientists Workshop, Post A3-2020 Symposium on Epigenetic Signature of Carcinogenesis* 2020.09.19 Seoul, Korea, Online
3. Akiyama Y, Shimada S, Tanabe M, Tanaka S. Loss of ARID1A increases a stemness gene ALDH1A1 expression through histone acetylation change in cholangiocarcinoma. *The 79th Annual Meeting of the Japanese Cancer Association* 2020.10.01 Yokohama, Online
4. Shimada S, Akiyama Y, Tanabe M, Tanaka S. Loss of KDM6A characterizes a poor prognostic subtype of pancreatic cancer and potentiates HDAC inhibitor lethali . *The 79th Annual Meeting of the Japanese Cancer Association* 2020.10.01 Yokohama, Online
5. Shu Shimada, Yoshimitsu Akiyama, Shigeki Arii, Minoru Tanabe, Shinji Tanaka. Comprehensive molecular and immunological classification of hepatocellular carcinoma. *The 56th Annual Meeting of Liver Cancer Study Group of Japan* 2020.12.22 Online

[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

Associate Professor: Takumi AKASHI

Assistant Professor: Susumu KIRIMURA, Shohei TOMII, Yuko KINOWAKI, Hiroshi Shintaku

Project Assistant Professor: 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) Development of novel markers significant for histopathological diagnosis
- 3) Clinico-pathological analysis of malignant mesothelioma
- 4) Clinico-pathological analysis of inflammatory bowel disease
- 5) Clinico-pathological analysis of glomerular disease
- 6) Clinico-pathological analysis of pancreatic neuroendocrine tumor
- 7) Clinico-pathological analysis of neuronal degenerative disease

(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 (40 case in a year), cytopathology services (8,696 cases in a year) and surgical pathology (11,670 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 2019.

(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. Kikuchi Y, Mori M, Fujioka T, Yamaga E, Oda G, Nakagawa T, Koyanagi A, Tomii S, Kubota K, Tateishi U. Feasibility of ultrafast dynamic magnetic resonance imaging for the diagnosis of axillary lymph node metastasis: A case report. *European journal of radiology open*. 2020; 7; 100261
2. 内田千恵, 並木剛, 三浦圭子, 田中顕太郎, 横関博雄. 円板状エリテマトーデスに発症した疣状癌・有棘細胞癌の1例 *Skin Cancer*. 2020.01; 35(1); 12-15
3. Iijima Yuki, Tateishi Tomoya, Tsuchiya Kimitake, Sumi Yuki, Akashi Takumi, Miyazaki Yasunari. 金属チタン研削粉の吸入により引き起こされた塵肺症 (Pneumoconiosis Caused by Inhalation of Metallic Titanium Grindings) *Internal Medicine*. 2020.02; 59(3); 425-428
4. Katsumi Oishi, Takashi Ito, Daisuke Sakonishi, Keisuke Uchida, Masaki Sekine, Mariko Negi, Daisuke Kobayashi, Keiko Miura, Takumi Akashi, Yoshinobu Eishi. Cancer gland rupture as a potential risk factor for lymph node metastasis in early colorectal adenocarcinoma with deep submucosal invasion. *Histopathology*. 2020.03; 76(4); 603-612
5. Hoshino Akihiro, Tokoro Shown, Akashi Takumi, Inoue Maiko, Takagi Masatoshi, Imai Kohsuke, Kanegane Hirokazu, Muraosa Yasunori, Kamei Katsuhiko, Morio Tomohiro. Disseminated fusariosis in a child after haploidentical hematopoietic stem cell transplantation. *Pediatrics International*. 2020.03; 62(3); 419-420
6. Yamamoto K, Abe S, Honda A, Hashimoto J, Aizawa Y, Ishibashi S, Takemura T, Hanagata N, Yamamoto M, Miura O, Kurata M, Kitagawa M.. Fatty acid beta oxidation enzyme HADHA is a novel potential therapeutic target in malignant lymphoma. *Lab Invest*. . 2020.03;
7. Akihiro Hoshino, Akira Nishimura, Takuya Naruto, Tsubasa Okano, Kazuaki Matsumoto, Keisuke Okamoto, Hiroshi Shintaku, Shown Tokoro, Hiroyuki Okamoto, Taizo Wada, Masatoshi Takagi, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio. High-throughput analysis revealed the unique immunoglobulin gene rearrangements in plasmacytoma-like post-transplant lymphoproliferative disorder. *Br. J. Haematol.*. 2020.05; 189(4); e164-e168
8. Al-Busani Hind, Namiki Takeshi, Miura Keiko, Yokozeki Hiroo. Mixed-pattern syphilitic alopecia of the scalp associated with uveitis and asymptomatic neurosyphilis *JOURNAL OF DERMATOLOGY*. 2020.05;
9. Hind Al-Busani, Takeshi Namiki, Shown Tokoro, Tsukasa Ugajin, Keiko Miura, Hiroo Yokozeki. Bilateral juvenile temporal arteritis mimicking clinical features of classic giant cell arteritis. *Int. J. Dermatol.*. 2020.06;

10. Keiko Miura, Takumi Akashi, Takeshi Namiki, Tsunekazu Hishima, Yuan Bae, Urara Sakurai, Keimei Murano, Junichi Shiraishi, Masahiro Warabi, Toru Tanizawa, Michio Tanaka, Ekapot Bhunchet, Jiro Kumagai, Shinya Ayabe, Takahiro Sekiya, Noboru Ando, Hiroshi Shintaku, Yuko Kinowaki, Shohei Tomii, Susumu Kirimura, Kou Kayamori, Kurara Yamamoto, Takashi Ito, Yoshinobu Eishi. Engrailed Homeobox 1 and Cytokeratin 19 Are Independent Diagnostic Markers of Eccrine Porocarcinoma and Distinguish It From Squamous Cell Carcinoma. *Am. J. Clin. Pathol.*. 2020.06;
11. MIHO HACHIYA, MIEKO OI, KEIKO MIURA, YUKO FUTEI, Ko-Ron CHEN. A case of neutrophilic dermatosis with various cutaneous eruptions 2020.07; 74(8); 571-577
12. Nakashima Y, Inamura K, Ninomiya H, Okumura S, Mun M, Kirimura S, Kobayashi M, Okubo K, Ishikawa Y. Frequent expression of conventional endothelial markers in pleural mesothelioma: usefulness of claudin-5 as well as combined traditional markers to distinguish mesothelioma from angiosarcoma. *Lung cancer (Amsterdam, Netherlands)*. 2020.10; 148; 20-27
13. Inoue Y, Okamoto T, Honda T, Nukui Y, Akashi T, Takemura T, Tozuka M, Miyazaki Y. Disruption in the balance between apolipoprotein A-I and mast cell chymase in chronic hypersensitivity pneumonitis. *Immunity Inflammation and Disease*. 2020.10; 8(4); 659-671
14. Katsukura N, Watanabe S, Shirasaki T, Hibiya S, Kano Y, Akahoshi K, Tanabe M, Kirimura S, Akashi T, Kitagawa M, Okamoto R, Watanabe M, Tsuchiya K. Intestinal phenotype is maintained by Atoh1 in the cancer region of intraductal papillary mucinous neoplasm. *Cancer science*. 2020.12;
15. Baba S, Akashi T, Kayamori K, Ohuchi T, Ogawa I, Kubota N, Nakano K, Nagatsuka H, Hasegawa H, Matsuzaka K, Tomii S, Uchida K, Katsuta N, Sekiya T, Ando N, Miura K, Ishibashi H, Ariizumi Y, Asakage T, Michi Y, Harada H, Sakamoto K, Eishi Y, Okubo K, Ikeda T. Homeobox transcription factor engrailed homeobox 1 is a possible diagnostic marker for adenoid cystic carcinoma and polymorphous adenocarcinoma. *Pathology international*. 2020.12;

[Conference Activities & Talks]

1. Shintaku Hiroshi, et al.. A coexistent case of primary gastric choriocarcinoma and alpha fetoprotein-producing gastric cancer. 2020

[Social Contribution]

1. The Japanese Society of Diagnostic Dermatopathology, Department of Diagnostic Pathology, Saitama Medical University International Medical Center, 2005.04.17 - Now
2. Ochanomizu Study Meeting of Dermatopathology, 2009.04 - Now

Signal Gene Regulation

Professor (Bio-Matrix, Medical Biochemistry) HATA Yutaka
Associate Professor FUNATO Noriko

(1) Research

1. Genetic regulators of craniofacial and bone development.
2. Molecular control of cleft lip and/or palate.
3. Study of wound healing and tissue regeneration.

(2) Education

Lecture

Goals/Outline:

Students will learn the basics in life sciences by understanding the regulation of signal transduction involved in cell proliferation, differentiation, and death.

Practice

Goals/Outline:

Students will learn to handle recombinant DNA molecules and analyze the data obtained from experiments.

Lab

Goals/Outline:

Students will learn basic molecular biology and genetic engineering techniques by observing and/or performing biochemical experiments using cultured cells and gene-engineered mice.

(3) Lectures & Courses

The aim of Research Core is to provide laboratory equipments, 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 and histology.

(4) Publications

[Original Articles]

1. N Funato*, D Srivastava, S Shibata, H Yanagisawa. TBX1 Regulates Chondrocyte Maturation in the Spheno-occipital Synchronosis. *Journal Dental Research*. 2020.09; 99(10); 1182-1191
2. Noriko Funato, Yuki Taga, Lindsay E Laurie, Chisa Tometsuka, Masashi Kusubata, Kiyoko Ogawa-Goto. The Transcription Factor HAND1 Is Involved in Cortical Bone Mass through the Regulation of Collagen Expression. *Int J Mol Sci*. 2020.11; 21(22); 8638

[Misc]

1. Funato N*. New Insights into Cranial Synchronosis Development: A Mini Review. *Frontiers in Cell and Developmental Biology*. 2020.08; 8(706); 1-9

[Conference Activities & Talks]

1. Funato N, Srivastava D, Shibata S, Yanagisawa H.. TBX1 regulates chondrocyte maturation in the spheno-occipital synchondrosis through TBX1-RUNX2 axis. the 62nd Annual Meeting of Japanese Association for Oral Biology 2020.09.12 Online
2. Identification of 3-hydroxyproline-containing tripeptide in human blood after oral ingestion of collagen hydrolysate. 2020.09.20
3. Noriko Funato, Yuki Taga, Lindsay E. Laurie, Chisa Tometsuka, Masashi Kusubata, Kiyoko Ogawa-Goto.. The bHLH transcription factor HAND1 is involved in cortical bone volume through the regulation of collagen expression.. the 68th Annual Meeting of Japanese Association for Dental Research 2020.11.07 Online
4. Funato N, Srivastava D, Shibata S, Yanagisawa H.. TBX1 suppresses transcriptional activity of RUNX2 and regulates chondrocyte maturation. *Cell Bio Virtual 2020-An Online ASCB—EMBO Meeting* 2020.12 Online

[Others]

1. Unboxing the role of TBX1 in palatal development: a gene profiling study, 2020.02
Atlas of Science - another view of science
(<https://atlasofscience.org>)

Applied Gene Medicine

Professor	Yoshio Miki
Associate Professor	Akira Nakanishi
Assistant Professor	Shigeaki Sunada
Project Assistant Professor	Ji Shuting
JSPS Research Fellowship for Young Scientists	Naoe Nihira
Ph.D. Student	Yo Tojo, Deng Yu, Enkhat Gerelmaa, Mio Hukuda, Zhang Dou Dou, Zhao Ying, Guo QianQian,
Master's student	Shiori Hirayama, Li Zi

(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. Kaneyasu T, Mori S, Yamauchi H, Ohsumi S, Ohno S, Aoki D, Baba S, Kawano J, Miki Y, Matsumoto N, Nagasaki M, Yoshida R, Akashi-Tanaka S, Iwase T, Kitagawa D, Masuda K, Hirasawa A, Arai M, Takei J, Ide Y, Gotoh O, Yaguchi N, Nishi M, Kaneko K, Matsuyama Y, Okawa M, Suzuki M, Nezu A, Yokoyama S, Amino S, Inuzuka M, Noda T, Nakamura S. Prevalence of disease-causing genes in Japanese patients with \geq BRCA1/2 \leq -wildtype hereditary breast and ovarian cancer syndrome. NPJ breast cancer. 2020; 6; 25
2. Yu Deng, Yoshio Miki, Akira Nakanishi. Estradiol/GPER affects the integrity of mammary duct-like structures in vitro Scientific reports. 2020.01;
3. Satoru Torii, Hirofumi Yamaguchi, Akira Nakanishi, Satoko Arakawa, Shinya Honda, Kenta Moriwaki, Hiroyasu Nakano, Shigeomi Shimizu. Identification of a phosphorylation site on Ulk1 required for genotoxic stress-induced alternative autophagy Nature Communications. 2020.04; 11; 1754
4. Ishigaki K, Akiyama M, Kanai M, Takahashi A, Kawakami E, Sugishita H, Sakaue S, Matoba N, Low SK, Okada Y, Terao C, Amariuta T, Gazal S, Kochi Y, Horikoshi M, Suzuki K, Ito K, Koyama S, Ozaki K, Niida S, Sakata Y, Sakata Y, Kohno T, Shiraishi K, Momozawa Y, Hirata M, Matsuda K, Ikeda M, Iwata N, Ikegawa S, Kou I, Tanaka T, Nakagawa H, Suzuki A, Hirota T, Tamari M, Chayama K, Miki D, Mori M, Nagayama S, Daigo Y, Miki Y, Katagiri T, Ogawa O, Obara W, Ito H, Yoshida T, Imoto I, Takahashi T, Tanikawa C, Suzuki T, Sinozaki N, Minami S, Yamaguchi H, Asai S, Takahashi Y, Yamaji K, Takahashi K, Fujioka T, Takata R, Yanai H, Masumoto A, Koretsune Y, Kutsumi H, Higashiyama M, Murayama S, Minegishi N, Suzuki K, Tanno K, Shimizu A, Yamaji T, Iwasaki M, Sawada N, Uemura H, Tanaka K, Naito M, Sasaki M, Wakai K, Tsugane S, Yamamoto M, Yamamoto K, Murakami Y, Nakamura Y, Raychaudhuri S, Inazawa J, Yamauchi T, Kadowaki T, Kubo M, Kamatani Y. Large-scale genome-wide association study in a Japanese population identifies novel susceptibility loci across different diseases. Nature genetics. 2020.07; 52(7); 669-679
5. Yang Gao, Naoe Taira Nihira 他. Acetylation-dependent regulation of PD-L1 nuclear translocation dictates the efficacy of anti-PD-1 immunotherapy Nature Cell Biology. 2020.08;
6. Ishiba Tohiyuki, Aruga Tomoyuki, Nara Miyako, Yabe Sakiko, Saita Chiaki, Onishi Mai, Iwamoto Naoko, Yonekura Rika, Miyamoto Hiromi, Honda Yayoi, Oda Goshi, Nakagawa Tsuyoshi, Nakanishi Akira, Uetake Hiroyuki, Miki Yoshio. Calretinin can be the specific marker for phyllodes tumor CANCER RESEARCH. 2020.08; 80(16);
7. Gao Y, Nihira NT, Bu X, Chu C, Zhang J, Kolodziejczyk A, Fan Y, Chan NT, Ma L, Liu J, Wang D, Dai X, Liu H, Ono M, Nakanishi A, Inuzuka H, North BJ, Huang YH, Sharma S, Geng Y, Xu W, Liu XS, Li L, Miki Y, Sicinski P, Freeman GJ, Wei W. Acetylation-dependent regulation of PD-L1 nuclear translocation dictates the efficacy of anti-PD-1 immunotherapy. Nature cell biology. 2020.09; 22(9); 1064-1075
8. Chin YM, Takahashi Y, Chan HT, Otaki M, Fujishima M, Shibayama T, Miki Y, Ueno T, Nakamura Y, Low SK. Ultradeep targeted sequencing of circulating tumor DNA in plasma of early and advanced breast cancer. Cancer science. 2020.10; 112(1); 454-464

[Conference Activities & Talks]

1. Deng Yu, Akira Nakanishi, Yoshio Miki. The role of BRCA2 in H3K4 methylation mediated by MLL. 第79回日本癌学会学術総会 2020.10.01
2. Gerelmaa Enkhbat, Uetake Hiroyuki, Akira Nakanishi, Yoshio Miki. Elucidation of the regulation mechanism of BRCA2 protein levels in the cell cycle. 第79回日本癌学会学術総会 2020.10.01
3. Yo Tojo, Akira Nakanishi, Yoshio Miki. The physiological role of centrosome pairs during S phase. 第79回日本癌学会学術総会 2020.10.01
4. Deng Yu, 大塚 菜央, 中西 啓, 三木 義男. MLL を介した H3K4 メチル化における BRCA2 の役割. 日本癌学会総会記事 2020.10.01
5. 東條 陽, 中西 啓, 三木 義男. S 期中心体対の生理的役割. 日本癌学会総会記事 2020.10.01

6. 張 抖抖, 砂田 成章, 三木 義男. Tioxolone による新たな合成致死療法の開発. 日本癌学会総会記事 2020.10.01
7. 趙 ニン, 砂田 成章, 三木 義男. ステロイドホルモンはトポイソメラーゼ 2 機能不全に伴う毒性を増強する. 日本癌学会総会記事 2020.10.01
8. 三木 義男, 砂田 成章, 中西 啓. 乳がん微小環境の特性と全身性応答、新しい治療展開 遺伝子修復を標的とする新しい治療法の開発. 日本癌学会総会記事 2020.10.01
9. Enkhbat Gerelmaa, Uetake Hiroyuke, 中西 啓, 三木 義男. 細胞周期における BRCA2 タンパク質レベルの制御メカニズムの解明 (Elucidation of the regulation mechanism of BRCA2 protein level in cell cycle). 日本癌学会総会記事 2020.10.01
10. 郭 倩倩, 徐 澤宇, 齊藤 広子, 砂田 成章, 三木 義男. 臨床的意義不明な BRCA2 バリエントの相同組換え活性. 日本癌学会総会記事 2020.10.01
11. 三木 義男, 砂田 成章, 中西 啓. 遺伝子異常を標的とした乳癌の治療戦略 BRCA1/2 変異 基礎から臨床へ. 日本癌治療学会学術集会抄録集 2020.10.01

Molecular Cytogenetics

Professor Johji Inazawa M.D., Ph.D.
 Associate Professor 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. Matsukawa T, Yamamoto T, Honda A, Toya T, Ishiura H, Mitsui J, Tanaka M, Hao A, Shinohara A, Ogura M, Kataoka K, Seo S, Kumano K, Hosoi M, Narukawa K, Yasunaga M, Maki H, Ichikawa M, Nannya Y, Imai Y, Takahashi T, Takahashi Y, Nagasako Y, Yasaka K, Mano KK, Matsukawa MK, Miyagawa T, Hamada M, Sakuishi K, Hayashi T, Iwata A, Terao Y, Shimizu J, Goto J, Mori H, Kunimatsu A, Aoki S, Hayashi S, Nakamura F, Arai S, Momma K, Ogata K, Yoshida T, Abe O, Inazawa J, Toda T, Kurokawa M, Tsuji S. Clinical efficacy of haematopoietic stem cell transplantation for adult adrenoleukodystrophy. *Brain communications*. 2020; 2(1); fcz048
2. Gokita K, Inoue J, Ishihara H, Kojima K, Inazawa J. Therapeutic Potential of LNP-Mediated Delivery of miR-634 for Cancer Therapy. *Molecular therapy. Nucleic acids*. 2020.03; 19; 330-338

3. Takahashi Kenta, Gen Yasuyuki, Tanimoto Kousuke, Kudo Atsushi, Oshima Noriko, Ban Daisuke, Takemoto Akira, Onishi Iichiro, Kumaki Yuichi, Yokobori Junko, Takamine Eriko, Kano Yoshihito, Miyake Satoshi, Miyasaka Naoyuki, Tanabe Minoru, Inazawa Johji, Ikeda Sadakatsu. Clinical impact of hemizygous deletion detection and panel-size in comprehensive genomic profiling. JOURNAL OF CLINICAL ONCOLOGY. 2020.05; 38(15);
4. Takagawa Yuki, Gen Yasuyuki, Muramatsu Tomoki, Tanimoto Kousuke, Inoue Jun, Harada Hiroyuki, Inazawa Johji. miR-1293, a Candidate for miRNA-Based Cancer Therapeutics, Simultaneously Targets BRD4 and the DNA Repair Pathway MOLECULAR THERAPY. 2020.06; 28(6); 1494-1505
5. Ishigaki K, Akiyama M, Kanai M, Takahashi A, Kawakami E, Sugishita H, Sakaue S, Matoba N, Low SK, Okada Y, Terao C, Amariuta T, Gazal S, Kochi Y, Horikoshi M, Suzuki K, Ito K, Koyama S, Ozaki K, Niida S, Sakata Y, Sakata Y, Kohno T, Shiraishi K, Momozawa Y, Hirata M, Matsuda K, Ikeda M, Iwata N, Ikegawa S, Kou I, Tanaka T, Nakagawa H, Suzuki A, Hirota T, Tamari M, Chayama K, Miki D, Mori M, Nagayama S, Daigo Y, Miki Y, Katagiri T, Ogawa O, Obara W, Ito H, Yoshida T, Imoto I, Takahashi T, Tanikawa C, Suzuki T, Sinozaki N, Minami S, Yamaguchi H, Asai S, Takahashi Y, Yamaji K, Takahashi K, Fujioka T, Takata R, Yanai H, Masumoto A, Koretsune Y, Kutsumi H, Higashiyama M, Murayama S, Minegishi N, Suzuki K, Tanno K, Shimizu A, Yamaji T, Iwasaki M, Sawada N, Uemura H, Tanaka K, Naito M, Sasaki M, Wakai K, Tsugane S, Yamamoto M, Yamamoto K, Murakami Y, Nakamura Y, Raychaudhuri S, Inazawa J, Yamauchi T, Kadowaki T, Kubo M, Kamatani Y. Large-scale genome-wide association study in a Japanese population identifies novel susceptibility loci across different diseases. Nature genetics. 2020.07; 52(7); 669-679
6. Inoue J, Fujiwara K, Hamamoto H, Kobayashi K, Inazawa J. Improving the Efficacy of EGFR Inhibitors by Topical Treatment of Cutaneous Squamous Cell Carcinoma with *miR-634* Ointment. Molecular therapy oncolytics. 2020.12; 19; 294-307

[Conference Activities & Talks]

1. Oligonucleotide therapeutics using a novel tumor-suppressive microRNA targeting MYC pathway. 2020.10.01
2. 劉暢, 玄泰行, 稲澤讓治. miR-3140はBRD4-MYCN経路を標的とし、神経芽腫細胞の増殖を抑制する. 日本癌学会総会記事 2020.10.01
3. 玄泰行, 稲澤讓治. MYC経路を標的とする新規腫瘍抑制型miRNAを用いた核酸抗癌薬の可能性. 日本癌学会総会記事 2020.10.01
4. 村松智輝, 徐博, 稲澤讓治. 口腔・食道がんにおいてピタバスタチンはAKT、ERKのシグナルを抑制し、細胞増殖を阻害する. 日本癌学会総会記事 2020.10.01
5. 高田亮, 赤松秀輔, 中川英刀, 高橋篤, 颯川晋, 鎌谷洋一郎, 稲澤讓治, 小川修, 小原航. 日本人前立腺癌の発癌に関する新規12遺伝子多型とポリジェニックリスクスコアの同定. 日本癌学会総会記事 2020.10.01
6. 稲澤讓治. 癌ゲノム学入門 がん精密医療を实践するために知っておきたい遺伝学の知識. 日本癌学会総会記事 2020.10.01
7. 井上純, 岸川正大, 朝蔭孝宏, 稲澤讓治. 食道癌における治療標的としての代謝関連分子の探索. 日本癌学会総会記事 2020.10.01

[Patents]

1. THERAPEUTIC AGENT FOR TREATING A CANCER IN WHICH NRF2 IS STABILIZED, Patent Number : EP2963125
2. METHOD FOR ASSAYING MICRORNA, CANCER THERAPEUTIC AGENT, AND MEDICINAL COMPOSITION CONTAINING SAME FOR CANCER THERAPY, Patent Number : US10876115

Hematology

Chair (Substitute) Shuji Tohda

Professor(Immunotherapy for Hematopoietic Disorders) Norihiko Kawamata

Junior Associate Professor Masahide Yamamoto

Assistant Professor Toshikage Nagao, Yoshihiro Umezawa, Keigo Okada

Project Assistant Professor Chizuko Sakashita

Assistant Professor (Department of Clinical Laboratory) Ayako Nogami

Senior Resident Tomoyuki Arimatu, Atsushi Takahata, Mai Kuboki, Moyu Kimura, Makiko Saito

Graduate Student Kota Yoshifuji, Sunichiro Yasuda, Satoru Aoyama

(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

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. Research focusing on Myeloproliferative Neoplasms (MPN): Tumorigenesis, Chemo-resistance, new drugs.
3. Signal transduction mechanisms from cytokine/growth factor receptors regulating proliferation, survival, and adhesion of hematopoietic cells including leukemia and lymphoma cells.
4. Molecular analysis of Chronic Myeloid Leukemia (CML): rare variants, chemo-resistance, target therapy.
5. Development of novel CAR-T technology: Chimeric Antigen Receptor T-cell targeting leukemia.

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 thrombocytopenia, with chemotherapeutics, molecularly-targeted drugs, immunosuppressive agents, hematopoietic cell transplantation, and CAR-T cell therapy.

(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. Nogami A, Yamamoto M, Yamamoto K, Ito M, Umezawa Y, Tohda S, Miura O, Fukuda T. Marginal zone lymphoma-like primary bone marrow lymphoma with long-term pancytopenia preceding diagnosis Rinsho ketsueki. 2020; 61(10); 1469-1475
2. Koji Nishikawa, Kiminori Kimura, Yoshinobu Kanda, Masaya Sugiyama, Kazuhiko Kakihana, Noriko Doki, Kazuteru Ohashi, Sung Kwan Bae, Kazuhiro Takahashi, Yuko Ishihara, Ishikazu Mizuno, Yasushi Onishi, Masahiro Onozawa, Makoto Onizuka, Masahide Yamamoto, Tetsuya Ishikawa, Kazuaki Inoue, Shigeru Kusumoto, Satoshi Hashino, Hidetsugu Saito, Tatsuya Kanto, Hisashi Sakamaki, Masashi Mizokami. A prospective trial of vaccine to prevent hepatitis B virus reactivation after hematopoietic stem cell transplantation. Bone Marrow Transplant.. 2020.02;
3. Akiyama H, Umezawa Y, Watanabe D, Okada K, Ishida S, Nogami A, Miura O. Inhibition of USP9X Downregulates JAK2-V617F and Induces Apoptosis Synergistically with BH3 Mimetics Preferentially in Ruxolitinib-Persistent JAK2-V617F-Positive Leukemic Cells. Cancers. 2020.02; 12(2);
4. Shunya Matsumoto, Toshiki Kijima, Yoh Matsuoka, Masahide Yamamoto, Yasuhisa Fujii. A case of recurrent thrombocytopenia involving divergent immune-related mechanisms associated with pembrolizumab. Eur. J. Cancer. 2020.03;
5. Ayako Arai, Hiroshi Takase, Mayumi Yoshimori, Kouhei Yamamoto, Manabu Mochizuki, Osamu Miura. Gene expression profiling of primary vitreoretinal lymphoma. Cancer science. 2020.04; 111(4); 1417-1421
6. Ichiro Yonese, Chizuko Sakashita, Ken-Ichi Imadome, Tohru Kobayashi, Masahide Yamamoto, Akihisa Sawada, Yoshinori Ito, Noriko Fukuhara, Asao Hirose, Yusuke Takeda, Masanori Makita, Tomoyuki Endo, Shun-Ichi Kimura, Masataka Ishimura, Osamu Miura, Shouichi Ohga, Hiroshi Kimura, Shigeyoshi Fujiwara, Ayako Arai. Nationwide survey of systemic chronic active EBV infection in Japan in accordance with the new WHO classification. Blood Adv. 2020.07; 4(13); 2918-2926

7. Towako Taguchi, Morito Kurata, Iichiroh Onishi, Yuko Kinowako, Yunosuke Sato, Sayuri Shiono, Sachiko Ishibashi, Masumi Ikeda, Masahide Yamamoto, Masanobu Kitagawa, Kouhei Yamamoto. SECISBP2 is a novel prognostic predictor that regulates selenoproteins in diffuse large B-cell lymphoma. *Lab Invest.* 2020.10;
8. Satoshi Koi, Kosuke Arai, Ayako Nogami, Hayato Toma, Masahide Yamamoto, Osamu Miura, Toshikage Nagao. Impaired hematopoiesis due to copper deficiency in a hemodialysis patient supplemented with zinc. *Rinsho Ketsueki.* 2020.10; 61(10); 1487-1491

[Conference Activities & Talks]

1. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Hiroki Akiyama, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura, Norihiko Kawamata. A Protease-Mediated Regulatory Chimeric Antigen Receptor (CAR): “Scissors” CAR Improves Target Specificity through Regulation of CAR-T Cell Activity. American Association for Cancer Research (AACR) annual meeting 2020 2020.06.22
2. Masahide Yamamoto, Maho Sato, Yasushi Onishi, Kenichi Matsuoka, Makoto Onizuka, Kenichiro Watanabe, Atsushi Kikuta, Chizuko Sakashita, Tohru Kobayashi, Tatsuo Ichinohe, Takahiro Fukuda, Masami Inoue, Yoshiko Atsuta, Ayako Arai. Outcome of hematopoietic stem cell transplantation for chronic active Epstein-Barr virus infection. The 83rd Annual Meeting of the Japanese Society of Hematology 2020.10
3. Yoshihiro Umezawa, Yotaro Motomura, Keigo Okada, Ayako Nogami, Toshikage Nagao, Norihiko Kawamata, Shuji Tohda, Osamu Miura, Masahide Yamamoto. Letermovir prophylaxis with comprehensive virus monitoring after hematopoietic-cell transplantation. The 82nd Annual Meeting of Japanese Society of Hematology 2020.10.10
4. Yotaro Motomura, Keigo Okada, Ayako Nogami, Yoshihiro Umezawa, Toshikage Nagao, Shuji Tohda, Ukihide Tateishi, Masahide Yamamoto. 18F-FDG PET/CT in patients with newly diagnosed plasma cell disorders. The 82nd Annual meeting of Japanese Society of Hematology 2020.10.10
5. Keisuke Tanaka, Masahide Yamamoto, Satoshi Koi, Mai Kubok, Fumihiko Ouchi, Naoya Nakamura, Shigeo Toyota. High dose methotrexate for central nerve system prophylaxis in diffuse large B-cell lymphoma. The 82nd Annual Meeting of Japanese Society of Hematology 2020.10.10
6. Daisuke Watanabe, Ayako Nogami, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa, Toshikage Nagao, Osamu Miura. FLT3-ITD activates RSK1 to upregulate mTORC1 and eIF4B and to inhibit BAD and BIM. The 82nd Annual meeting of Japanese Society of Hematology 2020.10.10
7. Toshikage Nagao, Ayako Nogami, Yoshihiro Umezawa, Keigo Okada. COT kinase regulates cell survival and proliferation in ABC like DLBCL. The 82nd Annual Meeting of the Japanese Society of Hematology 2020.10.10
8. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Hiroki Akiyama, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura, Norihiko Kawamata. Protease harboring Chimeric Antigen Receptor (CAR) Regulates CAR-T Cell Activity. The 82nd Annual Meeting of the Japanese Society of Hematology 2020.10.10
9. Shunichiro Yasuda, Satoru Aoyama, Ryoto Yoshimoto, Daisuke Watanabe, Kouhei Yamamoto, Takeo Fujiwara, Yoko Eda, Misa Imai, Marito Araki, Norio Komatsu, Osamu Miura, Norihiko Kawamata. Overexpression of MPL causes ruxolitinib-resistance in MPN with CALR frame-shift mutations. The 82nd Annual Meeting of Japanese Society of Hematology 2020.10.10
10. Shunichiro Yasuda, Satoru Aoyama, Ryoto Yoshimoto, Daisuke Watanabe, Hiroki Akiyama, Kouhei Yamamoto, Takeo Fujiwara, Emiko Sakaida, Yoko Eda, Misa Imai, Marito Araki, Norio Komatsu, Norihiko Kawamata. MPL Overexpression Induces a High Level of Mutant-Calr/MPL Complex: A Novel Mechanism of Ruxolitinib Resistance in Myeloproliferative Neoplasms with Calr Mutations. The 62nd Annual meeting of American Society of Hematology 2020.12.05 Online meeting
11. Satoru Aoyama, Shunichiro Yasuda, Daisuke Watanabe, Hiroki Akiyama, Keigo Okada, Yoshihiro Umezawa, Ayako Nogami, Osamu Miura, Norihiko Kawamata. A Protease-Mediated Regulatory Chimeric Antigen Receptor (CAR): “Double Arm” CAR System Improves Tumor-cell-Specificity of CAR-T Cell Therapy. 62nd American Society of Hematology (ASH) annual Meeting and Exposition 2020.12.06 virtual meeting

[Awards & Honors]

1. Shunichiro Yasuda ASH-JSH Abstract Achievement Award 2020, American society of hematology and Japanese society of hematology, 2020.12

Molecular Endocrinology and Metabolism

Professor: Tetsuya Yamada

Associate Professor: Kenji Ikeda, Hajime Izumiyama

Assistant Professor: Chikara Komiya, Kazutaka Tsujimoto, Kumiko Shiba, Masanori Murakami

Clinical Fellow: Shoko Mori, Jun Aoki, Takaaki Shigematsu, Akiko Horie, Yoko Nishiuchi

Resident: Miho Shiomura, Hidetoshi Nakashima, Keitaro Kawakami

Project Assistant Professor: Mitsuyuki Numasawa

Graduate Students (Doctor's course): Yoshihiro Niitsu, Akira Takeuchi, Masahiro Ando

(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 diabetes, 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) Mechanisms and development of new therapeutic strategies of diabetes and metabolic syndrome
- 2) Thermogenesis and energy metabolism
- 3) Induced molecular mechanism of thermogenic fat
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors

3. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- 1) diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- 2) diseases of the thyroid, pituitary and adrenal glands.
- 3) primary and secondary hypertension
- 4) disorders of calcium metabolism

(2) Publications

[Original Articles]

1. Fukuda T., Bouchi R., Asakawa M., Takeuchi T., Shiba K., Tsujimoto K., Komiya C., Yoshimoto T., Ogawa Y., Yamada T.. Sarcopenic obesity is associated with a faster decline in renal function in people with type 2 diabetes DIABETIC MEDICINE. 2020.01;
2. Takahiro Fukaishi, Isao Minami, Seizaburo Masuda, Yasutaka Miyachi, Kazutaka Tsujimoto, Hajime Izumiyama, Koshi Hashimoto, Masayuki Yoshida, Sayako Takahashi, Kenichi Kashimada, Tomohiro Morio, Kenjiro Kosaki, Yoshiro Maezawa, Koutaro Yokote, Takanobu Yoshimoto, Tetsuya Yamada. A

- case of generalized lipodystrophy-associated progeroid syndrome treated by leptin replacement with short and long-term monitoring of the metabolic and endocrine profiles. *Endocr. J.* 2020.02; 67(2); 211-218
3. Hayashi Ruriko, Minami Isao, Sasahara Yuriko, Izumiyama Hajime, Yoshimoto Takanobu, Kishino Mitsuhiro, Kudo Atsushi, Tateishi Ukihide, Tanabe Minoru, Yamada Tetsuya. Diagnostic accuracy of selective arterial calcium injection test for localization of gastrinoma *Endocrine Journal*. 2020.03; 67(3); 305-315
 4. Kobayashi Hiroki, Nakamura Yoshihiro, Abe Masanori, Kurihara Isao, Itoh Hiroshi, Ichijo Takamasa, Takeda Yoshiyu, Yoneda Takashi, Katabami Takuyuki, Tsuiki Mika, Wada Norio, Ogawa Yoshihiro, Sakamoto Ryuichi, Kawashima Junji, Sone Masakatsu, Inagaki Nobuya, Yoshimoto Takanobu, Yamada Tetsuya, Okamoto Ryuji, Matsuda Yuichi, Fujita Megumi, Watanabe Minemori, Tamura Kouichi, Tanabe Akiyo, Naruse Mitsuhide. Effect of cosyntropin during adrenal venous sampling on subtype of primary aldosteronism: analysis of surgical outcome *European Journal of Endocrinology*. 2020.03; 182(3); 265-273
 5. Hanzawa N, Hashimoto K, Yuan X, Kawahori K, Tsujimoto K, Hamaguchi M, Tanaka T, Nagaoka Y, Nishina H, Morita S, Hatada I, Yamada T, Ogawa Y. Targeted DNA demethylation of the *Fgf21* promoter by CRISPR/dCas9-mediated epigenome editing. *Scientific reports*. 2020.03; 10(1); 5181
 6. Tajima Kazuki, Ikeda Kenji, Tanabe Yuji, Thomson Ella A., Yoneshiro Takeshi, Oguri Yasuo, Ferro Marc D., Poon Ada S. Y., Kajimura Shingo. Wireless optogenetics protects against obesity via stimulation of non-canonical fat thermogenesis *Nature Communications*. 2020.04; 11(1); 1730
 7. Nakamura Yuki, Yokoyama Minato, Yoshida Soichiro, Tanaka Hajime, Kijima Toshiki, Ishioka Junichiro, Matsuoka Yoh, Saito Kazutaka, Minami Isao, Yoshimoto Takanobu, Naito Shotaro, Ogawa Yoshihiro, Yamada Tetsuya, Uchida Shinichi, Fujii Yasuhisa. Postoperative renal impairment and longitudinal change in renal function after adrenalectomy in patients with Cushing's syndrome(和訳中) *International Journal of Urology*. 2020.05; 27(5); 395-400
 8. Hosaka Shinichiro, Yamada Tetsuya, Takahashi Kei, Dan Takashi, Kaneko Keizo, Kodama Shinjiro, Asai Yoichiro, Munakata Yuichiro, Endo Akira, Sugawara Hiroto, Kawana Yohei, Yamamoto Junpei, Izumi Tomohito, Sawada Shojiro, Imai Junta, Miyata Toshio, Katagiri Hideki. Inhibition of Plasminogen Activator Inhibitor-1 Activation Suppresses High Fat Diet-Induced Weight Gain via Alleviation of Hypothalamic Leptin Resistance *Frontiers in Pharmacology*. 2020.06; 11; 943
 9. Ohno Y, Sone M, Inagaki N, Kawashima A, Takeda Y, Yoneda T, Kurihara I, Itoh H, Tsuiki M, Ichijo T, Katabami T, Wada N, Sakamoto R, Ogawa Y, Yoshimoto T, Yamada T, Kawashima J, Matsuda Y, Kobayashi H, Kamemura K, Yamamoto K, Otsuki M, Okamura S, Izawa S, Okamoto R, Tamura K, Tanabe A, Naruse M.. Nadir Aldosterone Levels After Confirmatory Tests Are Correlated With Left Ventricular Hypertrophy in Primary Aldosteronism. *Hypertension*. 2020.06; 75(6); 1475-1482
 10. Kobayashi Y, Haze T, Yano Y, Tamura K, Kurihara I, Ichijo T, Yoneda T, Katabami T, Tsuiki M, Wada N, Ogawa Y, Kawashima J, Sone M, Inagaki N, Yamada T, Okamoto R, Fujita M, Kamemura K, Yamamoto K, Izawa S, Tanabe A, Naruse M.. Associations Between Changes in Plasma Renin Activity and Aldosterone Concentrations and Changes in Kidney Function After Treatment for Primary Aldosteronism. *Kidney International Reports*. 2020.06; 5(8); 1291-1297
 11. Nakano Y, Komiya C, Shimizu H, Mishima H, Shiba K, Tsujimoto K, Ikeda K, Kashimada K, Dateki S, Yoshiura KI, Ogawa Y, Yamada T. A case of ezetimibe-effective hypercholesterolemia with a novel heterozygous variant in *ABCG5*. *Endocrine journal*. 2020.07;
 12. Oguri Yasuo, Shinoda Kosaku, Kim Hyeonwoo, Alba Diana L., Bolus W. Reid, Wang Qiang, Brown Zachary, Pradhan Rachana N., Tajima Kazuki, Yoneshiro Takeshi, Ikeda Kenji, Chen Yong, Cheang Rachel T., Tsujino Kazuyuki, Kim Caroline R., Greiner Vanille Juliette, Datta Ritwik, Yang Christopher D., Atabai Kamran, McManus Michael T., Koliwad Suneil K., Spiegelman Bruce M., Kajimura Shingo. CD81 Controls Beige Fat Progenitor Cell Growth and Energy Balance via FAK Signaling *Cell*. 2020.08; 182(3); 563-+
 13. Wallace PW, Conrad C, Brückmann S, Pang Y, Caleiras E, Murakami M, Korpershoek E, Zhuang Z, Rapizzi E, Kroiss M, Gudziol V, Timmers HJ, Mannelli M, Pietzsch J, Beuschlein F, Pacak K, Robledo M, Klink B, Peitzsch M, Gill AJ, Tischler AS, de Krijger RR, Papatomas T, Aust D, Eisenhofer G, Richter S. Metabolomics, machine learning and immunohistochemistry to predict succinate dehydrogenase

mutational status in pheochromocytomas and paragangliomas. *The Journal of pathology*. 2020.08; 251(4); 378-387

14. Sponton Carlos H., Hosono Takashi, Taura Junki, Jedrychowski Mark P., Yoneshiro Takeshi, Wang Qiang, Takahashi Makoto, Matsui Yumi, Ikeda Kenji, Oguri Yasuo, Tajima Kazuki, Shinoda Kosaku, Pradhan Rachana N., Chen Yong, Brown Zachary, Roberts Lindsay S., Ward Carl C., Taoka Hiroki, Yokoyama Yoko, Watanabe Mitsuhiro, Karasawa Hiroshi, Nomura Daniel K., Kajimura Shingo. The regulation of glucose and lipid homeostasis via PLTP as a mediator of BAT-liver communication *EMBO Reports*. 2020.09; 21(9);
15. Kaneko Keizo, Sawada Shojiro, Satake Chihiro, Kondo Keiichi, Izumi Tomohito, Tanaka Mamiko, Imai Junta, Yamada Tetsuya, Katsushima Hiroki, Fujishima Fumiyoshi, Katagiri Hideki. Extraordinarily long-inactive solitary fibrous tumor transformed to produce big insulin-like growth factor-2, leading to hypoglycemia and rapid liposarcoma growth: a case report *BMC Endocrine Disorders*. 2020.09; 20(1); 148
16. Kawahori K, Kondo Y, Yuan X, Kawasaki Y, Hanzawa N, Tsujimoto K, Wada F, Kohda T, Ishigami A, Yamada T, Ogawa Y, Hashimoto K. Ascorbic acid during the suckling period is required for proper DNA demethylation in the liver. *Scientific reports*. 2020.12; 10(1); 21228
17. Bouchi R, Sonoda N, Itoh J, Ono Y, Fukuda T, Takeuchi T, Kishimoto J, Yamada T, Ogawa Y. Effects of intensive exercise combined with dapagliflozin on body composition in patients with type 2 diabetes: a randomized controlled trial. *Endocrine Journal*. 2020.12;

[Misc]

1. Ikeda K, Yamada T.. UCP1 Dependent and Independent Thermogenesis in Brown and Beige Adipocytes *Frontiers in Endocrinology*. 2020.07;

[Conference Activities & Talks]

1. Masanori Murakami. In Situ Metabolomics (Mass spectrometry imaging) in Adrenal Tumor.. AOCE-SICEM 2020 (The 17th Asia-Oceania Congress of Endocrinology and the 8th Seoul International Congress of Endocrinology and Metabolism) 2020.10.28 Seoul, Korea

[Awards & Honors]

1. The 93rd Annual Congress of the Japan Endocrine Society, Young Investigator's Award (Masanori Murakami), The Japan Endocrine Society, 2020.07
2. The 93rd Annual Congress of the Japan Endocrine Society, Young Investigator's Award (Nozomi Hanzawa), The Japan Endocrine Society, 2020.07

Hepatobiliary and Pancreatic Surgery

Director & Professor

Minoru Tanabe MD, PhD

Associate Professor

Atsushi Kudo MD, PhD

Daisuke Ban MD, PhD (until March)

Assistant Professor

Hiroaki Ono MD, PhD

Kosuke Ogawa MD, PhD

Keiichi Akahoshi MD, PhD

Hiroki Ueda MD, PhD (from April)

Shuichi Watanabe MD, PhD

Yoshiya Ishikawa MD, PhD

Graduate School Students

Masafumi Akasu MD (until March)

Tomotaka Kato MD (until March)

Toshitaka Sugawara MD

Takeshi Ishii MD

Yoshiki Murase MD

Aya Maekawa MD

Kohei Yagi MD

Hironari Yamashita MD (from April)

Hiroyuki Ishida MD (from April)

Koichiro Morimoto MD (from 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 and pancreatic cancers

- Liver transplantation and organ preservation
- Treatments for neuroendocrine tumor
- Innovation of imaging modality for hepatobiliary and pancreatic cancers
- Establishment of PDX model in hepatobiliary and pancreatic cancer

(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) Lectures & Courses

Undergraduate education: Educate and acquire knowledge as a surgeon in general and basic knowledge, then more practical knowledge and stages, in accordance with the actual case as much as possible in a one-on-one system with a supervising doctor. At the same time, they will teach you how to be a doctor and learn morals according to specific cases such as how to treat patients and issues of illness notification. Basic surgical procedures will be entrusted to postgraduate education, but the aim is to gain many clinical experiences by assisting many patients with hepatobiliary and pancreatic surgery as high-assistance surgery.

Post-graduate education: The primary purpose is to develop surgeons with a high level of consulting skills in cooperation with related hospitals. Instruct students to have a viewpoint. We want to not only provide surgeons and gastroenterologists with training that can be obtained, but also motivate internationally competitive specialists and surgical researchers to make a leap forward.

(5) Clinical Services & Other Works

Diseases of hepatobiliary, pancreatic, and splenic areas are the targets of our department, and we mainly focus on multidisciplinary treatments for malignant tumors centering on surgical treatment. The mission of the university is to push the limits of surgical indications for highly advanced and refractory cancers, using preoperative simulation using a workstation and resection / reconstruction with vascular complications. In addition, arthroscopic surgery will be developed as a minimally invasive treatment. As an important treatment option for patients with end-stage liver disease, we also make indications for living donor liver transplantation. In laparoscopic surgery, we will develop new surgical instruments and procedures to promote safer, reduced port surgery that minimizes abdominal wall destruction, and expand the indication of minimally invasive operations.

(6) Clinical Performances

In 2020, the influence of surgery restrictions by COVID-19 was strong, and the total number of surgeries was 148 (255 in 2019), 61 hepatectomy and 70 pancreatic resection. It is one of the top-class high volume facilities in Japan and covers a wide variety of surgical procedures from characteristic minimally invasive surgery to extended surgery.

Laparoscopic surgery accounts for more than half of all cases, and laparoscopic surgery is about half for both hepatectomy and pancreatic resection, and the number of cases is increasing year by year. In addition, we started pancreatic resection by robotic surgery in 2020 and have successfully completed 3 robotic pancreatic resections.

The treatment of neuroendocrine tumors, which is a feature of our department, spans surgery, drug therapy, and radiotherapy, and we aim to improve results by performing multidisciplinary treatment. Last year, the cumulative number of first-visit patients exceeded 700, the largest number in Japan.

(7) Publications

[Original Articles]

1. Takao Ohtsuka, Masafumi Nakamura, Susumu Hijioka, Yasuhiro Shimizu, Michiaki Unno, Minoru Tanabe, Yuichi Nagakawa, Kyoichi Takaori, Seiko Hirono, Naoto Gotohda, Wataru Kimura, Kei Ito, Akio Katanuma, Tsuyoshi Sano, Takahiro Urata, Emiri Kita, Keiji Hanada, Minoru Tada, Takeshi Aoki, Masahiro Serikawa, Kojun Okamoto, Hiroyuki Isayama, Yoshitaka Gotoh, Kousei Ishigami, Hiroshi Yamaguchi, Kenji Yamao, Masanori Sugiyama, Kazuichi Okazaki. Prediction of the Probability of Malignancy in Mucinous Cystic Neoplasm of the Pancreas With Ovarian-Type Stroma A Nationwide Study in Japan *Pancreas*. 2020.02; 49(2); 181-186
2. Hiroaki Ono, Atsushi Kudo, Keiichi Akahoshi, Toshiro Ogura, Kosuke Ogawa, Daisuke Ban, Shinji Tanaka, Minoru Tanabe. Combination of weekly streptozocin and oral S-1 treatment for patients of unresectable or metastatic pancreatic neuroendocrine neoplasms *Journal of Cancer Research and Clinical Oncology*. 2020.03; 146(3); 793-799
3. Satoshi Koizumi, Shingo Yamashita, Satoshi Matsumura, Kazuhisa Takeda, Takuya Minagawa, Shinjiro Kobayashi, Taizo Hibi, Masahiro Shinoda, Itaru Endo, Minoru Tanabe, Masakazu Yamamoto, Takehito Otsubo. Significance of a preoperative tumor marker gradient for predicting microvascular invasion in cases of hepatocellular carcinoma *Molecular and clinical oncology*. 2020.03; 12(3); 290-294
4. Ruriko Hayashi, Isao Minami, Yuriko Sasahara, Hajime Izumiyama, Takanobu Yoshimoto, Mitsuhiro Kishino, Atsushi Kudo, Ukihide Tateishi, Minoru Tanabe, Tetsuya Yamada . Diagnostic accuracy of selective arterial calcium injection test for localization of gastrinoma *Endocrine Journal* . 2020.03; 67(3); 305-315
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[Books etc]

1. D. Asano, D. Ban, M. Tanabe. Colorectal Cancer Liver Metastases. Springer, 2020.08 (ISBN : 978-3-030-25485-8)

[Conference Activities & Talks]

1. Fukiko Kawai-Kitahata, Yasuhiro Asahina , Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka , Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Online
2. Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka, Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and aav/hepatitis b virus integration into genome on development of hepatocellular carcinoma in patients with prior hepatitis b virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Web 開催
3. Akiyama Y, Shimada S, Tanabe M, Tanaka S. Loss of ARID1A increases a stemness gene ALDH1A1 expression through histone acetylation change in cholangiocarcinoma. The 79th Annual Meeting of the Japanese Cancer Association 2020.10.01 Yokohama, Online
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5. Hiroaki Ono, Sadakatsu Ikeda, Yoshiya Ishikawa, Shuici Watanabe, Keiichi Akahoshi, Kosuke Ogawa, Daisuke Ban, Atsushi Kudo, Satoshi Miyake, Minoru Tanabe. Cross-sectional study of genomic sequencing in HBP malignancies. The 75th General Meeting of the Japanese Society of Gastroenterological Surgery 2020.12.16 Wakayama

6. Shu Shimada, Yoshimitsu Akiyama, Shigeki Arii, Minoru Tanabe, Shinji Tanaka. Comprehensive molecular and immunological classification of hepatocellular carcinoma. The 56th Annual Meeting of Liver Cancer Study Group of Japan 2020.12.22 Online

Orthopaedic and Spinal Surgery

Professor: Atsushi Okawa

Associate Professor: Toshitaka Yoshii

Junior Associate Professor: Takashi Hirai

Assistant Professor: Yuko Segawa, Masato Yuasa, Hidetoshi Kaburagi, Yu Matsukura, Ryohei Takada

Specially Appointed Assistant Professor: Shingo Morishita, Naoto Watanabe, Jae-Sung An

「Department of Orthopaedic and Trauma Research」

Associate Professor: Hiroyuki Inose

Junior Associate Professor: Hirotaka Koyanagi

Junior Associate Professor: Yoto Oh

「Joint Research Department of Advanced Technology in Medicine」

Joint Research Professor: Shigenori Kawabata

Visiting Professor : Kensuke Sekihara

Junior Associate Professor: Yuko Hoshino

「Joint Research Department of Functional Joint Anatomy」

Joint Research Professor: Akimoto Nimura

Junior Associate Professor: Koji Fujita

「Department of Nano-Bioscience」

Joint Research Professor: Yoshinori Asou

Assistant Professor: HAILATI AINI

(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

(3) Education

Our department has several regular programs 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 up-dated knowledge of clinical medicine through regularly-held journal clubs and research meetings.

(4) Lectures & Courses

Japanese orthopaedic research is characterized by the fact that surgeon himself participates in 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 device for measuring 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 musculoskeletal tumor. More than twenty registered orthopaedic surgeons belong to our department. We also organized 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 ossification of spinal ligaments, adult spinal deformity, and tumor of the spine are our other interest.

(7) Publications

[Original Articles]

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3. Norihiro Isogai, Naobumi Hosogane, Haruki Funao, Kenya Nojiri, Satoshi Suzuki, Eijiro Okada, Seiji Ueda, Tomohiro Hikata, Yuta Shiono, Kota Watanabe, Kei Watanabe, Takashi Kaito, Tomoya Yamashita, Hiroyasu Fujiwara, Yukitaka Nagamoto, Hidetomi Terai, Koji Tamai, Yuji Matsuoka, Hidekazu Suzuki, Hirosuke Nishimura, Atsushi Tagami, Shuta Yamada, Shinji Adachi, Seiji Ohtori, Sumihisa Orita, Takeo Furuya, Toshitaka Yoshii, Shuta Ushio, Gen Inoue, Masayuki Miyagi, Wataru Saito, Shiro Imagama, Kei Ando, Daisuke Sakai, Tadashi Nukaga, Katsuhito Kiyasu, Atsushi Kimura, Hirokazu Inoue, Atsushi Nakano, Katsumi Harimaya, Kenichi Kawaguchi, Nobuhiko Yokoyama, Hidekazu Oishi, Toshiro Doi, Shota Ikegami, Masayuki Shimizu, Toshimasa Futatsugi, Kenichiro Kakutani, Takashi Yurube, Masashi Oshima, Hiroshi Uei, Yasuchika Aoki, Masahiko Takahata, Akira Iwata, Shoji Seki, Hideki Murakami, Katsuhito Yoshioka, Hirooki Endo, Michio Hongo, Kazuyoshi Nakanishi, Tetsuya Abe, Toshinori Tsukanishi, Ken Ishii. The Surgical Outcomes of Spinal Fusion for Osteoporotic Vertebral

- Fractures in the Lower Lumbar Spine with a Neurological Deficit. *Spine Surg Relat Res.* 2020; 4(3); 199-207
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 7. Lu Zhao, Koji Makino, Koji Fujita, Toru Sasaki, Nobutaka Sato, Kazuki Yamada, Kensuke Koyama, Hirotaka Haro, Hidetsugu Terada. High-Accuracy Finger Force Distribution Measurement System with Precision Calibration Function 2020 IEEE/SICE International Symposium on System Integration. 2020.01;
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 13. Yusuke Minami, Shingo Sato, Hirotaka Koyanagi, Yuko Kinowaki. Malignant primary pulmonary meningioma with bone metastasis. *Oxf Med Case Reports.* 2020.02; 2020(2); omaa005
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 17. Takashi Hirai, Toshitaka Yoshii, Satoru Egawa, Kenichiro Sakai, Hiroyuki Inose, Masato Yuasa, Tsuyoshi Yamada, Shuta Ushio, Tsuyoshi Kato, Yoshiyasu Arai, Shigenori Kawabata, Shigeo Shindo, Osamu Nakai, Atsushi Okawa. Increased Height of Fused Segments Contributes to Early-Phase Strut Subsidence after Anterior Cervical Corpectomy with Fusion for Multilevel Ossification of the Posterior Longitudinal Ligament. *Spine Surg Relat Res.* 2020.03; 4(4); 294-299
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 19. Toshitaka Yoshii, Satoru Egawa, Hiroataka Chikuda, Norimitsu Wakao, Takeo Furuya, Tsukasa Kanchiku, Narihito Nagoshi, Yasushi Fujiwara, Masahiro Yoshida, Toshihiko Taguchi, Masahiko Watanabe. A systematic review and meta-analysis comparing anterior decompression with fusion and posterior laminoplasty for cervical spondylotic myelopathy. *J Orthop Sci.* 2020.03; (20); 30059-2
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 21. Kawabata A, Nimura A, Fujita K, Ishii S, Okawa A. Locking of the Distal Radioulnar Joint Caused by Dorsal Tear of the Triangular Fibrocartilage Complex A Case Report *JBJS Case Connector.* 2020.04; 10(2); e0143
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 23. Satoru Egawa, Keigo Hirai, Rempei Matsumoto, Toshitaka Yoshii, Masato Yuasa, Atsushi Okawa, Ken Sugo, Shinichi Sotome. Efficacy of Antibiotic-Loaded Hydroxyapatite/Collagen Composites Is Dependent on Adsorbability for Treating *Staphylococcus aureus* Osteomyelitis in Rats. *J Orthop Res.* 2020.04; 38(4); 843-851
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27. Hosono S, Fujita K, Nimura A, Akita K. Release of cervical muscular tension improved severe pruritus in moderate-to-severe atopic dermatitis: A case series. *JAAD case reports.* 2020.06; 6(6); 510-513
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33. Sasaki T, Makino K, Nimura A, Suzuki S, Kuroiwa T, Koyama T, Okawa A, Terada H, Fujita K. Assessment of grip-motion characteristics in carpal tunnel syndrome patients using a novel finger grip dynamometer system. *Journal of orthopaedic surgery and research.* 2020.07; 15(1); 245
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[Books etc]

1. Takashi Hirai, Toshitaka Yoshii, Atsushi Okawa, Yoshiharu Kawaguchi. *Ossification of the Posterior Longitudinal Ligament (Third Edition)*. Springer, 2020
2. Toshitaka Yoshii. *Ossification of the Posterior Longitudinal Ligament (Third Edition)*. Springer, 2020

[Conference Activities & Talks]

1. Jae-Sung An, Kunikazu Tsuji, Hiroaki Onuma, Takashi Hoshino, Kei Inomata, Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Jun Hino, Hiroshi Hosoda, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Pain Persistence And Articular Cartilage Degeneration Were Significantly Alleviated By An Anti-fibrotic Drug Treatment In Monoiodoacetate Induced Rat Arthritis Model. 2020 Orthopaedic Research Society 2020.02.08 Phonex, USA
2. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Koji Otabe, Hisako Katano, Nobutake Ozeki, Yuji Kohno, Tsuyoshi Kimura, Kunikazu Tsuji, Hideyuki Koga, Akio Kishida, Ichiro Sekiya. The amount of collagen is not related to mechanical properties in high hydrostatic pressure-decellularized menisci and freeze-thawed menisci. ORS Annual Meeting, 2020 2020.02.08 Phenix Arizona
3. Takafumi Koyama, Tomoyuki Kuroiwa, Koji Fujita, Aakimoto Nimura, Atsushi Okawa. Comparing Kapandji scores with thumb pronation and palmar abduction angles. APFSSH/APFSHT2020 2020.03.14 Melbourne, Australia
4. Koji Fujita, Aakimoto Nimura, Ryuichi Kato, Atsushi Okawa. Gait analysis of patients with distal radius fracture using a novel Laser-TUG system. APFSSH/APFSHT2020 2020.03.14 Melbourne, Australia
5. Kaku Takumi, Oh Yoto, Sato Shingo, Koyanagi Hirotaka, Hirai Takashi, Yuasa Masato, Yoshii Toshitaka, Okawa Atsushi. Atypical femoral fractures in patients with metastatic bone disease: An alert report. The 93th Annual Meeting of the Japanese Orthopaedic Association 2020.06.11
6. Koji Fujita, Aakimoto Nimura, Ryuichi Kato, Atsushi Okawa. Gait characteristics and fall tendency of patients with distal radius fracture. ASSH 2020 2020.10.02 Online

7. Hiroyuki Inose, Tsuyoshi Kato, Atsushi Okawa. Predictors of residual low back pain after acute osteoporotic compression fracture: a prospective, multicenter cohort study. EUROSPINE 2020 2020.10.09
8. Toshitaka Yoshii. Intraoperative CT/navigation assisted surgery for severe cervical OPLL.. CAOS-KOREA 2020.10.30 Soul (Web)
9. Shimano S., Ohkawa R., Nambu M., Sasaoka M., Yamazaki A., Fujii Y., Igarashi K., Horiuchi Y., Lai SJ., Kameda T., Ichimura N., Fujita K., Tohda S. and Tozuka M. Dramatic change of high-density lipoprotein structure and serum amyloid A distribution after orthopedic surgery. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line

[Patents]

1. NERVE STIMULATION APPARATUS AND BIOMAGNETIC FIELD MEASUREMENT SYSTEM, Patent Number : 10722701
2. MAGNETIC MEASURING DEVICE, Patent Number : 17759677.2
3. MAGNETIC MEASURING DEVICE, Patent Number : 17759677.2

[Awards & Honors]

1. Operation Impact Award(Takahisa Ogawa), Harvard Initiative for Learning and Teaching, 2020

Diagnostic Radiology and Nuclear Medicine

Professor Ukihide Tateishi

Project Professor Yukihisa Saida

Associate Professors Ichiro Yamada(∼ Mar.), Mitsuhiro Kishino(Apr. ∼),
Yoshio Kitazume(Department of medical informatics associate) professor)

Lecturers Mitsuhiro Kishino(∼ Mar.),Tomoyuki Fujioka,
Junichi Ysuchiya(Apr. ∼),Jun Oyama(Apr. ∼)

Research Associates Makiko Honda(∼ Sep.),Syuichiro Nakaminato(∼ Mar.),
Junichi Tsuchiya(∼ Mar.),Jun Oyama(∼ Mar.),Mio Mori,

Marie Takahashi,Ryosuke Watanabe,Kota Yokoyama,
Koichiro Kimura(Apr. ∼),Emi Yamaga(Apr. ∼),

Project Researchi Associates Osamu Manabe(Apr. ∼ Jun.),Takuya Adachi(Apr. ∼)

Hospital Staff members Sayumi Tsuyuzaki,Kouichiro Kimura(∼ Mar.),
Yuka Yashima(Oct. ∼),Kenji Nishida(∼ Mar.) Momo Wakui(∼ Mar.),

Resident Wu Xiaotong(∼ Mar.),Yuuki Yokoi(∼ Mar.)

Sayuri Okawa(Apr. ∼),Megumi Uemichi(Apr. ∼),Kanae Takahashi(Apr. ∼),
Mayumi Hara(Apr. ∼),Toshihiro Horii(Apr. ∼),

Graduate Students

Takuya Adachi,Takumi Ooshima,Takehiro Tamura,Hyeyel Bae,

Ryo Miyazawa,Ken Yamagiwa, Syuichi Yanai,Li Runan,Mirai Kawano,

Miyako Nara

(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), ^{62/64}Cu-ATSM (redox), ¹⁸F-FLT (DNA synthesis), ¹⁸F-NaF (bone metabolism), ⁶⁸Ga-DOTATATE (somatostatin receptor), and ¹⁸F-Fluorobetaipir (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: TACE 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 17 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 F-18 FLT PET/CT for 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]**

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[Books etc]

1. Harushi Mori, Akio Ogura. Diagnostic imaging to learn from mechanism of the human body. Medical view, 2020.02 (ISBN : 978-7583-2020-7 C3047)

[Misc]

1. Fujioka T, Mori M, Kubota K, Oyama J, Yamaga E, Yashima Y, Katsuta L, Nomura K, Nara M, Oda G, Nakagawa T, Kitazume Y, Tateishi U. The Utility of Deep Learning in Breast Ultrasonic Imaging: A Review. *Diagnostics (Basel, Switzerland).* 2020.12; 10(12);

[Conference Activities & Talks]

1. Tomoyuki Fujioka, Mori Mio, Kubota Kazunori, Kikuchi Yuka, Katsuta Leona, Kimura Mizuki, Kitazume Yoshio, Tateishi Ukihide. Breast Ultrasound Image Synthesis using Deep Convolutional Generative Adversarial Networks. The 79th Annual Meeting of the Japan Radiological Society 2020.05
2. Koichiro Kimura, Tomoyuki Fujioka, Takumi Hiraishi, Yuto Fukuda, Hiroto Hada, Takahiro Hamanaka, Ukihide Tateishi. Tin-filtered 140-kVp abdominopelvic unenhanced computed tomography: image quality and effect on radiation dose reduction. The 79th Annual Meeting of the Japan Radiological Society 2020.05.15
3. Tomoyuki Fujioka, Mio Mori, Kazunori Kubota, Yuka Yashima, Leona Katsuta, Mio Adachi, Goshi Oda, Tsuyoshi Nakagawa, Ukihide Tateishi. Initial Experience of Breast Ultrasound Image Synthesis using Deep Convolutional Generative Adversarial Networks. EUROPEAN CONGRESS OF RADIOLOGY 2020 2020.07 Vienna, Austria
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6. Koichiro Kimura, Tomoyuki Fujioka, Mio Mori, Takumi Hiraishi, Hiroto Hada, Ishikawa Toshiaki, Ukihide Tateishi. Clinical Utility of Tin Filter–Based Spectral Shaping Chest-Abdominal-Pelvic CT in Colorectal Cancer Patients with Radiation Reduction and High Diagnostic Performance . 106th RSNA Scientific Assembly and Annual Meeting 2020.11.29

Genomic Function and Diversity

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(1) Outline

Complex diseases such as immunological diseases, metabolic diseases and cancer diseases are caused by both genetic and environmental factors, with varying combinations in different individuals. Genome-wide association studies (GWAS) have led to the discovery of thousands of risk variants involved in these diseases, but the precise mechanisms of the diseases are not fully understood. Our laboratory aims to elucidate the disease etiology by dissecting the diversity of genomic function among individuals. To this end, we integrate bioinformatic approaches with molecular biology techniques in the analysis of genetic variants such as expression QTL and splicing QTL mapping. We will also establish to predict each individual's pathophysiology (disease severity, drug response, etc.) based on the individual's genome information to bring precision medicine into clinical practice.

(2) Research

1. To dissect pathological mechanism of complex traits, we integrated the disease GWAS data with expression QTL and splicing QTL data, and we comprehensively identified disease-associated alternative isoforms.
2. To further seek disease susceptible loci for rheumatoid arthritis and systemic lupus erythematosus, we are performing GWAS meta-analysis in world-wide collaboration.
3. Using polygenic risk score (PRS), we established a statistical model to predict radiographic progression in rheumatoid arthritis.
4. Using long-read sequencing technology, we unraveled disease-associated structural and repetitive variants.

(3) Education

We lectured how to understand the etiology of complex traits through big data such as GWAS and eQTL/sQTL for undergraduate students and postgraduate students.

(4) Lectures & Courses

With the advent of research methods and technologies such as GWAS and next-generation sequencers, we can easily access to disease big-data in public databases. We will bring up young researchers to have skills to understand the fundamental of disease etiology by data-driven approaches.

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

1. Aoi H, Lei M, Mizuguchi T, Nishioka N, Goto T, Miyama S, Suzuki T, Iwama K, Uchiyama Y, Mitsuhashi S, Itakura A, Takeda S, Matsumoto N. Nonsense variants of *STAG2* result in distinct congenital anomalies. *Human genome variation*. 2020; 7; 26
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10. Nakamura H, Doi H, Mitsuhashi S, Miyatake S, Katoh K, Frith MC, Asano T, Kudo Y, Ikeda T, Kubota S, Kunii M, Kitazawa Y, Tada M, Okamoto M, Joki H, Takeuchi H, Matsumoto N, Tanaka F. Long-read sequencing identifies the pathogenic nucleotide repeat expansion in RFC1 in a Japanese case of CANVAS. *Journal of human genetics*. 2020.05; 65(5); 475-480
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 27. Hiromoto Y, Azuma Y, Suzuki Y, Hoshina M, Uchiyama Y, Mitsuhashi S, Miyatake S, Mizuguchi T, Takata A, Miyake N, Kato M, Matsumoto N. Hemizygous FLNA variant in West syndrome without periventricular nodular heterotopia. *Human genome variation*. 2020.12; 7(1); 43
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Human Genetics and Disease Diversity

Professor, Toshihiro Tanaka
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. Higashijima Y, Matsui Y, Shimamura T, Nakaki R, Nagai N, Tsutsumi S, Abe Y, Link VM, Osaka M, Yoshida M, Watanabe R, Tanaka T, Taguchi A, Miura M, Ruan X, Li G, Inoue T, Nangaku M, Kimura H, Furukawa T, Aburatani H, Wada Y, Ruan Y, Glass CK, Kanki Y. Coordinated demethylation of H3K9 and H3K27 is required for rapid inflammatory responses of endothelial cells. *The EMBO journal*. 2020.03; e103949
2. Ishigaki K, Akiyama M, Kanai M, Takahashi A, Kawakami E, Sugishita H, Sakaue S, Matoba N, Low SK, Okada Y, Terao C, Amariuta T, Gazal S, Kochi Y, Horikoshi M, Suzuki K, Ito K, Koyama S, Ozaki K, Niida S, Sakata Y, Sakata Y, Kohno T, Shiraishi K, Momozawa Y, Hirata M, Matsuda K, Ikeda M, Iwata N, Ikegawa S, Kou I, Tanaka T, Nakagawa H, Suzuki A, Hirota T, Tamari M, Chayama K, Miki D, Mori M, Nagayama S, Daigo Y, Miki Y, Katagiri T, Ogawa O, Obara W, Ito H, Yoshida T, Imoto I, Takahashi T, Tanikawa C, Suzuki T, Sinozaki N, Minami S, Yamaguchi H, Asai S, Takahashi Y, Yamaji K, Takahashi K, Fujioka T, Takata R, Yanai H, Masumoto A, Koretsune Y, Kutsumi H, Higashiyama M, Murayama S, Minegishi N, Suzuki K, Tanno K, Shimizu A, Yamaji T, Iwasaki M, Sawada N, Uemura H, Tanaka K, Naito M, Sasaki M, Wakai K, Tsugane S, Yamamoto M, Yamamoto K, Murakami Y, Nakamura Y, Raychaudhuri S, Inazawa J, Yamauchi T, Kadowaki T, Kubo M, Kamatani Y. Large-scale genome-wide association study in a Japanese population identifies novel susceptibility loci across different diseases. *Nature genetics*. 2020.07; 52(7); 669-679
3. Todd A Johnson, Yoichi Mashimo, Jer-Yuarn Wu, Dankyu Yoon, Akira Hata, Michiaki Kubo, Atsushi Takahashi, Tatsuhiko Tsunoda, Kouichi Ozaki, Toshihiro Tanaka, Kaoru Ito, Hiroyuki Suzuki, Hiromichi

Hamada, Tohru Kobayashi, Toshiro Hara, Chien-Hsiun Chen, Yi-Ching Lee, Yi-Min Liu, Li-Ching Chang, Chun-Ping Chang, Young-Mi Hong, Gi-Young Jang, Sin-Weon Yun, Jeong-Jin Yu, Kyung-Yil Lee, Jae-Jung Kim, Taesung Park, , Jong-Keuk Lee, Yuan-Tsong Chen, Yoshihiro Onouchi. Association of an IGHV3-66 gene variant with Kawasaki disease. *J Hum Genet.* 2020.10;

Applied Regenerative Medicine

Professor: Ichiro SEKIYA

Assistant Professor: Koji OTABE, Hisako KATANO, Nobutake OZEKI

Project Assistant Professor: Mitsuru MIZUNO, Yuji KONO

Project Researcher : Kentaro ENDO

Specially Appointed Researcher : Keiichiro KOMORI, Kimiko TAKANASHI

Graduate Student: Naoto WATANABE, Yoshihisa KUSHIDA,

So SUZUKI, Akinobu HYODO,

Hayato AOKI, Kiyotaka HORIUCHI,

Rei KUBOTA, Shunichi FUJII,

Yugo MIURA, Sho SASAKI,

Assistant Researcher: Mika WATANABE, Kaoru KOMORIYA,

Assistant Clerk: Yuumi HIRAOKA

(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 the 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

Our mission is to establish a novel treatment for knee osteoarthritis. We have shown that synovial mesenchymal stem cells (MSCs) have a high chondrogenic potential, that transplantation of synovial MSCs accelerates the natural healing process, and that transplantation of synovial MSC can be performed by minimally invasive arthroscopic surgery. After these basic researches and two clinical studies, we started a physician-led clinical trial of autologous synovial MSCs for meniscus injury in August 2017. We concluded a patent license agreement with a company in March 2019 and completed a clinical trial in June 2019. After arranging the issues in the pre-application consultation of the PMDA for regenerative medical products, we are now preparing for the corporate clinical trial as a validation study.

We also started a clinical study "Intra-articular injection of synovial stem cells for knee osteoarthritis" in December 2017 under the support of the AMED Research Project for Practical Application of Regenerative Medicine (PI: Ichiro Sekiya) to develop a treatment through a new route for synovial stem cells, and completed the observation period for all study subjects in March 2020. We plan to conduct a comparative study to promote this treatment in the near future.

We further developed MRI 3D analysis software that can automatically display cartilage defects in knee joints. This system was installed in a volume analyzer and released commercially in 2019. It is currently used in medical practices.

(4) Publications

[Original Articles]

1. Nobutake Ozeki, Hideyuki Koga, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Tomoyuki Saito, Takeshi Muneta, Ichiro Sekiya. Biomechanical analysis of the centralization procedure for extruded lateral menisci with posterior root deficiency in a porcine model. *J Orthop Sci.* 2020.01; 25(1); 161-166
2. Mai Katakura, Kaori Nakamura, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *Knee.* 2020.01; 27(1); 95-101
3. Hajime Utsunomiya, Ichiro Sekiya, Soshi Uchida.. Editorial Commentary:Are We Ready to Apply Stem Cell Therapy in Rotator Curr Tear Surgery? *Arthroscopy.* 2020.01; 36(1); 86-87
4. Kaori Nakamura, Tomomasa Nakamura, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Masaki Amemiya, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Anatomic femoral tunnel placement is difficult by the transtibial technique: comparison of three different femoral tunnel drilling techniques in double-bundle anterior cruciate ligament reconstructions. *Knee Surg Sports Traumatol Arthrosc.* 2020.02; 28(2); 584-593
5. Masaki Amemiya, Kunikazu Tsuji, Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Synovial fluid-derived mesenchymal cells have non-inferior chondrogenic potential and can be utilized for regenerative therapy as substitute for synovium-derived cells. *Biochem. Biophys. Res. Commun.* 2020.03; 523(2); 465-472
6. Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Masafumi Horie, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Validity of intraoperative observation of graft length change pattern for medial patellofemoral ligament reconstruction. *J Orthop.* 2020.03; 21; 131-136
7. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Ichiro Sekiya. The effect of a centralization procedure for extruded lateral meniscus on load distribution in porcine knee joints at different flexion angles. *BMC Musculoskelet Disord.* 2020.04; 21(1); 205
8. Toshifumi Watanabe, Hideyuki Koga, Koji Otabe, Yusuke Nakagawa, Takeshi Muneta, Ichiro Sekiya, Tetsuya Jinno.. Coronal and sagittal laxity affects clinical outcomes in posterior-stabilized total knee arthroplasty: assessment of well-functioning knees. *Knee Surg Sports Traumatol Arthrosc.* . 2020.05; 28(5); 1400-1409
9. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Kei Inomata, Mio Udo, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Fibrotic changes in the infrapatellar fat pad induce new vessel formation and sensory nerve fiber endings that associate prolonged pain. *J. Orthop. Res.* 2020.06; 38(6); 1296-1306
10. So Suzuki, Mitsuru Mizuno, Yuriko Sakamaki, Ayako Mimata, Kentaro Endo, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Morphological changes in synovial mesenchymal stem cells during their adhesion to the meniscus. *Lab. Invest.* 2020.07; 100(7); 916-927
11. Naoko Araya, Kazumasa Miyatake, Kunikazu Tsuji, Hiroki Katagiri, Yusuke Nakagawa, Takashi Hoshino, Hiroaki Onuma, Saisei An, Hirofumi Nishio, Yoshitomo Saita, Ichiro Sekiya, Hideyuki Koga. Intra-articular Injection of Pure Platelet-Rich Plasma Is the Most Effective Treatment for Joint Pain by

Modulating Synovial Inflammation and Calcitonin Gene-Related Peptide Expression in a Rat Arthritis Model. *Am J Sports Med.* 2020.07; 48(8); 2004-2012

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13. Mitsuru Mizuno, Kentaro Endo, Hisako Katano, Ayako Tsuji, Naomi Kojima, Ken Watanabe, Norio Shimizu, Tomohiro Morio, Ichiro Sekiya. The environmental risk assessment of cell-processing facilities for cell therapy in a Japanese academic institution. *PLoS ONE.* 2020.08; 15(8); e0236600
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16. Hayato Aoki, Nobutake Ozeki, Hisako Katano, Akinobu Hyodo, Yugo Miura, Junpei Matsuda, Kimiko Takanashi, Kenji Suzuki, Jun Masumoto, Noriya Okanouchi, Takeo Fujiwara, Ichiro Sekiya. Relationship between medial meniscus extrusion and cartilage measurements in the knee by fully automatic three-dimensional MRI analysis. *BMC Musculoskelet Disord.* 2020.11; 21(1); 742
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18. Naoto Watanabe, Kentaro Endo, Keiichiro Komori, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Yuji Kohno, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Mesenchymal Stem Cells in Synovial Fluid Increase in Knees with Degenerative Meniscus Injury after Arthroscopic Procedures through the Endogenous Effects of CGRP and HGF. *Stem cell reviews and reports..* 2020.12; 16(6); 1305-1315
19. Yoshihisa Kushida, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Koichiro Kishima, Yoshio Soma, Ichiro Sekiya. Two- and three-dimensional optical coherence tomography to differentiate degenerative changes in a rat meniscectomy model. *J Orthop Res.* 2020.12; 38(12); 2592-2600

[Misc]

1. Naoko Araya, Hiroki Katagiri, Yusuke Nakagawa, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga.. Predictors of residual mechanical symptoms after meniscus surgery: data from the maks group Osteoarthritis and Cartilage. 2020.04; 28(1); S221-S223

[Conference Activities & Talks]

1. Nobutake Ozeki, Hideyuki Koga, Hayato Aoki, Akinobu Hyodo, Hiroki Katagiri, Yusuke Nakagawa, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. 3D MRI Analysis For Cartilage In Anterior Cruciate Ligament Deficient Knee.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA
2. Kiyotaka Horiuchi, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Comparison Between Cultured Mscs And Non-cultured Mscs After Cryopreservation For Intra-articular Injections Into The Knee In A Rat Oa Model.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA
3. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Yuji Kohno, Junpei Matsuda, Yoshihisa Kushida, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Ichiro Sekiya.. The Effect Of Centralization Procedure For Extruded Lateral Meniscus On Load Distributionin Porcine Knee Joints At 30-90 Degrees Of Flexion.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA

4. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Tsuyoshi Kimura, Kunikazu Tsuji, Akio Kishida, Ichiro Sekiya.. The Amount Of Collagen Is Not Related To Mechanical Properties Of High Hydrostatic Pressure-decellularized Meniscus And Freeze-thawed Meniscus.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.09 Phoenix,USA
5. Hayato Aoki, Nobutake Ozeki, Akinobu Hyodo, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kenji Suzuki, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Learning Times And Segmentation Accuracy Of U-net Convolutional Neural Networks On Automatic Segmentation For Mri Of Knee.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.09 Phoenix,USA
6. So Suzuki, Mitsuru Mizuno, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Quantitative Morphological Analysis Of Synovial Mesenchymal Stem Cells During Adhesion To The Meniscus.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.10 Phoenix,USA
7. Akinobu Hyodo. Nobutake Ozeki, Hayato Aoki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. Radial Projected Femoral Cartilage Area By Automatic Cartilage Segmentation For The Knee MRI.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.11 Phoenix,USA
8. Yoshihisa Kushida, Nobutake Ozeki, Hisako Katano, Mitsuru Mizuno, Ichiro Sekiya.. 2D And 3D Optical Coherence Tomography To Differentiate Degenerative Changes In A Rat Meniscectomy Model.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.11 Phoenix,USA

Medical Science Mathematics

Professor: Tatsuhiko Tsunoda, Junior Associate Professor: Fuyuki Miya,
Assistant Professor: Jo Nishino, Assistant Professor: Takashi Kamatani

(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. Nishiguchi Koji M., Fujita Kosuke, Miya Fuyuki, Katayama Shota, Nakazawa Toru. Single AAV-mediated mutation replacement genome editing in limited number of photoreceptors restores vision in mice NATURE COMMUNICATIONS. 2020.01; 11(1); 482
2. Jo Nishino, Shuichi Watanabe, Fuyuki Miya, Takashi Kamatani, Toshitaka Sugawara, Keith A Boroevich, Tatsuhiko Tsunoda. Quantification of multicellular colonization in tumor metastasis using exome-sequencing data. Int. J. Cancer. 2020.02; 146(9); 2488-2497
3. Shuai S; PCAWG Drivers and Functional Interpretation Working Group ((Tsunoda T et al), Gallinger S, Stein L; PCAWG Consortium.. Combined burden and functional impact tests for cancer driver discovery using DriverPower. Nat Commun. 2020.02; 11(1); 734
4. Paczkowska M, Barenboim J, Sintupisut N, Fox NS, Zhu H, Abd-Rabbo D, Mee MW, Boutros PC; PCAWG Drivers and Functional Interpretation Working Group (Tsunoda T et al), Reimand J; PCAWG Consortium.. Integrative pathway enrichment analysis of multivariate omics data. Nat Commun. 2020.02; 11(1); 735
5. Barenboim J, Wadi L, Dhingra P, Shrestha R, Getz G, Lawrence MS, Pedersen JS, Rubin MA, Wheeler DA, Brunak S, Izarzugaza JMG, Khurana E, Marchal K, von Mering C, Sahinalp SC, Valencia A; PCAWG Drivers and Functional Interpretation Working Group (Tsunoda T et al), Reimand J, Stuart JM, Raphael BJ; PCAWG Consortium.. Pathway and network analysis of more than 2500 whole cancer genomes. Nat Commun. 2020.02; 11(1); 729
6. Carlevaro-Fita J, Lanzós A, Feuerbach L, Hong C, Mas-Ponte D, Pedersen JS; PCAWG Drivers and Functional Interpretation Group (Tsunoda T et al), Johnson R; PCAWG Consortium.. Cancer LncRNA Census reveals evidence for deep functional conservation of long noncoding RNAs in tumorigenesis. Commun Biol. 2020.02; 3(1); 56

7. ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium.. Pan-cancer analysis of whole genomes. *Nature*. 2020.02; 578(7793); 82-93
8. Esther Rheinbay, Morten Muhlig Nielsen, Federico Abascal, Jeremiah A Wala, Ofer Shapira, Grace Tiao, Henrik Hornshøj, Julian M Hess, Randi Istrup Juul, Ziao Lin, Lars Feuerbach, Radhakrishnan Sabarinathan, Tobias Madsen, Jaegil Kim, Loris Mularoni, Shimin Shuai, Andrés Lanzós, Carl Herrmann, Yosef E Maruvka, Ciyue Shen, Samirkumar B Amin, Pratiti Bandopadhyay, Johanna Bertl, Keith A Boroevich, John Busanovich, Joana Carlevaro-Fita, Dimple Chakravarty, Calvin Wing Yiu Chan, David Craft, Priyanka Dhingra, Klev Diamanti, Nuno A Fonseca, Abel Gonzalez-Perez, Qianyun Guo, Mark P Hamilton, Nicholas J Haradhvala, Chen Hong, Keren Isaev, Todd A Johnson, Malene Juul, Andre Kahles, Abdullah Kahraman, Youngwook Kim, Jan Komorowski, Kiran Kumar, Sushant Kumar, Donghoon Lee, Kjong-Van Lehmann, Yilong Li, Eric Minwei Liu, Lucas Lochovsky, Keunchil Park, Oriol Pich, Nicola D Roberts, Gordon Saksena, Steven E Schumacher, Nikos Sidiropoulos, Lina Sieverling, Nasa Sinnott-Armstrong, Chip Stewart, David Tamborero, Jose M C Tubio, Husen M Umer, Liis Uusküla-Reimand, Claes Wadelius, Lina Wadi, Xiaotong Yao, Cheng-Zhong Zhang, Jing Zhang, James E Haber, Asger Hobolth, Marcin Imielinski, Manolis Kellis, Michael S Lawrence, Christian von Mering, Hidewaki Nakagawa, Benjamin J Raphael, Mark A Rubin, Chris Sander, Lincoln D Stein, Joshua M Stuart, Tatsuhiko Tsunoda, David A Wheeler, Rory Johnson, Jüri Reimand, Mark Gerstein, Ekta Khurana, Peter J Campbell, Núria López-Bigas, , , Joachim Weischenfeldt, Rameen Beroukhim, Iñigo Martincorena, Jakob Skou Pedersen, Gad Getz, . Analyses of non-coding somatic drivers in 2,658 cancer whole genomes. *Nature*. 2020.02; 578(7793); 102-111
9. PCAWG Transcriptome Core Group, Claudia Calabrese, Natalie R Davidson, Deniz Demircioğlu, Nuno A Fonseca, Yao He, André Kahles, Kjong-Van Lehmann, Fenglin Liu, Yuichi Shiraiishi, Cameron M Soulette, Lara Urban, Liliana Greger, Siliang Li, Dongbing Liu, Marc D Perry, Qian Xiang, Fan Zhang, Junjun Zhang, Peter Bailey, Serap Erkek, Katherine A Hoadley, Yong Hou, Matthew R Huska, Helena Kilpinen, Jan O Korbelt, Maximillian G Marin, Julia Markowski, Tannistha Nandi, Qiang Pan-Hammarström, Chandra Sekhar Pedamallu, Reiner Siebert, Stefan G Stark, Hong Su, Patrick Tan, Sebastian M Waszak, Christina Yung, Shida Zhu, Philip Awadalla, Chad J Creighton, Matthew Meyerson, B F Francis Ouellette, Kui Wu, Huanming Yang, , Alvis Brazma, Angela N Brooks, Jonathan Göke, Gunnar Rättsch, Roland F Schwarz, Oliver Stegle, Zemin Zhang, PCAWG Consortium (including Tsunoda T).. Genomic basis for RNA alterations in cancer. *Nature*. 2020.02; 578(7793); 129-136
10. Ludmil B Alexandrov, Jaegil Kim, Nicholas J Haradhvala, Mi Ni Huang, Alvin Wei Tian Ng, Yang Wu, Arnoud Boot, Kyle R Covington, Dmitry A Gordenin, Erik N Bergstrom, S M Ashiqul Islam, Nuria Lopez-Bigas, Leszek J Klimczak, John R McPherson, Sandro Morganello, Radhakrishnan Sabarinathan, David A Wheeler, Ville Mustonen, , Gad Getz, Steven G Rozen, Michael R Stratton, PCAWG Consortium (including Tsunoda T).. The repertoire of mutational signatures in human cancer. *Nature*. 2020.02; 578(7793); 94-101
11. Moritz Gerstung, Clemency Jolly, Ignaty Leshchiner, Stefan C Dentre, Santiago Gonzalez, Daniel Rosebrock, Thomas J Mitchell, Yulia Rubanova, Pavana Anur, Kaixian Yu, Maxime Tarabichi, Amit Deshwar, Jeff Wintersinger, Kortine Kleinheinz, Ignacio Vázquez-García, Kerstin Haase, Lara Jerman, Subhajt Sengupta, Geoff Macintyre, Salem Malikic, Nilgun Donmez, Dimitri G Livitz, Marek Cmero, Jonas Demeulemeester, Steven Schumacher, Yu Fan, Xiaotong Yao, Juhee Lee, Matthias Schlesner, Paul C Boutros, David D Bowtell, Hongtu Zhu, Gad Getz, Marcin Imielinski, Rameen Beroukhim, S Cenk Sahinalp, Yuan Ji, Martin Peifer, Florian Markowitz, Ville Mustonen, Ke Yuan, Wenyi Wang, Quaid D Morris, , Paul T Spellman, David C Wedge, Peter Van Loo, PCAWG Consortium (including Tsunoda T).. The evolutionary history of 2,658 cancers. *Nature*. 2020.02; 578(7793); 122-128
12. Yilong Li, Nicola D Roberts, Jeremiah A Wala, Ofer Shapira, Steven E Schumacher, Kiran Kumar, Ekta Khurana, Sebastian Waszak, Jan O Korbelt, James E Haber, Marcin Imielinski, , Joachim Weischenfeldt, Rameen Beroukhim, Peter J Campbell, PCAWG Consortium (including Tsunoda T).. Patterns of somatic structural variation in human cancer genomes. *Nature*. 2020.02; 578(7793); 112-121
13. Isidro Cortés-Ciriano, Jake June-Koo Lee, Ruibin Xi, Dhawal Jain, Youngsook L Jung, Lixing Yang, Dmitry Gordenin, Leszek J Klimczak, Cheng-Zhong Zhang, David S Pellman, , Peter J Park, PCAWG Consortium (including Tsunoda T).. Comprehensive analysis of chromothripsis in 2,658 human cancers using whole-genome sequencing. *Nat. Genet.* 2020.02;

14. Marc Zapatka, Ivan Borozan, Daniel S Brewer, Murat Iskar, Adam Grundhoff, Malik Alawi, Nikita Desai, Holger Sültmann, Holger Moch, , Colin S Cooper, Roland Eils, Vincent Ferretti, Peter Lichter, PCAWG Consortium (including Tsunoda T).. The landscape of viral associations in human cancers. *Nat. Genet.*.. 2020.02; 52(3); 320-330
15. Kadir C Akdemir, Victoria T Le, Sahaana Chandran, Yilong Li, Roel G Verhaak, Rameen Beroukhim, Peter J Campbell, Lynda Chin, Jesse R Dixon, P Andrew Futreal, PCAWG Consortium (including Tsunoda T).. Disruption of chromatin folding domains by somatic genomic rearrangements in human cancer. *Nat. Genet.*.. 2020.02; 52(3); 294-305
16. Bernardo Rodriguez-Martin, Eva G Alvarez, Adrian Baez-Ortega, Jorge Zamora, Fran Supek, Jonas Demeulemeester, Martin Santamarina, Young Seok Ju, Javier Temes, Daniel Garcia-Souto, Harald Detering, Yilong Li, Jorge Rodriguez-Castro, Ana Dueso-Barroso, Alicia L Bruzos, Stefan C Dentre, Miguel G Blanco, Gianmarco Contino, Daniel Ardeljan, Marta Tojo, Nicola D Roberts, Sonia Zumalave, Paul A W Edwards, Joachim Weischenfeldt, Montserrat Puiggròs, Zechen Chong, Ken Chen, Eunjung Alice Lee, Jeremiah A Wala, Keiran Raine, Adam Butler, Sebastian M Waszak, Fabio C P Navarro, Steven E Schumacher, Jean Monlong, Francesco Maura, Niccolo Bolli, Guillaume Bourque, Mark Gerstein, Peter J Park, David C Wedge, Rameen Beroukhim, David Torrents, Jan O Korbel, Inigo Martincorena, Rebecca C Fitzgerald, Peter Van Loo, Haig H Kazazian, Kathleen H Burns, , Peter J Campbell, Jose M C Tubio, PCAWG Consortium (including Tsunoda T).. Pan-cancer analysis of whole genomes identifies driver rearrangements promoted by LINE-1 retrotransposition. *Nat. Genet.*.. 2020.02; 52(3); 306-319
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18. Sergei Yakneen, Sebastian M Waszak, , Michael Gertz, Jan O Korbel, PCAWG Consortium (including Tsunoda T).. Butler enables rapid cloud-based analysis of thousands of human genomes. *Nat. Biotechnol.*.. 2020.02;
19. Wei Jiao, Gurnit Atwal, Paz Polak, Rosa Karlic, Edwin Cuppen, , Alexandra Danyi, Jeroen de Ridder, Carla van Herpen, Martijn P Lolkema, Neeltje Steeghs, Gad Getz, Quaid Morris, Lincoln D Stein, PCAWG Consortium (including Tsunoda T).. A deep learning system accurately classifies primary and metastatic cancers using passenger mutation patterns. *Nat Commun.* 2020.02; 11(1); 728
20. Marek Cmero, Ke Yuan, Cheng Soon Ong, Jan Schröder, , Niall M Corcoran, Tony Papenfuss, Christopher M Hovens, Florian Markowetz, Geoff Macintyre, PCAWG Consortium (including Tsunoda T).. Inferring structural variant cancer cell fraction. *Nat Commun.* 2020.02; 11(1); 730
21. Yulia Rubanova, Ruian Shi, Caitlin F Harrigan, Roujia Li, Jeff Wintersinger, Nil Sahin, Amit Deshwar, , Quaid Morris, PCAWG Consortium (including Tsunoda T).. Reconstructing evolutionary trajectories of mutation signature activities in cancer using TrackSig. *Nat Commun.* 2020.02; 11(1); 731
22. Yiqun Zhang, Fengju Chen, Nuno A Fonseca, Yao He, Masashi Fujita, Hidewaki Nakagawa, Zemin Zhang, Alvis Brazma, , , Chad J Creighton, PCAWG Consortium (including Tsunoda T).. High-coverage whole-genome analysis of 1220 cancers reveals hundreds of genes deregulated by rearrangement-mediated cis-regulatory alterations. *Nat Commun.* 2020.02; 11(1); 736
23. Vinayak Bhandari, Constance H Li, Robert G Bristow, Paul C Boutros, PCAWG Consortium (including Tsunoda T).. Divergent mutational processes distinguish hypoxic and normoxic tumours. *Nat Commun.* 2020.02; 11(1); 737
24. Lina Sieverling, Chen Hong, Sandra D Koser, Philip Ginsbach, Kortine Kleinheinz, Barbara Hutter, Delia M Braun, Isidro Cortés-Ciriano, Ruibin Xi, Rolf Kabbe, Peter J Park, Roland Eils, Matthias Schlesner, , Benedikt Brors, Karsten Rippe, David T W Jones, Lars Feuerbach, PCAWG Consortium (including Tsunoda T).. Genomic footprints of activated telomere maintenance mechanisms in cancer. *Nat Commun.* 2020.02; 11(1); 733
25. Kazunari Onodera, Daisuke Shimojo, Yasuharu Ishihara, Masato Yano, Fuyuki Miya, Haruhiko Banno, Naoko Kuzumaki, Takuji Ito, Rina Okada, Bruno de Araújo Herculano, Manabu Ohyama, Mari Yoshida,

- Tatsuhiko Tsunoda, Masahisa Katsuno, Manabu Doyu, Gen Sobue, Hideyuki Okano, Yohei Okada. Unveiling synapse pathology in spinal bulbar muscular atrophy by genome-wide transcriptome analysis of purified motor neurons derived from disease specific iPSCs. *Mol Brain*. 2020.02; 13(1); 18
26. Sato Taimu, Nishiguchi Koji M., Fujita Kosuke, Miya Fuyuki, Inoue Takashi, Sasaki Erika, Asano Toshifumi, Tsuda Satoru, Shiga Yukihiro, Kunikata Hiroshi, Nakazawa Mitsuru, Nakazawa Toru. Serum anti-recoverin antibodies is found in elderly patients with retinitis pigmentosa and cancer *ACTA OPHTHALMOLOGICA*. 2020.02;
 27. Hideki Mutai, Koichiro Wasano, Yukihide Momozawa, Yoichiro Kamatani, Fuyuki Miya, Sawako Masuda, Noriko Morimoto, Kiyomitsu Nara, Satoe Takahashi, Tatsuhiko Tsunoda, Kazuaki Homma, Michiaki Kubo, Tatsuo Matsunaga. Variants encoding a restricted carboxy-terminal domain of SLC12A2 cause hereditary hearing loss in humans. *PLoS Genet.*. 2020.04; 16(4); e1008643
 28. Wafaa Wardah, Abdollah Dehzangi, Ghazaleh Taherzadeh, Mahmood A Rashid, M G M Khan, Tatsuhiko Tsunoda, Alok Sharma. Predicting protein-peptide binding sites with a Deep Convolutional Neural Network. *J. Theor. Biol.*. 2020.04; 110278
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 30. Ronesh Sharma, Shiu Kumar, Tatsuhiko Tsunoda, Thirumananseri Kumarevel, Alok Sharma. Single-stranded and double-stranded DNA-binding protein prediction using HMM profiles. *Anal Biochem*. 2020.09; 612; 113954
 31. Bailey MH, Meyerson WU, Dursi LJ, Wang LB, Dong G, Liang WW, Weerasinghe A, Li S, Kelso S; MC3 Working Group; PCAWG novel somatic mutation calling methods working group, Saksena G, Ellrott K, Wendl MC, Wheeler DA, Getz G, Simpson JT, Gerstein MB, Ding L; PCAWG Consortium (including Tsunoda T).. Retrospective evaluation of whole exome and genome mutation calls in 746 cancer samples. *Nat Commun*. 2020.09; 11(1); 4748
 32. Jun Hosoe, Fuyuki Miya, Hiroko Kadowaki, Toyofumi Fujiwara, Ken Suzuki, Takashi Kato, Hironori Waki, Takayoshi Sasako, Katsuya Aizu, Natsumi Yamamura, Fusako Sasaki, Makoto Kurano, Kazuo Hara, Masaki Tanaka, Hiroyuki Ishiura, Shoji Tsuji, Kenjiro Honda, Jun Yoshimura, Shinichi Morishita, Fumiko Matsuzawa, Sei-Ichi Aikawa, Keith A Boroevich, Masaomi Nangaku, Yukinori Okada, Tatsuhiko Tsunoda, Nobuhiro Shojima, Toshimasa Yamauchi, Takashi Kadowaki. Clinical usefulness of multigene screening with phenotype-driven bioinformatics analysis for the diagnosis of patients with monogenic diabetes or severe insulin resistance. *Diabetes Res. Clin. Pract.*. 2020.09; 108461
 33. Todd A Johnson, Yoichi Mashimo, Jer-Yuarn Wu, Dankyu Yoon, Akira Hata, Michiaki Kubo, Atsushi Takahashi, Tatsuhiko Tsunoda, Kouichi Ozaki, Toshihiro Tanaka, Kaoru Ito, Hiroyuki Suzuki, Hiromichi Hamada, Tooru Kobayashi, Toshiro Hara, Chien-Hsiun Chen, Yi-Ching Lee, Yi-Min Liu, Li-Ching Chang, Chun-Ping Chang, Young-Mi Hong, Gi-Young Jang, Sin-Weon Yun, Jeong-Jin Yu, Kyung-Yil Lee, Jae-Jung Kim, Taesung Park, , Jong-Keuk Lee, Yuan-Tsong Chen, Yoshihiro Onouchi. Association of an IGHV3-66 gene variant with Kawasaki disease. *J Hum Genet*. 2020.10;
 34. Yasuyoshi Sato, Ikuo Wada, Kosuke Odaira, Akihiro Hosoi, Yukari Kobayashi, Koji Nagaoka, Takahiro Karasaki, Hirokazu Matsushita, Koichi Yagi, Hiroharu Yamashita, Masashi Fujita, Shuichi Watanabe, Takashi Kamatani, Fuyuki Miya, Junichi Mieno, Hidewaki Nakagawa, Tatsuhiko Tsunoda, Shunji Takahashi, Yasuyuki Seto, Kazuhiro Kakimi. Integrative immunogenomic analysis of gastric cancer dictates novel immunological classification and the functional status of tumor-infiltrating cells. *Clin Transl Immunology*. 2020.10; 9(10); e1194
 35. Kato Kohji, Miya Fuyuki, Oka Yasuyoshi, Mizuno Seiji, Saitoh Shinji. A novel missense variant in CUL3 shows altered binding ability to BTB-adaptor proteins leading to diverse phenotypes of CUL3-related disorders *JOURNAL OF HUMAN GENETICS*. 2020.10;
 36. Daichi Shigemizu, Shintaro Akiyama, Sayuri Higaki, Taiki Sugimoto, Takashi Sakurai, Keith A Boroevich, Alok Sharma, Tatsuhiko Tsunoda, Takahiro Ochiya, Shumpei Niida, Kouichi Ozaki. Prognosis prediction model for conversion from mild cognitive impairment to Alzheimer's disease created by integrative analysis of multi-omics data. *Alzheimers Res Ther*. 2020.11; 12(1); 145

37. Vineet Singh, Alok Sharma, Abdollah Dehzangi, Tatushiko Tsunoda. PupStruct: Prediction of Pupylylated Lysine Residues Using Structural Properties of Amino Acids. *Genes (Basel)*. 2020.11; 11(12); E1431
38. Abel Avitesh Chandra, Alok Sharma, Abdollah Dehzangi, Tatushiko Tsunoda. RAM-PGK: Prediction of Lysine Phosphoglycerylation Based on Residue Adjacency Matrix. *Genes (Basel)*. 2020.12; 11(12);

[Conference Activities & Talks]

1. Tatushiko Tsunoda. Personalized Cancer Medicine with Heterogeneity and Immunological Analysis. CREST International Symposium on Big Data Application 2020.01.13 Tokyo

[Patents]

1. METHOD FOR SELECTING IPS CELL CLONE, AND METHOD FOR SELECTING GENE USED IN METHOD FOR SELECTING SAME, Announcement Number : WO 2012/115270

Functional Material

Tsuyoshi KIMURA

(1) Research

1) Specific capture of Treg cells

In order to remove Treg cells, which induce immunotolerance, a device of capturing of Treg cells is developed.

2) Decellularization of native tissue for regenerative medicine

In order to obtain a novel scaffold, which can be applied for regenerative tissue, ultra-high pressurization method was developed for the complete elimination of the cells and inactivation of the viruses.

3) Inducing molecular aggregation using ultra-high pressurization

The basic and applied science on molecular aggregation triggered by hydrogen bonding at over 6,000 atm is studied. This technique is being applied for hybridization of DNA with polymer for drug delivery system.

4) Bio-interface

To investigate how the materials interact with biological cues such as phospholipids, proteins, or cells, precisely controlled surface via atomic transfer radical polymerization was prepared. The basic research on physical and biological properties of this surface is being investigated.

(2) Education

In order to develop technology, which may contribute to the advance in the medical science, lectures on functional molecules from basic to advanced knowledge on molecular design for specific purpose, mainly concentrated on medical application would be executed. Theories on functional molecules and overviews on medical system would be lectured in Graduate School of Medical and Dental Sciences. Students would have chances to learn about Genomics and Bio-intelligent system in Graduate School of Biomedical Science.

(3) Publications

[Original Articles]

1. Masaki Watanabe, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Characterization of engineering plastics plasticized using supercritical CO₂ Polymers. 2020.01; 12(1); 134
2. Yongwei Zhang, Kwangwoo Nam, Tsuyoshi Kimura, Pingli Wu, Naoko Nakamura, Yoshihide Hashimoto, Seiichi Funamoto, Akio Kishida. Preparation of gradient-type biological tissue-polymer complex for interlinking device Mater. Sci. Eng. C-Mater. Biol. Appl. 2020.09; 114; 111017
3. Mako Kobayashi, Junpei Kadota, Yoshihide Hashimoto, Toshiya Fujisato, Naoko Nakamura, Tsuyoshi Kimura, Akio Kishida. Elastic modulus of ECM hydrogels derived from decellularized tissue affects capillary network formation in endothelial cells Int. J. Mol. Sci. 2020.09; 21(17); 6304
4. Naoko Nakamura, Kazuki Saito, Tsuyoshi Kimura, Akio Kishida. Recellularization of decellularized cancellous bone scaffolds using low temperature cell seeding Tissue and Cell. 2020.10; 66; 101385

5. Mako Kobayashi, Masao Ohara, Yoshihide Hashimoto, Naoko Nakamura, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. In vitro evaluation of surface biological properties of decellularized cardiovascular use J. Mater. Chem. B. 2020.12; 2020(48); 10977-10989
6. Masaki Watanabe, Hanako Maeda, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Protein adsorption and cell adhesion behavior of engineering plastics plasticized by supercritical carbon dioxide Dent. Mater. J. 2020.12; 39(6); 1033-1038

JFCR Cancer Biology

Professor Takuro NAKAMURA

Professor Noriko SAITOH

Professor Kiyotaka SHIBA

Professor Kengo TAKEUCHI

Professor Akihiro TOMIDA

Professor Toru HIROTA

Graduate Student Yoshiharu Kusama, Ayumi
Fujimoto, Hironobu Sugita, Saho Matsui

(1) Research

Understanding the mechanisms of carcinogenesis and cancer progression. Studying the basics of personalized medicine for innovative cancer therapy.

(2) Education

We are committed to training talented and motivated graduate students, helping launch careers in basic and translational cancer research.

1. Molecular mechanisms of carcinogenesis and identification of cell-of-origin of cancer (Nakamura)
2. Understanding of molecular mechanisms for epigenetic regulation in breast cancer (Saitoh)
3. Application of nanobiotechnology in cancer diagnostics (Shiba)
4. Pathological and genetic analysis of human cancer such as malignant lymphoma and lung cancer (Takeuchi)
5. Strategy for innovative drug therapy based on cancer biology (Tomida)
6. To understand how chromosomes are assembled and segregated in mitosis, and to elucidate the pathology underlying chromosomal instability in cancers (Hirota)

(3) Publications

[Original Articles]

1. *Ochiai, H., Hayashi T., Umeda, M., Yoshimura, M., Harada, A., Shimizu, Y., Nakano, K., Saitoh, N., Liu, Z., Yamamoto, T., Okamura, T., Ohkawa, Y., Kimura, H., *Nikaido, I. (2020). Genome-wide analysis of kinetic properties of transcriptional bursting in mammalian cells. **Science Advances**, 6, eaaz6699.

2. #Yamamoto, T., *#Hirose, A., Nakamoto, M., Yoshida, R., Sakata, J., Matsuoka, Y., Kawahara, K., Nagao, Y., Nagata, M., Takahashi, N., Hiraki, A., Shinohara, M., Nakao, M., *Saitoh, N., Nakayama, H. (2020). BRD4 promotes metastatic potential in oral squamous cell carcinoma through the epigenetic regulation of the MMP2 gene. **Br. J. Cancer**, 123, 580–590.
3. #Fujita, R., #Yamamoto, T., Arimura, Y., Fujiwara, S., Tachiwana, H., Ichikawa, Y., Sakata, S., Yang, L., Maruyama, R., Hamada, M., Nakao, M., *Saitoh, N., *Kurumizaka, H. (2020). Nucleosome destabilization by nuclear non-coding RNAs. **Commun. Biol.**, 3 (1), 60.
4. Yasuda, Y., Tokunaga, K., Koga, T., Goldberg, I., Sakamoto, C., * Saitoh, N., *Nakao, M. (2020). Computational analysis of morphological and molecular features in gastric cancer tissues. **Cancer Med.** 9, 2223-2234.
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[Review Articles]

1. *Nozawa, R., Yamamoto, T., Takahashi, M., Tachiwana, H., Maruyama, R., Hirota T., *Saitoh, N. (2020). Nuclear microenvironment in cancer: control through liquid-liquid phase separation. **Cancer Sci**, 111, 3155–3163.
2. Tachiwana, H., Yamamoto, T., *Saitoh, N. (2020.) Gene regulation by non-coding RNAs in the 3D genome architecture. **Curr. Opin. Genet. Dev**, 61, 69–74.
3. Sakamoto K, Takeuchi K. Cytogenetics of Blastic Plasmacytoid Dendritic Cell Neoplasm: Chromosomal Rearrangements and DNA Copy-Number Alterations. **Hematol Oncol Clin North Am**. 2020;34:523-538.
4. Nakayama, I., Hirota, T., Shinozaki, E. (2020) BRAF mutation in colorectal cancers: from prognostic marker to targetable mutation. Review. **Cancers** 12: 3236.

[Conference Activities & Talks]

1. Yamamoto, T., Ichikawa, Y., Fukuoka, M., Saitoh, N. *Eleanor* ncRNAs modulate the 3D genome architecture in recurrent breast cancer. Cold Spring Harbor Laboratory Meeting: Genome Organization & Nuclear Function, April 30, 2020 (April 28, 2020, Virtual Meeting)
2. Toru Hirota: How activity of Aurora B is controlled at centromeres in mitosis. Seminar. Okinawa Institute of Science and Technology, Feb 5, 2020.
3. Eriko Sasaki and Toru Hirota: Symposium “How does genome reorganization drive ecological evolution?” The 43rd Annual meeting of the Molecular Biology Society of Japan (MBSJ). Kobe, Dec 3, 2020.

Organogenesis and Neogenesis

Professor TAKEBE Takanori
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(1) Outline

The Takebe Lab enjoys developing new technology and implementing fresh outlooks on discoveries that may be ignored, under-appreciated and overlooked by the traditional scientific community. The Takebe Lab takes a creative lead for the exploitation and dissemination of unpredictable, extraordinary and crazy paradigm by integrating discovery and technology, eventually revolutionizing science, and medico-health-care paradigm. The Takebe Lab is also lending its support to commercial execution to move forward.

The self-organizing tissue-based approach coupled with induced pluripotent stem cell (iPSC) technology has just begun as a promising field for designing a miniature organ, aka an organoid, in culture and is expected to achieve valuable outcomes in ‘(re-) generative medicine’ and ‘drug development’. However, how the complex but stereotyped tissue shapes self-organize still remains largely unknown. To understand such complex self-organizing mechanisms, Dr Takebe’s lab proposes to take a ‘reverse reductionism approach’ for a holistic mechanistic understanding of the dynamic nature of a self-developing system. We also seek to translate knowledge of living systems into a revolutionary technology platform towards practical biomedical use in clinics.

(2) Research

Organoids are multicellular structures that can be derived from adult organs or pluripotent stem cells. Early versions of organoids range from simple epithelial structures to complex, disorganized tissues with large cellular diversity. The current challenge is to engineer cellular complexity into organoids in a controlled manner that results in organized assembly and acquisition of tissue function. These efforts have relied on studies of organ assembly during embryonic development and have resulted in development of organoids with multilayer tissue complexity and higher order functions. To advance the field forward, Takebe Lab would like to achieve three interactive and complementary goals:

1. The deductive development of a complex human organoid model
2. The multidisciplinary dissection of self-driven mechanisms of organogenesis
3. The technology prototyping towards biomedical applications

Our early efforts are being made on liver organoid (liver bud or miniature liver) systems using human iPSC. For example, we have demonstrated successful integration of endothelial cells (Nature, 2013), mesenchymal cells (Cell Stem Cell, 2015) and macrophages (Cell Metab, 2019) into human liver organoids, allowing for the study of drug testing and transplant applications. More recently, we showed the inter-coordinated specification and invagination of the human hepato-biliary-pancreatic system from human pluripotent stem cells, thereby, connecting multi-organ systems in a dish (Nature, 2019). Thus we are tackling the questions how the next generation of organoids can be designed by utilizing an engineering-based narrative design, and what promise and impact will be brought towards future biomedical applications (Science, 2019). Our interested expertise includes cell biology, mathematics, bioinformatics, morphogenesis, genomics, bioengineering, chemistry or biomechanics. In a longer term, we seek to realize “organoid medicine” applications through human implementation of extracorporeal device, precision medicine, drug discovery and organ replacement therapy. We are accelerating such biomedical applications of organoids by collaborating with international and diverse industry collaborators, such as the Cincinnati Children’s Hospital and the Takeda-CiRA program.

(3) Publications

[Original Articles]

1. Hayashi H, Osaka S, Sakabe K, Fukami A, Kishimoto E, Aihara E, Sabu Y, Mizutani A, Kusuvara H, Naritaka N, Zhang W, Huppert SS, Sakabe M, Nakamura T, Hu YC, Mayhew C, Setchell K, Takebe T, Asai A. Modeling Human Bile Acid Transport and Synthesis in Stem Cell-Derived Hepatocytes with a Patient-Specific Mutation. *Stem cell reports*. 2020.12;
2. Sekine K, Ogawa S, Tsuzuki S, Kobayashi T, Ikeda K, Nakanishi N, Takeuchi K, Kanai E, Otake Y, Okamoto S, Kobayashi T, Takebe T, Taniguchi H. Generation of human induced pluripotent stem cell-derived liver buds with chemically defined and animal origin-free media. *Scientific reports*. 2020.10; 10(1); 17937
3. Shinozawa T, Kimura M, Cai Y, Saiki N, Yoneyama Y, Ouchi R, Koike H, Maezawa M, Zhang RR, Dunn A, Ferguson A, Togo S, Lewis K, Thompson W, Asai A, Takebe T. High-Fidelity Drug-Induced Liver Injury Screen Using Human Pluripotent Stem Cell-Derived Organoids. *Gastroenterology*. 2020.10;
4. Koido M, Kawakami E, Fukumura J, Noguchi Y, Ohori M, Nio Y, Nicoletti P, Aithal GP, Daly AK, Watkins PB, Anayama H, Dragan Y, Shinozawa T, Takebe T. Polygenic architecture informs potential vulnerability to drug-induced liver injury. *Nature medicine*. 2020.10; 26(10); 1541-1548
5. Okabe R, Chen-Yoshikawa TF, Yoshizawa A, Hirashima T, Saito M, Date H, Takebe T. Orthotopic foetal lung tissue direct injection into lung showed a preventive effect against paraquat-induced acute lung injury in mice. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*. 2020.09; 58(3); 638-645
6. Kobayashi Naritaka, Togo Shodai, Matsuzaki Takahisa, Hashiseko Kaede, Kawamura Ryuzo, Suganuma Masami, Nakabayashi Seiichiro, Yoneyama Yosuke, Ouchi Rie, Takebe Takanori, Yoshikawa Hiroshi Y.. Stiffness distribution analysis in indentation depth direction reveals clear mechanical features of cells and organoids by using AFM *APPLIED PHYSICS EXPRESS*. 2020.09; 13(9);
7. Kobayashi Naritaka, Togo Shodai, Matsuzaki Takahisa, Hashiseko Kaede, Kawamura Ryuzo, Suganuma Masami, Nakabayashi Seiichiro, Yoneyama Yosuke, Ouchi Rie, Takebe Takanori, Yoshikawa Hiroshi Y.. Stiffness distribution analysis in indentation depth direction reveals clear mechanical features of cells and organoids by using AFM *APPLIED PHYSICS EXPRESS*. 2020.09; 13(9);
8. Choi US, Kawaguchi H, Kida I. Cerebral artery segmentation based on magnetization-prepared two rapid acquisition gradient echo multi-contrast images in 7 Tesla magnetic resonance imaging. *NeuroImage*. 2020.08; 117259

9. Han L, Chaturvedi P, Kishimoto K, Koike H, Nasr T, Iwasawa K, Giesbrecht K, Witcher PC, Eicher A, Haines L, Lee Y, Shannon JM, Morimoto M, Wells JM, Takebe T, Zorn AM. Single cell transcriptomics identifies a signaling network coordinating endoderm and mesoderm diversification during foregut organogenesis. *Nature communications*. 2020.08; 11(1); 4158
10. Naganawa Shinji, Nakane Toshiki, Kawai Hisashi, Taoka Toshiaki, Kawaguchi Hirokazu, Maruyama Katsuya, Murata Katsutoshi, Koerzdoerfer Gregor, Pfeuffer Josef, Nittka Mathias, Sone Michihiko. Detection of IV-gadolinium Leakage from the Cortical Veins into the CSF Using MR Fingerprinting(和訳中) *Magnetic Resonance in Medical Sciences*. 2020.05; 19(2); 141-146
11. Sakabe K, Takebe T, Asai A. Organoid Medicine in Hepatology. *Clinical liver disease*. 2020.01; 15(1); 3-8
12. Naganawa Shinji, Nakane Toshiki, Kawai Hisashi, Taoka Toshiaki, Kawaguchi Hirokazu, Maruyama Katsuya, Murata Katsutoshi, Koerzdoerfer Gregor, Pfeuffer Josef, Nittka Mathias, Sone Michihiko. Detection of IV-gadolinium Leakage from the Cortical Veins into the CSF Using MR Fingerprinting *MAGNETIC RESONANCE IN MEDICAL SCIENCES*. 2020; 19(2); 141-146
13. Thompson WL, Takebe T. Generation of multi-cellular human liver organoids from pluripotent stem cells. *Methods in cell biology*. 2020; 159; 47-68
14. Okino R, Usui A, Yoneyama Y, Takahashi SI, Hakuno F. Myoblasts With Higher IRS-1 Levels Are Eliminated From the Normal Cell Layer During Differentiation. *Frontiers in endocrinology*. 2020; 11; 96

[Conference Activities & Talks]

1. Takebe T. Promise and Impact of Organoid Medicine. 金沢大学 NanoLSI 第 4 回国際シンポジウム 2020.11.26 Web
2. Takebe T. Organoids by Design. ISSCR Organoids Webinar 2020.10.27 Web
3. Takebe T. From pluripotency to organoids -finding a clue to reproducibility by live incubation monitoring. ISSCR 講演 2020.06.25 web
4. Sakurako Kobayashi, Satoshi Watanabe, Yosuke Yoneyama, Kousuke Tanimoto, Ryu Nishimura, Sayaka Nagata, Masami Inoue, Kouhei Suzuki, Sei Kakinuma, Kiichiro Tsuchiya, Ryuichi Okamoto, Mamoru Watanabe, Takanori Takebe, Shiro Yui. Conceptual basis of lineage shift between intestinal epithelium and hepatocytes. *Keystone Symposia, Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease* 2020.01.22 Vancouver (Canada)
1. A new approach for studying steatohepatitis in human with pluripotent stem cell-derived liver organoid system and biophysical analysis of fibrosis. 2020.07.01

[Awards & Honors]

1. National Institutes of Health, National Institutes of Health, 2020.10

Department of Integrated Analytics

Junior Associate Professor

HASEGAWA Takanori

Project Professor

SATORU Miyano

Project Assistant Professor

ITO Satoshi

Project Assistant Professor

KAKUTA Masanori

(1) Outline

We develop new mathematical analysis methods using bioinformatics and machine learning to analyze multidimensional and ultra-heterogeneous biological big data in the medical/dentistry and medical fields, and advance information processing technologies such as supercomputers. By using them, we aim to elucidate the biological and biological systems, discover drugs, and implement new treatment strategies.

Research Topics

1. Knowledge extraction from big data using supercomputers and artificial intelligence technology
2. Elucidation of cancer origin and diversity by large-scale data analysis and mathematical modeling
3. Multi-omics large-scale data analysis research
4. Research on system modeling and simulation of pathological conditions

(2) Research

■ Development and application of mathematical analysis methods for biological big data

The pathophysiology of the disease is a situation in which control abnormalities affect each other in a complex manner due to the influence of multiple genes and the environment including the intestine and skin, and in particular, cancer is a state that deviates from integrated control as a system. In the field of integrated data science, we will integrate ultra-multidimensional and ultra-heterogeneous biological big data such as genome and other omics data, pathological conditions, and environmental data by making full use of cutting-edge computational science strategies and information processing technologies such as supercomputers. Study mathematical methodologies to analyze and their applications. By doing so, we will clarify the mechanism of the breakdown of the biological and biological systems called pathological conditions, and develop the results into drug discovery and therapeutic method development.

Adopted by the Ministry of Education, Culture, Sports, Science and Technology "FUGAKU" result creation acceleration program, and conducted research on "elucidation of the origin and diversity of cancer by large-scale data analysis and artificial intelligence technology" (jointly with the field of AI technology development).

■ Construction of integrated analysis platform for M & D data and promotion of cooperation system

Medical dentistry and medical research are entering a new era in terms of both quality and quantity of

information. In the analysis of health status and diseases, it is common to acquire and use a large amount of biological information through genomic information analysis and single cell analysis, and by analyzing such information in an integrated manner, new findings and new findings can be obtained. It has become possible to create treatment strategies for diseases. Based on this situation, in the field of integrated analysis, we will practice integrated analysis of medical big data of our university by organically collaborating with existing organizations. Then we promote information education and the construction of information infrastructure necessary for integrated analysis.

In particular, we developed the activities of the "Medical Data Society Return WG" established at Tokyo Medical and Dental University. In addition, a new 1PB storage server was introduced to build a system that connects the hospital DWH and the disease bio-resource center. A new data science infrastructure was built.

(3) Education

[Undergraduate]

- Developed the "Introduction to Medical Care and AI / Big Data" curriculum for 2021.
- Acted in the Mathematical / DS / AI Education Literacy Level WG.
- The "Basic Research Physician Program" was established for 2021.
- Participation in "public health" was established for 2021.
- Activities of the Consortium for Strengthening Mathematical and Data Science Education.
- Supported the undergraduate mathematics club. In March 2021, it hosted the 3rd National Medical and AI Contest.
- Responded to inquiries about data science from undergraduate students.

【graduate School】

- The master's lecture "Introduction to Medical Data Science" was established for 2021.
- Decided to participate in "Data Science Special Lecture II (English version)" (hosted by Professor Kunihiko Takahashi).
- Decided to participate in "Data Science Special Lecture 1 (English version)" (hosted by Professor Kunihiko Takahashi).
- Provided support for research inquiries from graduate students.

(4) Lectures & Courses

The educational policy is to enable clinical and basic students to independently perform data science. With a mere data analysis support system, first-class human resources will not grow up at Tokyo Medical and Dental University.

(5) Clinical Services & Other Works

- To support COVID-19, Tokyo Medical and Dental University, Keio University School of Medicine, Department of Oncology, Graduate School of Medicine, Kyoto University, Department of Genetic Statistics, Graduate School of Medicine, Osaka University, Human Genome Analysis Center, Institute of Medical Science, University of Tokyo Became the main founder and created a network-type research organization called "Corona Suppression Task Force". About 120 hospitals from all over the country participated, and by March 2021, about 3,500 samples had been collected. Host whole-genome analysis and RNA sequence analysis are performed on 500 of these samples to search for aggravating factors.
- Through this task force, we are participating in the International COVID-19 Consortium.
- We actively conducted cancer genomics research with a group such as Professor Seishi Ogawa of Kyoto University.

(6) Publications

[Original Articles]

1. Naoki Ozato, Shinichiro Saito, Tohru Yamaguchi, Mitsuhiro Katashima, Itoyo Tokuda, Kaori Sawada, Yoshihisa Katsuragi, Masanori Kakuta, Seiya Imoto, Kazushige Ihara, Shigeyuki Nakaji. Association

- between breath methane concentration and visceral fat area: a population-based cross-sectional study. *J Breath Res.* 2020; 14(2); 026008
2. Noriaki Sato, Masanori Kakuta, Eiichiro Uchino, Takanori Hasegawa, Ryosuke Kojima, Wataru Kobayashi, Kaori Sawada, Yoshihiro Tamura, Itoyo Tokuda, Seiya Imoto, Shigeyuki Nakaji, Koichi Murashita, Motoko Yanagita, Yasushi Okuno. The relationship between cigarette smoking and the tongue microbiome in an East Asian population. *J Oral Microbiol.* 2020; 12(1); 1742527
 3. Kento Aoyama, Masanori Kakuta, Yuri Matsuzaki, Takashi Ishida, Masahito Ohue, Yutaka Akiyama. Development of computational pipeline software for genome/exome analysis on the k computer Supercomputing *Frontiers and Innovations* . 2020; 7(1); 37-54
 4. Noriaki Sato, Masanori Kakuta, Takanori Hasegawa, Rui Yamaguchi, Eiichiro Uchino, Wataru Kobayashi, Kaori Sawada, Yoshihiro Tamura, Itoyo Tokuda, Koichi Murashita, Shigeyuki Nakaji, Seiya Imoto, Motoko Yanagita, Yasushi Okuno. Metagenomic analysis of bacterial species in tongue microbiome of current and never smokers. *NPJ Biofilms Microbiomes.* 2020; 6(1); 11
 5. Takanori Hasegawa, Rui Yamaguchi, Masanori Kakuta, Kaori Sawada, Kenichi Kawatani, Koichi Murashita, Shigeyuki Nakaji, Seiya Imoto. Prediction of blood test values under different lifestyle scenarios using time-series electronic health record. *PLoS ONE.* 2020; 15(3); e0230172
 6. Tomoko Saito, Atsushi Niida, Ryutaro Uchi, Hidenari Hirata, Hisateru Komatsu, Shotaro Sakimura, Shuto Hayashi, Sho Nambara, Yosuke Kuroda, Shuhei Ito, Hidetoshi Eguchi, Takaaki Masuda, Keishi Sugimachi, Taro Tobo, Haruto Nishida, Tsutomu Daa, Kenichi Chiba, Yuichi Shiraishi, Tetsuichi Yoshizato, Masaaki Kodama, Tadayoshi Okimoto, Kazuhiro Mizukami, Ryo Ogawa, Kazuhisa Okamoto, Mitsutaka Shuto, Kensuke Fukuda, Yusuke Matsui, Teppei Shimamura, Takanori Hasegawa, Yuichiro Doki, Satoshi Nagayama, Kazutaka Yamada, Mamoru Kato, Tatsuhiko Shibata, Masaki Mori, Hiroyuki Aburatani, Kazunari Murakami, Yutaka Suzuki, Seishi Ogawa, Satoru Miyano, Koshi Mimori. A temporal shift of the evolutionary principle shaping intratumor heterogeneity in colorectal cancer. *Nat Commun.* 2020; 9(1); 2884
 7. Atsushi Niida, Takanori Hasegawa, Hideki Innan, Tatsuhiko Shibata, Koshi Mimori, Satoru Miyano. A unified simulation model for understanding the diversity of cancer evolution. *PeerJ.* 2020; 8; e8842
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57. Felix A Dingler, Meng Wang, Anfeng Mu, Christopher L Millington, Nina Oberbeck, Sam Watcham, Lucas B Pontel, Ashley N Kamimae-Lanning, Frederic Langevin, Camille Nadler, Rebecca L Cordell, Paul S Monks, Rui Yu, Nicola K Wilson, Asuka Hira, Kenichi Yoshida, Minako Mori, Yusuke Okamoto, Yusuke Okuno, Hideki Muramatsu, Yuichi Shiraishi, Masayuki Kobayashi, Toshinori Moriguchi, Tomoo Osumi, Motohiro Kato, Satoru Miyano, Etsuro Ito, Seiji Kojima, Hiromasa Yabe, Miharuru Yabe, Keitaro Matsuo, Seishi Ogawa, Berthold Göttgens, Michael R G Hodkinson, Minoru Takata, Ketan J Patel. Two Aldehyde Clearance Systems Are Essential to Prevent Lethal Formaldehyde Accumulation in Mice and Humans. *Mol Cell.* 2020.12; 80(6); 996-1012.e9
58. Heewon Park, Rui Yamaguchi, Seiya Imoto, Satoru Miyano. Automatic sparse principal component analysis *The Canadian J Statistics.* 2020.12; Online ahead of print;

[Misc]

1. Satoru Miyano. Genome Revolution-Preventive and Medical Innovation: Footprints of the Genome Revolution and the Near Future of Prevention and Medical Care *The Journal of Public Health Practice.* 2020.04; 84(4); 214-219
2. Imoto S, Hasegawa T, Yamaguchi R. Data science and precision health care. *Nutrition reviews.* 2020.12; 78(12 Suppl 2); 53-57

[Conference Activities & Talks]

1. Satoru Miyano. Cancer Genome Research and Medicine Accelerating with Artificial Intelligence and Supercomputers. The Annual Meeting of the Fukuoka Association of Medical Sciences 2020.01.02 Hall of the Fukuoka Association of Medical Sciences
2. Satoru Miyano. Cancer genomic medicine realized by supercomputer and artificial intelligence. The 3rd Kobe City Health/Medical Strategy Conference 2020.01.28 Institute of Biomedical Research and Innovation, Kobe
3. Satoru Miyano. Cancer Big Data Challenges by Supercomputers and Artificial Intelligence. International Conference on Cancer Systems Biology Beyond 2020.01.29 Sheraton Miyano Hotel Tokyo
4. Satoru Miyano. Doctors wearing artificial intelligence power suits have arrived for cancer medicine!. The 16th Industry-academia-government technology exchange meeting 2020.02.15 Tokyo Metropolitan Industrial Technology Research Institute
5. Satoru Miyano. Why AI and supercomputers are necessary for personalized cancer genomic medicine. Medical IT EXPO 2020.02.26 Intex Osaka
6. 宮城 洋平, 笠島 理加, 山口 類, 井元 清哉, 青木 一郎, 上村 博司, 清水 英悟, 宮野 悟. 日本人における前立腺癌のバリエーション分析と関連する生物学的経路の予測 (Variant analysis of prostate cancer in the Japanese and prediction of related biological pathways). 日本病理学会会誌 2020.03.01
7. Nobuyuki Kakiuchi, Kenichi Yoshida, Motoi Uchino, Takako Kihara, Akaki Kotaro, Yoshikage Inoue, Kenji Kawada, Satoshi Nagayama, Akira Yokoyama, Tomonori Hirano, Yasuhide Takeuchi, Hiroyuki Miyoshi, Yoshiharu Sakai, Hironori Haga, Seiichi Hirota, Hiroki Ikeuchi, Osamu Takeuchi, Satoru Miyano, Hiroshi Seno, Seishi Ogawa. Analysis of clonal expansion in epithelium affected by ulcerative colitis reveals frequent mutations affecting IL-17 signaling pathway and novel cancer vulnerability. AACR Annual Meeting 2020 2020.04.27 Online, Philadelphia, USA
8. Yasuhide Takeuchi, Annegret Kunitz, Adriane Halik, Hiromichi Suzuki, Kenichi Yoshida, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Nobuyuki Kakiuchi, Yusuke Shiozawa, Akira Yokoyama, Yoshikage Inoue, Tetsuichi Yoshizato, Kosuke Aoki, Yoichi Fujii, Yasuhito Nannya, Hideki Makishima, Satoru Miyano, Hironori Haga, Frederik Damm, Seishi Ogawa. Frequent abnormalities in TP53 and increased genetic instability in myxofibrosarcoma. AACR Annual Meeting 2020 2020.04.27 Online, Philadelphia, USA
9. Yoshikage Inoue, Nobuyuki Kakiuchi, Kenichi Yoshida, Yasuhide Takeuchi, Yusuke Shiozawa, Yuichi Shiraishi, Kenichi Chiba, Tetsuichi Yoshizato, Hiroko Tanaka, Ai Okada, Satoshi Nagayama, Satoru Miyano, Yoshiharu Sakai, Seishi Ogawa. Frequent genomic alterations to evade the immune system in colorectal cancer with POLE gene mutation. AACR Annual Meeting 2020 2020.04.27 Online, Philadelphia, USA
10. Yoichi Fujii, Yusuke Sato, Hiromichi Suzuki, Tetsuichi Yoshizato, Kenichi Yoshida, Yuichi Shiraishi, Taketo Kawai, Tohru Nakagawa, Hiroaki Nishimatsu, Toshikazu Nishimatsu, Masashi Sanada, Hideki Makishima, Satoru Miyano, Haruki Kume, Seishi Ogawa. Distinct molecular subtypes and a high diagnostic urinary biomarker of upper urinary tract urothelial carcinoma. AACR Annual Meeting 2020 2020.04.27 Online, Philadelphia, USA
11. Hirano Tomonori, Nobuyuki Kakiuchi, Yasuhide Takeuchi, Yoshikage Inoue, Tomomi Nishimura, Yoichi Fujii, Akira Yokoyama, Hideki Makishima, Toshihiko Masui, Shinji Uemoto, Sachiko Minamiguchi, Hironori Haga, Kenichi Chiba, Hiroko Tanaka, Yuichi Shiraishi, Satoru Miyano, Norimitsu Uza, Yuzo Kodama, Hiroshi Seno, Seishi Ogawa. Genetic analysis of metachronous pancreatic cancers. AACR Annual Meeting 2020 2020.04.27 Online, Philadelphia, USA
12. Satoru Miyano. Cancer Big Data Challenges from Genomes to Networks. The 24th International Conference on Research in Computational Molecular Biology (RECOBM 2020) 2020.06.23 Online
13. 井上 善景, 垣内 伸之, 吉田 健一, 塩澤 裕介, 竹内 康英, 千葉 健一, 吉里 哲一, 長山 聡, 宮野 悟, 坂井 義治, 小川 誠司. POLE 遺伝子に変異を持つ大腸癌における免疫回避機構. 日本癌学会総会記事 2020.10.01
14. 藤田 征志, 山口 類, 有廣 光司, 島田 周, 宮野 悟, 山上 裕機, 茶山 一彰, 垣見 和宏, 田中 真二, 井元 清哉, 中川 英刀. がん免疫ゲノム解析 肝臓がんの免疫ゲノム解析. 日本癌学会総会記事 2020.10.01

15. 佐伯 龍之介, 吉里 哲一, 白石 友一, 千葉 健一, 田中 洋子, 松田 浩一, 村上 善則, 久保 充明, 宮野 悟, 牧島 秀樹, 小川 誠司. クロウン造血における遺伝子変異とコピー数異常の統合解析. 日本癌学会総会記事 2020.10.01
16. 小笠原 辰樹, 藤井 陽一, 塩澤 裕介, 牧島 秀樹, 中村 英二郎, 田中 知明, 白石 友一, 宮野 悟, 小川 誠司. チアノーゼ性先天性心疾患に伴う多発パラングリオーマは異なる HIF2 α 変異を伴う平行進化を示した. 日本癌学会総会記事 2020.10.01
17. 関口 昌央, 関 正史, 吉田 健一, 田中 水緒, 白井 了太, 宗崎 良太, 白石 友一, 樋渡 光輝, 加藤 元博, 田口 智章, 田中 祐吉, 宮野 悟, 小川 誠司, 滝田 順子. マルチオミックス解析による肝芽腫の治療標的 NQO1、ODC1 の同定. 日本癌学会総会記事 2020.10.01
18. 藤井 陽一, 佐藤 悠佑, 鈴木 啓道, 吉里 哲一, 垣内 伸之, 吉田 健一, 千葉 健一, 白石 友一, 西松 寛明, 岡根谷 利一, 真田 昌, 南谷 泰仁, 牧島 秀樹, 宮野 悟, 久米 春喜, 小川 誠司. 上部尿路上皮癌の分子分類と新規バイオマーカー. 日本癌学会総会記事 2020.10.01
19. 西村 友美, 垣内 伸之, 吉田 健一, 竹内 康英, 前田 紘奈, 塩澤 裕介, 平田 勝啓, 片岡 竜貴, 桜井 孝規, 馬場 郷子, 竹内 賢吾, 羽賀 博典, 宮野 悟, 戸井 雅和, 小川 誠司. 乳がん微小環境の特性と全身性応答、新しい治療展開 乳管上皮増殖性病変から乳癌へ至るクロウン進化. 日本癌学会総会記事 2020.10.01
20. 垣内 伸之, 内野 基, 木原 多佳子, 赤木 宏太郎, 井上 善景, 横山 顕礼, 平野 智紀, 廣田 誠一, 池内 浩基, 竹内 理, 宮野 悟, 妹尾 浩, 小川 誠司. 大腸がんの診断・治療と発がん研究における新しい知見 潰瘍性大腸炎における大腸上皮クロウン進化から明らかとなった大腸がんの脆弱性. 日本癌学会総会記事 2020.10.01
21. 土方 康基, 横山 和明, 山口 貴世志, 池上 恒雄, 山口 類, 井元 清哉, 内丸 薫, 宮野 悟, 四柳 宏, 東條 有伸, 古川 洋一. 当院における標準治療不応進行がん患者を対象としたクリニカルシーケンスの検討. 日本癌学会総会記事 2020.10.01
22. 竹田 淳恵, 吉田 健一, 依田 成玄, 南谷 泰仁, 中川 正宏, 越智 陽太郎, 昆 彩奈, 吉里 哲一, 塩澤 裕介, 白石 友一, 千葉 健一, 田中 洋子, 真田 昌, 宮野 悟, 牧島 秀樹, 小川 誠司. 急性赤白血病における JAK 阻害剤の検討. 日本癌学会総会記事 2020.10.01
23. 越智 陽太郎, 吉田 健一, 佐々木 光, 細谷 紀子, 塩澤 裕介, 南谷 泰仁, 石川 隆之, 白石 友一, 千葉 健一, 田中 洋子, 真田 昌, 牧島 秀樹, 高折 晃史, 宮野 悟, 三谷 絹子, 小川 誠司. 慢性骨髄性白血病急性転化の遺伝学的機序と予後. 日本癌学会総会記事 2020.10.01
24. 平野 智紀, 垣内 伸之, 竹内 康英, 増井 俊彦, 上本 伸二, 南口 早智子, 羽賀 博典, 白石 友一, 宮野 悟, 宇座 徳光, 児玉 裕三, 妹尾 浩, 千葉 勉, 小川 誠司. 異時性多発腺癌の遺伝子解析. 日本癌学会総会記事 2020.10.01
25. 鎌谷 高志, 平田 真, 植田 幸嗣, 片山 琴絵, 山口 類, 松原 大祐, 藤田 征志, 高澤 豊, 山下 享子, 中村 卓郎, 井元 清哉, 宮野 悟, 中川 英刀, 松田 浩一, 角田 達彦. 粘液型脂肪肉腫におけるがん微小環境の免疫学的解析. 日本癌学会総会記事 2020.10.01
26. 竹内 康英, 鈴木 啓道, 吉田 健一, 白石 友一, 垣内 伸之, 塩澤 裕介, 井上 善景, 千葉 健一, 牧島 秀樹, 宮野 悟, 羽賀 博典, Damm Frederik, 小川 誠司. 粘液線維肉腫にみられる TP53 の異常と著明な遺伝的不安定性. 日本癌学会総会記事 2020.10.01
27. 大津 敬, 笠島 理加, 鷺見 公太, 廣島 幸彦, 片山 琴絵, 清水 英悟, 山口 類, 井元 清哉, 宮野 悟, 河村 大輔, 石川 俊平, 横瀬 智之, 比留間 徹, 宮城 洋平. 肉腫患者由来ゼノグラフトの RNA 発現解析. 日本癌学会総会記事 2020.10.01
28. 笠島 理加, 鈴木 理樹, 清水 英悟, 玉田 嘉紀, 新井田 厚司, 山口 類, 井元 清哉, 古川 洋一, 宮野 悟, 横瀬 智之, 宮城 洋平. 胎児性肺癌における遺伝子ネットワーク解析. 日本癌学会総会記事 2020.10.01
29. 垣内 伸之, 横山 顕礼, 内野 基, 木原 多佳子, 赤木 宏太郎, 井上 善景, 平野 智紀, 廣田 誠一, 池内 浩基, 竹内 理, 宮野 悟, 妹尾 浩, 小川 誠司. 遺伝子変異クロウンによる食道および大腸組織の再構築の解明. 第 79 回日本癌学会学術総会 2020.10.01
30. 古川 洋一, 山口 貴世志, 笠島 理加, 清水 英悟, 高根 希世子, 山口 類, 井元 清哉, 宮野 悟, 池上 恒雄. 遺伝性腫瘍-最新情報と今後の方向性 消化管遺伝性腫瘍の最前線. 日本癌学会総会記事 2020.10.01
31. 南谷 泰仁, 牧島 秀樹, 竹田 淳恵, 桃沢 幸秀, 佐伯 龍之介, 宮崎 泰司, 石川 隆之, 大屋敷 一馬, Hellstroem Lindberg Eva, Mario Cazzola, Torsten Haferlach, 鎌谷 洋一郎, 久保 充明, 宮野 悟, 小川 誠司. 骨髄系腫瘍における DDX41 変異の意義. 日本癌学会総会記事 2020.10.01

32. 藤田 征志、山口 類、有廣 光司、島田 周、宮野 悟、山上 裕 機、茶山 一彰、垣見 和宏、田中 真二、井元 清哉 2、中川 英刀. 肝臓がんの免疫ゲノム解析. 第 79 回日本癌学会学術総会 2020.10.01 リーガロイヤルホテル広島
33. 前田 紘奈、垣内 伸之、平野 智紀、竹内 康英、伊藤 孝司、小川 絵里、塩川 雅広、宇座 徳光、田中 洋子、南谷 泰仁、牧 島 秀樹、上本 伸二、宮野 悟、小川 誠司. 慢性炎症に伴う胆管上皮におけるクローン拡大. 第 79 回日本癌学会学術総会 2020.10.01 リーガロイヤルホテル広島
34. 宮野 悟. AI とがん研究・医療との対話 - がん研究・医療のための自然言語処理と説明可能 AI. 第 79 回日本癌学会学術総会 2020.10.02 リーガロイヤルホテル広島
35. 垣内 伸之、内野 基、木原 多佳子、赤木 宏太郎、井上 善景、横 山 顕礼、平野 智紀、廣田 誠一、池内 浩基、竹内 理、宮野 悟、妹尾 浩、小川 誠司. 潰瘍性大腸炎における大腸上皮クローン進化から明らかとなった大腸 がんの脆弱性. 第 79 回日本癌学会学術総会 2020.10.02 リーガロイヤルホテル広島
36. 渡邊 健太郎、加登 翔太、磯部 知弥、緒方 瑛人、田坂 佳資、上野 浩生、南谷 泰仁、田中 洋子、白石 友一、千葉 健一、梅田 雄嗣、樋渡 光輝、宮野 悟、小川 誠司、滝田 順子. 小児・AYA 腫瘍の最近の進歩 難治性骨肉腫における糖鎖遺伝子の役割と治療標的としての可能性. 第 79 回日本癌学会学術総会 2020.10.03 リーガロイヤルホテル広島
37. 渡邊 健太郎、加登 翔太、磯部 知弥、緒方 瑛人、田坂 佳資、上野 浩生、南谷 泰仁、田中 洋子、白石 友一、千葉 健一、梅田 雄嗣、樋渡 光輝、宮野 悟、小川 誠司、滝田 順子. 難治性骨肉腫における糖鎖遺伝子の役割と治療標的としての可能性. 2020.10.03 リーガロイヤルホテル広島
38. 古川 洋一、山口 貴世志、笠島 理加、清水 英悟、高根 希世子、山口 類、井元 清哉、宮野 悟、池上 恒雄. 消化管遺伝性腫瘍の最前線. 第 79 回日本癌学会学術総会 2020.10.03

[Works]

1. Virtual Grid Engine, Software, IEEE BIBM2018, 2018.12 - Now

[Awards & Honors]

1. The 16th Healthy Society Award (Pioneer Division), Healthysociety-Sho, 2020.11

[Others]

1. Nature index Artificial Intelligence: Japan's new centre of gravity for clinical data science, 2020.12
"Nature index Artificial Intelligence"
Japan's new centre of gravity for clinical data science.
On a mission to mine its wealth of data for clinical insights, the Tokyo Medical and Dental University has established itself as Japan's new hub for AI-driven clinical data science.

<https://www.nature.com/articles/d42473-020-00351-1>

Department of Biostatistics

Professor TAKAHASHI Kunihiko
Assistant Professor
ANZAI Tatsuhiko
Assistant Professor
ITOU Tsubasa

(1) Outline

Biostatistics has a central role in medical research. We aim to develop methodologies for data analysis focused on medical, dental and healthcare applications, and will collaborate on practical research.

(2) Research

1) Methodology development for data analysis in M&D field

We are developing biostatistical methodologies for data analysis in the field of M&D. Our focus includes methodologies and applications for spatial epidemiological research with geographic and temporal data, disease surveillance and monitoring, real-world data (RWD) analysis, meta-analysis, dynamic modeling, and their implementation in software.

2) Practical research on M&D field

Another focus is joint research in the field of M&D with medical, dental, and healthcare professionals. Some of our contributions include the design and analysis of any types of medical/clinical, health related studies.

(3) Education

[Data Science I (English)]

(4) Lectures & Courses

The objective of this course is to master methodologies in biostatistics, and will be able to interpret the results of data analysis in medical research.

(5) Publications

[Original Articles]

1. Tatsuhiko Anzai, Kunihiko Takahashi, Michiko Watanabe, Mayumi Mochizuki, Atsuko Murashima. Adverse event reports in patients taking psychiatric medication during pregnancy from spontaneous reports in Japan and the United States: an approach using latent class analysis. *BMC Psychiatry*. 2020; 20(1); 118

2. Tomohiro Ishimaru, Yoshihisa Fujino, Tatsuhiko Anzai, Shinya Matsuda, Yoshiya Tanaka. Validity and responsiveness of the Work Functioning Impairment Scale (WFun) in rheumatoid arthritis patients: A multicenter prospective study. *Modern Rheumatology*. 2020; 30(5); 821-827
3. Tasuku Fujii, Yasuyuki Shibata, Yasutaka Ban, Akira Shitaokoshi, Kunihiko Takahashi, Shigeyuki Matsui, Kimitoshi Nishiwaki. A single paravertebral injection via a needle vs. a catheter for the spreading to multiple intercostal levels: a randomized controlled trial. *J Anesth*. 2020; 34(1); 72-78
4. Kunihiko Takahashi, Hideyasu Shimadzu. Detecting multiple spatial disease clusters: information criterion and scan statistic approach. *Int J Health Geogr*. 2020; 19(1); 33
5. Tsubasa Ito, Tatsuya Kubokawa. Robust Estimation of Mean Squared Error Matrix of Small Area Estimators in a Multivariate Fay-Herriot Model. *Japanese Journal of Statistics and Data Science*. 2020; 3; 39-61
6. Tsubasa Ito, Tatsuya Kubokawa. Empirical Best Linear Unbiased Predictors in Multivariate Nested-Error Regression Models. *Communications in Statistics - Theory and Methods*. 2020;
7. Ryo Emoto, Atsushi Kawaguchi, Kunihiko Takahashi, Shigeyuki Matsui. Effect-Size Estimation Using Semiparametric Hierarchical Mixture Models in Disease-Association Studies with Neuroimaging Data. *Comput Math Methods Med*. 2020; 2020; 7482403
8. Yuma Yasuda, Mitsuaki Nishikimi, Kazuki Nishida, Kunihiko Takahashi, Atsushi Numaguchi, Michiko Higashi, Shigeyuki Matsui, Naoyuki Matsuda. Relationship Between Serum Norepinephrine Levels at ICU Admission and the Risk of ICU-Acquired Delirium: Secondary Analysis of the Melatonin Evaluation of Lowered Inflammation of ICU Trial. *Crit Care Explor*. 2020.02; 2(2); e0082
9. Masato Yoshihara, Hiroaki Kajiyama, Satoshi Tamauchi, Shohei Iyoshi, Akira Yokoi, Shiro Suzuki, Michiyasu Kawai, Tetsuro Nagasaka, Kunihiko Takahashi, Shigeyuki Matsui, Fumitaka Kikkawa. Prognostic impact of pelvic and para-aortic lymphadenectomy on clinically-apparent stage I primary mucinous epithelial ovarian carcinoma: a multi-institutional study with propensity score-weighted analysis. *Jpn J Clin Oncol*. 2020.02; 50(2); 145-151
10. Hiroshi Takagi, Daisuke Hagiwara, Tomoko Handa, Mariko Sugiyama, Takeshi Onoue, Taku Tsunekawa, Yoshihiro Ito, Shintaro Iwama, Motomitsu Goto, Hidetaka Suga, Ryoichi Banno, Kunihiko Takahashi, Shigeyuki Matsui, Hiroshi Arima. Diagnosis of central diabetes insipidus using a vasopressin radioimmunoassay during hypertonic saline infusion. *Endocr J*. 2020.03; 67(3); 267-274
11. Maki Takagishi, Nobutoshi Esaki, Kunihiko Takahashi, Masahide Takahashi. Cytoplasmic Dynein Functions in Planar Polarization of Basal Bodies within Ciliated Cells. *iScience*. 2020.06; 23(6); 101213
12. Kunihiko Takahashi, Hideto Takahashi, Tomoki Nakaya, Seiji Yasumura, Tetsuya Ohira, Hitoshi Ohto, Akira Ohtsuru, Sanae Midorikawa, Shinichi Suzuki, Hiroki Shimura, Shunichi Yamashita, Koichi Tanigawa, Kenji Kamiya. Factors Influencing the Proportion of Non-examinees in the Fukushima Health Management Survey for Childhood and Adolescent Thyroid Cancer: Results From the Baseline Survey. *J Epidemiol*. 2020.07; 30(7); 301-308
13. Hideto Takahashi, Seiji Yasumura, Kunihiko Takahashi, Tetsuya Ohira, Akira Ohtsuru, Sanae Midorikawa, Satoru Suzuki, Hiroki Shimura, Tetsuo Ishikawa, Akira Sakai, Shinichi Suzuki, Susumu Yokoya, Koichi Tanigawa, Hitoshi Ohto, Kenji Kamiya. Nested matched case control study for the Japan Fukushima Health Management Survey's first full-scale (second-round) thyroid examination. *Medicine (Baltimore)*. 2020.07; 99(27); e20440
14. Masato Yoshihara, Hiroaki Kajiyama, Satoshi Tamauchi, Shohei Iyoshi, Akira Yokoi, Shiro Suzuki, Michiyasu Kawai, Tetsuro Nagasaka, Kunihiko Takahashi, Shigeyuki Matsui, Fumitaka Kikkawa. Impact of uterus-preserving surgery on Stage I primary mucinous epithelial ovarian carcinoma: A multi-institutional study with propensity score-weighted analysis. *Int J Gynaecol Obstet*. 2020.08; 150(2); 177-183
15. Ryota Sato, Daisuke Hasegawa, Natsumi T Hamahata, Swetha Narala, Kazuki Nishida, Kunihiko Takahashi, Tomoki Sempokuya, Ehab G Daoud. The predictive value of airway occlusion pressure at 100 msec (P0.1) on successful weaning from mechanical ventilation: A systematic review and meta-analysis. *J Crit Care*. 2020.09;

16. Daisuke Kasugai, Akihiko Hirakawa, Masuyuki Ozaki, Kazuki Nishida, Takao Ikeda, Kunihiko Takahashi, Shigeyuki Matsui, Norimichi Uenishi. Maximum Norepinephrine Dosage Within 24 Hours as an Indicator of Refractory Septic Shock: A Retrospective Study. *J Intensive Care Med.* 2020.11; 35(11); 1285-1289
17. Takashi Yamauchi, Kunihiko Takahashi, Machi Suka, Takeshi Sasaki, Masaya Takahashi, Toru Yoshikawa, Hiroto Okoshi, Shigeo Umezaki, Hiroyuki Yanagisawa. Longitudinal association between near-misses/minor injuries and moderate/severe injuries in industrial settings by presence/absence of depressive symptoms in a nationally representative sample of workers in Japan. *Occup Environ Med.* 2020.12; 77(12); 832-838
18. Isumi A, Doi S, Yamaoka Y, Takahashi K, Fujiwara T. Do suicide rates in children and adolescents change during school closure in Japan? The acute effect of the first wave of COVID-19 pandemic on child and adolescent mental health. *Child Abuse Negl.* 2020.12; 110; 104680

Biomedical Devices and Instrumentation

Professor: Kohji Mitsubayashi
Junior Associate Professor: Takahiro Arakawa
Assistant Professor: Koji Toma
Lecturer (part-time): Kazuyoshi Yano
Lecturer (part-time): Naoya Takeda
Lecturer (part-time): Ming Ye

(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” and “Air bio-battery” based on chemo-mechanical energy conversion
Novel chemo-mechanical energy conversion systems (Organic engine and Air bio-battery) that utilize enzyme reactions and active transport of chemicals has 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. Iitani K, Toma K, Arakawa T, Mitsubayashi K. Transcutaneous Blood VOC Imaging System (Skin-Gas Cam) with Real-Time Bio-Fluorometric Device on Rounded Skin Surface. *ACS sensors*. 2020.02; 5(2); 338-345
2. Iitani K, Naisierding M, Toma K, Arakawa T, Mitsubayashi K. Evaluation for regional difference of skin-gas ethanol and sweat rate using alcohol dehydrogenase-mediated fluorometric gas-imaging system (sniff-cam). *The Analyst*. 2020.04; 145(8); 2915-2924
3. Takahiro Arakawa, Takashi Aota, Kenta Iitani, Koji Toma, Iwasaki Y, Kohji Mitsubayash. Skin ethanol gas measurement system with a biochemical gas sensor and gas concentrator toward monitoring of blood volatile compounds *Talanta*. 2020.05; 115; 887-895
4. Koji Mizukoshi Takahiro Arakawa Kohji Mitsubayashi. Convenience biosensing approach of lactic acid in stratum corneum for skin care assessment *Skin Research and Technology*. 2020.07; 26(4); 455-464
5. Takahiro Arakawa, Keisuke Tomoto, Hiroki Nitta, Koji Toma, Shuhei Takeuchi, Toshiaki Sekita, Shunsuke Minakuchi, Kohji Mitsubayashi. A Wearable Cellulose Acetate-Coated Mouthguard Biosensor for In Vivo Salivary Glucose Measurement. *Anal Chem*. 2020.09; 92(18); 12201-12207
6. Chien PJ, Suzuki T, Ye M, Toma K, Arakawa T, Iwasaki Y, Mitsubayashi K. Ultra-Sensitive Isopropanol Biochemical Gas Sensor (Bio-Sniffer) for Monitoring of Human Volatiles. *Sensors (Basel, Switzerland)*. 2020.11; 20(23);

[Books etc]

1. *Odor-Sensing Technologies*. 2020.08

[Conference Activities & Talks]

1. Toma K, Tsujii M, Arakawa T, Mitsubayashi K. Dual-target biochemical gas sensor for assessment of lipid metabolism from breath acetone and isopropanol. The 6th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2020.01.14 Bangkok, Thailand
2. Wanotayan Sittinadh, Misato Kato, Kanako Kurata, Naoyuki Yoshimura, Koji Toma, Takahiro Arakawa, Kiyoko Kanamori, Hiromi Yatsuda, Kohji Mitsubayashi. Precipitate-enhanced SAW immunosensor for sensitive mite allergen monitoring. The 6th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2020.01.14 Bangkok, Thailand
3. Toma K. 2D (concentration versus time) sensing of biochemical molecules for advanced environmental and clinical medicine. Seminar of the Petroleum and Petrochemical College, Chulalongkorn university 2020.01.15 Bangkok, Thailand
4. Kohji Mitsubayashi. Bio-fluorometric gas sensing and imaging of human volatiles (Bio-sniffer & Sniff-cam). 8th International Conference on Nanoscience and Nanotechnology (ICONN 2020) 2020.02.12 Brisbane, Australia

Medical Devices

5. Toma K, Ye M, Arakawa T, Mitsubayashi K. Biochemical acetone gas sensor for non-invasive and real-time assessment of lipid metabolism. The 7th Joint Symposium between IBB/TMDU and Chulalongkorn University on “Biomedical Materials and Engineering” 2020.12.22 Online

[Awards & Honors]

1. 2020 PROSE Award (Chemistry and Physics Category) by the Association of American Publishers, The Association of American Publishers, 2020.02

Biomedical Information

Professor Yoshikazu NAGAJIMA
 Associate Professor Shinya ONOGI
 Assistant Professor Toshihiro KAWASE
 Takaaki SUGINO
 Research Assistant Teruyo MORI
 Graduate Student Misato SHIMIZU
 Yutaro SUZUKI
 Rina SUZUKI
 Myuji MATSUDA
 Satoshi ISHIDA
 Jun Feng XUAN
 Xiaoxi ZHOU
 Ruiqi ZHANG
 Longfei ZHAO
 Haruka HORIUCHI
 Azusa MINEMURA

(1) Research

1. Medical data analysis with complex artificial intelligence
2. Deep-Learning Segmentation and Annotation of Brain MRI volumes
3. Surgical Navigation System with deformation tracking of soft tissues
4. Pneumatic Stiffness-Tunable Mechanism and its Application for Laparoscopic Surgeries

(2) Publications

[Original Articles]

1. Nakajima Y, Sohma Y, Jiang J . Laser-beam projection mapping with the compensation of soft-tissue deformation Sensors and Materials. 2020; 32(3); 935-945
2. Oda H, Roth HR, Sugino T, Sunaguchi N, Usami N, Oda M, Shimao D, Ichihara S, Yuasa T, Ando M, Akita T, Narita Y, Mori K. Cardiac fiber tracking on super high-resolution CT images: a comparative study. Journal of medical imaging (Bellingham, Wash.). 2020.03; 7(2); 026001
3. Victor R Barradas, Jason J Kutch, Toshihiro Kawase, Yasuharu Koike, Nicolas Schweighofer. When 90% of the variance is not enough: residual EMG from muscle synergy extraction influences task performance. Journal of neurophysiology. 2020.06; 123(6); 2180-2190
4. Nakajima Y, Suzuki R, Suzuki Y, Sugino T, Kawase T, Onogi S, Seki H, Fujiwara T, Ouchi K.. Suction-fixing surgical device for assisting liver manipulation with laparoscopic forceps. International

Journal of Computer Assisted Radiology and Surgery. 2020.07;

5. Ryu Nakadate, Tsutomu Iwasa, Shinya Onogi, Jumpei Arata, Susumu Oguri, Yasuharu Okamoto, Tomohiko Akahoshi, Masatoshi Eto, Makoto Hashizume. Surgical Robot for Intraluminal Access: An Ex Vivo Feasibility Study Cyborg and Bionic Systems. 2020.12; 2020; 8378025

[Conference Activities & Talks]

1. Tao Feng, Takahiro Kanno, Tetsuro Miyazaki, Toshihiro Kawase, Yoshikazu Nakajima, Kenji Kawashima, Norihiko Ito. Development of a robotic platform for OCT guided retinal surgery. 2020.10.09
2. Hiroyuki Hayashi, Toshihiro Kawase, Tetsuro Miyazaki, Takahiro Kanno, Yoshikazu Nakajima, Kenji Kawashima. Multi-joint motion estimation of an exoskeleton with artificial muscles using pneumatic reservoir computing. 2020.11.05
3. Toshihiro Kawase, Rina Suzuki, Takaaki Sugino, Shinya Onogi, Yoshikazu Nakajima. Effect of beam design on function of stiffness-tunable organ grasping device: a FEM study. 2020 Asian Conference on Computer Assisted Surgery (ACCAS 2020) 2020.11.27

[Patents]

1. FORCEPS SYSTEM, Patent Number : US10,675,047

Bioelectronics

Staff

Yuji Miyahara (Professor)
 Akira Matsumoto (Associate Professor)
 Tatsuro Goda (Assistant Professor)
 Miyuki Tabata (tenure track Assistant Professor)
 Yukichi Horiguchi (Assistant Professor)
 KHAN Thahomina Tareque (Project Assistant Professor)
 Siyuan Chen (Collaborative Researcher)
 Michiko Ito (Collaborative Researcher)
 Takuya Miyazaki (Collaborative Researcher)
 Hiroko Matsumoto (Technical Assistant)
 Yuki Morooka (Technical Assistant)
 Chiharu Mizoi (Technical Assistant)
 Sayo Kotaki (Technical Assistant)
 Sayaka Kanai (Technical Assistant)
 Kiyoshi Ikehara (Technical Assistant)
 Ulala Minamibata (Staff Assistant)

Graduate student

Hideki Fujisaki, Hiroaki Hatano, Chattarika KHAMHANGLIT,
 Ayumu Tsuchiya, Xinyue Liu, Ayano Mukaida, Kyouka Susawa

(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. Hai W, Pu S, Wang X, Bao L, Han N, Duan L, Liu J, Goda T, Wu W. Poly(3,4-ethylenedioxythiophene) Bearing Pyridylboronic Acid Group for Specific Recognition of Sialic Acid. *Langmuir : the ACS journal of surfaces and colloids*. 2020.01; 36(2); 546-553
2. Shiozaki Y, Sakurai S, Sakamoto R, Matsumoto A, Maruoka K. Iron-Catalyzed Radical Cleavage/C-C Bond Formation of Acetal-Derived Alkylsilyl Peroxides. *Chemistry, an Asian journal*. 2020.03; 15(5); 573-576
3. Khamhanglit Chattarika, Tabata Miyuki, Goda Tatsuro, Matsumoto Akira, Miyahara Yuji, Sriyudthsak Mana. Protein immobilization method on the ion-sensitive FET(和訳中) 生体医歯工学共同研究拠点成果報告書. 2020.04; 令和元年度; 162
4. Matsumoto Akira, Kuwata Hirohito, Kimura Shinichiro, Matsumoto Hiroko, Ochi Kozue, Moro-oka Yuki, Watanabe Akiko, Yamada Hironori, Ishii Hitoshi, Miyazawa Taiki, Chen Siyuan, Baba Toshiaki, Yoshida Hiroshi, Nakamura Taichi, Inoue Hiroshi, Ogawa Yoshihiro, Tanaka Miyako, Miyahara Yuji, Suganami Takayoshi. Hollow fiber-combined glucose-responsive gel technology as an in vivo electronics-free insulin delivery system *COMMUNICATIONS BIOLOGY*. 2020.06; 3(1); 313
5. Chen Siyuan, Miyazaki Takuya, Itoh Michiko, Matsumoto Hiroko, Moro-oka Yuki, Tanaka Miyako, Miyahara Yuji, Suganami Takayoshi, Matsumoto Akira. Temperature-Stable Boronate Gel-Based Microneedle Technology for Self-Regulated Insulin Delivery *ACS APPLIED POLYMER MATERIALS*. 2020.07; 2(7); 2781-2790
6. Osawa Shigehito, Matsumoto Akira, Maejima Yukie, Suzuki Toshihiro, Miyahara Yuji, Otsuka Hidenori. Direct Observation of Cell Surface Sialylation by Atomic Force Microscopy Employing Boronic Acid-Sialic Acid Reversible Interaction *ANALYTICAL CHEMISTRY*. 2020.09; 92(17); 11714-11720

7. Yukichi Horiguchi, Yuji Miyahara. Surface modification to suppress small pore clogging in resistive pulse sensing Applied Physics Express. 2020.10; 13; 115002
8. Tanaka Miyako, Saka-Tanaka Marie, Ochi Kozue, Fujieda Kumiko, Sugiura Yuki, Miyamoto Tomofumi, Kohda Hiro, Ito Ayaka, Miyazawa Taiki, Matsumoto Akira, Aoe Seiichiro, Miyamoto Yoshihiro, Tsuboi Naotake, Maruyama Shoichi, Suematsu Makoto, Yamasaki Sho, Ogawa Yoshihiro, Suganami Takayoshi. C-type lectin Mincle mediates cell death-triggered inflammation in acute kidney injury JOURNAL OF EXPERIMENTAL MEDICINE. 2020.11; 217(11);
9. Miyazaki Takuya, Uchida Satoshi, Hatano Hiroaki, Miyahara Yuji, Matsumoto Akira, Cabral Horacio. Guanidine-phosphate interactions stabilize polyion complex micelles based on flexible cationomers to improve mRNA delivery EUROPEAN POLYMER JOURNAL. 2020.11; 140;

[Conference Activities & Talks]

1. Protein Immobilization Method on the Ion-Sensitive FET. 2020.03.13
2. 劉 心月, 田畑美幸, 宮原裕二. Comparison of cell adhesion properties using different binding materials for cell-based bio-transistors application. 第 37 回「センサ・マイクロマシンと応用システム」シンポジウム 2020.10.17 オンライン会議
3. ガムヘンリット チャッターカ, 田畑美幸, 宮原裕二. バイオメディカル応用に向けた ISFET pH センサの表面化学修飾法の検討. 第 37 回「センサ・マイクロマシンと応用システム」シンポジウム 2020.10.17 オンライン会議
4. Polymer gel-based totally synthetic pancreas device. 2020.11.27
5. Miyuki Tabata, Yuji Miyahara. Detection of small nucleic acids using electrochemical devices for liquid biopsy. IEEE Nanomed2020 2020.12.15 オンライン会議

[Awards & Honors]

1. Soft Matter Presentation Prize, 2020.01

Material-Based Medical Engineering

Prof. Akio Kishida
Assoc. Prof. Tsuyoshi Kimura
Assist. Prof. Yoshihide Hashimoto
Secretary Naomi Hiwatari
Lecturer(part-time) Seiichi Funamoto
Lecturer(part-time) Akitatsu Yamashita
Lecturer(part-time) Masaki Tabuchi
Lecturer(part-time) Jun Negishi
Lecturer(part-time) Naoko Nakamura
Lecturer(part-time) Yongwei Zhang

Doctor Course Student
Masaki Watanabe
Takuya Konishi
Mako Kobayashi

(1) Outline

Our laboratory has dealt with many research topics from the fundamental study of biomaterials in terms of material engineering to the application study of the medical devices. The keywords 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 systems 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 researches aimed at specific clinical applications using cell engineering and genetic engineering techniques. Target fields are development of novel medical material, regenerative medicine, gene therapy, and treatment engineering.

(1) Regenerative medicine using decellularized biological tissue

For removing immunogenicity, biological tissues are decellularized using a novel processing method, high-hydrostatic pressure (HHP) method. We have demonstrated that decellularized biological tissues are promising materials in tissue engineering and regenerative medicine fields.

(2) Development of processing and high-performance technology for biological materials

This research focuses on developing functional materials with novel functions by processing biological materials. Specifically, we are conducting research on processing into powders, fibers, and hydrogels, and hybrid technology with functional molecules.

(3) Development of inflammatory evaluation method for biomaterials

Macrophages are polarized into an inflammatory type (M1 type) that contributes to inflammation and an anti-inflammatory type (M2 type) that contributes to healing. We are developing an inflammatory evaluation method for biomaterials using macrophage polarization in vitro.

(4) Immune control systems: technology of specific cell capture and release

In cancer immunotherapy, by removing regulatory T cells (Treg) that negatively regulate immune reactions, anti-tumor immune responses can be enhanced. We are developing novel biomaterials and technologies to capture and release Treg using interfacial science.

(3) Education

Our laboratory is in charge of lectures on "Medical Materials Engineering", "Applied Biomaterials", and "Medical, Dental and Pharmaceutical Industrial Engineering" in the graduate school, and "Biomedical Engineering" in the faculty.

Through these lectures, we will explain from the basic knowledge of various materials to the molecular design theory required for device development.

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

1. Masaki Watanabe, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Characterization of engineering plastics plasticized using supercritical CO₂ Polymers. 2020.01; 12(1); 134
2. Yongwei Zhang, Kwangwoo Nam, Tsuyoshi Kimura, Pingli Wu, Naoko Nakamura, Yoshihide Hashimoto, Seiichi Funamoto, Akio Kishida. Preparation of gradient-type biological tissue-polymer complex for interlinking device Mater. Sci. Eng. C-Mater. Biol. Appl. 2020.09; 114; 111017
3. Mako Kobayashi, Junpei Kadota, Yoshihide Hashimoto, Toshiya Fujisato, Naoko Nakamura, Tsuyoshi Kimura, Akio Kishida. Elastic modulus of ECM hydrogels derived from decellularized tissue affects capillary network formation in endothelial cells Int. J. Mol. Sci. 2020.09; 21(17); 6304
4. Naoko Nakamura, Kazuki Saito, Tsuyoshi Kimura, Akio Kishida. Recellularization of decellularized cancellous bone scaffolds using low temperature cell seeding Tissue and Cell. 2020.10; 66; 101385
5. Kotaro Yanagisawa, Seiichi Funamoto, Yoshihide Hashimoto, Jun Negishi. Introduction of cells into porous Poly (L-lactic) acid scaffolds using impregnation techniques Tissue Eng. Part C-Methods. 2020.12; 26(12); 608-616
6. Mako Kobayashi, Masao Ohara, Yoshihide Hashimoto, Naoko Nakamura, Toshiya Fujisato, Tsuyoshi Kimura, Akio Kishida. In vitro evaluation of surface biological properties of decellularized cardiovascular use J. Mater. Chem. B. 2020.12; 2020(48); 10977-10989
7. Masaki Watanabe, Hanako Maeda, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida. Protein adsorption and cell adhesion behavior of engineering plastics plasticized by supercritical carbon dioxide Dent. Mater. J. 2020.12; 39(6); 1033-1038

Chemical Bioscience

Professor	Takamitsu HOSOYA
Associate Professor	Suguru YOSHIDA
Assistant Professor	Junpei TAGUCHI
Assistant Professor	Yuki SAKATA
Technical Assistant	Yuki HAZAMA, Haruka HIRAYAMA, Satomi TOMITA
Graduate Students	Tsubasa MATSUZAWA, Tsuneyuki KOBAYASHI, Takahiro AIMI, Rika IDOGAWA, Akihiro KOBAYASHI, Kazuya SUGIYAMA, Hinano TAKEMURA, Mai MINOSHIMA, Takumi OZAWA, Minoru SUZUKI, Ryoto NABEKURA
Collaborators	Yohei OHATA, Yuta Omoto, Kota Kimura, Kento TOKUNAGA

(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 chemical modification methods of biomolecules by strained alkynes.
3. Target protein identification of bioactive compounds based on radioisotope-free (non-RI) photoaffinity labeling based on diazido probe strategy.
4. Development of new methods to efficiently connect multiple molecules based on the characteristic features of azido group.
5. Development of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

(3) Publications

[Original Articles]

1. Yazaki J, Kawashima Y, Ogawa T, Kobayashi A, Okoshi M, Watanabe T, Yoshida S, Kii I, Egami S, Amagai M, Hosoya T, Shiroguchi Ki, Ohara O. HaloTag-based conjugation of proteins to barcoding-oligonucleotides. *Nucleic Acids Res.* 2020.01; 48(2); e8
2. Kobayashi T, Hosoya T, Yoshida S. Consecutive Aryne Generation Strategy for the Synthesis of 1,3-Diarylpyrazoles. *J Org Chem.* 2020.02; 85(6); 4448-4462
3. Inouye S, Sahara-Miura Y, Nakamura M, Hosoya T. Expression, purification, and characterization of recombinant apoPholasin. *Protein Expr Purif.* 2020.02; 171; 105615

- Meguro T, Sakata Y, Morita T, Hosoya T, Yoshida S. Facile assembly of three cycloalkyne-modules onto a platform compound bearing thiophene *S,S*-dioxide moiety and two azido groups. *Chem Commun (Camb)*. 2020.04; 56(34); 4720-4723
- Kanemoto K, Sakata Y, Hosoya T, Yoshida S. Synthesis of Phenoxathiins and Phenothiazines by Aryne Reactions with Thiosulfonates. *Chem Lett*. 2020.05; 49(5); 593-596
- Inouye S, Miura-Sahara Y, Iimori R, Sakata Y, Hazama Y, Yoshida S, Nakamura M, Hosoya T. A novel yellow fluorescent protein of recombinant apoPholasin with dehydrocoelenterazine. *Biochem Biophys Res Commun*. 2020.05; 526(2); 404-409
- Kim Y, Kanemoto K, Shimomori K, Hosoya T, Yoshida S. Functionalization of a Single C-F Bond of Trifluoromethylarenes Assisted by an *ortho*-Silyl Group Using a Trityl-Based All-in-One Reagent with Ytterbium Triflate Catalysis. *Chem Eur J*. 2020.05; 26(28); 6136-6140
- Mutsuura K, Sakata Y, Uchida K, Hosoya T, Yoshida S. Synthesis of Thioxanthenes through Formal C-H Thiolation of Benzoic Acid Esters and Acid-mediated Direct Cyclization. *Chem Lett*. 2020.05; 49(7); 753-756
- Kobayashi A, Matsuzawa T, Hosoya T, Yoshida S. Sulfoxide synthesis from sulfinate esters under Pummerer-like conditions. *Chem Commun (Camb)*. 2020.05; 56(40); 5429-5432
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23. Nakamura Y, Sakata Y, Hosoya T, Yoshida S. Synthesis of Functionalized Benzopyran/Coumarin-Derived Aryne Precursors and Their Applications. *Org Lett*. 2020.10; 22(21); 8505-8510
24. Jonasson M, Nordeman P, Eriksson J, Wilking H, Wikström J, Takahashi K, Niwa T, Hosoya T, Watanabe Y, Antoni G, Sundström Poromaa I, Lubberink M, Comasco E. Quantification of aromatase binding in the female human brain using [¹¹C] cetrozole positron emission tomography. *J Neurosci Res*. 2020.11; 98(11); 2208-2218
25. Matsuzawa T, Hosoya T, Yoshida S. One-step synthesis of benzo[*b*] thiophenes by aryne reaction with alkynyl sulfides. *Chem Sci*. 2020.11; 11(35); 9691-9696
26. Nakano-Kobayashi A, Fukumoto A, Morizane A, Nguyen D T , Le T M, Hashida K, Hosoya T, Takahashi R, Takahashi J, Hori O, Hagiwara M. Therapeutics potentiating microglial p21-Nrf2 axis can rescue neurodegeneration caused by neuroinflammation. *Sci Adv*. 2020.11; 6(46); eabc1428
27. Terashima N, Sakata Y, Meguro T, Hosoya T, Yoshida S. Triazole formation of phosphinyl alkynes with azides through transient protection of phosphine by copper. *Chem Commun (Camb)*. 2020.11; 56(90); 14003-14006
28. Idogawa R, Kim Y, Shimomori K, Hosoya T, Yoshida S. Single C–F Transformations of *o*-Hydrosilyl Benzotrifluorides with Trityl Compounds as All-in-One Reagents. *Org Lett*. 2020.12; 22(23); 9292-9297
29. Takemura H, Goto S, Hosoya T, Yoshida S. 2-Azidoacrylamides as compact platforms for efficient modular synthesis. *Chem Commun (Camb)*. 2020.12; 56(99); 15541-15544

[Misc]

1. Niwa T, Hosoya T. Molecular Renovation Strategy for Expeditious Synthesis of Molecular Probes. *Bull Chem Soc Jpn*. 2020.02; 93(2); 230-248

Medicinal Chemistry

Professor Hirokazu TAMAMURA, Ph.D.
Assistant Professor Kohei TSUJI, Ph.D.
Assistant Professor Takuya KOBAYAKAWA, Ph.D.
Technical Assistant Ami MASUDA
Assistant Tomoe KAMEI

Graduate students

D3 Kiju KONNO, Kento EBIHARA, Kofi Baffour-Awuah Owusu
D1 WANG RONGYI
M2 Takumi KAMIMURA, Masaki KURAKAMI, Yuki WATANABE, LIU YISHAN, Tomoki KISHI,
Chika AZUMA, Takahiro ISHII, Miyuki NAKAYAMA, Sayaka BOKU, LIU YIJIE, YANG TINGTING
M1 Takato ONISHI, Akane KUDO, Hiroki NAKANO, Miki HORI, Naoya WADA

Internal Collaborators
ZHANG YAN, LI DONGRUI

External Collaborators
Syun KAWAKATSU

(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 proteins, TALEN and CRISPR-Cas9 for gene therapy and nanotechnology.

Utilizing DNA sequence-specific recognition of zinc finger proteins, TALEN and CRISPR-Cas9, 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. Daisuke Matsumoto, Hirokazu Tamamura, Wataru Nomura. TALEN-Based Chemically Inducible, Dimerization-Dependent, Sequence-Specific Nucleases *Biochemistry* . 2020.01; 59(2); 197-204
2. Takuya Kobayakawa, Hikaru Takano, Takahiro Ishii, Kohei Tsuji, Nami Ohashi, Wataru Nomura, Toshiaki Furuta, Hirokazu Tamamura. Synthesis of hydrophilic caged DAG-lactones for chemical biology applications. *Org. Biomol. Chem.* 2020.05; 18(22); 4217-4223
3. Kohei Tsuji, Kofi Baffour-Awuah Owusu, Takuya Kobayakawa, Rongyi Wang, Masayuki Fujino, Moemi Kaneko, Naoki Yamamoto, Tsutomu Murakami, Hirokazu Tamamura. Exploratory studies on CA-15L, an anti-HIV active HIV-1 capsid fragment. *Bioorg. Med. Chem.* 2020.06; 28(11); 115488

4. Junpeng Qi, Kohei Tsuji, David Hymel, Terrence R. Burke, Jr., Michael Hudecek, Christoph Rader, Haiyong Peng. Chemically Programmable and Switchable CAR-T Therapy *Angew. Chem., Int. Ed.* 2020.07; 59(29); 12178-12185
5. Kohei Tsuji, David Hymel, Terrence R. Burke, Jr.. A new genre of fluorescence recovery assay to evaluate polo-like kinase 1 ATP-competitive inhibitors. *Anal. Methods: advancing methods and applications.* 2020.09; 12(36); 4418-4421
6. Daisuke Matsumoto, Hirokazu Tamamura, Wataru Nomura. A cell cycle-dependent CRISPR-Cas9 activation system based on an anti-CRISPR protein shows improved genome editing accuracy *Communications Biology.* 2020.10; 3; 1-10
7. Stephen E. Miller, Kohei Tsuji, Rachel P.M. Abrams, Terrence R. Burke, Jr., Joel P. Schneider. Uncoupling the Folding-Function Paradigm of Lytic Peptides to Deliver Impermeable Inhibitors of Intracellular Protein-Protein Interactions. *J. Am. Chem. Soc.* 2020.11; 142(47); 19950-19955
8. Takuya Kobayakawa, Kento Ebihara, Kohei Tsuji, Takuma Kawada, Masayuki Fujino, Yuzuna Honda, Nami Ohashi, Tsutomu Murakami, Hirokazu Tamamura. Bivalent HIV-1 fusion inhibitors based on peptidomimetics. *Bioorg. Med. Chem.* 2020.12; 28(24); 115812

[Conference Activities & Talks]

1. Hirokazu Tamamura . Peptide-lead medicinal chemistry: anti-cancer & HIV agents. The 6th Joint Symposium between Chulalongkorn University and IBB/TMDU on Biomedical Materials and Engineering 2020.01.14 Bangkok, Thailand
2. Hirokazu Tamamura . Bivalent Ligands of GPCR as Molecular Measures, Bioprobes for Cancer Cells and Anti-cancer Agents. The 7th SNU Symposium on Medicinal Chemistry 2020.02.14 Seoul, Korea
3. Hirokazu Tamamura. Bivalent HIV-1 fusion inhibitors using peptidomimetics. 16th Chinese International Peptide Symposium 2020.09.25 online/Hefei, China (Keynote Speaker)
4. Chika Azuma, Takuya Kobayakawa, Kohei Tsuji, Hirokazu Tamamura. A convergent synthesis of chloroalkene dipeptide isosteres as peptidomimetics. The 57th Japanese Peptide Symposium 2020.11.09 online (Tottori)
5. Kofi Baffour-Awuah Owusu, Kohei Tsuji, Rongyi Wang, Takuya Kobayakawa, Moemi Kaneko, Tsutomu Murakami, Hirokazu Tamamura. Exploratory studies on the development of anti-HIV-1 peptides based on HIV-1 capsid fragments. The 57th Japanese Peptide Symposium 2020.11.10 online(Tottori)
6. Wataru Nomura, Takumi Kamimura, Takuya Kobayakawa, Hirokazu Tamamura. Endogenous protein expression imaging by fluorogenic ZIP tag-probe system. The 57th Japanese Peptide Symposium 2020.11.10 online (Tottori)
7. Kohei Tsuji, David Hyme, Buyong Ma, Ruth Nussinov, Hirokazu Tamamura, Terrence R. Burke, Jr.. Development of bivalent inhibitors of polo-like kinase 1 with great affinity enhancement. The 57th Japanese Peptide Symposium 2020.11.10 online (Tottori)
8. Kaho Matsumoto, Takeo Kuwata, Zahid Hasan, Yu Kaku, Shashwata Biswas, Shokichi Takahama, Hirokazu Tamamura and Shuzo Matsushita. The CD4 mimetic compound YIR-821-mediated enhancement of the neutralization activities of plasma IgG against autologous isolates in vitro.. 21st Kumamoto AIDS Seminar 2020.11.11 online(Kumamoto)
9. Hirokazu Tamamura. Bioimaging of GPCR dimers and its application to molecular probes for cancer cells. A3 Foresight & 5 Star Alliance Joint Workshop on Organic/Inorganic Hybrid Nano Materials and Bio Imaging 2020.12.03 online
10. Hirokazu Tamamura. Mid-size drugs based on peptidomimetics. The 7th Joint Symposium between Chulalongkorn University and IBB/TMDU on Biomedical Materials and Engineering 2020.12.22 online (Thailand)
11. Kohei Tsuji. Kinase inhibitors for anti-cancer drugs. The 7th Joint Symposium between Chulalongkorn University and IBB/TMDU on Biomedical Materials and Engineering 2020.12.22 online (Thailand)

Metallic Biomaterials

Takao HANAWA Prof
Maki ASHIDA Assist Prof
Peng CHEN 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. Namura Y, Uchida Y, Sato R, Shimizu N, Motoyoshi M, Tsutsumi Y, Hanawa T, Yoneyama T. Changes in surface properties of dental alloys with atmospheric plasma irradiation Dent. Mater. J.. 2020;
2. Hanawa T. Zirconia versus titanium in dentistry: A review Dent. Mater. J.. 2020.01; 39(1); 24-36

3. Chen P, Liu H, Niinomi M, Horita Z, Fujii H, Hanawa T. Fatigue property and cytocompatibility of a biomedical Co-Cr-Mo alloy subjected to a high pressure torsion and a subsequent short time annealing Mater Trans. 2020.01; 61(2); 361-367
4. Atsushi Takaichi, Yuka Kajima, Nuttaphon Kittikundecha, Hein Linn Htat, Hla Htoot Wai Cho, Takao Hanawa, Takayuki Yoneyama, Noriyuki Wakabayashi. Effect of heat treatment on the anisotropic microstructural and mechanical properties of Co-Cr-Mo alloys produced by selective laser melting. J Mech Behav Biomed Mater. 2020.02; 102;
5. Yuka Kajima, Atsushi Takaichi, Yusuke Tsutsumi, Takao Hanawa, Noriyuki Wakabayashi, Akira Kawasaki. Influence of magnetic susceptibility and volume on MRI artifacts produced by low magnetic susceptibility Zr-14Nb alloy and dental alloys. Dent Materials Journal. 2020.03; 39(2); 256-261
6. Ashida M, Tsutsumi Y, Homma K, Chen P, Shimojo M, Hanawa T. Design of zirconium quaternary system alloys and their properties Mater Trans. 2020.03; 61(4); 776-781
7. Correa DRN, Rocha LA, Donato TAG, Sousa KSJ, Grandini CR, Afonso CRM, Doi H, Tsutsumi Y, Hanawa T. On the mechanical biocompatibility of Ti-15Zr-based alloys for potential use as load-bearing implants J Mater Res Technol. 2020.03; 9(2); 1241-1250
8. Sun XH, Liu DB, Zhou WW, Nomura N, Tsutsumi Y, Hanawa T. Effects of process parameters on the mechanical properties of additively manufactured Zr-1Mo alloy builds J Mech Behavior Biomed Mater. 2020.04; 104; 103655
9. Shimabukuro M, Manaka T, Tsutsumi Y, Nozaki K, Chen P, Ashida M, Nagai A, Hanawa T. Corrosion Behavior and Bacterial Viability on Different Surface States of Copper Mater Trans. 2020.06; 61(6); 1143-1148
10. Namura Y, Uchida Y, Sato R, Shimizu N, Motoyoshi M, Tsutsumi Y, Hanawa T, Yoneyama T. Changes in surface properties of dental alloys with atmospheric plasma irradiation Dent Mater J. 2020.06; 39(3); 375-380
11. Shimabukuro M, Hiji A, Manaka T, Nozaki K, Chen P, Ashida M, Tsutsumi Y, Nagai A, Hanawa T. Time-transient effects of silver and copper in the porous titanium dioxide layer on antibacterial properties J Funct Biomater. 2020.06; 11(2); 44
12. Fukushima O, Tsutsumi Y, Hanawa T. Mechanism of electrodeposition process of poly (ethylene glycol) diamine to titanium surface Mater Trans. 2020.07; 61(7); 1346-1354
13. Dziaduszevska M, Shimabukuro M, Seramak T, Zielinski A, Hanawa T. Effects of micro-arc oxidation process parameters on characteristics of calcium-phosphate containing oxide layers on the selective laser melted Ti13Zr13Nb alloy Coatings. 2020.07; 10(8); 745
14. Shimabukuro M, Tsutsumi Y, Nozaki K, Chen P, Yamada R, Ashida M, Doi H, Nagai A, Hanawa T. Investigation of antibacterials effect of copper introduced titanium surface by electrochemical treatment against facultative anaerobic bacteria Dent Mater J. 2020.08; 39(4); 639-647
15. Rajan ST, Thampi A, Terada-Nakaishi M, Chen P, Hanawa T, Nandakumar AK, Subramanian B. Zirconium-based metallic glass and zirconia coatings to inhibit bone formation on titanium Biomed Mater. 2020.10; 15(6); 065019
16. Hiji A, Hanawa T, Shimabukuro M, Chen P, Ashida M, Ishikawa K. Initial formation kinetics of calcium phosphate on titanium in Hanks' solution characterized using XPS Surf Interface Anal. 2020.10; 53(2); 185-193
17. Sun XH, Liu DB, Chen MF, Zhou WW, Nomura N, Hanawa T. Hot isostatic pressing of MRI compatible Zr-1Mo components manufactured by laser powder bed fusion Mater Charact. 2020.11; 169; 110657
18. Tsutsumi Y, Muto I, Nakano S, Tsukada J, Manaka T, Chen P, Ashida M, Sugawara Y, Shimojo M, Hara N, Katayama H, Hanawa T. Effect of impurity elements on localized corrosion of zirconium in chloride containing environment J Electrochem Soc. 2020.11; 167(14); 141507
19. Yanagida S, Nagoshi T, Araki A, Chang TFM, Chen CY, Kobayashi E, Umise A, Hosoda H, Sato T, Sone M. Heterogeneous deformation behavior of Cu-Ni-Si alloy by micro-size compression testing Crystals. 2020.12; 10(12); 1162

[Conference Activities & Talks]

1. Hanawa T. Biofunctionalization of metals. The 6th Joint Symposium between IBB/TMDU and Chulalongkorn University on "Biomedical Materials and Engineering" 2020.01.14 Bangkok, Thailand
2. Chen P, Shinohara N, Shinonaga T, Ashida M, Sato Y, Tsutsumi Y, Tsukamoto M, Hanawa T. Improvement of osteoconduction of preosteoblast by titanium with patterned periodic nano surface topography fabricated by femtosecond laser irradiation. International Joint Symposium 2020 2020.12.14 オンライン
3. Ashida M. Strengthening of titanium alloy by severe plastic deformation for dental narrow implants. The 7th Joint Symposium between IBB/TMDU and Chulalongkorn University 2020.12.22 オンライン

Organic Biomaterials

Professor: Nobuhiko YUI
Associate Professor: Atsushi TAMURA
Assistant Professor: Yoshinori ARISAKA
Secretary: Nanae NISHI

(1) Research

1. Design of Polyrotaxane-based Surfaces and Three-dimensional Architectures

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. In addition, Polyrotaxane-based three-dimensional architectures such as hydrogels, scaffolds, and resins are developed for biologically active supramolecular biomaterials. The mobility and stimuli-responsively dissociative character of polyrotaxanes are integrated to the three-dimensional architectures to demonstrate novel functions in the Biomaterials.

2. Stimuli-labile Polyrotaxanes as a Therapeutic Agent for Intractable Diseases

Stimuli-labile polyrotaxanes that release threaded cyclodextrins under intracellular environments are developed and evaluated their activity in the treatment of various intractable diseases including lysosomal storage disorders.

3. Detachable Dental Adhesives Based on Photo-degradable Supermolecular Cross-linkers

Photo-degradable polyrotaxanes are developed as a component of detachable dental adhesive, cement, and resin. By the irradiation of light, the mechanical strength of the polyrotaxane-containing dental materials are found to decrease. Therefore, the photo-degradable polyrotaxanes-containing dental materials would be applied as detachable dental materials.

(2) Publications

[Original Articles]

1. Ruriko Sekiya-Aoyama, Yoshinori Arisaka, Nobuhiko Yui. Mobility tuning of polyrotaxane surfaces to stimulate myocyte differentiation *Macromolecular Bioscience*. 2020.02; 20(4); 1900424
2. Yoshinori Arisaka, Hiroki Masuda, Tetsuya Yoda, Nobuhiko Yui. Simple treatment of cell culture surfaces with water-dimethyl sulfoxide mixtures impacts YAP localization in vascular endothelial cells *Materials Letters*. 2020.03; 263; 127245
3. Hiroki Masuda, Yoshinori Arisaka, Ruriko Sekiya-Aoyama, Tetsuya Yoda, Nobuhiko Yui. Biological effects of polyrotaxane surfaces on cellular responses of fibroblast, preosteoblast, and preadipocyte cell lines *Polymers*. 2020.04; 12(4); 924
4. Asato Tonegawa, Atsushi Tamura, Shunyao Zhang, Nobuhiko Yui. Hydrophobicity of acyl groups in α -cyclodextrin-threaded polyrotaxanes dominates the formation and stability of self-assembled nanoparticles. *Polymer*. 2020.06; 200; 122537

5. Kei Nishida, Atsushi Tamura, Tae Woong Kang, Hiroki Masuda, Nobuhiko Yui. An antibody–supermolecule conjugate for tumor-specific targeting of tumoricidal methylated β -cyclodextrin-threaded polyrotaxanes. *Journal of Materials Chemistry B*. 2020.08; 8(31); 6975-6987
6. Asato Tonegawa, Atsushi Tamura, Nobuhiko Yui. Acetylation of cyclodextrin-threaded polyrotaxanes yields temperature-responsive phase transition and coacervate formation properties. *Macromolecular Rapid Communications*. 2020.09; 41(17); 2000322
7. Satomi Matsunaga, Atsushi Tamura, Mayu Fushimi, Hokuto Santa, Yoshinori Arisaka, Toru Nikaido, Junji Tagami, Nobuhiko Yui. Light-embrittled dental resin cements containing photodegradable polyrotaxane cross-linkers for attenuating debonding strength. *ACS Applied Polymer Materials*. 2020.12; 2(12); 5756-5766
8. Ruriko Sekiya-Aoyama, Yoshinori Arisaka, Masahiro Hakariya, Hiroki Masuda, Takanori Iwata, Tetsuya Yodad and Nobuhiko Yui . Dual effect of molecular mobility and functional groups of polyrotaxane surfaces on the fate of mesenchymal stem cells *Biomaterials Science*. 2020.12;

[Misc]

1. Arun Kumar Rajendan, Yoshinori Arisaka, Nobuhiko Yui, Sachiko Iseki. Polyrotaxanes as emerging biomaterials for tissue engineering applications: A brief review *Inflammation and Regeneration*. 2020.11; 40(1); 27

[Conference Activities & Talks]

1. Tae Woong Kang, 田村篤志, 有坂慶紀, 由井伸彦. Preparation and characterization of novel functionalized polyrotaxanes capped by bulky trithiocarbonate groups. 第 69 回高分子学会年次大会 2020.05.27 福岡国際会議場, 福岡県福岡市
2. Zhang Shunyao, 田村篤志, 由井伸彦. Design of pH-responsive anionic polyrotaxanes and the modulation of cellular internalization efficiency. 第 69 回高分子学会年次大会 2020.05.27 福岡国際会議場, 福岡県福岡市

Molecular Cell Biology

Professor Hiroshi Shibuya
Associate Professor Toshiyasu Goto
Assistant Professor Masahiro Shimizu

(1) Lectures & Courses

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. Sato Atsushi, Shimizu Masahiro, Goto Toshiyasu, Masuno Hiroyuki, Kagechika Hiroyuki, Tanaka Nobuyuki, Shibuya Hiroshi. WNK regulates Wnt signalling and beta-Catenin levels by interfering with the interaction between beta-Catenin and GID COMMUNICATIONS BIOLOGY. 2020.11; 3(1);

Developmental and Regenerative Biology

Professor Hiroshi Nishina, Ph.D.
Lecturer Satoshi Kofuji, Ph.D.
Assistant Professor Yasuhiro Nakano, Ph.D.
Technical Assistant Mizuki Kusaba
Secretary Kazuko Tanaka
Secretary Kaori Kofuji

(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
2. Studies on vertebrate organogenesis
3. Studies on organ homeostasis
4. Studies on behavioral rhythm

(3) Publications

[Original Articles]

1. Hirofumi Omori, Miki Nishio, Muneyuki Masuda, Yosuke Miyachi, Fumihito Ueda, Takafumi Nakano, Kuniaki Sato, Koshi Mimori, Kenichi Taguchi, Hiroki Hikasa, Hiroshi Nishina, Hironori Tashiro, Tohru Kiyono, Tak Wah Mak, Kazuwa Nakao, Takashi Nakagawa, Tomohiko Maehama, Akira Suzuki. YAP1 is a potent driver of the onset and progression of oral squamous cell carcinoma. *Sci Adv.* 2020; 6(12); eaay3324
2. Kenya Kamimura, Takeshi Yokoo, Hiroyuki Abe, Norihiro Sakai, Takuro Nagoya, Yuji Kobayashi, Masato Ohtsuka, Hiromi Miura, Akira Sakamaki, Hiroteru Kamimura, Norio Miyamura, Hiroshi Nishina, Shuji Terai. Effect of Diphtheria Toxin-Based Gene Therapy for Hepatocellular Carcinoma. *Cancers (Basel).* 2020.02; 12(2);

3. Hanzawa N, Hashimoto K, Yuan X, Kawahori K, Tsujimoto K, Hamaguchi M, Tanaka T, Nagaoka Y, Nishina H, Morita S, Hatada I, Yamada T, Ogawa Y. Targeted DNA demethylation of the Fgf21 promoter by CRISPR/dCas9-mediated epigenome editing. *Scientific reports*. 2020.03; 10(1); 5181
4. Erika Ishihara, Yuya Nagaoka, Toshiaki Okuno, Satoshi Kofuji, Mari Ishigami-Yuasa, Hiroyuki Kagechika, Kenya Kamimura, Shuji Terai, Takehiko Yokomizo, Yukihiko Sugimoto, Yasuyuki Fujita, Akira Suzuki, Hiroshi Nishina. Prostaglandin E 2 and its receptor EP2 trigger signaling that contributes to YAP-mediated cell competition *Genes Cells*. 2020.03; 25(3); 197-214
5. Kodaka Manami, Mao Fengju, Arimoto-Matsuzaki Kyoko, Kitamura Masami, Xu Xiaoyin, Yang Zeyu, Nakagawa Kentaro, Maruyama Junichi, Ishii Kana, Akazawa Chihiro, Oyaizu Takuya, Yamamoto Naoki, Ishigami-Yuasa Mari, Tsuemoto Nozomi, Ito Shigeru, Kagechika Hiroyuki, Nishina Hiroshi, Hata Yutaka. Characterization of a novel compound that promotes myogenesis via Akt and transcriptional co-activator with PDZ-binding motif (TAZ) in mouse C2C12 cells *PLOS ONE*. 2020.04; 15(4); e0231265
6. Yasuhiro Nakano, Akihide Kamiya, Hideaki Sumiyoshi, Kota Tsuruya, Tatehiro Kagawa, Yutaka Inagaki. A Deactivation Factor of Fibrogenic Hepatic Stellate Cells Induces Regression of Liver Fibrosis in Mice. *Hepatology*. 2020.04; 71(4); 1437-1452
7. Tanaka A, Watanabe A, Nakano Y, Matsumoto M, Okazaki Y, Miyajima A. Reversible expansion of pancreatic islet progenitors derived from human induced pluripotent stem cells. *Genes to cells : devoted to molecular & cellular mechanisms*. 2020.05; 25(5); 302-311
8. Shimizu T, Nakamura T, Inaba H, Iwasa H, Maruyama J, Arimoto-Matsuzaki K, Nakata T, Nishina H, Hata Y. The RAS-interacting chaperone UNC119 drives the RASSF6-MDM2-p53 axis and antagonizes RAS-mediated malignant transformation. *The Journal of biological chemistry*. 2020.06;
9. Kenji Kamimoto, Yasuhiro Nakano, Kota Kaneko, Atsushi Miyajima, Tohru Itoh. Multidimensional imaging of liver injury repair in mice reveals fundamental role of the ductular reaction. *Communications Biology*. 2020.06; 3(1); 289
10. Daigo Kasahara, Hideaki Sumiyoshi, Hitoshi Endo, Takayo Yanagawa, Yasuhiro Nakano, Yuki Matsuki, Sachie Nakao, Akihide Kamiya, Hiroshi Kimura, Yutaka Inagaki. Visualization and isolation of zone-specific murine hepatocytes that maintain distinct cytochrome P450 oxidase expression in primary culture. *Biochemical and Biophysical Research Communications*. 2020.06; 528(3); 420-425
11. Hideaki Sumiyoshi, Sachie Nakao, Hitoshi Endo, Takayo Yanagawa, Yasuhiro Nakano, Yosuke Okamura, Akira T Kawaguchi, Yutaka Inagaki. A Novel Composite Biomaterial Made of Jellyfish and Porcine Collagens Accelerates Dermal Wound Healing by Enhancing Reepithelization and Granulation Tissue Formation in Mice. *Advances in Wound Care*. 2020.06; 9(6); 295-311
12. Kofuji S, Sasaki AT. GTP Metabolic Reprogramming by IMPDH2: Unlocking Cancer Cells' Fueling Mechanism. *Journal of biochemistry*. 2020.07;
13. Nishio M, To Y, Maehama T, Aono Y, Otani J, Hikasa H, Kitagawa A, Mimori K, Sasaki T, Nishina H, Toyokuni S, Lydon JP, Nakao K, Wah Mak T, Kiyono T, Katabuchi H, Tashiro H, Suzuki A. Endogenous YAP1 activation drives immediate onset of cervical carcinoma in situ in mice. *Cancer science*. 2020.07;
14. Takako Ooshio, Masahiro Yamamoto, Kiyonaga Fujii, Bing Xin, Kenji Watanabe, Masanori Goto, Yoko Okada, Akira Suzuki, Josef M Penninger, Hiroshi Nishina, Yuji Nishikawa. Hepatocyte MKK7 Contributes to Restoration of the Liver Parenchyma Following Injury. *Hepatology*. 2020.09;
15. Kofuji Satoshi, Sasaki Atsuo T.. GTP metabolic reprogramming by IMPDH2: unlocking cancer cells' fuelling mechanism(和訳中) *The Journal of Biochemistry*. 2020.10; 168(4); 319-328
16. Raymond Wu, Stephanie Pan, Yibu Chen, Yasuhiro Nakano, Meng Li, Steven Balog, Hidekazu Tsukamoto. Fate and functional roles of Prominin 1+ cells in liver injury and cancer. *Scientific Reports*. 2020.11; 10; 19412
17. Satotaka Omori, Teh-Wei Wang, Yoshikazu Johmura, Tomomi Kanai, Yasuhiro Nakano, Taketomo Kido, Etsuo A Susaki, Takuya Nakajima, Shigeyuki Shichino, Satoshi Ueha, Manabu Ozawa, Kisho Yokote, Soichiro Kumamoto, Atsuya Nishiyama, Takeharu Sakamoto, Kiyoshi Yamaguchi, Seira Hatakeyama, Eigo Shimizu, Kotoe Katayama, Yasuhiro Yamada, Satoshi Yamazaki, Kanako Iwasaki, Chika Miyoshi,

Hiromasa Funato, Masashi Yanagisawa, Hiroo Ueno, Seiya Imoto, Yoichi Furukawa, Nobuaki Yoshida, Kouji Matsushima, Hiroki R Ueda, Atsushi Miyajima, Makoto Nakanishi. Generation of a p16 Reporter Mouse and Its Use to Characterize and Target p16high Cells In Vivo. *Cell Metabolism*. 2020.11; 32(5); 814-828

[Misc]

1. Yasuhiro Nakano, Yutaka Inagaki. Activation and deactivation of hepatic stellate cells: therapeutic implication in liver fibrosis *Experimental Medicine*. 2020.08; 38(12); 1994-1999

[Conference Activities & Talks]

1. Satoshi Kofuji, Atsuo T Sasaki. A chemical-induced catastrophic vacuolization: potential anti-tumor effect . 第 43 回日本分子生物学会 2020.12.04

[Awards & Honors]

1. AbbVie Award, The Japan Society of Hepatology, 2020.11

Immunology

Professor: Takeshi TSUBATA, M.D., Ph.D.
 Associate Professor: Takahiro ADACHI, Ph.D.
 Assistant Professor: Chizuru AKATSU, Ph.D.
 Project Assistant Professor: Shuichi KINPARA, Ph.D.
 Lecturer: Ji-Yang WANG, Ph.D.
 Researcher: Amin ALBORZIAN DE SHEIKH, Ph.D.
 Technician: Mikako AKAZAWA
 Secretary: Chikako SAWADA

Graduate Students: Hongrui YANG, Kyoko TAMEHIRO
 Graduate Students: Wang LONG, Yuming HUANG
 Graduate Students: Shinji KUNITAKE, Ayaka OOKAME
 Graduate Students: Kana MATSUMURA, Mizuki OOSUMI
 Graduate Students: Yang CUI, Yi DING
 Graduate Students: Tianyi YANG

Intern: Kennosuke KIYOTA

Collaborative Researcher: Wataru TAKASHIMA

(1) Research

Antibody responses to non-protein antigens such as polysaccharide and nucleic acids play crucial roles in host defense against pathogens, and autoimmune diseases. The mechanisms for antibody responses to non-protein antigens are distinct from those to protein antigens, but are largely unknown. We are elucidating mechanisms for antibody responses to non-protein antigens in normal immunity and autoimmunity, and also developing novel therapies and vaccines. Followings are our research subjects.

- 1) Study on the regulatory mechanisms of autoantibody production in systemic lupus erythematosus (SLE) and autoimmune neuropathy
- 2) Study on the B cell regulation by molecular interactions in glycocalyx
- 3) Study on the mechanisms for antibody production to polysaccharides
- 4) Development of novel therapies for autoimmune diseases and vaccines

(2) Education

Department of Immunology is responsible for the education on immunology provided by the PhD Program in Biomedical Sciences and Engineering, and the Master's Program in Medical and Dental Science and Technology.

Research projects in both the Master's and PhD Programs aim at training the students to acquire basic research skills on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

Lecture course on Immunology at the Master's Program aims at giving the students basic ideas how immune system recognizes and responds to the antigens, and how immune system efficiently removes pathogens without responding to self-antigens or environmental antigens. In the lecture course on Molecular Pathophysiology at the PhD Program, lectures on immune responses and pathophysiology of immunological diseases are given so that the students are introduced with the current topics in the field of humoral immune responses and immunological diseases.

(3) Publications

[Original Articles]

1. Kumazawa T, Kotake K, Nishimura A, Asai N, Ugajin T, Yokozeki H, Adachi T. Isolation of food-derived bacteria inducing interleukin-22 in B cells. *Bioscience of microbiota, food and health*. 2020; 39(1); 1-9
2. Aihara, Y., Fukuda, Y., Takizawa, A., Osakabe, N., Aida, T., Tanaka, K., Yoshikawa, S., Karasuyama, H., Adachi, T. Visualization of mechanical stress-mediated Ca(2+) signaling in the gut using intravital imaging. *Bioscience of Microbiota, Food and Health*. 2020; 39(4); 209-18
3. Hong, R., Lai, N., Xiong, E., Ouchida, R., Sun, J., Zhou, Y., Tang, Y., Hikida, M., Tsubata, T., Tagawa, M., Wang, Y. and Wang, J.-y. Distinct roles of BCNP1 in B cell development and activation. *International Immunology*. 2020.01; 32(1); 17-26
4. Nishimura Yuya, Fukuda Yota, Okonogi Toya, Yoshikawa Soichiro, Karasuyama Hajime, Osakabe Naomi, Ikegaya Yuji, Sasaki Takuya, Adachi Takahiro. Dual real-time in vivo monitoring system of the brain-gut axis *BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS*. 2020.04; 524(2); 340-345
5. Isobe, J., Maeda, S., Obata, Y., Iizuka, K., Nakamura, Y., Fujimura, Y., Kimizuka, T., Hattori, K., Kim, Y-G., Morita, T., Kimura, I., Offermanns, S., Adachi, T., Nakao, A., Kiyono, H., Takahashi, D., Hase, K. Commensal-bacteria-derived butyrate promotes the T-cell-independent IgA response in the colon. *International Immunology*. 2020.04; 32(4); 243-258
6. Yasuda, K., Nakashima, A., Murata, A., Suzuki, K., Adachi, T. *Euglena gracilis* and β -glucan paramylon induce Ca²⁺ signaling in intestinal tract epithelial, immune, and neural cells. *Nutrients*. 2020.07; 12(8); 2293
7. Alborzian Deh Sheikh, A., Gomaa, S., Li, X., Routledge, M., Saigoh, K., Numoto, N., Angata, T., Hitomi, Y., Takematsu, H., Tsuiji, M., Ito, N., Kusunoki, S., Tsubata, T. A Guillain-Barré syndrome-associated SIGLEC10 rare variant impairs its recognition of gangliosides. *Journal of Autoimmunity*. 2020.11; 116; 102571
8. Tsugawa, N., Yamada, D., Watabe, T., Onizawa, M., Wang, S., Nemoto, Y., Oshima, S., Tsubata, T., Adachi, T., Kawano, Y., Watanabe, M., Blumberg, R.S., Okamoto, R., Nagaishi, T. CEACAM1 specifically suppresses B cell receptor signaling-mediated activation. *Biochemical and Biophysical Research Communications*. 2020.12; 535; 99-105

[Books etc]

1. Alborzian Deh Sheikh, A., Akatsu, C. and Tsubata, T.. Identification of Siglec Cis-ligands by Proximity Labeling. In "Lectin Purification and Analysis: Methods and Protocols" ed. by Jun Hirabayashi. Springer, 2020 (ISBN : 978-1-0716-0430-4)
2. Tsubata, T.. Involvement of reactive oxygen species (ROS) in BCR signaling as a second messenger. In "B Cells in Immunity and Tolerance" ed. by Ji-Yang Wang. Springer, 2020 (ISBN : 978-981-15-3531-4)

[Conference Activities & Talks]

1. Chizuru Akatsu, Amin Alborzian Deh Sheikh and Takeshi Tsubata. The SHP-1-activating inhibitory co-receptor CD22 paradoxically augments BCR signaling in immunodeficient B cells. The 14th International Conference on Protein Phosphatase 2020.12.10 Kobe + WEB

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) Rational design of PDZ domain inhibitors involved in regulation of intracellular signaling
- 7) Structural basis of giant hemoglobins
- 8) Molecular basis of suppression of HIV-1
- 9) Structure based drug design for protein kinases
- 10) 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. Mizukami T, Furuzawa S, Itoh SG, Segawa S, Ikura T, Ihara K, Okumura H, Roder H, Maki K. Energetics and kinetics of substrate analog-coupled staphylococcal nuclease folding revealed by a statistical mechanical approach. *Proceedings of the National Academy of Sciences of the United States of America*. 2020.07;
2. Senga A, Numoto N, Yamashita M, Iida A, Ito N, Kawai F, Oda M. Multiple structural states of Ca²⁺-regulated PET hydrolase, Cut190, and its correlation with activity and stability. *Journal of biochemistry*. 2020.09;
3. Sasaki H, Masuno H, Kawasaki H, Yoshihara A, Numoto N, Ito N, Ishida H, Yamamoto K, Hirata N, Kanda Y, Kawachi E, Kagechika H, Tanatani A. Lithocholic Acid Derivatives as Potent Vitamin D Receptor Agonists. *Journal of medicinal chemistry*. 2020.12;
4. Iiyama M, Numoto N, Ogawa S, Kuroda M, Morii H, Abe R, Ito N, Oda M. Molecular interactions of the CTLA-4 cytoplasmic region with the phosphoinositide 3-kinase SH2 domains. *Molecular immunology*. 2020.12;
5. Emori Miho, Numoto Nobutaka, Senga Akane, Bekker Gert-Jan, Kamiya Narutoshi, Kobayashi Yuma, Ito Nobutoshi, Kawai Fusako, Oda Masayuki. Structural basis of mutants of PET-degrading enzyme from *Saccharomonospora viridis* AHK190 with high activity and thermal stability *PROTEINS-STRUCTURE FUNCTION AND BIOINFORMATICS*. 2020.12;

[Conference Activities & Talks]

1. Nobutoshi Ito. PDBx/mmCIF format for crystallographic deposition to the Protein Data Bank (PDB). Annual Meeting of The Federation of Korean Societies for Molecular & Biomedical Sciences (FKSBS) 2020.01.10 Gwangju, South Korea
2. Nobutaka Numoto, Takeshi Tsubata, Nobutoshi Ito. Crystal structure analysis of an autoimmune disease susceptible allele CD72c. The 20th Annual Meeting of the Protein Science Society of Japan 2020.07.15
3. Momoka Iiyama, Nobutaka Numoto, Nobutoshi Ito, Masayuki Oda. Analysis of intermolecular interaction between T cell receptor CTLA-4 and adapter molecule PI3K SH2. The 93rd Annual Meeting of the Japanese Biochemical Society 2020.09.15
4. Miho Emori, Akane Senga, Nobutaka Numoto, Nobutoshi Ito, Fusako Kawai, Masayuki Oda. Functional and structural analysis of the improved activity mutant of PET degrading enzyme Cut190. The 93rd Annual Meeting of the Japanese Biochemical Society 2020.09.15
5. Nobutaka Numoto, Narutoshi Kamiya, Fusako Kawai, Masayuki Oda. Reaction mechanism and high functionality of cutinase, an enzyme with PET degrading activity. The 93rd Annual Meeting of the Japanese Biochemical Society 2020.09.16
6. Momoka Iiyama, Nobutaka Numoto, Nobutoshi Ito, Masayuki Oda. Structural and characteristics analysis of intracellular signal transduction protein PI3K SH2. The 56th Japan Conference Calorimetry and Thermal Analysis 2020.10.26
7. Nobutaka Numoto, Kunio Hirata, Takeshi Tsubata, Nobutoshi Ito. Structure determination from cluster crystals of an inhibitory B cell co-receptor CD72. Annual Meeting 2020 and General Assembly of Crystallographic Society of Japan 2020.11.27
8. Nobutaka Numoto. A user review of automatic and remote measurement at SPring-8. Webinar on Annual Meeting 2020 and General Assembly of Crystallographic Society of Japan 2020.11.27

Epigenetic Epidemiology

Associate Professor
SATO Noriko

(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. Developmental Origin of Health and Diseases
3. Role of nutrition on epigenetic modification and health
4. Genetic factors that affect the severity of pathological atherosclerosis and the development of cancer
5. Application of personal genome to preemptive & preventive medicine.

(3) Education

[Doctor course]

Noriko Sato: Biomedical Science

[Master course]

Masaaki Muramatsu: Environmental Social Health

Masaaki Muramatsu: Health Care Informatics

Noriko Sato: Molecular and Cellular Biology

Noriko Sato: Introduction to Human Molecular Genetics

Noriko Sato: Big Data Analytics

[Undergraduate]

Noriko Sato: Bioinformatics

(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. Abudushataer M, Sato N, Mieno M, Sawabe M, Muramatsu M, Arai T. Association of CYP2A6 gene deletion with cancers in Japanese elderly: an autopsy study. *BMC Cancer*. 2020.03; 20(1); 186
2. Minn AKK, Sato N, Mieno MN, Arai T, Muramatsu M. Association study of long non-coding RNA HOTAIR rs920778 polymorphism with the risk of cancer in an elderly Japanese population. *Gene*. 2020.03; 729; 144263
3. Takahisa Watabe, Sho Kanzaki, Noriko Sato, Tatsuo Matsunaga, Masaaki Muramatsu, Kaoru Ogawa. Single nucleotide polymorphisms in tinnitus patients exhibiting severe distress. *Sci Rep*. 2020.08; 10(1); 13023

[Conference Activities & Talks]

1. Noriko Sato. Developmental Origin of Health and Disease (DOHaD) -what conveys the past in utero experience? . The 43rd Annual Meeting of the Molecular Biology Society of Japan 2020.12.03 On line

Department of Functional Genome Informatics

Professor NIKAIDO Itoshi

(1) Outline

We will develop human resources capable of development at an advanced level in molecular biology and data science technologies to measure genome function information at an unprecedented scale and accuracy and produce human resources that can promote the next generation of medicine creatively and proactively.

(2) Publications

[Original Articles]

1. Tsuyuzaki Koki, Sato Hiroyuki, Sato Kenta, Nikaido Itoshi. Benchmarking principal component analysis for large-scale single-cell RNA-sequencing *GENOME BIOLOGY*. 2020.01; 21(1); 9
2. Ozaki Haruka, Hayashi Tetsutaro, Umeda Mana, Nikaido Itoshi. Millefy: visualizing cell-to-cell heterogeneity in read coverage of single-cell RNA sequencing datasets *BMC GENOMICS*. 2020.03; 21(1); 177
3. Mereu Elisabetta, Lafzi Atefeh, Moutinho Catia, Ziegenhain Christoph, McCarthy Davis J., Alvarez-Varela Adrian, Batlle Eduard, Sagar, Gruen Dominic, Lau Julia K., Boutet Stephane C., Sanada Chad, Ooi Aik, Jones Robert C., Kaihara Kelly, Brampton Chris, Talaga Yasha, Sasagawa Yohei, Tanaka Kaori, Hayashi Tetsutaro, Braeuning Caroline, Fischer Cornelius, Sauers Sascha, Trefzer Timo, Conrad Christian, Adiconis Xian, Nguyen Lan T., Regev Aviv, Levin Joshua Z., Parekh Swati, Janjic Aleksandar, Wange Lucas E., Bagnoli Johannes W., Enard Wolfgang, Gut Marta, Sandberg Rickard, Nikaido Itoshi, Gut Ivo, Stegle Oliver, Heyn Holger. Benchmarking single-cell RNA-sequencing protocols for cell atlas projects *NATURE BIOTECHNOLOGY*. 2020.06; 38(6); 747+
4. Ochiai Hiroshi, Hayashi Tetsutaro, Umeda Mana, Yoshimura Mika, Harada Akihito, Shimizu Yukiko, Nakano Kenta, Saitoh Noriko, Liu Zhe, Yamamoto Takashi, Okamura Tadashi, Ohkawa Yasuyuki, Kimura Hiroshi, Nikaido Itoshi. Genome-wide kinetic properties of transcriptional bursting in mouse embryonic stem cells *SCIENCE ADVANCES*. 2020.06; 6(25); eaaz6699
5. Shiozawa Seiji, Nakajima Mayutaka, Okahara Junko, Kuortaki Yoko, Kisa Fumihiko, Yoshimatsu Sho, Nakamura Mari, Koya Ikuko, Yoshimura Mika, Sasagawa Yohei, Nikaido Itoshi, Sasaki Erika, Okano Hideyuki. Primed to Naive-Like Conversion of the Common Marmoset Embryonic Stem Cells *STEM CELLS AND DEVELOPMENT*. 2020.06; 29(12); 761-773
6. Michida Hiroki, Imoto Hiroaki, Shinohara Hisaaki, Yumoto Noriko, Seki Masahide, Umeda Mana, Hayashi Tetsutaro, Nikaido Itoshi, Kasukawa Takeya, Suzuki Yutaka, Okada-Hatakeyama Mariko. The Number of Transcription Factors at an Enhancer Determines Switch-like Gene Expression *CELL REPORTS*. 2020.06; 31(9); 107724
7. Sawada Tomoyo, Chater Thomas E., Sasagawa Yohei, Yoshimura Mika, Fujimori-Tonou Noriko, Tanaka Kaori, Benjamin Kynon J. M., Paquola Apua C. M., Erwin Jennifer A., Goda Yukiko, Nikaido Itoshi, Kato Tadafumi. Developmental excitation-inhibition imbalance underlying psychoses revealed by single-cell

analyses of discordant twins-derived cerebral organoids MOLECULAR PSYCHIATRY. 2020.08; 25(11);
2695-2711

RIKEN Molecular and Chemical Somatology

Visiting Professor	Ichiro Taniuchi
Visiting Professor	Mikiko Sodeoka
Visiting Professor	Nobumoto Watanabe
Visiting Professor	Shinya Hagihara
Visiting Professor	Motomasa Tanaka
Visiting Professor	Katsunori Tanaka
Visiting Lecturer	Nobuhiko Miyasaka
Visiting Lecturer	Fumiyoshi Myouga
Visiting Lecturer	Kazuko Yoshida
Visiting Lecturer	Kosuke Dodo
Visiting Lecturer	Ryo Endo
Visiting Lecturer	Hideyuki Yoshida
Visiting Lecturer	Yutaka Furutani
Visiting Lecturer	Qin Xian-Yang
Visiting Lecturer	Shunsuke Tagami
Visiting Lecturer	Krzyzanowski Marek
Graduate Students	D3 Chih-Hao Shen (Jan~Sep)
	D3 Ziyu Liu (Jan~Dec)
	D2 Xintong Liu (Jan~Dec)
	D2 Nayan Suryawanshi (Jan~Dec)
	D1 Chang Jingjie (Oct~Dec)

(1) Research

Molecular and Chemical Somatology is an interdisciplinary field for understanding of the 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 a variety of molecules that regulate cellular functions including low molecular weight organic compounds, proteins, sugars, and hormones. Students will learn and discuss about the outlines and/or the latest topics on discovery, structure, synthesis, biology, and management of the key molecules/factors, and deepen their understanding of this new research 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) Molecular Immunology

- Regulatory mechanisms for lymphocyte development

5) Molecular Neuropathology

- Molecular basis of neurodegenerative disorders and psychiatric diseases

(3) Publications

[Original Articles]

1. Shida T., Kamatari Y.O., Yoda T., Yamaguchi Y., Feig M., Ohhashi Y., Sugita Y., Kuwata K., and Tanaka M. Short disordered protein segment regulates cross-species transmission of a yeast prion. *Nat. Chem. Biol.*, 16, 756-765 (2020)
2. Seo, W., K. Shimizu, S., Kojo, A., Okeke, T., Kohwi-Shigematsu., Fujii S. I., and Taniuchi I. Runx-mediated regulation of CCL5 via antagonizing two enhancers influences immune cell function and anti-tumor immunity. *Nat Commun* 11: 1562 (2020).
3. Tenno, M., Wong A. Y. W., Ikegaya M, Miyauchi E., Seo W., See P., Kato T., Taida T., Ohno-Oishi M., Ohno, H., Yoshida H., Ginhoux F., and Taniuchi I. Essential functions of Runx/Cbfb in gut conventional dendritic cells for priming Rorgt⁺ T cells. *Life Sci Alliance* 3: e201900441 (2020).
4. Suvarna, K., Honda, K., Muroi, M., Kondoh, Y., Osada, H., and Watanabe, N. (2020) Measurement of ATPase activity of valosin-containing protein/p97. *Bio-protocol* 10, e3516.

5. Suvarna, K., Honda, K., Muroi, M., Kondoh, Y., Watanabe, N., and Osada, H. (2020) Identification of target protein for bio-active small molecule using photo-cross linked beads and MALDI-TOF mass spectrometry. *Bio-protocol* 10, e3517

[Review Articles]

1. Nomura, A., and Taniuchi I. The Role of CD8 Downregulation during Thymocyte Differentiation. *Trends Immunol* 41: 972-981 (2020).

[Conference Activities & Talks]

1. Taniuchi, I. “Molecular pathogenesis of PID by miss-sense variants of transcription factors”. The 48th Annula Meetign of the Japanese Soceity of Clinical Immunology. Oct 19, 2019. Online.
2. Liu, Z., Nogawa, T., Sanada, E., Okano, A., Ishikawa, K., Semba, K., Osada, H., and Watanabe, N. “Screening and analyses of c-Myc inhibitors using intrinsic transcriptional targets”. The 43th Annula Meetign of the Molecualr Bilogy Society of Japan. Dec 2-4, 2020. Online.

NCC Cancer Science

Visiting Professor	Hirofumi ARAKAWA
Visiting Professor	Kenkichi MASUTOMI
Visiting Professor	Ryuji HAMAMOTO
Visiting Associate Professor	Masahiro YASUNAGA
Visiting Lecturer	Tohru KIYONO
Visiting Lecturer	Kazunori AOKI
Visiting Lecturer	Takashi KOHNO
Visiting Lecturer	Yasuhito UEZONO
Visiting Lecturer	Naoto TSUCHIYA
Visiting Lecturer	Hiroyoshi NISHIKAWA
Visiting Lecturer	Issay KITABAYASHI
Visiting Lecturer	Tadashi KONDO
Graduate Students	D3 Tomoko WATANABE Kazuma KOBAYASHI Takahiro SHIRAI
	D2 Yamato OGIWARA Eri HASHIMOTO
	D1 Akira SAKAI Norio SHINKAI
	M2 Megumi KAMISHIMA Kurumi KISHIMOTO Yuma NOZUE Masako TSUDUKIHASHI Ai SASAKI
	M1 Yuma TAKAMOTO Rie SAWADO Tomomasa TANIYAMA

(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. Sano H, Futamura M, Gaowa S, Kamino H, Nakamura Y, Yamaguchi K, Tanaka Y, Yasufuku I, Nakakami A, Arakawa H, Yoshida K. p53/Mieap-regulated mitochondrial quality control plays an important role as a tumor suppressor in gastric and esophageal cancers. *Biochem Biophys Res Commun.* 529(3): 582-589, 2020.
2. Yasukawa M, Ando Y, Yamashita T, Matsuda Y, Shoji S, Morioka M, Kawaji H, Shiozawa K, Machitani M, Abe T, Yamada S, Kaneko M, Kato Y, Furuta Y, Kondo T, Shirouzu M, Hayashizaki Y, Kaneko S, Masutomi K. CDK1 dependent phosphorylation of hTERT contributes to cancer progression. *Nat. Commun.* 11(1): 1557, 2020.
3. Kobayashi K, Bolatkan A, Shiina S, Hamamoto R. Fully-Connected Neural Networks with Reduced Parameterization for Predicting Histological Types of Lung Cancer from Somatic Mutations. *Biomolecules.* 28: 1249, 2020.
4. Takahashi S, Asada K, Takasawa K, Shimoyama R, Sakai A, Bolatkan A, Shinkai N, Kobayashi K, Komatsu M, Kaneko S, Sese J, Hamamoto R. Predicting Deep Learning Based Multi-Omics Parallel Integration Survival Subtypes in Lung Cancer Using

Reverse Phase Protein Array Data. *Biomolecules*. 10: 1460, 2020.

5. Dozen A, Komatsu M, Sakai A, Komatsu R, Shozu K, Machino H, Yasutomi S, Arakaki T, Asada K, Kaneko S, Matsuoka R, Aoki D, Sekizawa A, Hamamoto R. Image Segmentation of the Ventricular Septum in Fetal Cardiac Ultrasound Videos Based on Deep Learning Using Time-Series Information. *Biomolecules*. 10: 1526, 2020.
6. Shozu K, Komatsu M, Sakai A, Komatsu R, Dozen A, Machino H, Yasutomi S, Arakaki T, Asada K, Kaneko S, Matsuoka R, Nakashima A, Sekizawa A, Hamamoto R. Model-Agnostic Method for Thoracic Wall Segmentation in Fetal Ultrasound Videos. *Biomolecules*. 10:1691, 2020.
7. Takashima H, Koga Y, Tsumura R, Yasunaga M, Tsuchiya M, Inoue T, Negishi E, Harada M, Yoshida S, Matsumura Y. Reinforcement of antitumor effect of micelles containing anticancer drugs by binding of an anti-tissue factor antibody without direct cytotoxic effects. *J Control Release*. 323: 138-150, 2020.
8. Numasawa K, Hanaoka K, Saito N, Yamaguchi Y, Ikeno T, Echizen H, Yasunaga M, Komatsu T, Ueno T, Miura M, Nagano T, Urano Y. et al, A Fluorescent Probe for Rapid, High-Contrast Visualization of Folate-Receptor-Expressing Tumors In Vivo. *Angew Chem Int Ed Engl*. 59(15): 6015-6020, 2020.
9. Watanabe T, Honda T, Totsuka H, Yoshida M, Tanioka M, Shiraishi K, Shimada Y, Arai E, Ushiyama M, Tamura K, Yoshida T, Kani Y, Kohno T. Simple prediction model for homologous recombination deficiency in breast cancers in adolescents and young adults. *Breast Cancer Res Treat*. 182(2): 491-502, 2020.
10. Hirose S, Murakami N, Takahashi K, Kuno I, Takayanagi D, Asami Y, Matsuda M, Shimada Y, Yamano S, Sunami K, Yoshida K, Honda T, Nakahara T, Watanabe T, Komatsu M, Hamamoto R, Kobayashi Kato M, Matsumoto K, Okuma K, Kuroda T, Okamoto A, Itami J, Kohno T, Kato T, Shiraishi K, Yoshida H. Genomic Alterations in STK11 Can Predict Clinical Outcomes in Cervical Cancer Patients. *Gynecol Oncol*. 156(1): 203-210, 2020.

[Reviews Articles]

1. Machitani M, Yasukawa M, Nakashima J, Furuichi Y, Masutomi K. RNA-dependent RNA polymerase, RdRP, a promising therapeutic target for cancer and potentially COVID-19. *Cancer Sci*. 111: 3976-3984, 2020.

2. Hamamoto R, Komatsu M, Takasawa K, Asada K, Kaneko S. Epigenetics Analysis and Integrated Analysis of Multiomics Data, Including Epigenetic Data, Using Artificial Intelligence in the Era of Precision Medicine. *Biomolecules*. 10: 62, 2020.
3. Hamamoto R, Suvarna K, Yamada M, Kobayashi K, Shinkai N, Miyake M, Takahashi M, Jinnai S, Shimoyama R, Sakai A, Takasawa K, Bolatkan A, Shozu K, Dozen A, Machino H, Takahashi S, Asada K, Komatsu M, Sese J, Kaneko S. Application of Artificial Intelligence Technology in Oncology: Towards the Establishment of Precision Medicine. *Cancers (Basel)*. 12: 3532, 2020.
4. Yasunaga M. Antibody therapeutics and immunoregulation in cancer and autoimmune disease. *Semin Cancer Biol*. 64: 1-12, 2020.

[Conference Activities & Talks]

1. Ryuji Hamamoto. Medical AI research for clinical applications. KAST-NAMOK Joint International Symposium 2020, Seoul (South Korea), October 2020.
2. Ryuji Hamamoto. Medical AI Research in the Era of Precision Medicine. Seoul Bio-Economy Forum 2020, Seoul (South Korea), November 2020.
3. Kamakura D, Yasunaga M, Asano R, Matsumura Y. Development of bispecific antibodies using molecular imaging. AACR Annual Meeting 2020, Online, June 2020.
4. Hirakawa T, Yasunaga M, Kawai T, Shimizu Y, Shitara K, Koganemaru S, Kuboki Y, Doi T, Matsumura Y. Discovery of novel biomarkers against refractory cancer using in situ level mass spectrometry informatics. AACR Annual Meeting 2020, Online, June 2020.
5. Takashima H, Koga Y, Onuki K, Manabe S, Tsumura R, Anzai T, Iwata N, Yasunaga M, Yang W, Yokokita T, Komori Y, Mori D, Haba H, Fujii H, Matsumura Y. Preclinical evaluation of astatine-211-conjugated anti-tissue factor antibody. AACR Annual Meeting 2020, Online, June 2020.

Cellular and Molecular Medicine

Associate Professor Junko Sasaki

(1) Outline

Phosphoinositides (PIPs) are the molecules that contain phosphatidylinositol, which has a glycerol backbone, two long-chain fatty acids, and an inositol head group. As a result of combinatorial phosphorylation of the hydroxyls of inositol ring, seven other PIPs classes can be generated. Each PIPs exhibits a unique stereochemistry and can bind to distinct cellular protein targets, thereby regulating a wide variety of cellular activities and responses. In terms of PIPs acyl chains, our knowledge about how much importance these hydrocarbon chains have is only limited, in contrast to the phosphorylation patterns. Our goal is to reveal the functions of each PIPs molecular species.

(2) Research

Recently, we revealed that the acyl profiles of phosphoinositides are altered in human prostate cancer tissues. Therefore we are currently studying the physiological and pathophysiological functions of each PIPs molecular species by three approaches.

1. Cellular analyses: We examine changes in PIPs molecular species regulating cellular responses, including cell migration, proliferation, and differentiation.
2. In vivo analyses: We examine changes in PIPs molecular species of diseased tissues from gene-targeted mice lacking PIPs metabolizing enzymes.
3. Molecular analyses: We find the binding proteins of each PIPs molecular species by developing new methods for studying lipid-protein interaction.

(3) Education

Topics of research for graduate student

1. Cancers and PIPs molecular species
2. Inflammations and PIPs molecular species
3. Disorders of sex development and PIPs molecular species

(4) Lectures & Courses

Each student has an independent research theme. Students are expected to have experimental science knowledge and skills.

The goal is to be able to plan, execute, and present original research in cooperation with other researchers.

(5) Publications

Division of Data Science Algorithm Design and Analysis

Professor BANNAI Hideo
 Assistant Professor
 KOEPPL Dominik

(1) Outline

The department of Data Science Algorithm Design and Analysis studies algorithms, which are an essential component of data science, especially for handling large data sets. Our aim is to design algorithms and data structures that are both effective and efficient, in order to help manage and analyze various types of medical data.

(2) Publications

[Original Articles]

1. Kohei Yamada, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Faster STR-EC-LCS Computation SOFSEM 2020: Theory and Practice of Computer Science. 2020; 125-135
2. Takuya Mieno, Yuki Kuhara, Tooru Akagi, Yuta Fujishige, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Minimal Unique Substrings and Minimal Absent Words in a Sliding Window SOFSEM 2020: Theory and Practice of Computer Science. 2020; 148-160
3. Dominik Köppl, Simon J. Puglisi, Rajeev Raman. Fast and Simple Compact Hashing via Bucketing. SEA. 2020; 7-14
4. Dominik Köppl, Tomohiro I, Isamu Furuya, Yoshimasa Takabatake, Kensuke Sakai, Keisuke Goto. Re-Pair in Small Space. DCC. 2020; 377
5. Kazuya Tsuruta, Dominik Köppl, Shunsuke Kanda, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. c-Trie++: A Dynamic Trie Tailored for Fast Prefix Searches. DCC. 2020; 243-252
6. Dominik Köppl, Daiki Hashimoto, Diptarama Hendrian, Ayumi Shinohara. In-Place Bijective Burrows-Wheeler Transforms. CPM. 2020; 21-15
7. Johannes Fischer, Tomohiro I, Dominik Köppl. Deterministic Sparse Suffix Sorting in the Restore Model. ACM Trans. Algorithms. 2020; 16(4); 50-53
8. Roland Glück, Dominik Köppl. Computational Aspects of Ordered Integer Partitions with Bounds. Algorithmica. 2020; 82(10); 2955-2984
9. Jarno Alanko, Hideo Bannai, Bastien Cazaux, Pierre Peterlongo, Jens Stoye. Finding all maximal perfect haplotype blocks in linear time Algorithms for Molecular Biology. 2020.02; 15(1);
10. Takaaki Nishimoto, Tomohiro I, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Dynamic index and LZ factorization in compressed space Discrete Applied Mathematics. 2020.03; 274; 116-129
11. Isamu Furuya, Takuya Takagi, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Takuya Kida. Practical Grammar Compression Based on Maximal Repeats Algorithms. 2020.04; 13(4); 103

12. Hideo Bannai, Travis Gagie, Tomohiro I. Refining the r-index *Theoretical Computer Science*. 2020.04; 812; 96-108
13. Kiichi Watanabe, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Fast Algorithms for the Shortest Unique Palindromic Substring Problem on Run-Length Encoded Strings *Theory of Computing Systems*. 2020.05;
14. Mitsuru Funakoshi, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda, Ayumi Shinohara. Detecting k-(Sub-)Cadences and Equidistant Subsequence Occurrences 31st Annual Symposium on Combinatorial Pattern Matching (CPM 2020). 2020.06; 12:1-12:11
15. Katsuhito Nakashima, Moriki Fujisato, Diptarama Hendrian, Yuto Nakashima, Ryo Yoshinaka, Shunsuke Inenaga, Hideo Bannai, Ayumi Shinohara, Masayuki Takeda. DAWGs for Parameterized Matching: Online Construction and Related Indexing Structures 31st Annual Symposium on Combinatorial Pattern Matching (CPM 2020). 2020.06; 26:1-26:14
16. Kazuya Tsuruta, Dominik Köppl, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Grammar-compressed Self-index with Lyndon Words *Transactions on mathematical modeling and its applications*. 2020.08; 13(2); 84-92
17. Hideo Bannai, Travis Gagie, Gary Hoppenworth, Simon J. Puglisi, Luís M. S. Russo. More Time-Space Tradeoffs for Finding a Shortest Unique Substring Algorithms. 2020.09; 13(234); 1-9
18. Jacqueline W. Daykin, Dominik Köppl, David Kübel, Florian Stober. On Arithmetically Progressed Suffix Arrays *Prague Stringology Conference 2020*. 2020.09; 96-110
19. Dominik Köppl, Tomohiro I, Isamu Furuya, Yoshimasa Takabatake, Kensuke Sakai, Keisuke Goto. Re-Pair in Small Space *Prague Stringology Conference 2020*. 2020.09; 134-147
20. Akihiro Nishi, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Towards Efficient Interactive Computation of Dynamic Time Warping Distance String Processing and Information Retrieval. 2020.10; 27-41
21. Takafumi Inoue, Shunsuke Inenaga, Hideo Bannai. Longest Square Subsequence Problem Revisited *String Processing and Information Retrieval*. 2020.10; 147-154
22. Kanaru Kutsukake, Takuya Matsumoto, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. On Repetitiveness Measures of Thue-Morse Words *String Processing and Information Retrieval*. 2020.10; 213-220
23. Hideo Bannai, Takuya Mieno, Yuto Nakashima. Lyndon Words, the Three Squares Lemma, and Primitive Squares *String Processing and Information Retrieval*. 2020.10; 265-273
24. Takuya Mieno, Dominik Köppl, Yuto Nakashima, Shunsuke Inenaga, Hideo Bannai, Masayuki Takeda. Space-efficient algorithms for computing minimal/shortest unique substrings 2020.12; 845; 230-242
25. Dominik Köppl, Tomohiro I, Isamu Furuya, Yoshimasa Takabatake, Kensuke Sakai, Keisuke Goto. Re-Pair in Small Space Algorithms. 2020.12; 14(1); 5
26. Shunsuke Kanda, Dominik Köppl, Yasuo Tabei, Kazuhiro Morita, Masao Fuketa. Dynamic Path-decomposed Tries *ACM Journal of Experimental Algorithmics*. 2020.12; 25; 1-28

[Awards & Honors]

1. SPIRE 2020 Best Paper Award, 27th International Symposium on String Processing and Information Retrieval (SPIRE 2020), 2020.10

Department of AI Technology Development

Heewon Park

(1) Outline

The department of AI Technology Development studies statistical methodologies and artificial intelligence technique that play a key role in uncovering disease mechanism based on complex biomedical data. Our mission is to develop novel AI and machine learning methodologies that attain statistical accuracy and better interpretability, simultaneously.

1. Statistical theory and data-analytic approaches
2. Explainable AI technologies for systematic understanding of diseases
3. Analysis of omics data for healthcare
4. Network biology for uncovering gene regulatory networks

(2) Research

We are research on statistical modeling and AI techniques for medical data analysis.

1) Statistical modeling and AI techniques for personalized medicine.

In recent years, genomic personalized medicine has been drawn a large amount of attention to identify individual genomic characteristics for each sample. One of our research topics is theoretical and practical studies on statistical modeling and AI technique to extract evidences and understand the mechanisms of disease.

2) Network Biology

Gene regulatory network is a crucial tool for identifying biomarkers having essential biological functions and uncover mechanism of disease. We are studying on gene network estimation and interpretation of the constructed network based on statistical and AI methodologies to understand complex mechanism of disease, find drug target, predict drug sensitivity, etc.

(3) Education

We are educating undergraduate and graduated students on the fields of data science and AI methodologies based on Mathematics and Statistics for analysis of data obtained from medical and dental area.

(4) Lectures & Courses

We aim to study knowledge for understanding statistical modeling and artificial intelligence, and encourages students to learn analysis of complex data obtained from medical and healthcare area based on the statistical and AI methodologies.

(5) Clinical Services & Other Works

Research support

We are providing support/ counseling data analysis of clinical data.

(6) Publications

[Original Articles]

1. Park H, Maruhashi K, Yamaguchi R, Imoto S, Miyano S. Global gene network exploration based on explainable artificial intelligence approach PLoS One. 2020.11; 15(11); e0246380.
2. Park H, Yamaguchi R, Imoto S, Miyano S. Automatic sparse principal component analysis CANADIAN JOURNAL OF STATISTICS-REVUE CANADIENNE DE STATISTIQUE. 2020.12; doi.org/10.1002/cjs.11579.
3. Park H, Konishi S. Sparse common component analysis for multiple high-dimensional datasets via noncentered principal component analysis STATISTICAL PAPERS. 2020.12; 61; 2283-2311.

Department of Anatomical and Physiological Science

Professor Osamu Hoshi
Assistant Professor Hitomi Fujishiro
(Doctor's Programs) Ayana Sugizaki, Miku Nakai

(1) Outline

Anatomy and physiology are the primary disciplines taught in the field of anatomy and physiological sciences. Anatomy explores the morphology and structure of the human body from the organ to cellular and molecular levels. It is the most fundamental area of medical science. Physiology investigates what kind of mechanism is needed for each structural component of the human body to function, and how such components are integrated into the whole human body. Anatomy and physiology function like two wheels of a cart for the scientific understanding of the human body. These two subjects lay down the foundation required to study advanced subjects. The teaching team is committed to providing students with education that helps them master the basics of the subjects and successfully transition to the clinic.

(2) Research

Morphology and biological information analysis uses various microscopic techniques including electron microscopy for observing the microstructure of the living tissue, with the primary aim of gaining new scientific knowledge. Cutting-edge research has been conducted in this area, such as the development of new imaging technologies and applying atomic force microscopy to biomedicine.

(3) Education

Examination for Technology Stream: Human Anatomy Lecture, Human Anatomy Practicum, Physiological Examination Lecture I, Physiological Examination Practicum I, Electron Microscopy, Theory of Advanced Medical Technology, General Lecture, Graduate Research Project

Examination for Nursing Stream: Anatomy, Physiology, Joint Practicum with Advanced and Basic Students (anatomy practicum)

Examination for Science Stream: Morphology and Biological Information Analysis Special Lecture A, Morphology and Biological Information Analysis Experiment A, Morphology and Biological Information Analysis Special Lecture

(4) Lectures & Courses

The teaching team provides students with education and research instructions that help them grow their interest to study and research in the field of medicine. The team simultaneously reviews feedback from students to improve the method of conducting lectures and practicums.

(5) Publications

[Original Articles]

1. Kensuke Kataoka, Ryota Kurimoto, Hiroki Tsutsumi, Tomoki Chiba, Tomomi Kato, Kana Shishido, Mariko Kato, Yoshiaki Ito, Yuichiro Cho, Osamu Hoshi, Ayako Mimata, Yuriko Sakamaki, Ryo Nakamichi, Martin K Lotz, Keiji Naruse, Hiroshi Asahara. In vitro Neo-Genesis of Tendon/Ligament-Like Tissue by Combination of Mohawk and a Three-Dimensional Cyclic Mechanical Stretch Culture System Front Cell Dev Biol. 2020; 8; 307
2. Masumi Saito, Yumi Makino, Kumi Inoue, Yoshino Watanabe, Osamu Hoshi, Tetsuo Kubota. Anti-DNA antibodies cross-reactive with β 2-glycoprotein I induce monocyte tissue factor through the TLR9 pathway. Immunol Med. 2020.07; 1-12

Department of Biochemistry and Biophysics

Assistant Professor: Yo Mabuchi
Project Assistant Professor: Chikako Hayashi

(1) Outline

Our department is in charge of education and research related to Biochemistry and Biophysics.

In particular, we provide education related to basic medicine, medical technology, and social medicine.

Yo Mabuchi (Assistant professor) and Chikako Hayashi (project assistant professor) are in charge of education and research.

(2) Research

Neural crest cell development and differentiation:

In vivo behavior of neural crest cells using Sox10 BAC transgenic mice, which a green fluorescent protein is inserted into a mouse BAC clone containing the entire promoter region of the gene Sox10. Neural crest cell development and differentiation is analyzed by imaging and cell sorting technology.

Diversity of mesenchymal stem cells:

Stem cells contained in somatic tissues are isolated by a cell sorter (flow cytometer) and their cell characteristics are examined. We aim to establish a cell therapy method by identifying the mechanism of tissue homeostasis and the cell population capable of tissue regeneration.

Molecular function analysis of Teneurin-4:

We analyze mice that have lost the function of the transmembrane protein Teneurin-4 as a model animal for tremor.

(3) Publications

[Original Articles]

1. Niibe K, Ohori-Morita Y, Zhang M, Mabuchi Y, Matsuzaki Y, Egusa H. A Shaking-Culture Method for Generating Bone Marrow Derived Mesenchymal Stromal/Stem Cell-Spheroids With Enhanced Multipotency *in vitro*. *Frontiers in bioengineering and biotechnology*. 2020; 8; 590332
2. Chikako Hayashi, Nobuharu Suzuki, Yo Mabuchi, Naomi Kikura, Yukina Hosoda, Susana de Vega, Chihiro Akazawa. The extracellular domain of teneurin-4 promotes cell adhesion for oligodendrocyte differentiation. *Biochem Biophys Res Commun*. 2020.02; 523(1); 171-176
3. Suto EG, Mabuchi Y, Toyota S, Taguchi M, Naraoka Y, Itakura N, Matsuoka Y, Fujii Y, Miyasaka N, Akazawa C.. Advantage of fat-derived CD73 positive cells from multiple human tissues, prospective isolated mesenchymal stromal cells *Scientific Reports*. 2020.09;

4. Harada S, Mabuchi Y, Kohyama J, Shimojo D, Suzuki S, Kawamura Y, Araki D, Suyama T, Kajikawa M, Akazawa C, Okano H, Matsuzaki Y. FZD5 regulates cellular senescence in human mesenchymal stem/stromal cells. *Stem cells (Dayton, Ohio)*. 2020.12; 39(3): 318-330

[Books etc]

1. Yo Mabuchi. *Neural Crest Contributions to Mesenchymal Stem Cells*. Oxford Academic Press, 2020.09

Department of Molecular and Cellular Biology

Nobuharu Suzuki, Associate Professor

(1) Outline

2020 is the 3rd year for our department, since it was started in 2018. The members were Assoc. Prof. Suzuki and 5 graduate students. Regarding our research, we have three main projects: 1) the molecular mechanism of myelination in the central nervous system, 2) the maintenance system of the stemness of somatic stem cells, and 3) the pericellular microenvironment organized by extracellular matrix molecules. In terms of education, we teach graduate and undergraduate students at lectures and laboratory classes of molecular biology and biochemistry, particularly related to medical tests/technologies. In addition, Suzuki is a member of the administrative offices of Lab Safety and of Open Innovation for Research and contributes to their activities.

(2) Research

1) Molecular mechanism of myelination in the central nervous system

In the central nervous system, myelin is formed by oligodendrocytes and is essential for rapid propagation of neuronal signal. In our department, we investigate its cellular and molecular mechanism using the mutant mouse line that develops hypomyelination in the central nervous system and expand the results of our research to application studies. In 2020, we published two original articles regarding the molecular mechanism of myelination in the central nervous system by the transmembrane protein teneurin-4 and the developmental defect of the specific subtype of oligodendrocytes in the teneurin-4 deficient mice, and one review including our recent research results. In addition, we gave 6 presentations of our recent data at international and domestic meetings. Two of the 6 presentations got awards at the meeting for neurochemistry. Also, we got an award at the pitch contest for Cryo-EM Gateway in TMDU. Further, we obtained the Grant-in-Aid for Scientific Research (C) and the Fund for the Promotion of Joint International Research (Fostering Joint International Research (B)) of the Ministry of Education, Culture, Sports, Science, and Technology (MEXT) in Japan, and the Grant for Basic Science Research Projects from The Sumitomo Foundation.

2) Pericellular microenvironment organized by extracellular matrix molecules

In recent years, research of pericellular microenvironment by extracellular matrix molecules has become popular. In our department, we examine functions of extracellular matrix proteins in myelination in the central nervous system. In 2020, we reported that a significance of basement membrane protein laminin for oligodendrocyte precursor cells at the Neurochemistry Meeting.

(3) Education

For undergraduate students, Suzuki teaches “Biochemistry”, “Biochemistry, Lecture”, “Medical Genetics and Human Genome Science, Lecture”, “Biochemistry, Laboratory”, and “Medical Genetics, Laboratory” as a subject-responsible person, and parts of “Advanced Laboratory Sciences”, “Practice of Medical Science”, and “General Medical Technology”.

For graduate students, Suzuki teaches parts of “Medical Technology I”, “Development of Novel Technologies for Clinical Tests” (Ph.D. course), and “Biomedical Laboratory Science Seminar I” (master and Ph.D. courses).

(4) Lectures & Courses

At first, we well-explain the fundamental mechanism of phenomena in organisms to students at any classes, since we want them to have curiosity as much as possible. Based on that, we teach them more expertized knowledge and techniques that are essential for medical technologists in order to let them to achieve at a high level of acquisition. In laboratory, we teach students from fundamental to advanced parts of our research field at lectures, journal clubs, and discussions to let them understand the history and our position in the current research field. Finally, we make efforts for students to have high motivation with their research and study and to enjoy new findings.

(5) Clinical Services & Other Works

Suzuki is Special Volunteer at National Institutes of Health (NIH) and a visiting fellow at National Center of Neurology and Psychiatry (NCNP) and contributes to relationships between the research institutes and universities, internationally and domestically. Also, Suzuki is a member of Society for Neuroscience (SfN), The American Society for Cell Biology (ASCB), The Molecular Biology Society of Japan (MBSJ), The Japan Neuroscience Society (JNS), The Japanese Society for Neurochemistry (JSN), and The Japanese Society for Matrix Biology and Medicine (JSMBM) and contributes to their activities.

(6) Publications

[Original Articles]

1. Chikako Hayashi, Nobuharu Suzuki, Yo Mabuchi, Naomi Kikura, Yukina Hosoda, Susana de Vega, Chihiro Akazawa. The extracellular domain of teneurin-4 promotes cell adhesion for oligodendrocyte differentiation. *Biochem Biophys Res Commun.* 2020.02; 523(1); 171-176
2. Chikako Hayashi, Nobuharu Suzuki, Riko Takahashi, Chihiro Akazawa. Development of type I/II oligodendrocytes regulated by teneurin-4 in the murine spinal cord. *Sci Rep.* 2020.05; 10(1); 8611

[Misc]

1. Nobuharu Suzuki, Miho Iwase, Momona Yamada. The mechanism of axon maintenance by myelin in the central nervous system 2020.12; 9(2); 103-109

[Conference Activities & Talks]

1. Nobuharu Suzuki, Chikako Hayashi, Yo Mabuchi, Naomi Kikura, Yukina Hosoda, Susana de Vega, Chihiro Akazawa. Teneurin-4 gene associated with mental disorders regulates CNS myelination through cell adhesion between oligodendrocytes and neuronal axons. The 10th Takeda Science Foundation Symposium on PharmaSciences 2020.01.24
2. Chikako Hayashi, Yukina Hosoda, Chinami Onchi, Nobuharu Suzuki. The mechanism of myelination through oligodendrocyte adhesion by teneurin-4. The 5th Annual Meeting of Japanese Society for Myelin 2020.02.22
3. Chikako Hayashi, Yukina Hosoda, Chinami Onchi, Nobuharu Suzuki. Teneurin-4 positively regulates oligodendrocyte-axon adhesion and myelination through the binding with teneurins.. 12th FENS Forum of Neuroscience 2020.07.12
4. Momo Ooishi, Chinami Onchi, Momona Yamada, Chikako Hayashi, Nobuharu Suzuki. Promoted oligodendrocyte precursor cell proliferation and survival via laminin E3 fragments.. 第 63 回日本神経化学学会大会 2020.09.10
5. Nobuharu Suzuki. Cell Adhesion Proteins Regulate Myelination of Small Caliber Axons Critically Involved in Myelin-related Diseases. 第 63 回日本神経化学学会大会 2020.09.10
6. Riko Takahashi, Chikako Hayashi, Miho Iwase, Nobuharu Suzuki. Teneurin-4 regulates the generation of type I/II oligodendrocytes that myelinate small diameter axons.. 第 63 回日本神経化学学会大会 2020.09.11

7. Yuki Munakata, Yukina Hosoda, Hiromi Kurumada, Chikako Hayashi, Nobuharu Suzuki. The crucial role of teneurin-4 associated with actin binding protein CNP in myelination and axonal maintenance.. 第63回日本神経化学会大会 2020.09.11

[Awards & Honors]

1. The silver award at the pitch contest for cryo-EM gateway, Tokyo Medical and Dental University, 2020.03
2. The Excellent Poster Presentation Award at the 63rd Annual Meeting of the Japanese Society for Neurochemistry , The Japanese Society for Neurochemistry, 2020.09
3. The Excellent Poster Presentation Award at the 63rd Annual Meeting of the Japanese Society for Neurochemistry , The Japanese Society for Neurochemistry, 2020.09

Department of Molecular Pathology

Professor: Motoji Sawabe

Assistant Professor: Yurie Soejima

Graduate student Doctoral Program

Graduated in March 2020: Tamami Denda, Ayana Horiguchi, Nobuyuki Nakamura, Kana Miyata

Enrolled in 2020: Yuichi Koyama, Mizuho Sato, Yoshifumi Morita, Mayumi Kinoshita, Akiya Tatsumi, Minami Kikuchi, HATTHAKONE THAVISOUK

Graduate student Master's Program

Graduated in March 2020: Miho Takeuchi, Satsuki Yuba, HATTHAKONE THAVISOUK

Enrolled in 2020: Nao Miyamoto, KO PO JUI, SAKHA SUJATA, Shiori Watabe, OUNDAVONG SUNTI

Clerical assistant: Hitomi Sasaki

(1) Outline

Pathology is the basic science of medicine that involved both the basic and clinical stages to elucidate the essence of diseases.

Pathological techniques play a role in conducting higher quality diagnoses by various examinations and methods such as histology, cytology, immunohistochemistry, electron microscopy, and genetic analysis. We explore the essence of the diseases in both aspects of pathology and pathological techniques.

(2) Research

In our department, we research the following programs in order to investigate and elucidate the etiology and pathophysiology, and further to explore and develop the theoretics and methods of examination that can contribute to the diagnosis.

1. Immunohistochemical analysis of human and mouse cardiac conduction system
2. Proteomic analysis of human cardiac aging
3. Proteome analysis and immunohistochemical study of arterial and cardiac aging
4. Molecular epidemiologic and clinicopathological study of Lipoprotein(a)
5. Molecular pathological study of hepatobiliary tumors
6. Histological and cytological analysis for early diagnosis of biliary tract cancer

(3) Education

In the undergraduate course, students learn the etiology and pathophysiology of basic disease in Pathological Technology, lecture and practice (Medical Technology), and Pathology (Nursing science).

In graduate school, we provide education and conduct the research with the aim of exploring, developing, and systematizing the theoretics and methods of molecular pathological techniques with a higher level of pathological

expertise and a broad international perspective.

(4) Lectures & Courses

In order to cultivate medical professionals with interdisciplinary and international perspectives, precious humanity and high ethical values, the ability of self-problem raising and solution, life-long-thinking, the following education are providing.

1) Undergraduate education

- In the second grade of Medical Technology and Nursing science, students learn common changes in disease, the essence of pathogenesis, and their origins systematically in the general theory of Pathology/Pathological technology.
- In the second grade of Medical Technology, practical training of pathological examination is organized to contributes to the diagnosis of diseases and elucidation the pathogenesis, such as various special staining methods, immunohistochemistry, cytology, and frozen section, in addition to visual inspection of organs, basic preparation of specimens and observation.
- In the second grade of Nursing science, we have pathological anatomical observation as a part of the Practice of Medical Sciences.
- In the fourth grade of Medical Technology, we provide the education of the basics of research, such as how to proceed with the study and how to write the research paper as the Undergraduate Research, and pathological examination practice is carried out at the Department of Pathology in TMDU hospital as Clinical Practice.

2) Graduate education

- In the Master' s Program, we discuss essentials of diseases, with the investigation and understanding the origin, pathophysiology, and pathological characteristics (macroscopical, histological, cytological and molecular pathological) of the disease. Furthermore, students learn the theory and method of pathological techniques (immunohistochemistry, electron microscopy, image analysis, etc.), which useful for elucidation pathophysiology and diagnosis. In addition, students will acquire the skills of quality management and problem-solving in the laboratory. We participate in various research meetings and academic societies and learn about the current status and prospects of international and interdisciplinary research in the pathology/pathological techniques field. Through this course, students will complete their research as a Master' s thesis and acquire basic research ability.
- In the Doctoral Program, we provide higher education, research instruction and medical English learning to acquire the independent research skills that internationally applicable.

(5) Clinical Services & Other Works

- In the Pathology department of the Medical hospital, Sawabe participates in the pathological diagnosis of autopsy cases, Soejima participates in the cytological diagnosis.
- In 2020, Soejima participated in the PCR screening test for the COVID-19 in the Medical hospital.

(6) Publications

[Original Articles]

1. Denda Tamami, Kamoshida Shingo, Kuwao Sadahito, Kawamura Jumpei, Ota Yasunori, Soejima Yurie, Akiyama Masako, Sawabe Motoji. solute carrier トランスポーター類に属し、膀胱癌において高グレードな悪性度を表す免疫組織化学マーカーとしての還元型葉酸キャリア 1 と受動拡散型ヌクレオシドトランスポーター 1(Solute carrier transporters, reduced folate carrier 1 and equilibrative nucleoside transporter 1, as immunohistochemical markers for high-grade malignancy in bladder cancer) Journal of Medical and Dental Sciences. 2020; 67; 11-20
2. Horiguchi Ayana, Umezawa Takashi, Umemori Miyaka, Ito Satoshi, Tsuchiya Sachiko, Hirooka Shinichi, Kiyokawa Takako, Ikegami Masahiro, Takahashi Hiroyuki, Soejima Yurie, Sawabe Motoji. Application of

- cell block preparation in effusion cytology: Analysis of mismatched diagnosis and utility of immunostaining
Journal of Medical and Dental Sciences. 2020; 67; 21-29
3. Wang Tan, Matsuda Yoko, Nonaka Keisuke, Kakizaki Mototsune, Ishiwata Toshiyuki, Kanazawa Nobuo, Uegaki Satoko, Muramatsu Masaaki, Sawabe Motoji, Mori Seijiro, Tanaka Masashi, Kitagawa Masanobu, Arai Tomio. Clinicopathological characteristics of gastric cancer with carbohydrate antigen 19-9 expression occurring in elderly individuals: An autopsy study(和訳中) *Pathology International*. 2020.02; 70(2); 92-100
 4. Abudushataer M, Sato N, Mieno M, Sawabe M, Muramatsu M, Arai T. Association of CYP2A6 gene deletion with cancers in Japanese elderly: an autopsy study. *BMC Cancer*. 2020.03; 20(1); 186
 5. Morita Yoshifumi, Kurano Makoto, Sakai Eri, Nishikawa Takako, Nishikawa Masako, Sawabe Motoji, Aoki Junken, Yatomi Yutaka. Analysis of urinary sphingolipids using liquid chromatography-tandem mass spectrometry in diabetic nephropathy *Journal of Diabetes Investigation*. 2020.03; 11(2); 441-449
 6. Govind P, Pavethynath S, Sawabe M, Arai T, Muramatsu M. Association between rs1229984 in ADH1B and cancer prevalence in a Japanese population. *Molecular and clinical oncology*. 2020.06; 12(6); 503-510
 7. Kensuke Ihara, Tetsuo Sasano, Yuichi Hiraoka, Marina Togo-Ohno, Yurie Soejima, Motoji Sawabe, Megumi Tsuchiya, Hidesato Ogawa, Tetsushi Furukawa, Hidehito Kuroyanagi. A missense mutation in the RSRSP stretch of Rbm20 causes dilated cardiomyopathy and atrial fibrillation in mice. *Sci Rep*. 2020.10; 10(1); 17894
 8. Morita Yoshifumi, Kurano Makoto, Morita Eriko, Shimamoto Satoshi, Igarashi Koji, Sawabe Motoji, Aoki Junken, Yatomi Yutaka. Urinary autotaxin concentrations are associated with kidney injury *CLINICA CHIMICA ACTA*. 2020.10; 509; 156-165
 9. Koyama Yuichi, Morikawa Teppei, Miyama Yu, Miyakawa Jimpei, Kawai Taketo, Kume Haruki, Sawabe Motoji, Ushiku Tetsuo. B7-H3 expression in upper tract urothelial carcinoma associates with adverse clinicopathological features and poor survival *PATHOLOGY RESEARCH AND PRACTICE*. 2020.12; 216(12); 153219

[Books etc]

1. Yoshihisa Takahashi, Keiichiro Sugimoto, Yurie Soejima, Arisa Kumagai, Tatsuki Koeda, Aiko Shojo, Kazuya Nakagawa, Naoki Harada, Ryoichi Yamaji, Hiroshi Inui, Toshikazu Yamanouchi and Toshio Fukusato. *Prime Archives in Biomedical Sciences*. Vide Leaf, 2020.08
2. Fukusato T, Kondo F, Soejima Y. *Liver Cancer. Tumor pathological differential diagnosis atlas*. 2nd ed. . Bunkodo, 2020.11 (ISBN : 978-4-8306-2254-0)

[Conference Activities & Talks]

1. Yurie Soejima, Hitoshi Abe, Kyoko Komatsu, Sadayuki Hiroi, Tomoo Itoh, Tomoko Wakasa, Motoji Sawabe, Kaori Ohara, Noriko Fujita, Toshiaki Kawai. Launch of a system of immunohistochemistry at a national hospital for cancer treatment in Cambodia. The 109th Annual Meeting of the Japanese Society of Pathology 2020.07.01 Fukuoka (web)
2. Tomoko Wakasa, Toshiaki Kawai, Eisuke Enoki, Tomoo Itoh, Kyoko Komatsu, Sadayuki Hiroi, Hitoshi Abe, Yurie Soejima, Kaori Ohara, Yasuyo Matsumoto, Noriko Fujita. Project For System Developments For Pathological Diagnosis In Cambodia, The Problems To Start IHC. The 109th Annual Meeting of the Japanese Society of Pathology 2020.07.01 Fukuoka (web)
3. Sadayuki Hiroi, Kyoko Komatsu, Hironori Katayama, Yurie Soejima, Yasuyo Matsumoto, Eisuke Enoki, Kaori Ohara, Tomoko Wakasa, Noriko Fujita, Toshiaki Kawai. Establishment in the pathology laboratory in Cambodia National Maternal and Child Health Center. The 109th Annual Meeting of the Japanese Society of Pathology 2020.07.01 Fukuoka (web)
4. Motoji Sawabe, Yurie Soejima. Search for a Practical Immunohistochemical Method to Identify Human Atrioventricular Conduction Axis. The 109th Annual Meeting of the Japanese Society of Pathology 2020.07.01 Fukuoka (web)

5. Yurie Soejima. International Slide Conference Lymph node Respondent. The 59th Annual Autumn Meeting of the Japanese Society of Clinical Cytology 2020.11.21 Yokohama
6. Yurie Soejima, Miho Takeuchi, Nao Miyamoto, Motoji Sawabe. ITGB6 knockout and functional analysis in cholangiocarcinoma cells. The 56th Annual Meeting of Liver Cancer Study Group of Japan 2020.12.22 Osaka (web)

Department of Respiratory and Nervous System Science

Professor: Yuki Sumi, MD, PHD.

Assistant Professor: Miho Akaza, MD, PHD.

Part-time: Keiko Hara, MD, PHD. Katsuya Ota, MD, PHD.

Doctoral: Yuri Ichikawa, MT, Msc.

Master's: Sayuri Kaminaka MT. Ryusuke Mizuguchi MT. Luna Okubo MT.

Students: Yuka Hosoya, Chiune Funaita, Gengen Ko, Sayuri Ishii,

Sayaka Ishikawa, Misaki Yagi.

(1) Outline

We research and educate on the respiratory and nerves systems. Our interests are looking at the living body as an integrated system from the molecular and cellular level to the organs and looking at the relationship between clinical medicine and physiological tests.

Previously, research and education on respiratory, cardiovascular, and nerves were conducted by the name of "Biofunctional Informatics". At the time of reorganization of Tokyo Medical and Dental University, cardiovascular division separated, and we moved from "Graduate School of Health Care Sciences" to "Graduate School of Medical and Dental Sciences" and was renamed to "Respiratory and Nervous System Science".

(2) Research

The research is conducted independently in each field by specialists in the respiratory and nervous system.

In the respiratory field, we are studying the clinical significance of new lung function tests, mechanisms and endotype classification of bronchial asthma and COPD, gene therapy for lung diseases, and diagnosis using AI. In the central nervous system area, we are researching on electroencephalogram (EEG) and epilepsy, and in the peripheral nervous system area, we are developing a new imaging methods.

(3) Education

In education, we provide education in general clinical medicine and acquire theory and skills through lectures and practical training in physiological function tests (lung function, EEG, peripheral nerve tests, various sonography, etc.). Undergraduate and graduate research educations are conducted in each specialized field.

1) Undergraduate student education

In the 1st year, a lecture on "Respiratory and Nervous System Science" is given on Advanced Laboratory Sciences. Second-year students have Physiological Laboratory Science, Lecture(I). Here students learn the basics of EEG, lung function tests, and sonographies. Physiological Laboratory Science, Lecture(II) and Physiological Laboratory Science, Laboratory(II) will be conducted jointly with the cardiovascular field in the 3rd years (2nd and 3rd years in the new curriculum). The contents include neurophysiological examination, respiratory examination, circulatory examination, ultrasonic examination, image analysis, thermography, sense of equilibrium function examination, fundus examination, and other basic examinations such as blood sampling practice, sample collection, etc. We also provide education on clinical techniques in general, including taking vital signs and procedures for critical care. In the 4th graders, students undergo Undergraduate research given on the research methods and minds, focusing on the research theme assigned to each person. In the clinical training, practical training of respiratory tests including blood gas measurement, EEG, evoked potential test,

and abdominal ultrasonography will be given during two weeks.

In addition, the educational effort equal to or higher than the lecture training in our Department is given to the 1st to 6th grade medical students and residents. (Details omitted)

2) Graduate education

In the Master's course, we are in charge of Medical Technology I, Medical Technology II, Seminar of Respiratory and Nervous System Science, Practice of Respiratory and Nervous System Science, and Respiratory and Nervous System Analysis Research for Thesis. Medical Technology I deepens the understanding of the scientific knowledge that is the basis of clinical tests currently being conducted in the medical field from various levels of genes, molecules, cells, tissues, and individuals, and further toward the future. The purpose is to reinforce the foundation for studying research topics. The purpose of Medical Technology II is to deepen the understanding of clinical tests currently being conducted in the medical field and to develop the ability to consider future research issues. In each lecture of Respiratory and Nervous Systems Science, we educate new knowledge and techniques, clarify areas that have already been elucidated and areas that do not, and acquire scientific research attitudes to clarify areas that are still unknown.

In the Doctoral course, we are in charge of Clinical Reasoning and Respiratory and Nervous System Science. In the Clinical Reasoning, we aim to cultivate the clinical laboratory technologists who can discuss with physicians of inferring disease conditions from laboratory data. In the Respiratory and Nervous System Science, we aim to teach the theory and techniques to inspect the living body as an integrated system. In particular, students learn the cutting edge medical knowledge in the respiratory or nervous system, the methodology to analyze the relationship between the biological information obtained by the examination and the pathogenesis, and the theory and techniques to developed novel examination methods.

(4) Lectures & Courses

What is important in education is to motivate learning. In particular, in the lower grades of undergraduate students, many students do not understand how basic learning is useful, and are not motivated to study despite being important. For this reason, we have increased practical training, conducted early exposure to understand how it is needed in the clinical setting. We wish students to be eager to learn and to acquire competency as if the water is soaking into dry sand.

In particular, as the physiological function testing is a clinical front line that is conducted in direct contact with patients, we educates from the standpoint of clinical medicine. The goal is that students learn theories and techniques of clinical physiological examinations in nerves, respiration, cardiovascular, digestive organs, and diagnostic imaging, and be able to apply them to researches. Physiological function testing involves not only device operation, safety measures, recording of biological phenomena, data organization / analysis techniques and knowledge, but also testing directly in contact with humans, so medical knowledge about diseases, medical ethics and communication skills are also required. It is also important to cultivate the ability to quickly recognize and take appropriate measures for test results that require emergency treatment of patients. In addition to these, we are also educating students on how to respond to sudden changes in patients during testing.

(5) Clinical Services & Other Works

Dr. Sumi is a Respiratory specialist and Respiratory instructor, and Allergy specialist certified by the academic society. He treats patients at respiratory medicine department in the hospital. He also takes care of the study groups of doctors and takes part in as discussant. He gave lecture at Evening seminar for medical interns, at CC (Clinical Clerkship) in respiratory medicine for undergraduate 5th and 6th grade medical students, at PCC (Preparation for Clinical Clerkship) in respiratory internal medicine for 4th year undergraduate medical students, at Respiratory Internal medicine for 3rd year undergraduate medical students, at Respiratory physiology for 2nd year undergraduate medical students, and at MIC (Medical Introductory Course) for 1st year undergraduate medical students.

The neurologist, Dr. Akaza, is familiar with peripheral neuropathy in addition to neurological diseases in general, and plays a central role in performing peripheral nerve tests and evaluating results in medical hospitals.

Dr. Hara is the psychiatrist, Mental health designated physician, specialist / instructor of the Japan Epilepsy Society, certified by the Japanese Society of Clinical Neurophysiology (EEG), and Delegate of the Japanese Society of Clinical Neurophysiology, Councilor of the Japan Pharmaco-EEG Society, Board secretary of the Japan Epilepsy Society. She examines many patients with epilepsy in the outpatient department including second opinions. In cooperation with the Department of Neurosurgery, she attends weekly EEG conferences,

monthly EEG and epilepsy lectures, and analyzes high frequency EEG (HFO). She also performs intraoperative electroencephalogram measurements in many brain surgeries.

(6) Clinical Performances

Dr. Akaza is a specialist in peripheral nerve function testing and performs most tests for neurological patients. She is conducting clinical research on peripheral neuropathy in diabetic patients.

Dr. Hara treats many patients with epilepsy including second opinions. She specializes in the treatment of pregnant women with epilepsy. In cooperation with obstetrics and gynecology doctors, patients with epilepsy are referred to her consultant before pregnancy since 2013.

(7) Publications

[Original Articles]

1. Oyama Saki, Otani Yoshio, Furuie Wakaba, Koike Fumika, Miyoshi Takao, Akaza Miho, Sumi Yuki. Cluster analysis of patients with cough, mainly cough variant asthma, showing a good response to asthma therapy(和訳中) *Journal of Medical and Dental Sciences*. 2020; 67; 1-10
2. Ichikawa Yuri, Maeda Tomoko, Takahashi Tetsuya, Ashikaga Kohei, Tanaka Shiori, Sumi Yuki, Itoh Haruki. Changes in oxygen uptake kinetics after exercise caused by differences in loading pattern and exercise intensity *ESC HEART FAILURE*. 2020.06; 7(3); 1109-1117
3. Okubo Luna, Takeda Naoya, Suzuki Yoshihiro, Nakashima Kuniya, Asano Motoyo, Koike Fumika, Ide Akane, Akaza Miho, Miyazaki Yasunari, Sumi Yuki. 喘息発作を起こした患者のサイトカインプロファイル (Cytokine profile in patients with asthma attack) *アレルギー*. 2020.10; 69(臨時増刊号); 114
4. Akaza Miho, Kawabata Shigenori, Watanabe Taishi, Miyano Yuki, Mizuguchi Ryusuke, Kaminaka Saeri, Iida Shintaro, Sasaki Toru, Adachi Yoshiaki, Sekihara Kensuke, Sumi Yuki, Okawa Atsushi, Yokota Takanori. 磁場の測定と超音波造影 (US) による位置情報を用いた神経活動の測定 (The evaluation of nerve activity using magnetic field measurement and positional information by US) *臨床神経学*. 2020.11; 60(Suppl.); S488
5. Miho Akaza, Shigenori Kawabata, Isamu Ozaki, Yuki Miyano, Taishi Watanabe, Yoshiaki Adachi, Kensuke Sekihara, Yuki Sumi, Takanori Yokota. Noninvasive measurement of sensory action currents in the cervical cord by magnetospinography. *Clin Neurophysiol*. 2020.12; 132(2); 382-391

Department of Clinical and Diagnostic Laboratory Science

Professor

Sei Kakinuma, M.D., Ph.D. (June, 2020-)

Graduate Students, Doctoral Program.

Hiroaki Komuro, M.S. (Biomedical Science and Engineering Track)

Jun Tsuchiya, M.D., Taro Shimizu, M.D., Keiya Watakabe, M.D.

(in collaboration with Department of Gastroenterology and Hepatology, Medical and Dental Science Track)

(1) Outline

Patients died from chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic liver disease, and the development of effective treatment for progressive liver diseases has been quite essential. Moreover, patients died from biliary and pancreatic cancer are more than 50,000 persons per a year in Japan. It is still difficult to detect such diseases at early stages and to establish the standard therapeutic strategy for them. It is urgently needed to address this issue as well as that of chronic liver diseases.

We believe that an essential role of departments in the Graduate school in Division of Biomedical Laboratory Sciences, TMDU, in medical science is to provide a basis for the innovative medical examination and to establish the treatment in next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutic strategy established upon basic research are required.

Our department is founded in June, 2020, which is standing by such principles. Our research projects focus on hepatology, including the field of hepato-biliary-pancreatic diseases. The goal of our education is to promote students to become a well-developed hepatologist, and also leading experts in the field of hepato-biliary-pancreatic diseases and medical technology.

(2) Research

Our principle of research is to achieve studies evoked from various clinical problems, and also directs to launch innovative diagnostic and therapeutic procedures. We focus on the basic studies of novel disease models using human iPS cells to elucidate the pathophysiology. We also focus on analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases. We focus other projects described as below, and promote them using molecular and cellular biologic approaches. We are collaborating with Department of Gastroenterology and Hepatology (Medical and Dental Science Track, Graduate school, TMDU), a lot of departments in TMDU, and several departments in other universities in Japan.

Research Projects:

- (1) Development of novel disease models using human iPS cells to elucidate the pathophysiology
- (2) Analysis of cell-to-cell interaction regulating development and progression of hepatobiliary diseases
- (3) Development of hepatobiliary and pancreatic disease models using organoid culture system
- (4) Molecular mechanisms regulating homeostasis of stem/progenitor cells in gastrointestinal, hepatobiliary, and pancreatic tissue

(5) Research on molecular mechanisms regulating liver regeneration and hepatic fibrosis

(3) Education

Undergraduate students.

We are teaching the courses of physiological function tests and clinical pathophysiology for undergraduate students of medical technologists in School of Medicine, TMDU. We also teach about basic techniques and scientific thinking necessary to advance the scientific research of undergraduate students in TMDU.

Graduate students

Primary goal for education of graduate students is to train highly educated and experienced clinical and technological scientists in the field of hepatology, including the field of hepato-biliary-pancreatic diseases. Our goal for education of graduate students is to produce clinical and technological scientists thinking from a wide perspective and to bring up leaders of hepatologist in next generation.

(4) Lectures & Courses

Undergraduate students.

- # Clinical Medicine (II)
- # Physiological Laboratory Science
- # Advanced physiological function
- # Analysis of Electrocardiogram

Graduate students.

- # Clinical and Diagnostic Laboratory Science

Our lectures and courses are collaboration with Department of Respiratory and Nervous System Science in undergraduate course, and with Department of Gastroenterology and Hepatology in graduate course. We also educate residents and medical technologist in Medical Hospital of TMDU.

Goals for education in scientific research

- #1. Students should master the strategy of research for molecular, regenerative, and stem cell biology to reveal the pathophysiology of Hepato-Biliary-Pancreatic diseases.
- #2. Students should master the theory and techniques about physiological laboratory and diagnostic imaging in the field of Hepato-Biliary-Pancreatic diseases.
- #3. Students should learn about the research strategy to develop a novel diagnostic and therapeutic methods.

(5) Clinical Services & Other Works

We pursue development 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 clinical study collaborating with the Department of Gastroenterology and Hepatology in TMDU.

We participate in eight research projects for treatment and eradication of hepatitis virus and one for cancer research and clinical evolution, 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. 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 contribute to the management of the activities and academic meetings held by the American Association for the Study of Liver Disease, the Japanese Society of Gastroenterology, the Japanese Society of Hepatology, the Japanese Society for Regenerative Medicine, and the Japanese Society for the Research of Hepatic cells.

(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 established the outpatient section specialized for chronic hepatitis, cirrhosis, and HCC. We are operating several multicenter studies about hepatitis and liver cancer, including one named as “Ochyanomizu Liver Conference”. More than 2000 patients with viral hepatitis were enrolled in such studies, and they 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 biomarkers, and dynamic contrast-enhanced ultrasonography.

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

1. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient *Hepatol Res.* 2020; 50(4); 524-531
2. Hiroaki Komuro, Masahiro Yamazoe, Kosuke Nozaki, Akiko Nagai, Tetsuo Sasano. Cardiomyocyte uptake mechanism of a hydroxyapatite nanoparticle mediated gene delivery system. *Beilstein J Nanotechnol.* 2020; 11; 1685-1692
3. Ayako Sato, Sei Kakinuma, Masato Miyoshi, Akihito Kamiya, Tomoyuki Tsunoda, Shun Kaneko, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Vasoactive intestinal peptide derived from liver mesenchymal cells mediates tight junction assembly in mouse intrahepatic bile ducts. *Hepatol Commun.* 2020.02; 4(2); 235-254
4. Komuro Hiroaki, Wint Wit Y., Horiuchi Naohiro, Nozaki Kosuke, Sasano Tetsuo, Miyashin Michiyo, Yamashita Kimihiro, Nagai Akiko. An oriented hydroxyapatite film with arrayed plate-like particles enhance chondrogenic differentiation of ATDC5 cells *JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A.* 2020.03; 108(3); 537-544
5. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient. *Hepatol Res.* 2020.04; 50(4); 524-531
6. Mina Nakagawa, Nobutoshi Nawa, Eiko Takeichi, Taro Shimizu, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Takeo Fujiwara, Mamoru Watanabe, Yujiro Tanaka, Yasuhiro Asahina. Mac-2 binding protein glycosylation isomer as a novel predictive biomarker for patient survival after hepatitis C virus eradication by DAAs. *J Gastroenterol.* 2020.08; 55; 990-999

[Conference Activities & Talks]

1. Sakurako Kobayashi, Satoshi Watanabe, Yosuke Yoneyama, Kousuke Tanimoto, Ryu Nishimura, Sayaka Nagata, Masami Inoue, Kouhei Suzuki, Sei Kakinuma, Kiichiro Tsuchiya, Ryuichi Okamoto, Mamoru Watanabe, Takanori Takebe, Shiro Yui. Conceptual basis of lineage shift between intestinal epithelium and hepatocytes. *Keystone Symposia, Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease* 2020.01.22 Vancouver (Canada)
2. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka, Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. *EASL The Digital International Liver Congress 2020* 2020.08.28 Online

Department of Analytical Laboratory Chemistry

Professor:

· 2020.1-12 : Ryunosuke Ohkawa

Assistant Professor:

· 2020.1-12 : Takahiro Kameda

Graduate Students:

(Master students)

· 2020.1-3 : Mayu Nambu, Yuka Yamagata

· 2020.4-12 : Ayuko Hara, Yume Mutsuda

(Doctoral Students)

· 2020-1-3 : Yuna Horiuchi, Shao Jui Lai

· 2020-4-12 : Yuna Horiuchi

· 2020-1-3 : Yuko Mishima, Tamaki Kobayasi

· 2020-4-12 : Tamaki Kobayasi

(Research Students)

· 2020-4-12 : Shao Jui Lai, Sun Chengman

(Under Graduate Students)

· 2020.1-3 : Ayuko Hara, Yume Mutsuda

· 2020.4-12 : Mei Ogino, Rina Kawaguchi, Marino Shibuya, Motoki Nakamura, Takako Yamada

(1) Outline

The central mission of the Analytical Laboratory Chemistry is to educate and research through “Clinical Chemistry” in Clinical Laboratory Science. Our topic is “Development of a new biomarker to predict a risk for cardiovascular disease”. To achieve our goal, skill and ability to create new reliable method are required. Development of students who can give back to a society through active outreach like publishing a paper and presenting at a congress is most important. We also aim to develop a Biomedical Laboratory Scientist who not only plays a pivotal role in medical front but also be active in education or research institutes. For that reason, creation of a laboratory where students can throw themselves into their research with enjoyment is essential.

(2) Research

We analyze lipoproteins and its components; cholesterol, triglyceride, apolipoproteins and their metabolites. Through these studies, we are aiming toward developing a new biomarker to predict a risk for cardiovascular disease in an early stage. In detail, we are focusing on cholesterol efflux capacity (reverse cholesterol transport), antioxidant ability and anti-inflammatory effect of high-density lipoprotein (HDL) and its main apolipoprotein, apolipoprotein A-I. Our hypothesis is that evaluation of these capacities would be available to make a specific diagnosis for coronary artery disease (CAD). Moreover, it is known that HDL is not structurally homogeneous but heterogeneous in size, density and chemical composition. We are investigating the mechanism of the HDL

diversification through the interactions with other lipoproteins and tissue, and its effect on the HDL character and functions. We are further studying the red blood cell-related lipids metabolism.

Many risk factors for CAD have been reported and testing these factors have been contributing to reduce the risk in some patients with CAD. However, despite many people are trying to keep their health to reduce their risk for heart disease, the actual number of heart event have not been decreased. We believe that investigating the above mechanisms would lead to find useful biomarker and establish new assay for diagnosis for cardiovascular disease.

Research Focus

- Development of a new biomarker to estimate residual risk for cardiovascular disease
- Mechanism of HDL diversification and its effect on the character and function
- Molecular mechanism of red blood cell-related lipids metabolism

(3) Lectures & Courses

Undergraduate education: Main topic is Analytical Laboratory Chemistry which includes Urinalysis & Body Fluid Tests and Clinical Chemistry. In addition, Associate Professor Masayuki Hara from General Isotope Research Division helps to educate radioisotope. We aim to educate student to become a leader of biomedical laboratory scientist in hospital or company. Our final goal is that student develop their creativities to think, solve a problem and improve by themselves.

Graduate education: Analytical skill is essential for research. There is no research achievement without analytical skill. Our first purpose is to understand an importance of reliable analytical skill and obtain the skill. Next, by using these skills, we aim to find new biomarker and develop a novel assay for the biomarker. Though these research process, students can obtain the analytical skill and cultivate capacity as researcher to make a research plan and choose the optimal way to proceed by themselves. Moreover, students can develop their outreach skill through presenting their research achievements at a congress and publishing their papers.

(4) Publications

[Original Articles]

1. Yuna Horiuchi, Shao-Jui Lai, Takahiro Kameda, Minoru Tozuka, Ryunosuke Ohkawa. Comparison of a novel cholesterol efflux assay using immobilized liposome-bound gel beads with the conventional method. *Biosci. Rep.* 2020.07;
2. Hann Low, Nigora Mukhamedova, Luciano Dos Santos Aggum Capettini, Yining Xia, Irena Carmichael, Stephen H Cody, Kevin Huynh, Michael Ditiatkovski, Ryunosuke Ohkawa, Michael Bukrinsky, Peter J Meikle, Soo-Ho Choi, Seth Field, Yury I Miller, Dmitri Sviridov. Cholesterol Efflux-Independent Modification of Lipid Rafts by AIBP (Apolipoprotein A-I Binding Protein). *Arterioscler. Thromb. Vasc. Biol.* 2020.08; ATVBAHA120315037
3. Ryunosuke Ohkawa, Hann Low, Nigora Mukhamedova, Ying Fu, Shao-Jui Lai, Mai Sasaoka, Ayuko Hara, Azusa Yamazaki, Takahiro Kameda, Yuna Horiuchi, Peter J Meikle, Gerard Pernes, Graeme Lancaster, Michael Ditiatkovski, Paul Nestel, Boris Vaisman, Denis Sviridov, Andrew Murphy, Alan T Remaley, Dmitri Sviridov, Minoru Tozuka. Cholesterol transport between red blood cells and lipoproteins contributes to cholesterol metabolism in blood. *J Lipid Res.* 2020.12; 61(12); 1577-1588

[Conference Activities & Talks]

1. Ryunosuke Ohkawa. Various types of research networks for medical technology, Keynote Speech. the 5th congress of AASMT (ASEAN Association of Schools of Medical Technology) 2020.11.05 Viet Nam (on-line)
2. Ryunosuke Ohkawa. Japanese laboratory medicine and its education, Country Reports. the 5th congress of AASMT (ASEAN Association of Schools of Medical Technology) 2020.11.05 Viet Nam (on-line)
3. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for

application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16
On-line

4. Shimano S., Ohkawa R., Nambu M., Sasaoka M., Yamazaki A., Fujii Y., Igarashi K., Horiuchi Y., Lai SJ., Kameda T., Ichimura N., Fujita K., Tohda S. and Tozuka M. Dramatic change of high-density lipoprotein structure and serum amyloid A distribution after orthopedic surgery. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
5. Ohkawa R., Low H., Mukhamedova N., Fu Y., Lai SJ., Sasaoka M., Horiuchi Y., Ditiatkovski M., Nestel P., Sviridov D., and Tozuka M. Evaluation of cholesterol uptake and efflux by red blood cells. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line

Department of Laboratory Molecular Genetics of Hematology

Associate professor :
Miwako NISHIO

Adjunct Lecturer :
Kumiko SAEKI, Ken-ichi IMADOME, Yoichi NAKAYAMA

Graduate Student :
Shiho HASHIMOTO, Shisei GO, Megumi TATEISHI, Yuki KUMAKI, Ayaka Mimura, Masato YAMAGUTI

(1) Outline

For undergraduate education, we are in charge of Clinical Laboratory Hematology, Hematology, Clinical Practice, Clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, mechanisms of coagulation and fibrinolysis, pathology and clinical features of main hematological disorders as well as fundamental laboratory practices.

For graduate education, we focus on clarifying molecular mechanisms of development of hematological disorders. We apply the results to develop new diagnostic procedures and treatment strategies. Our current research subject is EB virus-positive T- and NK-cell neoplasms.

(2) Research

Our research goals:

1. Clarifying pathogenesis of hematopoietic malignancies and innovation of a new treatment strategies
2. Clarifying mechanisms of EB virus-positive T- and NK-cell neoplasms and developing new treatment strategies
3. Creating new methods for diagnosing hematopoietic tumors
4. Development of new treatment methods using regenerative medicine technology

We collaborate on several researches with doctors of Deps. Hematology, Pediatrics, Neurology, Molecular Virology, Center for Stem Cell and Regenerative Medicine, Ophthalmology, Dermatology, Department of Comprehensive Pathology, and Diagnostic Radiology on-campus in TMDU. We are also doing research with members of National Center for Child Health and Development, Osaka Women's and Children's Hospital, Biochemistry department at Justus-Liebig Universität (Gießen). We collaborate with several companies as well.

(3) Education

1. Undergraduate Education

We are in charge of Clinical Laboratory Hematology, Clinical Hematology, clinical clerkship (School of Medicine), Clinical Hematology (Track of Nursing Science). We provide lectures on hematopoiesis, hematological disorders,

mechanism of coagulation and fibrinolysis, hematopoietic malignancies as well as fundamental laboratory practices.

Students are also involved in Undergraduate Research, which objective is to learn basis of research including how to plan and carry out research activities, how to write theses, and how to give an academic presentation. They also experience as trainees for Clinical Practice for hematological examination in cooperation with Clinical Laboratory at Medical Hospital. These lectures and practices are conducted in collaboration with the members of Departments of Hematology and Pediatrics.

2. Graduate Education

For graduate education, we focus on clarifying molecular mechanisms of development of hematological neoplasms. We apply the results to develop new diagnostic procedures and treatment strategies for these disorders. Our current research subject is EB virus-positive T- and NK-cell neoplasms. We instruct students to summarize what they investigated and complete English manuscripts for publication.

Detailed educational contents are shown below:

- 1) Investigating and understanding pathogenesis and pathology of hematopoietic disorders, especially neoplasms
- 2) Acquiring skills for cellular, molecular and genetic examination that play significant roles for diagnosing and clarifying cause and state of diseases. These molecular techniques are useful not only for clinical situation, but also for elucidating mechanisms of developing diseases
- 3) Acquiring current information for diagnosis and treatment of hematological diseases
- 4) Publishing papers on hematological laboratory testing and clinical hematology on main international academic journals and present them at international conferences

(4) Lectures & Courses

Cultivating interdisciplinary- and internationally-minded medical staffs with rich humanity, a strong sense of ethics, and ability to suggest and solve unmet medical issues

(5) Clinical Services & Other Works

Research:

Our research group is also a principal investigator of Japan Agency for Medical Research and Development (AMED) study group ‘the Investigator-initiated clinical research of a JAK1/2 inhibitor ruxolitinib for chronic active Epstein-Barr virus infection’ .

We are supporting patients with chronic active Epstein-Barr virus infection (CAEBV) through CAEBV patient’s association (SHAKE).

<http://caebv.com/>

(6) Clinical Performances

We are the only group that specialize EBV-positive T- or NK-cell neoplasms especially chronic active EBV infection. We accept referral patients with CAEBV from all over Japan and abroad. We analyze the blood sample in CAEBV patients.

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

1. Oka M, Kobayashi N, Matsumura K, Nishio M, Nakano K, Okamura T, Okochi H, Minamisawa T, Shiba K, Saeki K. New Role for Growth/Differentiation Factor 15 in the Survival of Transplanted Brown Adipose Tissues in Cooperation with Interleukin-6. *Cells*. 2020.06; 9(6);
2. Hashimoto S, Nakajima F, Imanishi T, Kawai Y, Kato K, Kimura T, Miyata S, Takanashi M, Nishio M, Tokunaga K, Satake M. Implications of HLA diversity among regions for bone marrow donor searches in Japan. *HLA*. 2020.07; 96(1); 24-42

[Misc]

1. Miwako Nishio, Kumiko Saeki.. The remaining Mysteries about Brown Adipose Tissues. *Cells*. 2020.11; 9(11); 2449

[Conference Activities & Talks]

1. HLA diversity among prefectures for bone marrow donor in Japan. 2020.03.07
2. M.Yoshimori, M.Tateishi, A.Ohashi, S.Wu, K.Imadome, N.Shimizu, M.Nishio, A.Arai. Products of EBV-Positive Neoplastic NK-Cells Induce Differentiation into Macrophages and Procoagulant Activity of Monocytes, which Leads to HLH. European Hematology Association (EHA) 2020.06
3. Megumi Tateishi, Mayumi Yoshimori, Ayaka Ohashi, Shixing Wu, Norio Shimizu, Miwako Nishio, Ayako Arai. The cytokines of EBV+neoplastic NK-cells enhance the procoagulant activity of monocytes causing DIC. 日本血液学会 2020.10.10
4. Mayumi Yoshimori, Megumi Tateishi, Ayaka Ohashi, Shixing Wu, Kenichi Imadome, Norio Shimizu, Miwako Nishio, Ayako Arai. EBV-positive neoplastic NK-cells induce macrophage differentiation from monocytes, leading to HLH. 日本血液学会 2020.10.10
5. Shixing Wu, Mayumi Yoshimori, Megumi Tateishi, Ayaka Ohashi, Norio Shimizu, Miwako Nishio, Ayako Ara. The elucidation of targets of EBV-derived micro-RNA in chronic active EBV infection. 日本血液学会 2020.10.10
6. Miwako Nishio. Molecular diagnosis of Chronic Active Epstein-Barr Virus (CAEBV). Medlab Asia 2020 2020.10.22
7. S Hashimoto, F Nakajima, T Imanishi, Y Kawai, K Kato, T Kimura, M Nishio, M Takanashi, S Miyata, K Tokunaga, M Satake. HLA DIVERSITY AMONG REGIONS AND PREFECTURES FOR BONE MARROW DONOR SEARCHES IN JAPAN. ISBT 2020.12.12

Department of Molecular Microbiology

Associate Professor (August, 2020-, Professor) : Ryoichi SAITO

Graduate Student (doctor's course): Miyuki MIZOGUCHI, Alafate AYIBIEKE, Yuko KAMICHI

Graduate Student (master's course): Yukino USUI, Wakana SATO, Akari SAMEJIMA, Eimi HASEGAWA

(1) Outline

Our department is engaged in both lecture and practical course for medical microbiology. These include education on prevention, diagnosis and treatment of infectious diseases for both undergraduate and graduate students. Regarding our research, we are interested in investigating molecular mechanisms of antibiotic resistance and virulence gene regulation in bacteria.

(2) Research

Research Interests:

1. Molecular mechanism of antibiotic resistance in bacteria
2. Mechanism of sporulation, spore germination and toxin production in *Clostridioides difficile* and *Clostridium perfringens*

(3) Education

Our course provides the conceptual basis for understanding pathogenic microorganisms including host response in infectious diseases, antimicrobial resistance, and epidemiologic surveillance. It also provides opportunities for undergraduate and graduate students to gain basic techniques, such as identification of microorganisms and antimicrobial susceptibility testing which are performed in the clinical laboratory at medical facilities.

(4) Publications

[Original Articles]

1. Yukino Usui, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Draft Genome Sequence of a *Clostridioides difficile* Sequence Type 97 Strain Belonging to Hypervirulent Clade 2. *Microbiol Resour Announc.* 2020.04; 9(14); e00245-20
2. Yukino Usui, Alafate Ayibieke, Yuko Kamiichi, Shu Okugawa, Kyoji Moriya, Shuji Tohda, Ryoichi Saito. Impact of deoxycholate on *Clostridioides difficile* growth, toxin production, and sporulation. *Heliyon.* 2020.04; 6(4); e03717
3. Yuta Okada, SHU OKUGAWA, Mahoko Ikeda, Tatsuya Kobayashi, Ryoichi Saito, Yoshimi Higurashi, Kyoji Moriya. Genetic Diversity and Epidemiology of Accessory Gene Regulator Loci in *Clostridioides difficile*. *Access Microbiology.* 2020.05;
4. Miyuki Mizoguchi, Yoshimi Matsumoto, Ryoichi Saito, Tomoaki Sato, Kyoji Moriya. Direct antibiotic susceptibility testing of blood cultures of gram-negative bacilli using the Drug Susceptibility Testing Microfluidic (DSTM) device. *J. Infect. Chemother.* 2020.06; 26(6); 554-562

5. Koh Okamoto, Alafate Ayibieke, Ryoichi Saito, Kenichi Ogura, Yuki Magara, Reiko Ueda, Hina Ogawa, Shuji Hatakeyama. A nosocomial cluster of *Roseomonas mucosa* bacteremia possibly linked to contaminated hospital environment. *J. Infect. Chemother.* 2020.08; 26(8); 802-806
6. Prah I, Ayibieke A, Huong NTT, Iguchi A, Mahazu S, Sato W, Hayashi T, Yamaoka S, Suzuki T, Iwanaga S, Ablordey A, Saito R. Virulence profile of diarrhoeagenic *Escherichia coli* from the Western region of Ghana. *Japanese journal of infectious diseases.* 2020.08;
7. Alafate Ayibieke, Ayumi Kobayashi, Masato Suzuki, Wakana Sato, Samiratu Mahazu, Isaac Prah, Miyuki Mizoguchi, Kyoji Moriya, Takaya Hayashi, Toshihiko Suzuki, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Prevalence and characterization of carbapenem-hydrolyzing class D β -lactamase-producing *Acinetobacter* isolates from Ghana. *Front Microbiol.* 2020.11; 11; 587398

[Misc]

1. Ryoichi Saito. Introduction to researchers for biomedical laboratory scientist. *Kensa to Gijutsu.* 2020.09; 48(9); 922-927

[Conference Activities & Talks]

1. Ryoichi Saito. Investigation of transport system in *Neisseria meningitidis*. The 31th Annual Meeting of Japanese Society for Clinical Microbiology 2020.02.01 Ishikawa, Japan
2. Ryoichi Saito. Antimicrobial susceptibility among clinical isolates of *Neisseria meningitidis* from patients with invasive meningococcal disease in Japan. The 31th Annual Meeting of Japanese Society for Clinical Microbiology 2020.02.01 Ishikawa, Japan
3. Alafate Ayibieke, Kageto Yamada, Yoshibumi Aiso, Yoshiro Hadano, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Epidemiological characteristics of bloodstream *S. epidermidis* isolates from two hospitals in Tokyo.. The 93th Annual Meeting of Japanese Society for Bacteriology 2020.02.20
4. Isaac Prah, Alafate Ayibieke, Atsushi Iguchi Samiratu Mahazu, Wakana Sato, Toshihiko Suzuki, Shoji Yamaoka, Shiroh Iwanaga, Anthony Ablordey, Ryoichi Saito. Virulence Profile of Diarrhegenic *E. coli* from the Western region of Ghana. The 93th Annual Meeting of Japanese Society for Bacteriology 2020.02.20 Aichi, Japan
5. Y. Nukui, R. Saito, K. Aoki, Y. Ishii, Y. Aiso, M. Shima, K. Sonobe, S. Tohda, R. Koike.. Molecular Epidemiological Analysis of Multidrug-Resistant *Achromobacter xylosoxidans* that Caused an Outbreak in Japan. *ASM Microbe 2020* 2020.06.18 Chicago, IL, USA
6. Yuta Okada, Shu Okugawa, Mahoko Ikeda, Tatsuya Kobayashi, Ryoichi Saito, Yoshimi Higurashi, Kyoji Moriya.. Genetic diversity and Epidemiology of Accessory Gene Regulator Loci in the Clinical Isolates of *Clostridioides difficile*. *ASM Microbe 2020* 2020.06.18 Chicago, IL, USA
7. Yoko Nukui, Ryoichi Saito, Tetushi Aiso, Kento Inoue, Yoshiro Hadano, Shuji Toda, Ryuji Koike. Case report caused by an NDM-5- and OXA-1-co-producing *Klebsiella oxytoca* isolate from Japan. The 94th Annual Meeting of the Japanese association for infectious diseases 2020.08.19 Tokyo, Japan

[Awards & Honors]

1. Wakana Sato, The Biomedical Research Award (Master's Program), Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, 2020.03

Department of Liver Disease Control

Professor : Yasuhiro ASAHINA

Professor : Sei KAKINUMA

Graduate Student

(collaboration with Department of Gastroenterology and Hepatology in TMDU)

Ayako SATO, Jun TUCHIYA, Taro SHIMIZU, Eiko TAKEICHI, Keiya WATAKABE

(1) Outline

Patients died of chronic liver diseases, including liver cancer, are about 40,000 persons per a year in Japan. Liver transplantation remains the only effective treatment available to patients with end-stage liver diseases. Because of a serious shortage of donors for allogeneic liver transplantation, an alternative therapy is needed. Prevention of hepatocarcinogenesis and hepatic fibrosis is also necessary for patients with chronic hepatitis, and the development of effective treatment for progressive liver diseases has been quite essential. We believe that the central role of clinical departments in the graduate school of TMDU is to establish basis for the innovative medical treatment in the next generation. To achieve our mission, both basic research lead by clinical concepts and development of novel therapeutics established upon basic research are required.

Our section is a donation-funded department collaborating with the Department of Gastroenterology and Hepatology in TMDU. Most of basic research projects, education for students, and clinical contributions including multicenter studies are collaboration with the Department of Gastroenterology and Hepatology in TMDU. The goal of our education is to promote students to become a well-developed hepatologist, and also a leading expert in the field of Hepatology and Gastroenterology.

(2) Research

Our principle is to achieve a research evoked from various clinical problems, and also directed to launch innovative therapeutic procedures to the daily clinical practice.

We focus on the basic studies of molecular mechanism regulating development, pathophysiology, progression, and therapeutic resistance of hepatocellular carcinoma (HCC). We also focus on the development of novel disease models using human induced pluripotent stem cells, the research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis, the study for molecular mechanisms regulating differentiation of hepatic stem/progenitor cells, analysis of mechanisms regulating escape of hepatitis viruses from innate immune systems in host cells, and factors for therapeutic resistance against antiviral agents.

Research projects

- Research for mechanism regulating development, pathophysiology, progression, and therapeutic resistance of HCC, based on molecular biology and genome informatics
- Development of novel disease models using human induced pluripotent stem cells to elucidate the pathophysiology of liver diseases
- Research for molecular mechanisms regulating liver tissue regeneration and hepatic fibrogenesis
- 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 8 research projects for treatment and eradication of hepatitis virus funded by Japan Agency for Medical Research and Development (AMED). From April 2019, our clinical research program, “Development of innovative disease models using hepatic organoids derived from human induced pluripotent stem cells and construction of new treatments to suppress carcinogenesis in liver”, was started as Programs for Basic and Clinical Research on Hepatitis in Division of infectious disease research, AMED. This program is primarily operated by our department in cooperation with several departments in TMDU and other institute. We are trying to develop novel therapeutic strategies to treat progressive liver diseases. 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. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe,

- Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient *Hepatol Res.* 2020; 50(4); 524-531
2. Ayako Sato, Sei Kakinuma, Masato Miyoshi, Akihide Kamiya, Tomoyuki Tsunoda, Shun Kaneko, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Sayuri Nitta, Fukiko Kawai-Kitahata, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Naohiko Koshikawa, Motoharu Seiki, Hiromitsu Nakauchi, Yasuhiro Asahina, Mamoru Watanabe. Vasoactive intestinal peptide derived from liver mesenchymal cells mediates tight junction assembly in mouse intrahepatic bile ducts. *Hepatol Commun.* 2020.02; 4(2); 235-254
 3. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Itsui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient. *Hepatol Res.* 2020.04; 50(4); 524-531
 4. Ryoichi Ando, Yasuhiro Asahina, Kazuaki Chayama, Naoki Hiramatsu, Toru Ikegami, Namiki Izumi, Kan Kikuchi, Kazuhiko Koike, Masayuki Kurosaki, Satoshi Mochida, Fumitaka Suzuki, Tetsuo Takehara, Hajime Takikawa, Atsushi Tanaka, Eiji Tanaka, Yasuhito Tanaka, Hiroshi Yotsuyanagi; Drafting Committee for Hepatitis Management Guidelines, the Japan Society of Hepatology. JSH guidelines for the management of hepatitis B virus infection: 2019 Update. *Hepatol Res.* 2020.04;
 5. Sakura Kirino, Kaoru Tsuchiya, Masayuki Kurosaki, Shun Kaneko, Kento Inada, Koji Yamashita, Leona Osawa, Yuka Hayakawa, Shuhei Sekiguchi, Mao Okada, Wan Wang, Mayu Higuchi, Kenta Takaura, Chiaki Maeyashiki, Nobuharu Tamaki, Yutaka Yasui, Hiroyuki Nakanishi, Jun Itakura, Yuka Takahashi, Yasuhiro Asahina, Namiki Izumi. Relative dose intensity over the first four weeks of lenvatinib therapy is a factor of favorable response and overall survival in patients with unresectable hepatocellular carcinoma. *PLoS One.* 2020.04; 15(4); e0231828
 6. Tetsuo Takehara, Kazuaki Chayama, Masayuki Kurosaki, Hiroshi Yatsuhashi, Yasuhito Tanaka, Naoki Hiramatsu, Naoya Sakamoto, Yasuhiro Asahina, Akito Nozaki, Toshikazu Nakano, Yosuke Hagiwara, Hiroko Shimizu, Hiroki Yoshida, Yuhuan Huang, Michael Biermer, Leen Vijgen, Norio Hayashi. JNJ-4178 (adafosbuvir, odalasvir, and simeprevir) in Japanese patients with chronic hepatitis C virus genotype 1 or 2 infection with or without compensated cirrhosis: the Phase IIa OMEGA-3 study. *J Gastroenterol.* 2020.06; 55(6); 640-652
 7. Yasuhiro Asahina, and Drafting Committee for Hepatitis Management Guidelines, the Japan Society of Hepatology. JSH guidelines for the management of hepatitis C virus infection, 2019 update; protective effect of antiviral therapy against hepatocarcinogenesis. *Hepatol Res.* 2020.07; 50(7); 775-790
 8. Ryoichi Ando, Yasuhiro Asahina, Kazuaki Chayama, Naoki Hiramatsu, Toru Ikegami, Namiki Izumi, Kan Kikuchi, Kazuhiko Koike, Masayuki Kurosaki, Satoshi Mochida, Fumitaka Suzuki, Tetsuo Takehara, Hajime Takikawa, Atsushi Tanaka, Eiji Tanaka, Yasuhito Tanaka, Hiroshi Yotsuyanagi; Drafting Committee for Hepatitis Management Guidelines, the Japan Society of Hepatology. Japan Society of Hepatology guidelines for the management of hepatitis C virus infection: 2019 update. *Hepatol Res.* 2020.07; 50(7); 791-816
 9. Mina Nakagawa, Nobutoshi Nawa, Eiko Takeichi, Taro Shimizu, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Takeo Fujiwara, Mamoru Watanabe, Yujiro Tanaka, Yasuhiro Asahina. Mac-2 binding protein glycosylation isomer as a novel predictive biomarker for patient survival after hepatitis C virus eradication by DAAs. *J Gastroenterol.* 2020.08; 55; 990-999
 10. Yuki Tahata, Hayato Hikita, Satoshi Mochida, Norifumi Kawada, Nobuyuki Enomoto, Akio Ido, Hitoshi Yoshiji, Daiki Miki, Yoichi Hiasa, Yasuhiro Takikawa, Ryotaro Sakamori, Masayuki Kurosaki, Hiroshi Yatsuhashi, Ryosuke Tateishi, Yoshiyuki Ueno, Yoshito Itoh, Taro Yamashita, Tatsuya Kanto, Goki Suda, Yasunari Nakamoto, Naoya Kato, Yasuhiro Asahina, Kentaro Matsuura, Shuji Terai, Kazuhiko Nakao, Masahito Shimizu, Taro Takami, Norio Akuta, Ryoko Yamada, Takahiro Kodama, Tomohide Tatsumi, Tomomi Yamada, Tetsuo Takehara. Sofosbuvir plus velpatasvir treatment for hepatitis C virus in patients with decompensated cirrhosis: a Japanese real-world multicenter study. *J Gastroenterol.* 2020.10; Online ahead of print.

11. Yasuhiro Asahina, Chun-Jen Liu, Edward Gane, Yoshito Itoh, Norifumi Kawada, Yoshiyuki Ueno, Jin Youn, Chen-Yu Wang, Joe Llewellyn, Takuma Matsuda, Anuj Gaggar, Hongmei Mo, Hadas Dvory-Sobol, Gerald Crans, Wan-Long Chuang, Pei-Jer Chen, Nobuyuki Enomoto. Twelve weeks of ledipasvir/sofosbuvir all-oral regimen for patients with chronic hepatitis C genotype 2 infection: Integrated analysis of three clinical trials. *Hepatology*. 2020.10; 50(10); 1109-1117

[Conference Activities & Talks]

1. Sakurako Kobayashi, Satoshi Watanabe, Yosuke Yoneyama, Kousuke Tanimoto, Ryu Nishimura, Sayaka Nagata, Masami Inoue, Kouhei Suzuki, Sei Kakinuma, Kiichiro Tsuchiya, Ryuichi Okamoto, Mamoru Watanabe, Takanori Takebe, Shiro Yui. Conceptual basis of lineage shift between intestinal epithelium and hepatocytes. Keystone Symposia, Tissue Organoids as Models of Host Physiology and Pathophysiology of Disease 2020.01.22 Vancouver (Canada)
2. Fukiko Kawai-Kitahata, Yasuhiro Asahina, Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka, Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Online

Department of Advanced Therapeutics for GI Diseases

Associate Professor : Takashi NAGAISHI
Assistant Professor : Yasuhiro NEMOTO
Graduate Student : Naoya TSUGAWA, Daiki YAMADA, Takehito ASAKAWA,
Ai MASUMOTO, Yuria TAKEI, Shohei TANAKA, Ryo MORIKAWA,
Yuki YONEMOTO

(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. Shohei Tanaka, Yasuhiro Nemoto, Yuria Takei, Ryo Morikawa, Shigeru Oshima, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Susanne Stutte, Mamoru Watanabe. High-fat diet-derived free fatty acids impair the intestinal immune system and increase sensitivity to intestinal epithelial damage. *Biochem Biophys Res Commun.* 2020.02; 522(4); 971-977
2. Yuria Takei, Yasuhiro Nemoto, Ryo Morikawa, Shohei Tanaka, Shigeru Oshima, Takashi Nagaishi, Ryuichi Okamoto, Kiichiro Tsuchiya, Tetsuya Nakamura, Mamoru Watanabe. T cells show amoeboid shape and frequent morphological change in vitro, and localize to small intestinal intraepithelial region in vivo. *Biochem Biophys Res Commun.* 2020.03; 523(2); 328-335

[Conference Activities & Talks]

1. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Taro Watabe, Michio Onizawa, Mamoru Watanabe. B cell receptor signaling in lymphoid tissues may be regulated by CEACAM1.. ECCO2020 2020.02.14 Vienna (Austria)
2. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Taro Watabe, Michio Onizawa, Yudai Kojima, Richard S. Blumberg, Mamoru Watanabe. BCR signaling in lymphoid tissues is regulated by the long isoform of Ceacam1.. MICS2020 2020.07.20 Web 開催
3. Takashi Nagaishi, Daiki Yamada, Naoya Tsugawa, Taro Watabe, Eiko Saito, Masayoshi Fukuda, Ayako Arai, Kazuo Ohtsuka, Mamoru Watanabe. A case of villous atrophy with CCR4+ T cell infiltration in the small intestine.. UEGW2020 2020.10.10 Web 開催
4. Takashi Nagaishi, Naoya Tsugawa, Daiki Yamada, Yudai Kojima, Michio Onizawa, Taro Watabe, Richard S. Blumberg, Mamoru Watanabe. BCR signaling in lymphoid tissues regulated by the long isoform of Ceacam1.. FOCIS2020 2020.10.28 Web 開催

Respiratory Physiology and Sleep Medicine

Professor: Yasunari Miyazaki
Associate Professor: Meiyo Tamaoka
Lecturer: Tomoya Tateishi
Technician: Miri Takahashi, Shisei Go

(1) Outline

The Department of Respiratory Physiology and Sleep Medicine aims to elucidate the mechanism of sleep disordered breathing including sleep apnea syndrome physiologically and biochemically. Also we aim to develop the novel diagnostic approach and therapeutic method for obstructive sleep apnea in our "Clinical Center for Pleasant Sleep" in collaboration with many other departments.

(2) Research

Research Subject:

1. Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
2. Development of Non-contact polysomnograph system.
3. The association between OSA and short term blood-pressure variability.
4. The association between OSA and interstitial pneumonia.
5. Snore sound analysis for detecting OSA severity
6. The effect of Tongue Exercise on OSA

(3) Education

Education of sleep medicine for students, residents and technicians

(4) 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. Jitoku (Psychiatry)

PM Dr. Kobayashi, Dr. Ejima, Dr. Kawahara (Respiratory Medicine),

Tuesday: AM Dr. Hirai (Psychiatry)

Wednesday: AM Dr. Miyazaki (Respiratory Medicine)

Thursday: AM Dr. Tamaoka

PM Dr. Tamaoka (Respiratory Physiology and Sleep Medicine)

Friday: AM Dr. Takagi (Psychiatry)

AM Dr. Tateishi (Respiratory Medicine)

PM Dr. Iijima (Respiratory Medicine)

· Outpatient visits: 5,439 (New:223) for FY 2020

· Examination: polysomnography: 67 patients for FY 2020

(5) Clinical Performances

We aim to establish personalized medicine for OSA in collaboration with the Dental Clinic for Sleep Disorders.

(6) Publications

[Original Articles]

1. Iijima Y, Sakakibara R, Ishizuka M, Honda T, Shirai T, Okamoto T, Tateishi T, Sakashita H, Tamaoka M, Takemoto A, Kumaki Y, Ikeda S, Miyazaki Y. Notable response to nivolumab during the treatment of SMARCA4-deficient thoracic sarcoma: a case report. *Immunotherapy*. 2020.01; 12(8); 563-569
2. Hayashi S, Tamaoka M, Tateishi T, Murota Y, Handa I, Miyazaki Y. A New Feature with the Potential to Detect the Severity of Obstructive Sleep Apnoea via Snoring Sound Analysis. *International Journal of Environmental Research and Public Health*. 2020.04; 17(8); 2951

Department of Nutrition and Metabolism in Cardiovascular Disease

Makiko Egawa
Mizuko Osaka

(1) Outline

This course was established as a donated research division attached to the Department of Life Sciences and Medical Ethics.

The main themes are investigating the mechanism of arteriosclerosis development, which are one of the main causes of lifestyle-related diseases such as cardiovascular diseases and diabetes. This course also has been interested in the treatment and prevention of atherosclerosis and its relationship toward pregnancy in women. Our education is being developed with the aim of training excellent researchers and highly specialized professionals with specialized knowledge and abilities capable of playing an active role in the international community.

(2) Publications

[Original Articles]

1. Higashijima Y, Matsui Y, Shimamura T, Nakaki R, Nagai N, Tsutsumi S, Abe Y, Link VM, Osaka M, Yoshida M, Watanabe R, Tanaka T, Taguchi A, Miura M, Ruan X, Li G, Inoue T, Nangaku M, Kimura H, Furukawa T, Aburatani H, Wada Y, Ruan Y, Glass CK, Kanki Y. Coordinated demethylation of H3K9 and H3K27 is required for rapid inflammatory responses of endothelial cells. *The EMBO journal*. 2020.03; e103949
2. Egawa M, Hara K, Ikeda M, Kono E, Miyashita S, Miyasaka N, Inaji M, Maehara T, Yoshida M. Role of obstetricians in promoting pregnancy-related knowledge among women with epilepsy in Japan. *Epilepsy & behavior : E&B*. 2020.06; 111; 107176
3. Terui-Kohbata Hiroko, Egawa Makiko, Yura Kei, Yoshida Masayuki. Knowledge and attitude of hereditary breast cancer among Japanese university female students *Journal of Human Genetics*. 2020.07; 65(7); 591-599
4. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a stimulation of differentiated HL60 induces THP-1 chemotaxis via MCP-1 dependent pathway(和訳中) 日本動脈硬化学会総会プログラム・抄録集. 2020.07; 52 回; 268
5. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a Elevates MCP-1 Expression in Neutrophil-like Differentiated HL60 via NF- κ B Signaling Pathway(和訳中) 日本循環器学会学術集会抄録集. 2020.07; 84 回; OE122-6
6. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver(和訳中) 日本循環器学会学術集会抄録集. 2020.07; 84 回; PE28-2
7. Egawa M, Hara K, Ikeda M, Yoshida M. Questionnaire dataset: Attitude of epileptologists and obstetricians to pregnancy among women with epilepsy. *Data in brief*. 2020.08; 31; 105948

8. Tsuru H, Osaka M, Hiraoka Y, Yoshida M. HFD-induced hepatic lipid accumulation and inflammation are decreased in Factor D deficient mouse. *Scientific reports*. 2020.10; 10(1); 17593
9. Inoue Reiko, Nishi Hiroshi, Osaka Mizuko, Yoshida Masayuki, Nangaku Masaomi. NEUTROPHIL INTERFERON-INDUCED, DOUBLE-STRANDED RNA-ACTIVATED PROTEIN KINASE (EIF2AK2) PROMOTES ADHESION IN NON-VIRAL INFLAMMATORY KIDNEY DISEASE NEPHROLOGY. 2020.10; 25; 35

[Conference Activities & Talks]

1. 大坂 瑞子、出牛 三千代、吉田 雅幸. 選択的 PPAR α アゴニスト、ペマフィブラートは LDL 受容体欠損マウス大腿動脈における高中性脂肪血症を改善し、白血球接着を抑制する. 第 52 回日本動脈硬化学会総会・学術集会 2020.07.17 名古屋
2. Syed Masudur Rahman Dewan, Michiyo Deushi, Mizuko Osaka, Masayuki Yoshida. C5a elevates MCP-1 expression in neutrophil-like differentiated HL60 via NF- κ B signaling pathway. 第 84 回日本循環器学会学術集会 2020.07.27 京都
3. Hiromi Tsuru, Mizuko Osaka, Masayuki Yoshida. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver . 第 84 回日本循環器学会学術集会 2020.07.27 Kyoto
4. 大坂瑞子. 動脈硬化症関連血管炎症反応における好中球でのヒストンシトルリン化の重要性. 第 43 回日本分子生物学会年会 2020.12.02

Department of Lifetime Clinical Immunology

MORI Masaaki
SUGIHARA Takahiko
YAMAZAKI Susumu
NARUTO Takuya

(1) Outline

(Overview)

In response to the rapid rise of social interest, the importance of medical care throughout lifelong, including the development of transitional medical care, has been reviewed. In addition, since 2015, the incurable disease policy in Ministry of Health, Labor and Welfare has been enriched as a national policy. However, the university courses in Japan have not successfully departed from the traditional framework of internal medicine and pediatrics so far; and these two departments have developed separately. Especially in intractable immune diseases, because the cause has not yet been fully elucidated; the commonalities and differences between children, adults, and the elderly in these diseases have not at all been sorted out, and studies of these diseases have independently been developed by age groups with little being merged across groups. The universal and uniform diagnostic methods and/or treatment for a lifetime have not yet been available in the current situation.

Therefore, it is now required to establish a system to study of and treat immune intractable diseases such as rheumatic diseases seamlessly from children to the elderly. Following such circumstances, in 2016, our university established a donation course in cooperation with a course in which specialists in immunological intractable diseases play an important role (Rheumatology and Pediatrics), and Masaaki Mori who had been conducting Pediatric rheumatology at Yokohama City University joined as a member. Pediatrics staff and Rheumatology staff shared a room, and very started the course as a "mixed team". This course, with the cooperation of Department of Rheumatology and Pediatrics, promotes the integration of research, education, and clinical system for life-long immunological intractable diseases which have not been achieved by existing courses, and aims to develop a new course that leads the reform and enhancement of medical care and learning for all intractable diseases.

(2) Research

(Research activities)

1) Establishment of a research system in cooperation with Pediatrics and Rheumatology

This course clarifies the differences and similarities of rheumatic diseases between children and adults, and develops and embodies a universal approach to "countermeasures for intractable diseases throughout life-full courses". Especially in the transitional phase from pediatric to adult, there may be many transition-specific problems such as changes in the department/physician in charge from pediatrics to internal medicine, and changes in the required amount of medication due to changes in drug metabolism and physique.

In addition, we will propose treatment strategies that consider the needs and issues of those who wish to have children and are restricted from treatment with immunosuppressive drugs, and the elderly who are concerned about complications and compliance.

2) Clinical epidemiological study aiming to construct a database in the transition from childhood to adulthood

This course will lead the construction of a nationwide database of pediatric rheumatic diseases that has not been organized in Japan so far. The cohort studies in Japan have independently investigated children and adults in the recognition as "specified pediatric chronic diseases" and "designated intractable diseases" by the Ministry of Health, Labor and Welfare.

This course will construct a database of patients from childhood to adulthood in cooperation with the international community to clarify the current situation of the treatment of patients with childhood rheumatism and collagen diseases in Japan. Then, basic data to unify the description of registered items will be presented for immune intractable diseases that cross both the childhood chronic specific disease system and the designated intractable disease system.

Specifically, we will complete CoNinJa, a database focusing on JIA patients, based on NinJa which is a database that focuses on adult patients with rheumatoid arthritis. We will collect data in the future and clarify the actual situation of JIA medical treatment.

3) Genomic and immunological marker studies related to differences and similarities between children and adults

In this course, we will utilize the disease bioresource center of our university, which has the latest technology such as whole exome sequencing, next-generation sequence analysis and immunomarker research to make an effort to clarify all the intractable diseases of children and adults (rheumatic and collagen diseases, vascular inflammatory diseases, primary immunodeficiency syndrome, and autoinflammatory syndrome), and comprehensively explore the childhood-onset, transition from childhood to adulthood, adult onset, and elderly.

4) Development and expansion of new treatments through doctor-initiated clinical trials, etc.

Clinical tests (clinical trials) for drug approval have rapidly been globalizing, and an increasing number of people have been participating in international joint trials. In addition, the review period has been significantly reduced following the establishment of a drug approval review system, and improvements in medical drug lag are expected.

In this course, we will actively promote clinical tests and trials of new drugs in the transitional phase, which are considered difficult to be implemented in the transition period between children and adults. As a result, it is expected that the therapeutic goals of rheumatic/collagen diseases for children through adults will be advanced, and that the treatment options will be complicated and diverse; hence, the direction of establishing the tailor-made treatments for children to the elderly are explored, considering the actual use of these drugs.

5) Implementation of clinical studies for adults to the elderly and preparation of clinical guidelines.

The following studies were conducted in cooperation with the rheumatology. Rheumatoid arthritis: analysis of cohort study of the elderly-onset rheumatoid arthritis, analysis of NinJa of elderly patient data, systematic review of elderly rheumatoid arthritis and preparation of clinical guidelines for rheumatoid arthritis, continuation of a multi-center prospective cohort study of rheumatoid arthritis, and implementation of a new prospective cohort study of middle age to the elderly. Vasculitis syndrome: Implementation of a cohort study of large and small vasculitis, data analysis, preparation of clinical guidelines for vasculitis, establishment of the remission criteria and treatment strategies for large vessel vasculitis, and starting a cohort study using an intractable disease platform. Adult-onset Still's disease, systemic juvenile idiopathic arthritis: Implementation of a Tokyo Medical and Dental University cohort study for children and adults, preparation of a prospective cohort study using intractable disease platform.

(3) Education

(Educational activities)

Fostering a "hybrid physician" who can provide consistent medical care from children to adults

The clinical system so far has been separated for children and adults. From the perspective of patients, many feel confused and anxious about the change of the department in charge and the attending physician once they reach a certain age when they grow up despite the same disease. The adult physicians also often struggle with how those patients have progressed the diseases, what problems or worries of patients have had other than medical concerns while growing up, and whether those patients in carry-over case can be treated in the same manner as adults. For this purpose, this course plays a central role in providing an educational system for fostering "hybrid physicians" who are specialists in rheumatism treatment, are well familiar with treatment for both children and adults, and transcend the boundaries between children and adults.

(4) Lectures & Courses

(Education policy)

In this course, with the cooperation of Department of Rheumatology and Pediatrics, we will promote the integration of research, education, and clinical systems for intractable immune diseases throughout the life of patients, and further aim to be a pioneer of renovation and enhancement of medical treatment and academics for intractable diseases. And this course is intending to foster pediatricians and adult physicians who can solve various problems for patients in the transition from childhood to adulthood and from adulthood to the elderly.

(5) Clinical Services & Other Works

(Clinical and off-campus activities)

Clinical activities

Pediatrics and rheumatology cooperated to provide treatment for collagen and rheumatic diseases from children to the elderly.

Off-campus activities

Professor Masaaki Mori plays a role as the research representative in the followings.

1. Health and Labor Sciences Research Fund Grant/Refractory Disease Policy Research Project (Immune and Allergic Disease Policy Research Project (Immune and Allergic Disease Policy Research Field)(Ministry of health, labor and welfare 2017 2019)

"Analysis of national survey data of patients with pediatric rheumatism in childhood and a transitional phase to adulthood, and standardization of standard treatment by establishing a nationwide "seamless" clinical network based on their differences and similarities"

2. Health and Labor Sciences Research Fund Grants/Refractory Disease Policy Research Project (Refractory Disease Policy Research Project)

(2017-2019, Ministry of Health, Labor and Welfare) "Research on autoimmune diseases" [Research representative: XXX]

3. Research Grant for NPO Japan Kawasaki Disease Research Center (2017/2018, Japan Kawasaki Disease Research Center) "Elucidation of Kawasaki disease by clustering based on clinical information and new biomarkers"

Associate Professor XXXX works as a research coordinator for the followings:

Research designated by the Ministry of Health, Labor and Welfare, research to support for patients with rheumatoid arthritis according to life stages

Health Labor Administration Promotion Research Project Subsidy, Immune/Allergic Disease Policy Research Project, Clinical epidemiological study in regard to standardization of rheumatoid arthritis medical care in Japan

Health and Labor Sciences Research Grants, Intractable Disease Policy Research Project, Investigation and research on intractable vasculitis

#AMED multi-layer study for CQ solution of intractable vasculitis treatment

Health and Labor Sciences Research Grants, Intractable Disease Policy Research Project, Investigation and research on autoimmune diseases

The results of the research indicated above were reported at academic conferences and workshops in Japan and overseas.

(6) Clinical Performances

(Clinical features)

The Lifelong Intractable Immunological Diseases Lecture, "is a unique university course that cannot be found elsewhere in the world, which aims to integrate research, education, and treatment systems for "immune intractable diseases", such as collagen and rheumatic diseases, for a lifetime from children to adults and the elderly". This course in our University has assessed various problems for patients with intractable diseases in

the transitional phase from pediatric to adult or adult to elderly, which have not been solved by conventional medical system of Pediatrics and Internal medicine.

(7) Publications

[Original Articles]

1. Kobayashi, I. and Akioka, S. and Kobayashi, N. and Iwata, N. and Takezaki, S. and Nakaseko, H. and Sato, S. and Nishida, Y. and Nozawa, T. and Yamasaki, Y. and Yamazaki, K. and Arai, S. and Nishino, I. and Mori, M.. Clinical practice guidance for juvenile dermatomyositis (JDM) 2018-Update *Mod Rheumatol.* 2020; 1-13
2. Matsumoto, T. and Matsui, T. and Hirano, F. and Tohma, S. and Mori, M.. Disease activity, treatment and long-term prognosis of adult juvenile idiopathic arthritis patients compared with rheumatoid arthritis patients *Mod Rheumatol.* 2020; 30(1); 78-84
3. Shimizu, M. and Mizuta, M. and Okamoto, N. and Yasumi, T. and Iwata, N. and Umebayashi, H. and Okura, Y. and Kinjo, N. and Kubota, T. and Nakagishi, Y. and Nishimura, K. and Mohri, M. and Yashiro, M. and Yasumura, J. and Wakiguchi, H. and Mori, M.. Tocilizumab modifies clinical and laboratory features of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis *Pediatr Rheumatol Online J.* 2020; 18(1); 2
4. Tanaka, Y. and Kuwana, M. and Fujii, T. and Kameda, H. and Muro, Y. and Fujio, K. and Itoh, Y. and Yasuoka, H. and Fukaya, S. and Ashihara, K. and Hirano, D. and Ohmura, K. and Tabuchi, Y. and Hasegawa, H. and Matsumiya, R. and Shirai, Y. and Ogura, T. and Tsuchida, Y. and Ogawa-Momohara, M. and Narazaki, H. and Inoue, Y. and Miyagawa, I. and Nakano, K. and Hirata, S. and Mori, M.. 2019 Diagnostic criteria for mixed connective tissue disease (MCTD): From the Japan research committee of the ministry of health, labor, and welfare for systemic autoimmune diseases *Mod Rheumatol.* 2020; 1-5
5. Masako Utsunomiya, Hiroaki Dobashi, Toshio Odani, Kazuyoshi Saito, Naoto Yokogawa, Kenji Nagasaka, Kenchi Takenaka, Makoto Soejima, Takahiko Sugihara, Hiroyuki Hagiyama, Shinya Hirata, Kazuo Matsui, Yoshinori Nonomura, Masahiro Kondo, Fumihito Suzuki, Yasushi Nawata, Makoto Tomita, Mari Kihara, Waka Yokoyama-Kokuryo, Fumio Hirano, Hayato Yamazaki, Ryoko Sakai, Toshihiro Nanki, Ryuji Koike, Nobuyuki Miyasaka, Masayoshi Harigai. prophylaxis: results of 52-week follow-up. *Rheumatol Adv Pract.* 2020; 4(2); rkaa029
6. Mitsuaki Isobe, Koichi Amano, Yoshihiro Arimura, Akihiro Ishizu, Shuichi Ito, Shinya Kaname, Shigeto Kobayashi, Yoshinori Komagata, Issei Komuro, Kimihiro Komori, Kei Takahashi, Kazuo Tanemoto, Hitoshi Hasegawa, Masayoshi Harigai, Shouichi Fujimoto, Tatsuhiko Miyazaki, Tetsuro Miyata, Hidehiro Yamada, Akitoshi Yoshida, Takashi Wada, Yoshinori Inoue, Haruhito A Uchida, Hideki Ota, Takahiro Okazaki, Mitsuho Onimaru, Tamihito Kawakami, Reiko Kinouchi, Atsushi Kurata, Hisanori Kosuge, Ken-Ei Sada, Kunihiro Shigematsu, Eiichi Suematsu, Eijun Sueyoshi, Takahiko Sugihara, Hitoshi Sugiyama, Mitsuhiro Takeno, Naoto Tamura, Michi Tsutsumino, Hiroaki Dobashi, Yoshikazu Nakaoka, Kenji Nagasaka, Yasuhiro Maejima, Hajime Yoshifuji, Yoshiko Watanabe, Shoichi Ozaki, Takeshi Kimura, Hiroshi Shigematsu, Keiko Yamauchi-Takihara, Toyoaki Murohara, Shin-Ichi Momomura, . JCS 2017 Guideline on Management of Vasculitis Syndrome - Digest Version. *Circ J.* 2020.01; 84(2); 299-359
7. Shimizu Masaki, Mizuta Mao, Okamoto Nami, Yasumi Takahiro, Iwata Naomi, Umebayashi Hiroaki, Okura Yuka, Kinjo Noriko, Kubota Tomohiro, Nakagishi Yasuo, Nishimura Kenichi, Mohri Mariko, Yashiro Masato, Yasumura Junko, Wakiguchi Hiroyuki, Mori Masaaki. Tocilizumab modifies clinical and laboratory features of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis *PEDIATRIC RHEUMATOLOGY.* 2020.01; 18(1); 2
8. Tamura D, Kawahara Y, Mori M, Yamagata T.. Multifocal and extrapulmonary tuberculosis due to immunosuppressants. *Pediatr Int.* 2020.01;
9. Aya Kawasaki, Natsumi Namba, Ken-Ei Sada, Fumio Hirano, Shigeto Kobayashi, Kenji Nagasaka, Takahiko Sugihara, Nobuyuki Ono, Takashi Fujimoto, Makio Kusaoi, Naoto Tamura, Kunihiro Yamagata, Takayuki Sumida, Hiroshi Hashimoto, Shoichi Ozaki, Hirofumi Makino, Yoshihiro Arimura, Masayoshi Harigai, Naoyuki Tsuchiya. Association of TERT and DSP variants with microscopic polyangiitis and

- myeloperoxidase-ANCA positive vasculitis in a Japanese population: a genetic association study. *Arthritis Res Ther.* 2020.01; 22(1); 246
10. Susumu Yamazaki, Asami Shimbo, Yuko Akutsu, Hiroshi Takase, Tomohiro Morio, Masaaki Mori. Importance of pediatric rheumatologists and transitional care for juvenile idiopathic arthritis-associated uveitis: a retrospective series of 9 cases. *Pediatr Rheumatol Online J.* 2020.03; 18(1); 26
 11. Takahiko Sugihara, Hitoshi Hasegawa, Haruhito A Uchida, Hajime Yoshifuji, Yoshiko Watanabe, Eisuke Amiya, Yasuhiro Maejima, Masanori Konishi, Yohko Murakawa, Noriyoshi Ogawa, Shunsuke Furuta, Yasuhiro Katsumata, Yoshinori Komagata, Taio Naniwa, Takahiro Okazaki, Yoshiya Tanaka, Tsutomu Takeuchi, Yoshikazu Nakaoka, Yoshihiro Arimura, Masayoshi Harigai, Mitsuaki Isobe, . Associated factors of poor treatment outcomes in patients with giant cell arteritis: clinical implication of large vessel lesions. *Arthritis Res. Ther.* 2020.04; 22(1); 72
 12. Soya Kobayashi, Ayano Inui, Tomoyuki Tsunoda, Syuichiro Umetsu, Tsuyoshi Sogo, Masaaki Mori, Masato Shinkai, Tomoo Fujisawa. Liver cirrhosis in a child associated with Castleman's disease: A case report. *World J Clin Cases.* 2020.05; 8(9); 1656-1665
 13. Ichiro Kobayashi, Shinji Akioka, Norimoto Kobayashi, Naomi Iwata, Shunichiro Takezaki, Haruna Nakaseko, Satoshi Sato, Yutaka Nishida, Tomo Nozawa, Yuichi Yamasaki, Kazuko Yamazaki, Satoru Arai, Ichizo Nishino, Masaaki Mori. Clinical practice guidance for juvenile dermatomyositis (JDM) 2018-Update. *Mod Rheumatol.* 2020.05; 30(3); 411-423
 14. Hiroshi Yokomichi, Keiko Tanaka-Taya, Rie Koshida, Takashi Nakano, Yoshinori Yasui, Masaaki Mori, Yuka Ando, Saeko Morino, Hideo Okuno, Hiroshi Satoh, Satoru Arai, Mie Mochizuki, Zentaro Yamagata. Immune thrombocytopenic purpura risk by live, inactivated and simultaneous vaccinations among Japanese adults, children and infants: a matched case-control study. *Int J Hematol.* 2020.07; 112(1); 105-114
 15. Toru Igarashi, Syuji Takei, Eriko Tanaka, Utako Kaneko, Tomohiro Kubota, Keisuke Okamoto, Shiro Ohshima, Masaaki Mori. Investigation of dual-energy X-ray absorptiometry units necessary for pediatric rheumatologists in Japan and a proposal for shared access to equipment among hospitals. *J Nippon Med Sch.* 2020.08;
 16. Kazuko Yamazaki, Akiko Ohta, Shinji Akioka, Yuichi Yamasaki, Asami Ohara, Haruna Nakaseko, Kenichi Nishimura, Norimoto Kobayashi, Yutaka Nishida, Satoshi Sato, Shunichiro Takezaki, Takayuki Kishi, Motomu Hashimoto, Ichiro Kobayashi, Masaaki Mori. External validation of the EULAR/ACR idiopathic inflammatory myopathies classification criteria with a Japanese paediatric cohort. *Rheumatology (Oxford).* 2020.08;
 17. Tomoya Kaneda, Eriko Tanaka, Yuko Akutsu, Toru Kanamori, Mariko Mouri, Tomohiro Morio, Masaaki Mori. Refractory secondary thrombotic microangiopathy with kidney injury associated with systemic lupus erythematosus in a pediatric patient *CEN Case Rep.* 2020.09; 9(4); 301-307
 18. Minako Tomiita, Ichiro Kobayashi, Yasuhiko Itoh, Yuzaburo Inoue, Naomi Iwata, Hiroaki Umebayashi, Nami Okamoto, Yukiko Nonaka, Ryoki Hara, Masaaki Mori. Clinical practice guidance for Sjögren's syndrome in pediatric patients (2018) - summarized and updated. *Mod Rheumatol.* 2020.09; 1-11
 19. Naomi Iwata, Minako Tomiita, Ichiro Kobayashi, Yusaburo Inoue, Yukiko Nonaka, Nami Okamoto, Hiroaki Umebayashi, Ryoki Hara, Yasuhiko Ito, Yasunori Sato, Masaaki Mori. Utility of the EULAR Sjögren syndrome disease activity index in Japanese children: a retrospective multicenter cohort study. *Pediatr Rheumatol Online J.* 2020.09; 18(1); 73
 20. Keisuke Okamoto, Tomohiro Morio, Yoshikazu Nakamura, Hiroshi Hataya, Koichi Mizuta, Masaaki Mori. Hospitalisations due to respiratory syncytial virus infection in children with Down syndrome before and after palivizumab recommendation in Japan. *Acta Paediatr.* 2020.10;
 21. Masaaki Mori. What are the main revised points in the 6th diagnostic guidelines for Kawasaki disease? *Pediatr Int.* 2020.10; 62(10); 1133-1134
 22. Takumi Matsumoto, Masaaki Mori. Questionnaire survey on transitional care for patients with juvenile idiopathic arthritis (JIA) and families. *Mod Rheumatol.* 2020.10; 1-6

23. Takehiko Mori, Masuho Saburi, Maki Hagihara, Masaaki Mori, Rie Yamazaki, Jun Kato. Long-term remission of cryopyrin-associated periodic syndrome after allogeneic haematopoietic stem cell transplantation. *Ann Rheum Dis.* 2020.11;
24. Tadashi Hosoya, Takahiko Sugihara, Nobuyuki Miyasaka, Shinsuke Yasuda. Novel treatment strategy of polymyalgia rheumatica targeting drug-free remission. *Clin Exp Rheumatol.* 2020.11;

[Misc]

1. Kenji Okada, Mihoko Mizuno, Hiroyuki Moriuchi, Satoshi Kusuda, Ichiro Morioka, Masaaki Mori, Keisuke Okamoto, Kuniyuki Okada, Shigemi Yoshihara, Hiroyuki Yamagishi, Utako Yokoyama, Tomohiro Kubota, Kazuko Kudo, Masatoshi Takagi, Shuichi Ito, Yutaka Kanamori, Yoji Sasahara. The Working Group for Revision of "Guidelines for the Use of Palivizumab in Japan": A Committee Report. *Pediatr Int.* 2020.11; 62(11); 1223-1229

[Conference Activities & Talks]

1. Ruperto N, Brunner HI , Mori M , Clinch J, Syed R, Iwata N , Bass DL , Ji B , Hammer AE , Okily M , Eriksson G , Quasny H. . PLUTO Trial: Sensitivity Analyses of SRI4 response with Belimumab vs Placebo in Paediatric Patients With Childhood-Onset Systemic Lupus Erythematosus (cSLE). . *European League Against Rheumatism 2020* 2020.06.01
2. 森 雅亮. アニュアルレクチャー. 小児リウマチ性疾患における移行期医療の取り組みと実際. . 第 64 回日本リウマチ学会総会・学術集会. 2020.08.01
3. Clinical feature and genetic alteration of Myeloid/Natural killer cell precursor acute leukemia (MNKPL). 2020.11.21

Department of Collaborative Medicine for Gastroenterology and Hepatology (CMGH)

Associate Professor : Seishin Azuma
Assistant Professor : Kento Takenaka

(1) Outline

Our department was established for the aim to support the medical care at Tokyo Medical and Dental University (TMDU), and to foster experts in the field of gastroenterology and hepatology who engaged a community medicine such as Ibaraki prefecture. In collaboration with the Department of Gastroenterology and Hepatology in TMDU, we will strengthen an information sharing system and an education training support system that build up with Tsuchiura Kyodo General Hospital and other related facilities. We hope to develop the community medicine through the communication and personal exchanges between such hospitals and us.

(2) Research

- Clinical research on liver diseases related to lifestyle-related diseases
- Establishment of optimized therapy in hepatobiliary diseases
- Development of evaluation and treatment of small bowel lesions in Crohn's disease.
- Development of support technology for diagnosis of digestive and liver diseases by artificial intelligence (AI).

(3) Education

Primary goal for education in our department is to train highly educated and experienced clinicians in the field of gastroenterology and hepatology. Therefore, our goal for education of graduate students is to produce clinicians thinking from a wide perspective and to bring up leaders of the next generation in the field of gastroenterology and hepatology.

(4) Lectures & Courses

Our lectures and courses for medical students 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, TMDU in collaboration with such department.

(5) Clinical Services & Other Works

In collaboration with the Department of Gastroenterology and Hepatology, we mainly provide outpatient and inpatient care of gastrointestinal and hepatobiliary diseases. In addition, we are managing a lot of multicenter studies including Tsuchiura Kyodo General Hospital. We are conducting industry-academic collaborative research in the field of AI research using the comprehensive collaboration program of TMDU.

(6) Clinical Performances

In collaboration with the Department of Gastroenterology and Hepatology, TMDU, we provide a medical care of liver and inflammatory bowel diseases. We have recently established special outpatient clinics for chronic hepatitis, liver cirrhosis, hepatocellular carcinoma and inflammatory bowel diseases.

We are operating a lot of multicenter studies. One of the multicenter studies evaluates the efficacy of treatment against viral hepatitis, named as “Ochanomizu Liver Conference”, in which more than 2,000 patients have been enrolled. We approach to improve the safety and reliance of treatment for hepatocellular carcinoma, the patients are treated using multilateral approaches by 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 have also performed balloon-assisted enteroscopy for the small intestine. The patients’ number were top-class in the world.

(7) Publications

[Original Articles]

1. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient *Hepatol Res.* 2020; 50(4); 524-531
2. Kento Takenaka, Kazuo Ohtsuka, Toshimitsu Fujii, Mariko Negi, Kohei Suzuki, Hiromichi Shimizu, Shiori Oshima, Shintaro Akiyama, Maiko Motobayashi, Masakazu Nagahori, Eiko Saito, Katsuyoshi Matsuoka, Mamoru Watanabe. Development and Validation of a Deep Neural Network for Accurate Evaluation of Endoscopic Images From Patients With Ulcerative Colitis. *Gastroenterology.* 2020.02;
3. Takenaka K, Kitazume Y, Fujii T, Tsuchiya K, Watanabe M, Ohtsuka K. Objective evaluation for treat to target in Crohn’s disease. *Journal of gastroenterology.* 2020.03;
4. Kento Takenaka, Yoshio Kitazume, Toshimitsu Fujii, Kiichiro Tsuchiya, Mamoru Watanabe, Kazuo Ohtsuka. Objective evaluation for treat to target in Crohn’ s disease. *J Gastroenterol.* 2020.03; 55(3); 579-587
5. Kento Takenaka, Toshimitsu Fujii, Kohei Suzuki, Hiromichi Shimizu, Maiko Motobayashi, Shuji Hibiya, Eiko Saito, Masakazu Nagahori, Mamoru Watanabe, Kazuo Ohtsuka. Small bowel healing detected by endoscopy in patients with Crohn’s disease after treatment with antibodies against tumor necrosis factor. *Clin Gastroenterol Hepatol.* 2020.06; 18(7); 1545-1552
6. Shigeki Bamba, Ryosuke Sakemi, Toshimitsu Fujii, Teruyuki Takeda, Shin Fujioka, Kento Takenaka, Hiroki Kitamoto, Shotaro Umezawa, Hirotake Sakuraba, Toshihiro Inokuchi, Norimasa Fukata, Shinta Mizuno, Masaki Yamashita, Shinichiro Shinzaki, Hiroki Tanaka, Hidetoshi Takedatsu, Ryo Ozaki, Kei Moriya, Manabu Ishii, Tetsu Kinjo, Keiji Ozeki, Makoto Ooi, Ryohei Hayashi, Kazuki Kakimoto, Yuichi Shimodate, Kazuya Kitamura, Akihiro Yamada, Akira Sonoda, Yu Nishida, Kyouko Yoshioka, Shinya Ashizuka, Fumiaki Takahashi, Toshio Shimokawa, Taku Kobayashi, Akira Andoh, Toshifumi Hibi. A nationwide, multi-center, retrospective study of symptomatic small bowel stricture in patients with Crohn’s disease. *J Gastroenterol.* 2020.06; 55(6); 615-626
7. Hiromichi Shimizu, Toshimitsu Fujii, Shuji Hibiya, Maiko Motobayashi, Kohei Suzuki, Kento Takenaka, Eiko Saito, Masakazu Nagahori, Kazuo Ohtsuka, Mamoru Watanabe. Rapid prediction of 1-year efficacy of tofacitinib for treating refractory ulcerative colitis. *Intest Res.* 2020.06; Online ahead of print.
8. Mina Nakagawa, Nobutoshi Nawa, Eiko Takeichi, Taro Shimizu, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Takeo Fujiwara, Mamoru Watanabe, Yujiro Tanaka, Yasuhiro Asahina. Mac-2 binding protein glycosylation isomer as a novel predictive biomarker for patient survival after hepatitis C virus eradication by DAAs. *J Gastroenterol.* 2020.08; 55; 990-999
9. Yoshio Kitazume, Junichi Tsuchiya, Kento Takenaka, Kazuo Ohtsuka, Koichiro Kimura, Ryosuke Watanabe, Tomoyuki Fujioka, Toshimitsu Fujii, Mamoru Watanabe, Ukihide Tateisi. High b-value

computed diffusion-weighted imaging for differentiating bowel inflammation in Crohn's disease. *Eur J Radiol.* 2020.10; 133; 109362

[Conference Activities & Talks]

1. Real world experience with tofacitinib in refractory ulcerative colitis.. 2020.02.07
2. Toshimitsu Fujii, Shuji Hibiya, Chiaki Maeyashiki, Eiko Saito, Kento Takenaka, Maiko Motobayashi, Hiromichi Shimizu, Masakazu Nagahori, Kazuo Ohtsuka, Masayuki Kurosaki, Tsunehito Yauchi, Mamoru Watanabe. Intolerance to 5-aminosalicylate is a risk of poor prognosis in Ulcerative colitis patients.. ECCO2020 2020.02.14 Vienna (Austria)
3. Fukiko Kawai-Kitahata, Yasuhiro Asahina , Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka , Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Online

Department of Child Health and Development

Professor: Hirokazu KANEGANE
Junior Assistant Professor: Masaki SHIMIZU

(1) Outline

In addition to acute diseases of medicine and child health care, “growth and medical care” include transition to the chronic phase, long-term medical treatment of patients with intractable diseases, medicine encompassing healthy growth of children. As a philosophy of “growth and medical care”, we establish a developmental and medical system closely related to regional medical care in the suburbs of the metropolitan area, and to foster human resources of pediatricians responsible for next-generation medical care.

(2) Research

We conduct survey research and education based on the organic collaboration between Tokyo Medical and Dental University and Kashiwa City Kashiwa Hospital.

The current main projects are the following.

- 1.Establishment of pediatric medical system in Kashiwa city.
- 2.Study of primary immunodeficiency (PID) predisposing to Epstein-Barr virus infection
- 3.Study of primary antibody deficiency
- 4.Etiologic and pathophysiological analysis of cytokine storm syndrome, especially of macrophage activation syndrome.
- 5.Etiologic and pathophysiological analysis of juvenile idiopathic arthritis (JIA), the most common type of pediatric rheumatic diseases.
- 6.Registry study on pediatric kidney disease in Kashiwa city.

(3) Education

We conduct a broader range of more specialized clinical education for acquiring pediatric specialists at the University Hospital.

(4) Lectures & Courses

We mainly train young pediatric researchers and specialists. We make them to be familiar with chronic diseases and intractable diseases of childhood and to be responsible for next generation medical care.

(5) Clinical Services & Other Works

We treat children with PID, hematological malignancies, hematological disorders, and malignant solid tumors in the University Hospital.

At Kashiwa City Kashiwa Hospital, we provide pediatric medicine mainly for acute diseases, cooperating with medical facilities in the suburbs, and establish a reliable medical system for children in the local residents.

(6) Clinical Performances

We provide diagnosis, treatment of pathological analysis of primary immunodeficiency (PID) and hematological malignancies, and perform hematopoietic cell transplantation for refractory diseases. Especially, we treat the largest number of patients with PID in Japan.

Our university hospital is one of the largest core centers for pediatric rheumatic diseases in Japan. Pediatric rheumatologists, adult rheumatologists, pediatric orthopedic surgeons and pediatric ophthalmologists cooperatively provide seamless medical cares for pediatric rheumatic diseases from children to adults.

(7) Publications

[Original Articles]

1. Irabu H, Shimizu M, Kaneko S, Inoue N, Mizuta M, Ohta K, Yachie A. Clinical Significance of Serum Galactose-Deficient IgA1 Level in Children with IgA Nephropathy. *Journal of immunology research*. 2020; 2020; 4284379
2. Yasumura J, Shimizu M, Toma T, Yashiro M, Yachie A, Okada S. Clinical Significance of Serum Soluble TNF Receptor I/II Ratio for the Differential Diagnosis of Tumor Necrosis Factor Receptor-Associated Periodic Syndrome From Other Autoinflammatory Diseases. *Frontiers in immunology*. 2020; 11; 576152
3. Tanaka T, Shimizu M, Tokuda O, Yamamoto H, Matsunoshita N, Takenaka K, Kawasaki K. Kawasaki Disease with an Initial Manifestation Mimicking Bacterial Inguinal Cellulitis. *Case reports in pediatrics*. 2020; 2020; 8889827
4. Sakumura N, Irabu H, Inoue N, Mizuta M, Shimizu M. Clinical usefulness of longitudinal IL-6 monitoring in a patient with Takayasu aortitis receiving tocilizumab. *Rheumatology*. 2020.01; 59(1); 252-254
5. Shimizu Masaki, Mizuta Mao, Okamoto Nami, Yasumi Takahiro, Iwata Naomi, Umebayashi Hiroaki, Okura Yuka, Kinjo Noriko, Kubota Tomohiro, Nakagishi Yasuo, Nishimura Kenichi, Mohri Mariko, Yashiro Masato, Yasumura Junko, Wakiguchi Hiroyuki, Mori Masaaki. Tocilizumab modifies clinical and laboratory features of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis *PEDIATRIC RHEUMATOLOGY*. 2020.01; 18(1); 2
6. Tao Xu, Qin Zhao, Wenyan Li, Xuemei Chen, Xiuhong Xue, Zhi Chen, Xiao Du, Xiaoming Bai, Qian Zhao, Lina Zhou, Xuemei Tang, Xi Yang, Hirokazu Kanegane, Xiaodong Zhao. X-linked lymphoproliferative syndrome in mainland China: review of clinical, genetic, and immunological characteristic. *Eur. J. Pediatr.*. 2020.02; 179(2); 327-338
7. Takuro Nishikawa, Ken Okamura, Mizuki Moriyama, Kenji Watanabe, Atsuko Ibusuki, Seiji Sameshima, Izumi Masamoto, Ieharu Yamazaki, Kay Tanita, Takuro Kanekura, Hirokazu Kanegane, Tamio Suzuki, Yoshifumi Kawano. Novel AP3B1 compound heterozygous mutations in a Japanese patient with Hermansky-Pudlak syndrome type 2. *J. Dermatol.*. 2020.02; 47(2); 185-189
8. Shimizu M, Shimizu H, Jinkawa A, Yamamiya M, Shinozaki E, Yokoyama T, Ohta K, Sakumura N, Takakuwa M, Fujita S, Fusagawa S, Nakagishi Y, Nariai E, Yachie A. Cytokine Profiles in Human Parechovirus Type 3-induced Sepsis-like Syndrome. *The Pediatric infectious disease journal*. 2020.02; 39(2); 137-139
9. Hoshino Akihiro, Tokoro Shown, Akashi Takumi, Inoue Maiko, Takagi Masatoshi, Imai Kohsuke, Kanegane Hirokazu, Muraosa Yasunori, Kamei Katsuhiko, Morio Tomohiro. Disseminated fusariosis in a child after haploidentical hematopoietic stem cell transplantation. *Pediatrics International*. 2020.03; 62(3); 419-420

10. Irabu H, Shimizu M, Kaneko S, Inoue N, Mizuta M, Nakagishi Y, Yachie A. Comparison of serum biomarkers for the diagnosis of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis during tocilizumab therapy. *Pediatric research*. 2020.03;
11. Shimizu M. Pathogenic functions and diagnostic utility of cytokines/chemokines in EHEC-HUS. *Pediatrics international : official journal of the Japan Pediatric Society*. 2020.03; 62(3); 308-315
12. Tzu-Wen Yeh, Tsubasa Okano, Takuya Naruto, Motoi Yamashita, Miko Okamura, Kay Tanita, Likun Du, Qiang Pan-Hammarström, Noriko Mitsui, Satoshi Okada, Hirokazu Kanegane, Kohsuke Imai, Tomohiro Morio. APRIL-dependent life-long plasmacyte maintenance and immunoglobulin production in humans. *J. Allergy Clin. Immunol.* 2020.04; S0091-6749(20); 30432-2
13. Tomonori Kadowaki, Hidenori Ohnishi, Norio Kawamoto, Saori Kadowaki, Tomohiro Hori, Kenichi Nishimura, Chie Kobayashi, Tomonari Shigemura, Shohei Ogata, Yuzaburo Inoue, Eitaro Hiejima, Kazushi Izawa, Tadashi Matsubayashi, Kazuaki Matsumoto, Kohsuke Imai, Ryuta Nishikomori, Shuichi Ito, Hirokazu Kanegane, Toshiyuki Fukao. Immunophenotyping of A20 haploinsufficiency by multicolor flow cytometry. *Clin. Immunol.* 2020.04; 108441
14. Shimizu M, Inoue N, Mizuta M, Sakakibara Y, Hamaguchi Y, Yachie A. Periorbital Edema as the Initial Sign of Juvenile Dermatomyositis. *Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases*. 2020.04; 26(3); e61
15. Akihiro Hoshino, Akira Nishimura, Takuya Naruto, Tsubasa Okano, Kazuaki Matsumoto, Keisuke Okamoto, Hiroshi Shintaku, Shown Tokoro, Hiroyuki Okamoto, Taizo Wada, Masatoshi Takagi, Kohsuke Imai, Hirokazu Kanegane, Tomohiro Morio. High-throughput analysis revealed the unique immunoglobulin gene rearrangements in plasmacytoma-like post-transplant lymphoproliferative disorder. *Br. J. Haematol.* 2020.05; 189(4); e164-e168
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17. Hitoshi Irabu, Masaki Shimizu, Shuya Kaneko, Natsumi Inoue, Mao Mizuta, Yuko Tasaki, Kazuhide Ohta, Akihiro Yachie, Taizo Wada. Apoptosis inhibitor of macrophage as a biomarker for disease activity in Japanese children with IgA nephropathy and Henoch-Schönlein purpura nephritis. *Pediatr. Res*. 2020.05;
18. Kaneko S, Shimizu M, Inoue N, Mizuta M, Yachie A. Chronic recurrent multifocal osteomyelitis with myositis: A case report and review of the literature. *Pediatrics international : official journal of the Japan Pediatric Society*. 2020.05; 62(5); 644-645
19. Inoue N, Shimizu M, Mizuta M, Yachie A. Successful treatment of tumor necrosis factor inhibitor-resistant cutaneous polyarteritis nodosa with tocilizumab. *Pediatrics international : official journal of the Japan Pediatric Society*. 2020.06; 62(6); 753-755
20. Miho Maeda, Akira Morimoto, Yoko Shioda, Takeshi Asano, Yuhki Koga, Yozo Nakazawa, Hirokazu Kanegane, Kazuko Kudo, Shouichi Ohga, Eiichi Ishii, . Long-term outcomes of children with extracutaneous juvenile xanthogranulomas in Japan. *Pediatr Blood Cancer*. 2020.07; 67(7); e28381
21. Tsubasa Okano, Kohsuke Imai, Takuya Naruto, Satoshi Okada, Motoi Yamashita, Tzu-Wen Yeh, Shintaro Ono, Keisuke Tanaka, Keisuke Okamoto, Kay Tanita, Kazuaki Matsumoto, Etsushi Toyofuku, Eri Kumaki-Matsumoto, Miko Okamura, Hiroo Ueno, Seishi Ogawa, Osamu Ohara, Masatoshi Takagi, Hirokazu Kanegane, Tomohiro Morio. Whole-Exome Sequencing-Based Approach for Germline Mutations in Patients with Inborn Errors of Immunity. *The Journal of Clinical Immunology* . 2020.07; 40((5)); 729-740
22. Kensaku Kohroggi, Masahiro Migita, Tadashi Anan, Takeshi Sugahara, Kazuhiko Yoshimoto, Hirokazu Kanegane, Kimitoshi Nakamura. Successful Artery Embolization in a Patient with Autoimmune Lymphoproliferative Syndrome Associated with Splenic Rupture. *J. Clin. Immunol.* 2020.07; 40(5); 780-782
23. Mizuta M, Shimizu M, Irabu H, Usami M, Inoue N, Nakagishi Y, Wada T, Yachie A. Comparison of serum cytokine profiles in macrophage activation syndrome complicating different background rheumatic diseases in children. *Rheumatology (Oxford, England)*. 2020.07;

24. Nishimura K, Hara R, Umebayashi H, Takei S, Iwata N, Imagawa T, Shimizu M, Tomiita M, Seko N, Kitawaki T, Yokota S. Efficacy and safety of canakinumab in systemic juvenile idiopathic arthritis: 48-week results from an open-label phase III study in Japanese patients. *Modern rheumatology*. 2020.07; 1-9
25. Tomoo Osumi, Satoshi Yoshimura, Mayumi Sako, Toru Uchiyama, Takashi Ishikawa, Toshinao Kawai, Eisuke Inoue, Tetsuya Takimoto, Ichiro Takeuchi, Masaki Yamada, Kenichi Sakamoto, Kaoru Yoshida, Yui Kimura, Yukihiro Matsukawa, Kana Matsumoto, Ken-Ichi Imadome, Katsuhiko Arai, Takao Deguchi, Kohsuke Imai, Yuki Yuza, Kimikazu Matsumoto, Masafumi Onodera, Hirokazu Kanegane, Daisuke Tomizawa, Motohiro Kato. A prospective study of allogeneic hematopoietic stem cell transplantation with post-transplantation cyclophosphamide and anti-thymoglobulin from HLA-mismatched related donors for non-malignant diseases. *Biol. Blood Marrow Transplant.* 2020.08;
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30. Takashi Uchida, Tasuku Suzuki, Atsuo Kikuchi, Fumihiko Kakuta, Takashi Ishige, Yoshiko Nakayama, Hirokazu Kanegane, Yuri Etani, Tatsuki Mizuochi, Shin-Ichi Fujiwara, Ryusuke Nambu, Kazuhide Suyama, Masanori Tanaka, Atsushi Yoden, Daiki Abukawa, Yoji Sasahara, Shigeo Kure. Comprehensive Targeted Sequencing Identifies Monogenic Disorders in Patients With Early-onset Refractory Diarrhea. *J Pediatr Gastroenterol Nutr*. 2020.09; 71(3); 333-339
31. Yasushi Kasahara, Masaru Imamura, Chansu Shin, Hiroshi Shimizu, Jirou Utsumi, Ryosuke Hosokai, Haruko Iwabuchi, Takayuki Takachi, Akiyoshi Kakita, Hirokazu Kanegane, Akihiko Saitoh, Chihaya Imai. Fatal Progressive Meningoencephalitis Diagnosed in Two Members of a Family With X-Linked Agammaglobulinemia. *Front Pediatr*. 2020.09; 8; 579
32. Kazuki Nemoto, Toshinori Kawanami, Takayuki Hoshina, Masataka Ishimura, Kei Yamasaki, Satoshi Okada, Hirokazu Kanegane, Kazuhiro Yatera, Koichi Kusuvara. Impaired B-Cell Differentiation in a Patient With STAT1 *Front Immunol*. 2020.09; 11; 557521
33. Tsukasa Tanaka, Masaki Shimizu, Oshi Tokuda, Hiroko Yamamoto, Natsuki Matsunoshita, Kanae Takenaka, Keiichiro Kawasaki. Kawasaki Disease with an Initial Manifestation Mimicking Bacterial Inguinal Cellulitis Case Reports in Pediatrics. 2020.10;
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 39. Mizuta M, Shimizu M, Inoue N, Ikawa Y, Nakagishi Y, Yasuoka R, Iwata N, Yachie A. Clinical significance of interleukin-18 for the diagnosis and prediction of disease course in systemic juvenile idiopathic arthritis. *Rheumatology (Oxford, England).* 2020.11;
 40. Chiaki Hosoda, Takashi Ishiguro, Yoshihiko Shimizu, Hirokazu Kanegane, Noboru Takayanagi. Infection Presenting as an Endobronchial Polyp and Upper Lobe Atelectasis. *Am J Respir Crit Care Med.* 2020.12; 202(11); e144-e145
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[Misc]

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[Conference Activities & Talks]

1. Takahiro Tomoda, Tsubasa Okano, Kento Inoue, Motoi Yamashita, Takahiro Kamiya, Takeshi Isoda, Masakatsu Yanagimachi, Hirokazu Kanegane, Masatoshi Takagi, Tomohiro Morio, Kohsuke Imai. An intractable case of hyper IgE syndrome. *APSID (Asia Pacific Society for Immunodeficiencies) School cum Workshop* 2020.02.06 Chandigarh, India.
2. Miko Okamura, Kay Tanita, Hidetoshi Takada, Tetsuo Mitsui, Yoshiyuki Minegishi, Kohsuke Imai, Tomohiro Morio, Hirokazu Kanegane. Somatically reverted T cells in dedicator of cytokinesis 8 deficiency modify cellular immunity. *3rd Scientific Congress of Asia Pacific Society for Immunodeficiencies* 2020.02.09 Chandigarh, India
3. Takahiro Tomoda, Tsubasa Okano, Kento Inoue, Motoi Yamashita, Takahiro Kamiya, Takeshi Isoda, Masakatsu Yanagimachi, Hirokazu Kanegane, Masatoshi Takagi, Tomohiro Morio, Kohsuke Imai. Second transplantation rescued the graft failure after hematopoietic stem cell transplantation. *3rd Scientific Congress of Asia Pacific Society for Immunodeficiencies* 2020.02.09 Chandigarh, India.
4. Genomics analysis of leukemia predisposition in X-linked agammaglobulinemia. 2020.02.16

5. 175 cases of genetic testing by health insurance for primary immunodeficiency in Japan. 2020.02.16
6. Yoonsun Yoon, Ji-man Kang, Junsik Choi, Kangmo Ahn, Keon Hee Yoo, Eun-Suk Kang, Kyoung-Mee Kim, Jung Eun Lee, Geum-Youn gawk, Kihyun Kim, Kosuke Imai, Hirokazu Kanegane, Yae-jean Kim. Cancer development in a Korean family with CTLA-4 haploinsufficiency. The 3rd Annual Scientific Meeting of the Japanese Society for Immunodeficiency and Autoinflammatory Diseases (JSIAD) 2020.02.16 東京
7. K. Tanita, F. Sakura, M. Tsumura, H. Ohnishi, A. Hoshino, K. Suzuki, S. Okada, R. Nambu, S. Umetsu, K. Imai, T. Morio, H. Kanegane. PATIENTS WITH THE GAIN-OF-FUNCTION MUTATIONS IN STAT3 PRESENT WITH A VARIETY OF AUTOIMMUNE DISEASES. 19th Biennial Meeting of The European Society of immunodeficiencies (ESID 2020) 2020.10.14 web
8. Masaki Shimizu. Macrophage Activation Syndrome: Analysis of various Cytokines. 22nd Asia-Pacific League of Associations for Rheumatology Congress 2020.10.24 Kyoto
9. Akihiro Hoshino, Yuya Koda, Jun Kato, Kay Tanita, Hirokazu Kanegane . A plastic anemia as an initial manifestation in a patient with SAP deficiency. The 27th Annual Meeting of the Japan Childhood Aplastic Anemia Study Group 2020.11.08 Web 開催
10. CAR-T Therapy Practice: Through experience under various situations. 2020.11.21
11. A case of relapsed infant ALL with MLL rearrangement who underwent CAR-T cell therapy. 2020.11.21
12. Allogeneic hematopoietic stem cell transplantation from haploidentical donors for non-malignant diseases with post-transplantation cyclophosphamide and anti-thymoglobulin. 2020.11.22
13. Inflammatory bowel disease associated with XIAP deficiency can be cured by allogeneic hematopoietic cell transplantation. 2020.11.22
14. Salvage haploidentical bone marrow transplant using post-transplant cyclophosphamide for graft failure in a patient with EDA-ID due to NEMO deficiency. 2020.11.22
15. Pediatric Hodgkin's lymphoma subsequently diagnosed as common variable immunodeficiency with FAS mutation. 2020.11.22
16. Ruxolitinib administration for two cases with steroid-refractory lung GVHD. 2020.11.22
17. A retrospective study of six cases of HLA haplo-identical hematopoietic stem cell transplantation with Post-Transplant Cyclophosphamide. 2020.11.22

Department of Tokyo Metropolitan Health Policy Advise ment

Professor, Kazushi Yamauchi (until December)
Associate Professor, Mutsuko Moriwaki
Researcher, Chihiro Takahashi

(1) Outline

There is an urgent need to develop a regional healthcare system that can respond to the rapid changes in the disease structure in the greater Tokyo area due to the aging of the population. Since its founding in 2019, this department endowed by the Tokyo Metropolitan Government has advanced research, education and practice to promote the Regional Medical Care Visions and develop measures to secure healthcare professionals in Tokyo.

(2) Research

Below is a sampling of the Department's research topics:

- Analysis of the current situation and problems of each medical area and examination of countermeasures based on various healthcare statistical data
 - Analysis and examination of measures to secure healthcare professionals
 - Research that contributes to strengthen outpatient medical services
 - Research on revision of the hospital bed allocation plan based on changing trends in patient healthcare use
 - Research on the promotion of the Medical Care Plans and the Regional Medical Care Vision
- etc.

(3) Education

The department provides healthcare professionals with various opportunities to learn about assessment of healthcare system and development of regional healthcare programs.

(4) Clinical Services & Other Works

As Regional Medical Care Visions Advisors of Tokyo, faculty commit themselves to work with the Tokyo Metropolitan Government to analyze the current situation of each medical area, create solutions to problems, and promote regional healthcare policy.

(5) Publications

[Original Articles]

1. Ogawa Takahisa, Yoshii Toshitaka, Moriwaki Mutsuko, Morishita Shingo, Oh Yoto, Miyatake Kazumasa, Nazarian Ara, Shiba Koichiro, Okawa Atsushi, Fushimi Kiyohide, Fujiwara Takeo. Association between Hemiarthroplasty vs. Total Hip Arthroplasty and Major Surgical Complications among Patients with Femoral Neck Fracture JOURNAL OF CLINICAL MEDICINE. 2020.10; 9(10);

2. Takahisa Ogawa, Toshitaka Yoshii, Shingo Morishita, Mutsuko Moriwaki, Atsushi Okawa, Ara Nazarian, Kiyohide Fushimi, Takeo Fujiwara. Seasonal impact on surgical site infections in hip fracture surgery: Analysis of 330,803 cases using a nationwide inpatient database. *Injury*. 2020.10;

[Conference Activities & Talks]

1. Mutsuko Moriwaki, Hitomi Yuasa, Hideaki Suzuki, Yasuki Kobayashi. Study on the effect of mother's burden as caregiver in children with cerebral palsy. The Japanese Society of Child Neurology (JSCN) 2020.09.01
2. Yoshiko Sakamoto, Takako Arai, Mutsuko Moriwaki, Keiko Osada. Extraction of screening implementation and improvement issues related to discharge support . 2020.10.07
3. Mutsuko Moriwaki, Hitomi Yuasa, Hideaki Suzuki, Masayuki Kakehashi, Yasuki Kobayashi. Study on the effect of mother's burden as caregiver in children with cerebral palsy. Japanese Society of Public Health (JPHA) 2020.10.23 Kouchi

Lifetime Oral Health Care Sciences

Professor Shinichi ARAKAWA
Junior Associate Professor Keiko KONDO
Specially Appointed Assistant Professor Masayuki TOI
Graduate Student Nami ISHIZAKA
Resident Shinta SUZUKI

(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 (OUFBW) :antimicrobial 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. Seki N, Moross J, Otsuka H, Sunaga M, Naito M, Kondo K, Shinada K, Morio I, Kinoshita A. Dental Hygiene Learning Outcomes Obtained Through Computer-Assisted Simulation Modules The Journal of Dental Hygiene. 2020.02; 94(1); 32-38

[Conference Activities & Talks]

1. 荒川真一. 高齢者に対する口腔衛生・機能管理. 令和元年度愛媛県前科術生士会第51司第5次生涯研修市I]度専門研修会 2020.12.15 愛媛県松山市堀之内

Oral Care for Systemic Health Support

Professor Yuhji Kabasawa
Assistant Professor Kanade Ito
Postgraduate student(Master's course) Shiori Tokura

(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, 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.

We also working about the Research on social inequalities in oral health.

(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. Research for safety in supplements in oral functions
3. Research on social inequalities in oral health.
4. Basic research for bone regeneration using FGF-2.

(3) Education

Team medical practice, clinical practice, clinical practice, oral surgery and dental anesthesiology, clinical medicine, graduation research, health care services, biomaterials science, oral disease prevention basics and practical training, clinical oral health practice, Dental practice support theory,etc

(4) Lectures & Courses

The purpose is to develop dental hygienist who can contribute to oral and general health. Train student who can contribute to the health and welfare of people based on the knowledge and skills for oral health activities, understanding oral medicine and social environmental factors that affect health.

(5) 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.

(6) Clinical Performances

Based on knowledge of oral medicine through oral care department, we are conducting perioperative oral function management with more specialized expertise.

(7) Publications

[Original Articles]

1. Kagifuku Y, Tohara H, Wakasugi Y, Susa C, Nakane A, Toyoshima M, Nakakuki K, Kabasawa Y, Harada H, Minakuchi S. What Factors Affect Changes in Body Composition and Swallowing Function in Patients Hospitalized for Oral Cancer Surgery? *Clinical Interventions in Aging*. 2020.01; 15; 1-7
2. 貴島逸斗、河野弥生、中村耕一郎、樺沢勇司、田畑泰彦、古屋純一、花輪剛久. Application of a Gelatin Nonwoven Fabric as a Novel Oral Care Product *日本医歯科機器学会誌*. 2020.04; 25(1); 33-38
3. Takenouchi A, Otani E, Sunaga M, Toyama T, Uehara H, Akiyama K, Kawashima T, Ito K, Izuno H, Kinoshita A. Development and evaluation of e-learning materials for dental hygiene students in six schools: using smartphones to learn dental treatment procedures. *International journal of dental hygiene*. 2020.06;
4. Kanade Ito, Noriko Cable, Tatsuo Yamamoto, Kayo Suzuki, Katsunori Kondo, Ken Osaka, Georgios Tsakos, Richard G Watt, Jun Aida. Wider Dental Care Coverage Associated with Lower Oral Health Inequalities: A Comparison Study between Japan and England. *International journal of environmental research and public health*. 2020.07; 17(15);
5. Suga T, Tu TTH, Takenoshita M, Higashihori N, Kabasawa Y, Ono T, Moriyama K, Toyofuku A. Psychosocial Indication for Orthognathic Surgery in Patients with Psychiatric Comorbidities. *Psychiatry and clinical neurosciences*. 2020.08;

[Misc]

1. Oral health care by dentists and dental hygienists 2020.11; (312); 38-42

[Conference Activities & Talks]

1. YUJI KABASAWA. A case of extensive severe intractable stomatitis caused by rituximab.. The 29th Annual Meeting of Japanese Society of Dentistry for Medically Compromised Patients 2020.02.28 Kobe (web meeting)
2. Seki N, Moross J, Kanamori Y, Kanazawa M, Komagamine Y, Mizutani K, Liao S, Kabasawa Y, Iseki S, Morio I. Importance of preparatory courses for international/global dental student exchange programs. Annual Meeting of the 39th Japanese Dental Education Association 2020.09.25 Paper/Online Base

Preventive Oral Health Care Sciences

Professor Kayoko SHINADA
Assistant Professor Naoko ADACHI(April-)
Kanako TODA(-March)
Part-time lecturer Atsushi OHYAMA,
Kenichi TANAKA
Kanako TODA(April-)
Chie YOSHIZU(April-)
Mamoru MURATA (May-)
Technical assistant Xu Zheng Yang(-May)
Graduate Students Master Course
Sakura Hayashi(-March), Liu Zhenyan(-March),
Miyu YASUI, HSU CHEN WEI,(April-),
WANG LIYANG (April-)
Graduate Students(research) WANG LIYANG (-March),WANG RAN, Yuko HIROTA (April-)

(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. Adachi Naoko, Kobayashi Yasuki. One-year follow-up study on associations between dental caries, periodontitis, and metabolic syndrome JOURNAL OF ORAL SCIENCE. 2020.01; 62(1); 52-56
2. Naoko Seki, Janelle Moross, Hiromi Otsuka, Masayo Sunaga, Mio Naito, Keiko Kondo, Kayoko Shinada, Ikuko Morio, Atsuhiko Kinoshita. Dental Hygiene Learning Outcomes Obtained Through Computer-Assisted Simulation Modules. J Dent Hyg. 2020.02; 94(1); 32-38

[Conference Activities & Talks]

1. Kayoko SHINADA. AI and Oral Health. 20th Anniversary Lecture on School of Oral Health, Taipei Medical University 2020.11.07 Taipei city (Online lecture, Tokyo)
2. Liao S, Seki N, Akiyama M, Shinada K, Morio I . Perceived stress and career planning of undergraduate dental hygiene students. The 85th Annual Meeting of the Stomatological Society 2020.12.05 Tokyo

Oral Health Sciences for Community Welfare

Professor Junichi FURUYA
Assistant Professor Rena Hidaka
Graduate Student Akane BENIYA
Graduate Student Ayano AKATSUKA
Graduate Student Nei KOSHITANI
Graduate Student Saki MIYAJIMA
Graduate Research Student Junji TOKUNAGA
Graduate Student (Gerodontology and Oral rehabilitation) Chiaki MATSUBARA
Graduate Student (Dysphagia Rehabilitation) Michiyo OBANA

(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. Oral function, mastication, swallowing and dentures for dysphagia rehabilitation of older people
2. Oral health management for multidisciplinary team approach (NST and palliative care team) in medical care and community welfare
3. Frailty, malnutrition and oral frailty of older people
4. Oral function of patients with stroke and dementia
5. Home care dentistry and team approach for enjoyment of oral intake in community welfare

(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. Yoshimi K, Nakagawa K, Hara K, Yamaguchi K, Nakane A, Kubota K, Furuya J, Tohara H. Relationship between tongue pressure and back muscle strength in healthy elderly individuals. *Aging Clinical and Experimental Research*. 2020.01;
2. Hidaka R, Furuya J, Suzuki H, Matsubara C, Obana M, Tokunaga J, Endo K. Survey on the oral health status of community-dwelling older people with visual impairment. *Spec Care Dentist*. 2020.03; 40(2); 192-197
3. Yamaguchi K, Hara K, Nakagawa K, Namiki C, Chantaramanee A, Yoshimi K, Nakane A, Kubota K, Furuya J, Tohara H. Association of Aging and Tooth Loss With Masseter Muscle Characteristics: An Ultrasonographic Study. *Clinical Oral Investigation*. 2020.03; 24(11); 3881-3888
4. 貴島逸斗、河野弥生、中村耕一郎、樺沢勇司、田畑泰彦、古屋純一、花輪剛久. Application of a Gelatin Nonwoven Fabric as a Novel Oral Care Product *日本医用歯科機器学会誌*. 2020.04; 25(1); 33-38
5. Yasushi Tamada, Junichi Furuya, Hiroyuki Suzuki, Shohei Onodera, Hisanori Yamamoto, Tomohide Sato, Taro Nomura, Hisatomo Kondo. Denture Wearing Status of Dysphagia Inpatients in an Acute Hospital *Japanese Journal of Gerodontology*. 2020.04; 34(4); 503-509
6. Hara Koji, Tohara Haruka, Namiki Chizuru, Yamaguchi Kohei, Chantaramanee Ariya, Kobayashi Kenichiro, Saito Takayuki, Nakagawa Kazuharu, Okumura Takuma, Yoshimi Kanako, Nakane Ayako, Furuya Junichi, Minakuchi Shunsuke. Relationship between displacement of the masseter muscle during biting and masseter muscle quality and bite force in healthy elderly persons *JOURNAL OF ORAL REHABILITATION*. 2020.04; 47(4); 441-448
7. Furuya J, Suzuki H, Tamada Y, Onodera S, Nomura T, Hidaka R, Minakuchi S, Kondo H. Food intake and oral health status of inpatients with dysphagia in acute care settings. *J Oral Rehabil*. 2020.06; 47(6); 736-742
8. Furuya J, Beniya A, Suzuki H, Hidaka R, Matsubara C, Obana M, Yoshimi K, Yamaguchi K, Hara K, Nakagawa K, Nakane A, Tohara H, Minakuchi S. Factors associated with the number of microorganisms on the tongue surface in patients following acute stroke. *J Oral Rehabil*. 2020.11; 47(11); 1403-1410
9. Yamaguchi K, Hara K, Nakagawa K, Yoshimi K, Chantaramanee A, Nakane A, Furuya J, Tohara H. Ultrasonography shows age-related changes and related factors in the tongue and suprahyoid muscles *Journal of the American Medical Directors Association*. 2020.11;
10. M Shirobe, R Hidaka, H Hirano, Y Ohara, K Endo, Y Watanabe, C Hakuta.. The effectiveness of a desensitization technique for mitigating oral and facial tactile hypersensitivity in institutionalized older persons: A randomized controlled trial *Journal of Dental Sciences*. 2020.11;

[Conference Activities & Talks]

1. Junji Tokunaga, Junichi Furuya, Hiroyuki Suzuki, Yasushi Tamada, Taro Nomura, Hisatomo Kondo. The relationship between nutrition intake and oral function in acute care hospital inpatients with dysphagia. The 12th Scientific Meeting of Japan Denture Care Society 2020.02.22 Nagoya
2. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Yasuhiro Yamazaki, Rena Hidaka, Kanako Yoshimi, Haruka Tohara, Shunsuke Minakuchi. Oral status and function in Mild Cognitive Impairment patients. The 129th Annual Meeting of the Japan Prosthodontic Society 2020.06.28 Online
3. Hiroyuki Suzuki, Junichi Furuya, Chiaki Matsubara, Rena Hidaka, Haruka Tohara, Shunsuke Minakuchi.. The features of oral health status and functions in Mild Cognitive Impairment (MCI) patients. 30th Annual congress of European College of Gerodontology 2020.10.10 Online

Oral Health Care Education

Professor Naomi Yoshida
Assistant Professor Hitomi Suzuki
Part-time Lecturer Kumiko Sugimoto

(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. Yoshiaki Nomura, Naomi Yoshida, Noriko Takei, et al.. Factors affecting on the leaving job and reentry for the Japanese dental hygienist 2020.05;
2. Yoshiaki Nomura, Naomi Yoshida, Noriko Takei. Prioritization of the skills to be mastered for the daily jobs of Japanese dental hygienists International Journal of Dentistry. 2020.06;
3. Hitomi Suzuki, Koichiro Matsuo . Oral health management of a patient with tuberous sclerosis complex for oral mucositis under everolimus: A case report International Journal of Disability and Oral Health. 2020.06; 16(1); 42-47

[Conference Activities & Talks]

1. 岩下亜未、雨河茂樹、佐々木好幸、鈴木瞳、吉田直美. 某中規模病院における周術期患者の全身状況・生活習慣および口腔内状況の探索研究. 第15回日本歯科衛生学会 2020.09.20 大阪→誌上開催

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:

Other education.

- Human anatomy (in School of Medicine, Faculty of Medicine).
- Head and neck basic medical sciences (in School of Medicine, Faculty of Medicine and School of Dentistry, Faculty of Dentistry).
- Structure and function of human body (in Course for Oral Health Engineering, School of Oral Health Care Sciences, Faculty of Dentistry).
- Oral health generic care sciences (in Health Sciences and Biomedical Engineering, Graduate School of Medical and Dental Sciences).

Basic Oral Health Engineering

Professor Kazuhiro Aoki
Associate Professor Meiko Oki
Assistant Professor Shingo Kamijo
Technical Assistant Masud Khan

(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 non-invasive methods of bone mass augmentation (Interdisciplinary research)
- 2) Research related to the connection between oral bacteria and systemic diseases
- 3) The development of novel bone anabolic reagents targeting RANKL (International collaboration)
- 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 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 Services & Other Works

Clinical activities

- Maxillofacial prosthetic rehabilitation for patients with maxillofacial defects

- Making dental and maxillofacial prostheses

(5) Publications

[Original Articles]

1. Shigeki Nagahiro, Tomoki Uehara, Mariko Yamamoto Kawai, Preksa Keo, Hiroki Ochi, Shingo Sato, Shinji Kuroda, Takashi Ono, Michiyo Miyashin, Kazuhiro Aoki. RANKL-binding peptide promotes ectopic bone formation induced by BMP-2 gene transfer in murine gastrocnemius muscle Dental, Oral and Maxillofacial Research. 2020.01; 6(1);
2. Takakura N, Matsuda M, Khan M, Hiura F, Aoki K, Hirohashi Y, Mori K, Yasuda H, Hirata M, Kitamura C, Jimi E. A novel inhibitor of NF- κ B-inducing kinase prevents bone loss by inhibiting osteoclastic bone resorption in ovariectomized mice. Bone. 2020.03; 135; 115316
3. Keo P, Matsumoto Y, Shimizu Y, Nagahiro S, Ikeda M, Aoki K, Ono T. A pilot study to investigate the histomorphometric changes of murine maxillary bone around the site of mini-screw insertion in regenerated bone induced by anabolic reagents. European journal of orthodontics. 2020.03;
4. Tun PS, Churei H, Hikita K, Kamijo S, Oki M, Tanabe G, Hayashi K, Aung TK, Win A, Hlaing S, Takahashi H, Ueno T. Fabrication of shock absorbing photopolymer composite material for 3D printing sports mouthguard JOURNAL OF PHOTOPOLYMER SCIENCE AND TECHNOLOGY. 2020.12; 33(6); 615-622

[Conference Activities & Talks]

1. Tun PS, Churei H, Tanabe G, Aung TK, Kamijo S, Oki M, Takahashi H, Hikita K, Ueno T. Shock-absorbing capability of laminated type of 3D printing materials compared to conventional mouthguard materials. 40th Myanmar Dental Conference 2020.02.07

Oral Biomaterials Development Engineering

Professor Hidekazu TAKAHASHI
Assistant Professor Naohiko IWASAKI
Assistant Professor Yumi TSUCHIDA

Research student Ha Rou Bing (until March)
Graduate student (Master course) Ha Rou Bing (from April)
Graduate student (Doctor course) Patcharanun CHAIAMORNSUP (Advanced Biomaterials) (until March)

(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

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.

(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. Chaiamornsop P, Iwasaki N, Yasue T, Uo M, Takahashi H. Effects of build conditions and angle acuteness on edge reproducibility of casting patterns fabricated using digital light projection. *Dental materials journal*. 2020.01; 39(1); 135-140
2. Tanabe Gen, Churei Hiroshi, Wada Takahiro, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine *JOURNAL OF ORAL SCIENCE*. 2020.01; 62(1); 23-27
3. Takahiro Wada, Hiroshi Churei, Mako Yokose, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Application of Glass Fiber and Carbon Fiber-Reinforced Thermoplastics in Face Guards. *Polymers (Basel)*. 2020.12; 13(1); 18
4. Fujita Haruka, Otomaru Takafumi, Takahashi Hidekazu, Iwasaki Naohiko, Sumita Yuka. Effect of Direct Retainer Types of Dent-Maxillary Prosthesis in Maxillectomy Patients: An In Vitro Study *The Journal of Indian Prosthodontic Society*. 2020.12; 43(2); 73-84

[Conference Activities & Talks]

1. Hao Jialin, Murakami Natsuko, Yamazaki Toshiki, Iwasaki Naohiko, Yatabe Masaru, Takahashi Hidekazu, Wakabayashi Noriyuki. Flexural Behavior of Machinable Polyester Denture Material Under Cyclic Loading. 2020 IADR/AADR/CADR General Session 2020.03 Washington, D.C., USA
2. Chaiamornsop Patcharanun, Yumi Tsuchida, Naohiko Iwasaki, Takahiro Wada, Motohiro Uo, Hidekazu Takahashi. Effects of build angle and DLP machine on adaptability of bridge casting pattern. 学際・国際高度人材育成ライフイノベーション材料創製共同研究プロジェクト 第4回 公開討論会 2020.03.04 東京
3. Takahiro Wada, Yasuhito Takashima, Rio Kinjo, Kasei Aoyagi, Hiroshi Churei, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takashi, Fumiyoshi Minami, Motohiro Uo. Strain distribution analysis of face guards made of carbon fiber-reinforced thermoplastics during shock absorption test using high-speed camera and digital image correlation. 4th open forum for "Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development" 2020.03.04 Tokyo, Japan
4. Tsuchida Y, Iwasaki N, Shiozawa M, Ha RB, Takahashi H. Evaluation on accuracies of 3-D facial scanner. 2020.10.31
5. Iwasaki N, Shiozawa M, Tsuchida Y, Ha Roubing, Takahashi H. Filler shape and elements of composite resin block for CAD/CAM. 2020.10.31 Tokyo Japan

Oral Prosthetic Engineering

Professor Noriyuki WAKABAYASHI
Junior Associate Professor Masaomi IKEDA
Assistant Professor 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) Advanced technology which utilized a CAD/CAM system.
- 2) 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, Teeth Morphological Curving, Advanced Teeth Morphological Curving, Conservative Dentistry, Science of Occlusion, Advanced Science of Occlusion, Communication Theory, Health Promotion, Basic Fixed Prosthodontics, Advanced Fixed Prosthodontics, Complete Denture Prosthodontics, Removable Partial Prosthodontics, Globalization for Oral Health Engineering, Gerodontology, Laws for Dental Technologists, CAD/CAM System Technology, CAD/CAM System Technology Practice, Special Lectures for Advanced Technology, Management and Regulation for Dental Technologists, Oral Appliances, Aesthetic Dentistry Practice, Orthodontic Dentistry, Comprehensive Oral Rehabilitation Engineering Practice, Graduation Research

(4) Publications

[Original Articles]

1. Keo P, Matsumoto Y, Shimizu Y, Nagahiro S, Ikeda M, Aoki K, Ono T. A pilot study to investigate the histomorphometric changes of murine maxillary bone around the site of mini-screw insertion in regenerated bone induced by anabolic reagents. *Eur J Orthod.* 2020.03;

2. Ko AK, Matsui N, Nakamoto A, Ikeda M, Nikaido T, Burrow MF, Tagami J. Effect of silver diammine fluoride application on dentin bonding performance) *Dental Materials J.* 2020.06; 39(3); 407-414
3. Khanlar LN, Takagaki T, Inokoshi M, Ikeda M, Nikaido T, Tagami J. The effect of carboxyl-based monomers on resin bonding to highly translucent zirconia ceramics. *Dent Mater J.* 2020.11; 39(6); 956-962
4. Koko M, Takagaki T, Abdou A, Inokoshi M, Ikeda M, Wada T, Uo M, Nikaido T, Tagami J. Effects of the ratio of silane to 10-methacryloyloxydecyl dihydrogenphosphate (MDP) in primer on bonding performance of silica-based and zirconia ceramics. *J Mech Behav Biomed Mater.* 2020.08; 112; 104026
5. Yonekura K, Hosaka K, Tichy A, Taguchi K, Ikeda M, Thanatvarakorn O, Prasansuttiorn T, Nakajima M, Tagami J. Air-blowing strategies for improving the microtensile bond strength of one-step self-etch adhesives to root canal dentin. *Dental Materials J.* 2020.09; 39(5); 892-899
6. Muta S, Ikeda M, Nikaido T, Sayed M, Sadr A, Suzuki T, Tagami J. Chairside fabrication of provisional crowns on FDM 3D-printed PVA model. *J Prosthodont Res.* 2020.10; 64(4); 401-407
7. Madrigal EL, Tichy A, Hosaka K, Ikeda M, Nakajima M, Tagami J. The effect of curing mode of dual-cure resin cements on bonding performance of universal adhesives to enamel, dentin and various restorative materials. *Dent Mater J.* 2020.11;
8. Aung SSMP, Takagaki T, Ikeda M, Tagami J. Ultra-morphological studies on enamel-universal adhesive interface. *Journal of dentistry.* 2020.11; 104; 103527
9. Koshimitsu Y, Inoue G, Sayed M, Saad A, Ikeda M, Tagami J. Transverse Micro Radiography Analysis of the Effect of Experimental Calcium-Containing Primer System on Demineralized Enamel. *CRYSTALS.* 2020.12; 10(12);
10. Kobayashi T, Takagaki T, Takahashi R, Ikeda M, Tagami J. Bonding performance of self-adhesive luting agents to highly translucent zirconia ceramics *Asian Pac J Dent.* 2020.12; 20(2); 29-33

[Conference Activities & Talks]

1. Tsuchida Y, Iwasaki N, Shiozawa M, Ha RB, Takahashi H. Evaluation on accuracies of 3-D facial scanner. 2020. 10. 31

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 2019. 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 June 2018. 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. Sayuri Nitta, Kazuaki Takahashi, Fukiko Kawai-Kitahata, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Miyako Murakawa, Yasuhiro Istui, Mina Nakagawa, Seishin Azuma, Sei Kakinuma, Mamoru Watanabe, Yasuhiro Asahina. Time course alterations of virus sequences and immunoglobulin titers in a chronic hepatitis E patient *Hepatol Res.* 2020; 50(4); 524-531
2. Nogami A, Yamamoto M, Yamamoto K, Ito M, Umezawa Y, Tohda S, Miura O, Fukuda T. Marginal zone lymphoma-like primary bone marrow lymphoma with long-term pancytopenia preceding diagnosis *Rinsho ketsueki.* 2020; 61(10); 1469-1475
3. Yukino Usui, Yoko Nukui, Ryuji Koike, Shuji Tohda, Ryoichi Saito. Draft Genome Sequence of a *Clostridioides difficile* Sequence Type 97 Strain Belonging to Hypervirulent Clade 2. *Microbiol Resour Announc.* 2020.04; 9(14); e00245-20
4. Yukino Usui, Alafate Ayibieke, Yuko Kamiichi, Shu Okugawa, Kyoji Moriya, Shuji Tohda, Ryoichi Saito. Impact of deoxycholate on *Clostridioides difficile* growth, toxin production, and sporulation. *Heliyon.* 2020.04; 6(4); e03717
5. Tatsuya Saito, Mai Itoh, Shuji Tohda. Metformin suppresses the growth of leukemia cells partly through downregulation of AXL receptor tyrosine kinase. *Leuk Res.* 2020.05; 94; 106383
6. Salwa M Okasha, Mai Itoh, Shuji Tohda. Sirtuin 1 Activation Suppresses the Growth of T-lymphoblastic Leukemia Cells by Inhibiting NOTCH and NF- κ B Pathways. *Anticancer Res.* 2020.06; 40(6); 3155-3161
7. Mina Nakagawa, Nobutoshi Nawa, Eiko Takeichi, Taro Shimizu, Jun Tsuchiya, Ayako Sato, Masato Miyoshi, Fukiko Kawai-Kitahata, Miyako Murakawa, Sayuri Nitta, Yasuhiro Itsui, Seishin Azuma, Sei Kakinuma, Takeo Fujiwara, Mamoru Watanabe, Yujiro Tanaka, Yasuhiro Asahina. Mac-2 binding protein glycosylation isomer as a novel predictive biomarker for patient survival after hepatitis C virus eradication by DAAs. *J Gastroenterol.* 2020.08; 55; 990-999
8. Satoshi Koi, Kosuke Arai, Ayako Nogami, Hayato Toma, Masahide Yamamoto, Osamu Miura, Toshikage Nagao. Impaired hematopoiesis due to copper deficiency in a hemodialysis patient supplemented with zinc. *Rinsho Ketsueki.* 2020.10; 61(10); 1487-1491

[Conference Activities & Talks]

1. Fukiko Kawai-Kitahata, Yasuhiro Asahina , Sei Kakinuma, Miyako Murakawa, Sayuri Nitta, Masato Miyoshi, Ayako Sato, Jun Tsuchiya, Taro Shimizu, Eiko Takeichi, Mina Nakagawa, Yasuhiro Itsui, Seishin Azuma, Shinji Tanaka , Minoru Tanabe, Shinya Maekawa, Nobuyuki Enomoto and Mamoru Watanabe. Comprehensive analysis of cancer-related genes and AAV/Hepatitis B virus integration into genome on development of hepatocellular carcinoma in patients with prior Hepatitis B virus infection. EASL The Digital International Liver Congress 2020 2020.08.28 Online
2. Daisuke Watanabe, Ayako Nogami, Keigo Okada, Hiroki Akiyama, Yoshihiro Umezawa:, Toshikage Nagao, Osamu Miura. FLT3-ITD activates RSK1 to upregulate mTORC1 and eIF4B and to inhibit BAD and BIM. The 82nd Annual meeting of Japanese Society of Hematology 2020.10.10
3. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
4. Shimano S., Ohkawa R., Nambu M., Sasaoka M., Yamazaki A., Fujii Y., Igarashi K., Horiuchi Y., Lai SJ., Kameda T., Ichimura N., Fujita K., Tohda S. and Tozuka M. Dramatic change of high-density lipoprotein structure and serum amyloid A distribution after orthopedic surgery. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line
5. Horiuchi Y., Lai SJ., Shimano S., Kameda T., Ichimura N., Tohda S., Tozuka M. and Ohkawa R. Novel cholesterol efflux assay using immobilized liposome-bound gel beads: confirmation and improvement for application in clinical laboratory. 2020 AACC Annual Scientific Meeting & Clinical Lab Expo 2020.12.16 On-line

Hyperbaric Medical Center

Senior Director and Associate Professor; Kazuyoshi YAGISHITA
Assistant Professor ; Toshiyuki OHHARA
Specially Appointed Assistant Professor ; Mikio SHIODA, Naoki YAMAMOTO
Adjunct Lecturer; Yasushi KOJIMA, Yumi NIIZEKI
Researcher; Masaki HORIE, Toshihiro KONDOH, Naohiro MITSUMOTO
Akira KAMEI
Staff Assistant; Kiyomi ITOH

(1) Outline

Hyperbaric oxygen therapy (HBO), which can dissolve oxygen in serum in population to atomic pressure and transport oxygen to ischemic tissue, is an established therapy for treatment of several conditions, including decompression illness, carbon monoxide poisoning, acute anterior disturbance, and peripheral ischemic disease. The mechanism of HBO can be described as hyperoxygenation in ischemic soft tissues, reduction of edema, stimulation of fibroblast proliferation and differentiation, increased collagen formation and cross-linking, angiogenesis, and improved preservation of energy metabolism.

This curious treatment has clinically many kinds of efficacy, however, the mechanism of the effect has not been fully understood, and many researchers in the world still attempt to reveal the mechanism of the effect of HBO. This HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(2) Research

Research Subjects

- 1) Soft tissue injuries related with sports activities
- 2) HBO for conditioning in sports activities
- 3) Diving medicine
- 4) Hyperbaric oxygen therapy

(3) Education

HBO can stimulate the interest of medical students, basic researchers, and clinical doctors, and this hyperbaric medical center can provide opportunities to study hyperbaric oxygen therapy field.

(4) Clinical Services & Other Works

In 2020, 203 times hyperbaric oxygen therapy (HBO) in 1,897 patients were performed in the university hospital.

(5) Clinical Performances

HBO is applied for several conditions, including decompression illness, carbon monoxide poisoning, infection, wound healing, delayed radiation injury, acute arterial disturbance, and peripheral ischemic disease. Recently, for the purpose of rapid recovery from injury, we perform HBO aggressively for soft tissue injury related with sports activities including compartment syndrome, ankle sprain, knee ligament injury, and muscle contusion.

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

1. Naoki Yamamoto, Takuya Oyaizu, Mitsuhiro Enomoto, Masaki Horie, Masato Yuasa, Atsushi Okawa, Kazuyoshi Yagishita. VEGF and bFGF induction by nitric oxide is associated with hyperbaric oxygen-induced angiogenesis and muscle regeneration. *Sci Rep.* 2020.02; 10(1); 2744
2. Watanabe D, Hatakeyama K, Ikegami R, Eshima H, Yagishita K, Poole DC, Kano Y. Sex differences in mitochondrial Ca²⁺ handling in mouse fast-twitch skeletal muscle in vivo. *Journal of applied physiology* (Bethesda, Md. : 1985). 2020.02; 128(2); 241-251
3. Takehiro OHMI, Junya AIZAWA, Kenji HIROHATA, Shunsuke OHJI, Kazuyoshi YAGISHITA. Developing Direct Arch Measurement under Quantitative Partial Weight Bearing and Reliability and Validity 2020.04; 35(2); 179-185
4. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Okawa Atsushi, Testuya Jinnō, Kazuyoshi Yagishita. The gap between dichotomous responses regarding return to sports and subjective athletic performance intensity after anterior cruciate ligament reconstruction 2020.04;
5. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Kazuyoshi Yagishita. The difference of ground reaction force during anterior step motion in collegiate male long-distance runners between with or without a history of medial tibial stress syndrome. *Japanese Journal of Clinical Sports Medicine.* 2020.04; 28(2); 313-320
6. Kojima Y, Kojima A, Niizeki Y, Yagishita K. Recreational diving-related injury insurance claims among Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014. *Diving and hyperbaric medicine.* 2020.06; 50(2); 92-97
7. Kenji Hirohata, Junya Aizawa, Hidetaka Furuya, Sho Mitomo, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Kate E Webster. The Japanese version of the anterior cruciate ligament-return to sport after injury (ACL-RSI) scale has acceptable validity and reliability. *Knee Surg Sports Traumatol Arthrosc.* 2020.08; 28(8); 2519-2525

Sports Medicine Center

Director and Associate Professor; Kazuyoshi YAGISHITA
Head Physical Therapist ; Junya AIZAWA (~ 2020.3)
Head Physical Therapist ; Kenji HIROHATA (2020.4 ~)
Assistant Professor ; Toshiyuki OHHARA
Specially Appointed Assistant Professor ; Mikio SHIOTA
Physical Therapist ; Takehiro OHMI, Sho MITOMO (2020.4 ~) ,
Shunsuke OHJI
Adjunct Lecturer ; Tomohiko TATEISHI
Staff Assistant; Kiyomi ITOH

(1) Publications

[Original Articles]

1. Junya Aizawa , Kenji Hirohata , Shunsuke Ohji , Takehiro Ohmi , Hideyuki Koga , Kazuyoshi Yagishita. Factors associated with psychological readiness to return to sports with cutting, pivoting, and jump-landings after primary anterior cruciate ligament reconstruction Orthopaedic Journal of Sports Medicine. 2020;
2. Naoki Yamamoto, Takuya Oyaizu, Mitsuhiro Enomoto, Masaki Horie, Masato Yuasa, Atsushi Okawa, Kazuyoshi Yagishita. VEGF and bFGF induction by nitric oxide is associated with hyperbaric oxygen-induced angiogenesis and muscle regeneration. Sci Rep. 2020.02; 10(1); 2744
3. Watanabe D, Hatakeyama K, Ikegami R, Eshima H, Yagishita K, Poole DC, Kano Y. Sex differences in mitochondrial Ca²⁺ handling in mouse fast-twitch skeletal muscle in vivo. Journal of applied physiology (Bethesda, Md. : 1985). 2020.02; 128(2); 241-251
4. Sadanori Shimizu, Tsuyoshi Nagase, Tomohiko Tateishi, Teruhiko Nakagawa, Masamitsu Tsuchiya. Second Anterior Cruciate Ligament Injuries After Anterior Cruciate Ligament Reconstruction in Professional Sumo Wrestlers: A Case Series. Orthop J Sports Med. 2020.02; 8(2); 2325967120903698
5. Takehiro OHMI, Junya AIZAWA, Kenji HIROHATA, Shunsuke OHJI, Kazuyoshi YAGISHITA. Developing Direct Arch Measurement under Quantitative Partial Weight Bearing and Reliability and Validity 2020.04; 35(2); 179-185
6. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Okawa Atsushi, Testuya Jinno, Kazuyoshi Yagishita. The gap between dichotomous responses regarding return to sports and subjective athletic performance intensity after anterior cruciate ligament reconstruction 2020.04;
7. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Kazuyoshi Yagishita. The difference of ground reaction force during anterior step motion in collegiate male long-distance runners between with or without a history of medial tibial stress syndrome. Japanese Journal of Clinical Sports Medicine. 2020.04; 28(2); 313-320
8. Araya N, Katagiri H, Nakagawa Y, Ohara T, Shioda M, Kohno Y, Amemiya M, Sekiya I, Koga H. PREDICTORS OF RESIDUAL MECHANICAL SYMPTOMS AFTER MENISCUS SURGERY: DATA FROM THE MAKS GROUP OSTEOARTHRITIS AND CARTILAGE. 2020.04; 28; S221-S223

9. Kojima Y, Kojima A, Niizeki Y, Yagishita K. Recreational diving-related injury insurance claims among Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014. *Diving and hyperbaric medicine*. 2020.06; 50(2); 92-97
10. Kenji Hirohata, Junya Aizawa, Hidetaka Furuya, Sho Mitomo, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Kate E Webster. The Japanese version of the anterior cruciate ligament-return to sport after injury (ACL-RSI) scale has acceptable validity and reliability. *Knee Surg Sports Traumatol Arthrosc*. 2020.08; 28(8); 2519-2525
11. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Koga Hideyuki, Okawa Atsushi, Jinno Tetsuya, Yagishita Kazuyoshi. The Gap Between Subjective Return to Sports and Subjective Athletic Performance Intensity After Anterior Cruciate Ligament Reconstruction *ORTHOPAEDIC JOURNAL OF SPORTS MEDICINE*. 2020.09; 8(9); 2325967120947402
12. Koga H, Nakamura T, Katagiri H, Nakagawa Y, Ozeki N, Ohara T, Shioda M, Kohno Y, Amemiya M, Sekiya I. Two-Year Outcomes After Meniscopectomy by Capsular Advancement With the Application of Arthroscopic Centralization Technique for Lateral Compartment Knee Osteoarthritis. *The American journal of sports medicine*. 2020.10; 363546520957367
13. Furuya H, Ito T, Hirohata K, Mitomo S, Yamasaki K, Igarashi H, Omori K, Hoshino M, Hart RA. Construct validity and reliability of the Japanese Version of the Lumbar Stiffness Disability Index. *Spine*. 2020.11;
14. Aizawa J, Hirohata K, Ohji S, Ohmi T, Koga H, Yagishita K. Factors Associated With Psychological Readiness to Return to Sports With Cutting, Pivoting, and Jump-Landings After Primary ACL Reconstruction. *Orthopaedic journal of sports medicine*. 2020.11; 8(11); 2325967120964484

[Conference Activities & Talks]

1. The Gait Analysis of the patients with Rotating Hinge knee in revision Total Knee Arthroplasty in initial stance phase. 2020.02.22

Center for Transfusion Medicine and Cell Therapy

Director: Ichiro Sekiya (Center for Stem Cell and Regenerative Medicine/Professor)
Vise Director: Michiko Kajiwara (Center for Transfusion Medicine and Cell Therapy/Junior Associate Professor)
Vise Director: Hisako Katano (Center for Stem Cell and Regenerative Medicine/Assistant Professor)
Quality control manager: Norio Shimizu (Center for Stem Cell and Regenerative Medicine/Associate Professor)
Product manager: Mitsuru Mizuno (Center for Stem Cell and Regenerative Medicine/Project Assistant Professor)
Specially Appointed Assistant Professor: Shihoko Suwa (Center for Transfusion Medicine and Cell Therapy)
Project Researcher: Kei-ichiro Komori (Center for Stem Cell and Regenerative Medicine)
Head Medical Technologist: Naoki Ohtomo
Section Chief Medical Technologist: Keiko Aikawa
Assisitant Section Chief Medical Technologist: Yukiko Ohishi
Medical Technologist: Yukari Usui, Chihiro Itoh, Miho Yamasaki, Misaki Chiba, Akiko Shiraishi, Mei Tanaka
Technician: Ayako Tsuji, Yuri Kohno
Clerical Assistant: Jun Kusano, Saki Nishimura

(1) Outline

Center for Transfusion Medicine and Cell Therapy provides “Blood Transfusion”, “Cell Therapy” and “Regenerative Medicine” to assist and regenerate dysfunctional tissues and organs.

In the Blood Transfusion group, Japan Society of Blood Transfusion and Cell Therapy Association certified doctors, certified blood transfusion laboratory stuffs, and cell therapy certified administrators enroll. We cover blood transfusion testing, blood product management, safety measures up to the implementation of blood transfusion including blood transfusion certification, and blood transfusion history management. We perform safe and appropriate blood transfusion therapy and hematopoietic stem cell transplantation.

In the Cell Therapy group, we set up a cell processing facility with the aim of putting the world’s top level of regenerative medicine and cell therapy into practical use. Japan Society of Regenerative Medicine certified doctors and clinical culture specialists process cells for clinical research and trials there. We support the practical application of useful regenerative medicine procedures inside and outside our university.

(2) Research

· Blood Transfusion group

- 1) The practice of safe and appropriate transfusion therapy
(including prevention of medical accident related transfusion)
- 2) Basic and clinical research of hematopoietic stem cell transplantation

· Cell Therapy group

- 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 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)
 6) Development of organoid-based therapy for inflammatory bowel disease
 (Department of Gastroenterology & Hepatology, Advanced Research Institute)

(3) Education

· Blood Transfusion group

Transfusion therapy is 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 the most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of the medical treatment. From this point of view, we educate the students of the school of medicine, school of allied health sciences, a graduate school of medical and dental sciences, medical doctors, and co-medicals.

· Cell Therapy group

Center of Cell Therapy assist 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 were recently installed at the CPC annex.

(4) Clinical Services & Other Works

Blood transfusion Services (The result of 2020)

- 1) The number of blood products used
 - Red cell component products 9,765 Units (4,968 bags)
 - Platelet concentration 26,250 Units (2,282 bags)
 - Fresh frozen plasma 6,733 Units (3,197 bags)
- 2) Autologous blood collection and transfusion
 - Autologous blood collection 176 cases (254 times, 494 Units)
 - Autologous blood transfusion 148 cases (388 Units)
- 3) The number of clinical tests of transfusion
 - Blood typing 6,992
 - Anti-red blood cell antibody test 4,317
 - Crossmatch tests 7,645

Cell Therapy Services (The result of 2020)

- 1) Hematopoietic stem cell harvest
 - Autologous peripheral blood stem cell harvest 8 cases 8 times
 - Allogenic peripheral blood stem cell harvest 9 cases 10 times
 - Allogenic bone marrow harvest 9 cases 9 times
(Including Japan Marrow Donor Program donors)
- 2) Cryopreservation of hematopoietic stem cell
 - 18 times
- 3) Hematopoietic stem cell transplantation
(The evaluation and preservation of the stem cells were done in our department)
 - Autologous peripheral blood stem cell transplantation 6 cases 6 times
 - Allogenic peripheral blood stem cell transplantation 10 cases 10 times
 - Allogenic bone marrow transplantation 12 cases 12 times
 - Allogenic umbilical cord blood transplantation 3 cases 3 times
- 4) CAR-T therapy
 - Obtained Kimria facility certification at the end of October 2019
 - 2020 Autologous peripheral blood mononuclear cell collection 10 cases 10 times
 - Tisagen Releucell administration 9 cases 9 times

The cell products currently prepared in our center include

- #1 Synovium-derived mesenchymal stem cells
- #2 Regenerative Medicine (HeartSheet)
- #3 Autologous Protein Solution (APS: concentrated Platelet-Rich Plasma)

(5) Clinical Performances

· Blood Transfusion group

We provide safe and wide of variation transfusion therapy. We cope with highly urgent blood transfusion of critical care center and blood transfusion with a high specialty such as NICU. In the area of hematopoietic stem cell transplantation, we closely cooperate with the clinical department. Transfusion medicine staffs mainly conduct collection, evaluation, processing, and storage of cells.

· Cell Therapy group

Our center in TMDU Medical Hospital was renovated and re-started operation as of March 2015. We have five Central Clinical Facilities 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.

(6) Publications

[Original Articles]

1. Nobutake Ozeki, Hideyuki Koga, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kunikazu Tsuji, Tomoyuki Saito, Takeshi Muneta, Ichiro Sekiya. Biomechanical analysis of the centralization procedure for extruded lateral menisci with posterior root deficiency in a porcine model. *J Orthop Sci.* 2020.01; 25(1); 161-166
2. Mai Katakura, Kaori Nakamura, Toshifumi Watanabe, Masafumi Horie, Tomomasa Nakamura, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Toshiyuki Ohara, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Risk factors for residual anterolateral rotational instability after double bundle anterior cruciate ligament reconstruction: Evaluation by quantitative assessment of the pivot shift phenomenon using triaxial accelerometer. *Knee.* 2020.01; 27(1); 95-101
3. Hajime Utsunomiya, Ichiro Sekiya, Soshi Uchida.. Editorial Commentary:Are We Ready to Apply Stem Cell Therapy in Rotator Curr Tear Surgery? *Arthroscopy.* 2020.01; 36(1); 86-87
4. Kaori Nakamura, Tomomasa Nakamura, Masafumi Horie, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Masaki Amemiya, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Anatomic femoral tunnel placement is difficult by the transtibial technique: comparison of three different femoral tunnel drilling techniques in double-bundle anterior cruciate ligament reconstructions. *Knee Surg Sports Traumatol Arthrosc.* 2020.02; 28(2); 584-593
5. Masaki Amemiya, Kunikazu Tsuji, Hiroki Katagiri, Kazumasa Miyatake, Yusuke Nakagawa, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Synovial fluid-derived mesenchymal cells have non-inferior chondrogenic potential and can be utilized for regenerative therapy as substitute for synovium-derived cells. *Biochem. Biophys. Res. Commun.* 2020.03; 523(2); 465-472
6. Chiaki Yamada, Akihiro Takeshita, Hitoshi Ohto, Ken Ishimaru, Kinuyo Kawabata, Yuriko Nomaguchi, Yasue Haraguchi, Misao Abe, Koki Sobue, Hiroyuki Takenouchi, Junko Takadate, Masami Kamimura, Akiko Katai, Daisuke Kasai, Yumiko Minami, Tatsuya Sugimoto, Junko Michino, Kazuhiro Nagai, Mikako Kumagai, Yuichi Hasegawa, Keiko Ishizuka, Naoki Ohtomo, Naotomo Yamada, Kazuo Muroi, Tadashi Matsushita, Koki Takahashi . A Japanese multi - institutional collaborative study of antigen - positive red blood cell (RBC) transfusions in patients with corresponding RBC antibodies *Vox Sanguinis.* 2020.03;
7. Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Masafumi Horie, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Validity of intraoperative observation of graft length change pattern for medial patellofemoral ligament reconstruction. *J Orthop.* 2020.03; 21; 131-136

8. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Junpei Matsuda, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Ichiro Sekiya. The effect of a centralization procedure for extruded lateral meniscus on load distribution in porcine knee joints at different flexion angles. *BMC Musculoskelet Disord.* 2020.04; 21(1); 205
9. Toshifumi Watanabe, Hideyuki Koga, Koji Otabe, Yusuke Nakagawa, Takeshi Muneta, Ichiro Sekiya, Tetsuya Jinno. Coronal and sagittal laxity affects clinical outcomes in posterior-stabilized total knee arthroplasty: assessment of well-functioning knees. *Knee Surg Sports Traumatol Arthrosc.* . 2020.05; 28(5); 1400-1409
10. Hiroaki Onuma, Kunikazu Tsuji, Takashi Hoshino, Kei Inomata, Mio Udo, Yusuke Nakagawa, Hiroki Katagiri, Kazumasa Miyatake, Toshifumi Watanabe, Ichiro Sekiya, Takeshi Muneta, Hideyuki Koga. Fibrotic changes in the infrapatellar fat pad induce new vessel formation and sensory nerve fiber endings that associate prolonged pain. *J. Orthop. Res.*. 2020.06; 38(6); 1296-1306
11. Katsutsugu Umeda, Kohsuke Imai, Masakatsu Yanagimachi, Hiromasa Yabe, Masao Kobayashi, Yoshiyuki Takahashi, Michiko Kajiwara, Nao Yoshida, Yuko Cho, Masami Inoue, Yoshiko Hashii, Yoshiko Atsuta, Tomohiro Morio. Impact of graft-versus-host disease on the clinical outcome of allogeneic hematopoietic stem cell transplantation for non-malignant diseases. *Int J Hematol.* 2020.06; 111(6); 869-876
12. So Suzuki, Mitsuru Mizuno, Yuriko Sakamaki, Ayako Mimata, Kentaro Endo, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya. Morphological changes in synovial mesenchymal stem cells during their adhesion to the meniscus. *Lab. Invest.*. 2020.07; 100(7); 916-927
13. Naoko Araya, Kazumasa Miyatake, Kunikazu Tsuji, Hiroki Katagiri, Yusuke Nakagawa, Takashi Hoshino, Hiroaki Onuma, Saisei An, Hirofumi Nishio, Yoshitomo Saita, Ichiro Sekiya, Hideyuki Koga. Intra-articular Injection of Pure Platelet-Rich Plasma Is the Most Effective Treatment for Joint Pain by Modulating Synovial Inflammation and Calcitonin Gene-Related Peptide Expression in a Rat Arthritis Model. *Am J Sports Med.* 2020.07; 48(8); 2004-2012
14. Yoichi Murata, Soshi Uchida, Hajime Utsunomiya, Akihisa Hatakeyama, Hirotaka Nakashima, Toshiharu Mori, Yoshiaki Yamanaka, Manabu Tsukamoto, Ichiro Sekiya, Johnny Huard, Marc J Philippon, Akinori Sakai. Differentiation Potential of Synovial Mesenchymal Stem Cells Isolated From Hip Joints Affected by Femoroacetabular Impingement Syndrome Versus Osteoarthritis. *Arthroscopy.* 2020.08; 36(8); 2122-2133
15. Mitsuru Mizuno, Kentaro Endo, Hisako Katano, Ayako Tsuji, Naomi Kojima, Ken Watanabe, Norio Shimizu, Tomohiro Morio, Ichiro Sekiya. The environmental risk assessment of cell-processing facilities for cell therapy in a Japanese academic institution. *PLoS ONE.* 2020.08; 15(8); e0236600
16. Nakano S, Tomaru Y, Kubota T, Takase H, Mochizuki M, Shimizu N, Sugita S, Direct Strip PCR Project Groups. Multiplex solid-phase real-time polymerase chain reaction without DNA extraction: A rapid intraoperative diagnosis using microvolumes. *Ophthalmology.* 2020.09;
17. Akihiro Takeshita, Hiroko Watanabe, Chiaki Yamada, Veera Sekaran Nadarajan, Parichart Permpikul, Attapong Sinkitjasub, Chan Pui Ha Nataie, Shuming Zhao, Kyou Aup Han Dae Won Kim, Jang Soo Suh, Hyun Ok Kim, Kinuyo Kawabata, Ken Ishimaru, Naoki Ohtomo, Naotomo Yamada, Yutaka Tomoda, Kimiko Yurugi, Hitoshi Ohto. Erythrocyte Alloimmunity and Genetic Variance: Results from the Collaborative Study of Alloimmunity to Antigen Diversity in Asian Populations (All ADP). *Transfusion and Apheresis Science.* 2020.10; 59(5); 102944
18. Yoshie Seki, Hiroki Katagiri, Koji Otabe, Yusuke Nakagawa, Kazumasa Miyatake, Ichiro Sekiya, Hideyuki Koga. Investigation of association between the preoperative intra-articular anesthetic test and persistent pain after total knee arthroplasty. *J Orthop Sci.* 2020.11; 25(6); 1055-1060
19. Hideyuki Koga, Tomomasa Nakamura, Hiroki Katagiri, Yusuke Nakagawa, Nobutake Ozeki, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya. Two-Year Outcomes After Meniscopectomy by Capsular Advancement With the Application of Arthroscopic Centralization Technique for Lateral Compartment Knee Osteoarthritis. *Am J Sports Med.* 2020.11; 48(13); 3154-3162
20. Hayato Aoki, Nobutake Ozeki, Hisako Katano, Akinobu Hyodo, Yugo Miura, Junpei Matsuda, Kimiko Takanashi, Kenji Suzuki, Jun Masumoto, Noriya Okanouchi, Takeo Fujiwara, Ichiro Sekiya. Relationship between medial meniscus extrusion and cartilage measurements in the knee by fully automatic three-dimensional MRI analysis. *BMC Musculoskelet Disord.* 2020.11; 21(1); 742

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22. Hajime Utsunomiya, Ichiro Sekiya, Soshi Uchida. Editorial Commentary: Mesenchymal Stem Cell Preparation Methods Affect the Properties of Shoulder Subacromial Bursa-Derived Cells. Arthroscopy. 2020.11; 36(11); 2803-2804
23. Naoto Watanabe, Kentaro Endo, Keiichiro Komori, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Yuji Kohno, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Mesenchymal Stem Cells in Synovial Fluid Increase in Knees with Degenerative Meniscus Injury after Arthroscopic Procedures through the Endogenous Effects of CGRP and HGF. Stem cell reviews and reports.. 2020.12; 16(6); 1305-1315
24. Yoshihisa Kushida, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Kunikazu Tsuji, Hideyuki Koga, Koichiro Kishima, Yoshio Soma, Ichiro Sekiya. Two- and three-dimensional optical coherence tomography to differentiate degenerative changes in a rat meniscectomy model. J Orthop Res. 2020.12; 38(12); 2592-2600
25. Endo Akifumi, Yamashita Motoi, Kamiya Takahiro, Mitsuki Noriko, Isoda Takeshi, Imai Kohsuke, Takagi Masatoshi, Kajiwara Michiko, Kanegane Hirokazu, Morio Tomohiro. A Retrospective Study of Six Cases of HLA Haplo-Identical Hematopoietic Stem Cell Transplantation with Post-Transplant Cyclophosphamide PEDIATRIC BLOOD & CANCER. 2020.12; 67;
26. Miyamoto Satoshi, Yanagimachi Masakatsu, Umeda Katsutsugu, Iguchi Akihiro, Sasahara Yoji, Takada Hidetoshi, Yamada Masafumi, Ishimura Masataka, Koike Takashi, Yasui Masahiro, Takahashi Yoshiyuki, Kawaguchi Hiroshi, Kajiwara Michiko, Inoue Masami, Kato Koji, Hashii Yoshiko, Atsuta Yoshiko, Yabe Hiromasa, Imai Kohsuke, Morio Tomohiro. Hematopoietic Stem Cell Transplantation for Inborn Errors of Immunity in Japan: Overview of a Nationwide Retrospective Analysis BONE MARROW TRANSPLANTATION. 2020.12; 55(SUPPL 1); 102-103
27. Miyamoto Satoshi, Yanagimachi Masakatsu, Umeda Katsutsugu, Iguchi Akihiro, Sasahara Yoji, Takada Hidetoshi, Takahashi Yoshiyuki, Kajiwara Michiko, Inoue Masami, Kato Koji, Hashii Yoshiko, Atsuta Yoshiko, Yabe Hiromasa, Imai Kohsuke, Morio Tomohiro. Hematopoietic Stem Cell Transplantation for Severe Combined Immunodeficiency in Japan: A Nationwide Retrospective Analysis BONE MARROW TRANSPLANTATION. 2020.12; 55(SUPPL 1); 443

[Misc]

1. Naoko Araya, Hiroki Katagiri , Yusuke Nakagawa, Toshiyuki Ohara, Mikio Shioda, Yuji Kohno, Masaki Amemiya, Ichiro Sekiya, Hideyuki Koga.. Predictors of residual mechanical symptoms after meniscus surgery: data from the maks group Osteoarthritis and Cartilage. 2020.04; 28(1); S221-S223

[Conference Activities & Talks]

1. Nobutake Ozeki, Hideyuki Koga, Hayato Aoki, Akinobu Hyodo, Hiroki Katagiri, Yusuke Nakagawa, Yuji Kohno, Mitsuru Mizuno, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. 3D MRI Analysis For Cartilage In Anterior Cruciate Ligament Deficient Knee.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA
2. Kiyotaka Horiuchi, Nobutake Ozeki, Mitsuru Mizuno, Hisako Katano, Koji Otabe, Keiichiro Komori, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Comparison Between Cultured Mscs And Non-cultured Mscs After Cryopreservation For Intra-articular Injections Into The Knee In A Rat Oa Model.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA
3. Rei Kubota, Hideyuki Koga, Nobutake Ozeki, Yuji Kohno, Junpei Matsuda, Yoshihisa Kushida, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Ichiro Sekiya.. The Effect Of Centralization Procedure For Extruded Lateral Meniscus On Load Distributionin Porcine Knee Joints At 30-90 Degrees Of Flexion.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.08 Phoenix,USA

4. Naoto Watanabe, Mitsuru Mizuno, Junpei Matsuda, Naoko Nakamura, Tsuyoshi Kimura, Kunikazu Tsuji, Akio Kishida, Ichiro Sekiya.. The Amount Of Collagen Is Not Related To Mechanical Properties Of High Hydrostatic Pressure-decellularized Meniscus And Freeze-thawed Meniscus.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.09 Phoenix,USA
5. Hayato Aoki, Nobutake Ozeki, Akinobu Hyodo, Yuji Kohno, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kenji Suzuki, Jun Masumoto, Hideyuki Koga, Ichiro Sekiya.. Learning Times And Segmentation Accuracy Of U-net Convolutional Neural Networks On Automatic Segmentation For Mri Of Knee.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.09 Phoenix,USA
6. So Suzuki, Mitsuru Mizuno, Yuji Kohno, Nobutake Ozeki, Koji Otabe, Hisako Katano, Kunikazu Tsuji, Hideyuki Koga, Ichiro Sekiya.. Quantitative Morphological Analysis Of Synovial Mesenchymal Stem Cells During Adhesion To The Meniscus.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.10 Phoenix,USA
7. Akinobu Hyodo. Nobutake Ozeki, Hayato Aoki, Mitsuru Mizuno, Koji Otabe, Hisako Katano, Kenji Suzuki, Jun Masumoto, Ichiro Sekiya.. Radial Projected Femoral Cartilage Area By Automatic Cartilage Segmentation For The Knee MRI.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.11 Phoenix,USA
8. Yoshihisa Kushida, Nobutake Ozeki, Hisako Katano, Mitsuru Mizuno, Ichiro Sekiya.. 2D And 3D Optical Coherence Tomography To Differentiate Degenerative Changes In A Rat Meniscectomy Model.. Orthopaedic Research Society 2020 Annual Meeting 2020.02.11 Phoenix,USA

Dental Clinic for Sleep Disorders (Apnea and Snoring)

Junior Associate Professor (Clinic Chief) Masayuki HIDEISHIMA
Project Assistant Professor Shuhei NAKAMURA (~ July)
Hospital Staff Mai MIYACHI (August ~)
Project Assistant Professor Hiroyuki ISHIYAMA (concurrently with TMJ CLinic)

(1) Publications

[Misc]

1. Mai Miyachi. The Perspective of Dental Sleep Medicine the Quintessence. 2020.07; 39(7); 90-113
2. Hideshima M, Ishihara N, Ishiyama H. Oral appliance therapy for sleep apnea and development of the prognosis model for treatment effect Cell. 2020.09; 52 (697); 570-573

[Conference Activities & Talks]

1. KANAMORI Yuna, NORITAKE Kanako, UMEMORI Sachi, IWAKI Maiko, KIDO Daisuke, HIDEISHIMA Masayuki, KIMURA Yasuyuki, HATTORI Akitaka, TONAMI Ken-ichi, EBIHARA Arata, ARAKI Kouji, NITTA Hiroshi. TMDU trainee residents' feedback on the trial of objective clinical skills examinations. 2020.09.26
2. Mai Miyachi, Masayuki Hideshima, R. Merrill, S. Arman. Clinical practice and education system for dental sleep medicine in the United States. The Japanese Academy of Dental Sleep Medicine 2020.11.22 online

Clinical Center for Sports Medicine and Sports Dentistry

Clinical Center of Sports Medicine
Center Chief and Junior Associate Professor ; Kazuyoshi YAGISHITA
Assistant Professor ; Toshoyuki OHHARA
Specially Appointed Assistant Professor ; Mikio SHIODA
Physical therapy operator chief ; Junya AIZAWA (~ 2020.3)
Physical therapy operator chief ; Kenji HIROHATA(2020.4 ~)
Physiotherapist; Takehiro OHMI,Sho (2020.4 ~) ,Shunsuke OHJI
Staff Assistant; Kiyomi ITOH

Sports Medicine/Dentistry
Associate Professor; Toshiaki UENO
Assistant Professor; Hiroshi CHUREI
Specially Appointed Assistant Professor ; Kairi HAYASHI

(1) Outline

Center of Sports Medicine and Sports Dentistry was established as a bridgehead for sports medical science and sports dental science which deals the clinical management of trauma and disorder for athletes and sports-active people, and the safety measures and prevention of sports-related traumatic injuries and disorders. Center of Sports Medicine and Sports Dentistry is consisted of Clinical Center of Sports Medicine in University Hospital of Medicine and Sports Medicine/Dentistry and Sports dentistry clinic in University Hospital of Dentistry.

(2) Research

○ Clinical Center of Sports Medicine

- 1) Athletic rehabilitation for rapid recovery from injury and high performance in athletes.
 - 1)-a Intervention of core strength in patients with anterior cruciate ligament reconstruction.
 - 1)-b Treatment from the aspect of core function in patients with overuse and fatigue fracture.
- 2) Evaluation methods for core function.
- 3) Development of dynamic stability.
- 4) Hyperbaric oxygen treatment
 - 4)-a Soft tissue injuries related with sports activities.
 - 4)-b Conditioning in sports activities

○ Sports Medicine/Dentistry

- 1) Oral health promotion of athletes and sports-active people
 - 1)-a Field survey of oral health conditions in athletes and sports-active people
 - 1)-b Changes of oral environment associated with physical and sporting activities
 - 1)-c Influences of sports drinks and supplements on oral health
- 2) Safety measures of sports-related dental and maxillofacial traumatic injuries
 - 2)-a Diagnosis and treatment techniques for sports-related dental and maxillofacial injuries
 - 2)-b Development and innovation of sports mouthguard
 - 2)-c Development and innovation of sports faceguard
 - 2)-d Development and innovation of scuba diving mouthpiece

- 3) Correlations between occlusion and general motor functions
- 3)-a Biomechanical assessment of motor performance associated with occlusion
- 3)-b Electrophysiological analysis of neuromuscular function associated with occlusion
- 4) Correlations between occlusion and body posture
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

(3) Clinical Services & Other Works

Center of Sports Medicine and Sports Dentistry clinic offers comprehensive care and clinical management for athletes and sports-active people suffered traumatic injuries, overuse disorders, disorders related with internal medicine, and dental diseases.

○ Clinical Center of Sports Medicine

Number of patients (From January 2020 to December 2020)

Section of out-patient clinic: 2,314

Section of athletic rehabilitation: 2,810

○ Sports Medicine/Dentistry, Sports dentistry clinic

Sports dentistry clinic 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.

(4) Publications

[Original Articles]

1. Junya Aizawa , Kenji Hirohata , Shunsuke Ohji , Takehiro Ohmi , Hideyuki Koga , Kazuyoshi Yagishita. Factors associated with psychological readiness to return to sports with cutting, pivoting, and jump-landings after primary anterior cruciate ligament reconstruction Orthopaedic Journal of Sports Medicine. 2020;
2. Tanabe G, Churei H, Wada T, Uo M, Takahashi H, Ueno T. Influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine J Oral Sci. 2020.01; 62(1); 23-27
3. Tanabe Gen, Churei Hiroshi, Wada Takahiro, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine JOURNAL OF ORAL SCIENCE. 2020.01; 62(1); 23-27
4. Naoki Yamamoto, Takuya Oyaizu, Mitsuhiro Enomoto, Masaki Horie, Masato Yuasa, Atsushi Okawa, Kazuyoshi Yagishita. VEGF and bFGF induction by nitric oxide is associated with hyperbaric oxygen-induced angiogenesis and muscle regeneration. Sci Rep. 2020.02; 10(1); 2744
5. Watanabe D, Hatakeyama K, Ikegami R, Eshima H, Yagishita K, Poole DC, Kano Y. Sex differences in mitochondrial Ca²⁺ handling in mouse fast-twitch skeletal muscle in vivo. Journal of applied physiology (Bethesda, Md. : 1985). 2020.02; 128(2); 241-251
6. Aung Thet Khaing , Churei Hiroshi, Kinjo Rio, Tun Phyu Sin , Tanabe Gen, Ueno Toshiaki. フェイスガードの異なるクッション材料の換気率と衝撃吸収能の比較 (Ventilation rate and shock absorbing ability of different types of cushion materials in face guard) スポーツ歯学. 2020.02; 23(2); 88-89
7. Tun Phyu Sin , Tanabe Gen, Kamijo Shingo, Aung Thet Khaing , Oki Meiko, Churei Hiroshi, Hikita Kazuhiro, Ueno Toshiaki. 光学 3D スキャナーを用いて個別調整したマウスガード適合性に関するデジタル評価法 (Digital evaluation of the fit of custom-made mouthguard using optical 3D scanner) スポーツ歯学. 2020.02; 23(2); 94-95
8. Takehiro OHMI, Junya AIZAWA, Kenji HIROHATA, Shunsuke OHJI, Kazuyoshi YAGISHITA. Developing Direct Arch Measurement under Quantitative Partial Weight Bearing and Reliability and Validity 2020.04; 35(2); 179-185

9. Ito D, Tanaka T, Kunieda Y, Kimura Y, Ishiyama D, Nishio N, Otobe Y, Koyama S, Ohji S, Suzuki M, Ichikawa T, Ogawa H, Narita Y, Yoshida T, Yamada M, Kondo K. Factors associated with post-stroke apathy in subacute stroke patients. *Psychogeriatrics : the official journal of the Japanese Psychogeriatric Society*. 2020.04;
10. Shunsuke Ohji, Junya Aizawa, Kenji Hirohata, Takehiro Ohmi, Hideyuki Koga, Okawa Atsushi, Testuya Jinno, Kazuyoshi Yagishita. The gap between dichotomous responses regarding return to sports and subjective athletic performance intensity after anterior cruciate ligament reconstruction 2020.04;
11. Takehiro Ohmi, Junya Aizawa, Kenji Hirohata, Shunsuke Ohji, Kazuyoshi Yagishita. The difference of ground reaction force during anterior step motion in collegiate male long-distance runners between with or without a history of medial tibial stress syndrome. *Japanese Journal of Clinical Sports Medicine*. 2020.04; 28(2); 313-320
12. Araya N, Katagiri H, Nakagawa Y, Ohara T, Shioda M, Kohno Y, Amemiya M, Sekiya I, Koga H. PREDICTORS OF RESIDUAL MECHANICAL SYMPTOMS AFTER MENISCUS SURGERY: DATA FROM THE MAKS GROUP OSTEOARTHRITIS AND CARTILAGE. 2020.04; 28; S221-S223
13. Leyang Li, Hiroyuki Yokoyama, Hidetoshi Kaburagi, Takashi Hirai, Kunikazu Tsuji, Mitsuhiro Enomoto, Yoshiaki Wakabayashi, Atsushi Okawa. Remnant neuromuscular junctions in denervated muscles contribute to functional recovery in delayed peripheral nerve repair. *Neural Regen Res*. 2020.04; 15(4); 731-738
14. Kojima Y, Kojima A, Niizeki Y, Yagishita K. Recreational diving-related injury insurance claims among Divers Alert Network Japan members: Retrospective analysis of 321 cases from 2010 to 2014. *Diving and hyperbaric medicine*. 2020.06; 50(2); 92-97
15. Kyohei Sakaki, Yuko Hoshino, Shigenori Kawabata, Yoshiaki Adachi, Taishi Watanabe, Kensuke Sekihara, Senichi Ishii, Masaki Tomori, Shoji Tomizawa, Mitsuhiro Enomoto, Atsushi Okawa. Evaluation of neural activity by magnetospinography with 3D sensors. *Clin Neurophysiol*. 2020.06; 131(6); 1252-1266
16. Kairi Hayashi, Hiroshi Churei, Gen Tanabe, Kaito Togawa, Ruman Uddin Chowdhury, Toshiaki Ueno. Improving the Wearing Rate of Mouthguards in the Youth Rugby Category Affects the Total Future Mouthguard Wearing Rate. *Dent J (Basel)*. 2020.07; 8(3); e77
17. Yamamoto Naoki, Oyaizu Takuya, Yagishita Kazuyoshi, Enomoto Mitsuhiro, Horie Masaki, Ohara Toshiyuki, Shioda Mikio, Takada Ryohei, Okawa Atsushi. Hyperbaric Oxygen Therapy Promotes Muscle Recovery After Contusion Injury Via Angiogenesis By Reactive Nitrogen Species *MEDICINE AND SCIENCE IN SPORTS AND EXERCISE*. 2020.07; 52(17); 929
18. Kenji Hirohata, Junya Aizawa, Hidetaka Furuya, Sho Mitomo, Takehiro Ohmi, Shunsuke Ohji, Toshiyuki Ohara, Hideyuki Koga, Kazuyoshi Yagishita, Kate E Webster. The Japanese version of the anterior cruciate ligament-return to sport after injury (ACL-RSI) scale has acceptable validity and reliability. *Knee Surg Sports Traumatol Arthrosc*. 2020.08; 28(8); 2519-2525
19. Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita YI, Chowdhury RU, Chowdhury NU, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment: A case report *Journal of Prosthodontic Research*. 2020.09; Sep 15 published online;
20. Ohji Shunsuke, Aizawa Junya, Hirohata Kenji, Ohmi Takehiro, Koga Hideyuki, Okawa Atsushi, Jinno Tetsuya, Yagishita Kazuyoshi. The Gap Between Subjective Return to Sports and Subjective Athletic Performance Intensity After Anterior Cruciate Ligament Reconstruction *ORTHOPAEDIC JOURNAL OF SPORTS MEDICINE*. 2020.09; 8(9); 2325967120947402
21. Ito Daisuke, Tanaka Tomoya, Kunieda Yota, Kimura Yosuke, Ishiyama Daisuke, Nishio Naohito, Otobe Yuhei, Koyama Shingo, Ohji Shunsuke, Suzuki Mizue, Ichikawa Takeo, Ogawa Hideyuki, Narita Yuya, Yoshida Taiki, Yamada Minoru, Kondo Kunitsugu. Factors associated with post-stroke apathy in subacute stroke patients(和訳中) *Psychogeriatrics*. 2020.09; 20(5); 780-781
22. Koga H, Nakamura T, Katagiri H, Nakagawa Y, Ozeki N, Ohara T, Shioda M, Kohno Y, Amemiya M, Sekiya I. Two-Year Outcomes After Meniscopectomy by Capsular Advancement With the Application of Arthroscopic Centralization Technique for Lateral Compartment Knee Osteoarthritis. *The American journal of sports medicine*. 2020.10; 363546520957367

23. Kimura Y, Ohji S, Nishio N, Abe Y, Ogawa H, Taguchi R, Otobe Y, Yamada M. The impact of wheelchair propulsion based physical activity on functional recovery in stroke rehabilitation: a multicenter observational study. *Disability and rehabilitation*. 2020.10; 1-6
24. Furuya H, Ito T, Hirohata K, Mitomo S, Yamasaki K, Igarashi H, Omori K, Hoshino M, Hart RA. Construct validity and reliability of the Japanese Version of the Lumbar Stiffness Disability Index. *Spine*. 2020.11;
25. Aizawa J, Hirohata K, Ohji S, Ohmi T, Koga H, Yagishita K. Factors Associated With Psychological Readiness to Return to Sports With Cutting, Pivoting, and Jump-Landings After Primary ACL Reconstruction. *Orthopaedic journal of sports medicine*. 2020.11; 8(11); 2325967120964484
26. Hiroyuki Yokoyama, Takashi Hirai, Tetsuya Nagata, Mitsuhiro Enomoto, Hidetoshi Kaburagi, Li Leiyo, Takayuki Motoyoshi, Toshitaka Yoshii, Atsushi Okawa, Takanori Yokota. DNA Microarray Analysis of Differential Gene Expression in the Dorsal Root Ganglia of Four Different Neuropathic Pain Mouse Models. *J Pain Res*. 2020.11; 13; 3031-3043
27. Tun PS, Churei H, Hikita K, Kamiyo S, Oki M, Tanabe G, Hayashi K, Aung TK, Win A, Hlaing S, Takahashi H, Ueno T. Fabrication of shock absorbing photopolymer composite material for 3D printing sports mouthguard *JOURNAL OF PHOTOPOLYMER SCIENCE AND TECHNOLOGY*. 2020.12; 33(6); 615-622
28. Takahiro Wada, Hiroshi Churei, Mako Yokose, Naohiko Iwasaki, Hidekazu Takahashi, Motohiro Uo. Application of Glass Fiber and Carbon Fiber-Reinforced Thermoplastics in Face Guards. *Polymers (Basel)*. 2020.12; 13(1); 18

[Conference Activities & Talks]

1. Churei H. Sports Dentistry. University of Dental Medicine, Yangon/Special Lecture 2020.02.06 Yangon, Myanmar
2. Aung TK, Churei H, Kinjo R, Tun PS, Tanabe G, Ueno T. Shock absorbing ability of different cushion materials used in face guard. 40th Myanmar Dental Conference 2020.02.07
3. Tun PS, Churei H, Tanabe G, Aung TK, Kamiyo S, Oki M, Takahashi H, Hikita K, Ueno T. Shock-absorbing capability of laminated type of 3D printing materials compared to conventional mouthguard materials. 40th Myanmar Dental Conference 2020.02.07
4. The Gait Analysis of the patients with Rotating Hinge knee in revision Total Knee Arthroplasty in initial stance phase. 2020.02.22
5. Takahiro Wada, Yasuhito Takashima, Rio Kinjo, Kasei Aoyagi, Hiroshi Churei, Naohiko Iwasaki, Toshiaki Ueno, Hidekazu Takashi, Fumiyoshi Minami, Motohiro Uo. Strain distribution analysis of face guards made of carbon fiber-reinforced thermoplastics during shock absorption test using high-speed camera and digital image correlation. 4th open forum for "Creation of Life Innovation Materials for Interdisciplinary and International Researcher Development" 2020.03.04 Tokyo, Japan
6. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Uo Motohiro, Ueno Toshiaki. Development of wearable mouth-guard device for monitoring teeth clenching during exercise. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)
7. Aung TK, Churei H, Kinjo R, Tun PS, Tanabe G, Takahashi Y, Hayashi T, Ueno T. Shock absorbing ability of 3D printed thermoplastic ABS compatible with face guard material. 第31回日本スポーツ歯科医学会 2020.12.05 広島市+ WEB 開催
8. Tun PS, 中禮宏, 疋田一洋, 上條真悟, 大木明子, 田邊元, 林海里, Aung TK, 高橋英和, 上野俊明. Production of shock absorbing photopolymer composite material for 3D printing sports mouthguard. 第31回日本スポーツ歯科医学会 2020.12.05 広島市+ WEB 開催

Sports Dentistry

(1) Publications

[Original Articles]

1. Tanabe Gen, Churei Hiroshi, Wada Takahiro, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine JOURNAL OF ORAL SCIENCE. 2020.01; 62(1); 23-27
2. Tanabe Gen, Churei Hiroshi, Wada Takahiro, Takahashi Hidekazu, Uo Motohiro, Ueno Toshiaki. 歯科用熱成形機でマウスガードを製造する際の温度がシート積層工程に及ぼす影響 (The influence of temperature on sheet lamination process when fabricating mouthguard on dental thermoforming machine) Journal of Oral Science. 2020.01; 62(1); 23-27
3. Aung Thet Khaing , Churei Hiroshi, Kinjo Rio, Tun Phyu Sin , Tanabe Gen, Ueno Toshiaki. フェイスガードの異なるクッション材料の換気率と衝撃吸収能の比較 (Ventilation rate and shock absorbing ability of different types of cushion materials in face guard) スポーツ歯学. 2020.02; 23(2); 88-89
4. Tun Phyu Sin , Tanabe Gen, Kamijo Shingo, Aung Thet Khaing , Oki Meiko, Churei Hiroshi, Hikita Kazuhiro, Ueno Toshiaki. 光学3D スキャナーを用いて個別調整したマウスガード適合性に関するデジタル評価法 (Digital evaluation of the fit of custom-made mouthguard using optical 3D scanner) スポーツ歯学. 2020.02; 23(2); 94-95
5. Kairi Hayashi, Hiroshi Churei, Gen Tanabe, Kaito Togawa, Ruman Uddin Chowdhury, Toshiaki Ueno. Improving the Wearing Rate of Mouthguards in the Youth Rugby Category Affects the Total Future Mouthguard Wearing Rate. Dent J (Basel). 2020.07; 8(3); e77
6. Hayashi K, Churei H, Shrestha A, Suzuki T, Matsubara H, Otomaru T, Sumita Y, Uddin Chowdhury R, Uddin Chowdhury N, Ueno T. Fabrication technique of obturator-type sports mouthguard for a patient who had undergone maxillectomy and its speech intelligibility assessment:A case report. Journal of prosthodontic research. 2020.09;

[Conference Activities & Talks]

1. Kinjo Rio, Wada Takahiro, Churei Hiroshi, Hayashi Kairi, Uo Motohiro, Ueno Toshiaki. Development of wearable mouth-guard device for monitoring teeth clenching during exercise. The Chubu and Kanto Conference of the Japanese Society for Dental Materials and Devices 2020.10.31 Tokyo, Japan (Hybrid Conference)

Life Science and Bioethics Research Center

Masayuki Yoshida
Yusuke Ebana
Hiroko Kohbata
Mizuko Osaka

(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. Takahiro Fukaiishi, Isao Minami, Seizaburo Masuda, Yasutaka Miyachi, Kazutaka Tsujimoto, Hajime Izumiyama, Koshi Hashimoto, Masayuki Yoshida, Sayako Takahashi, Kenichi Kashimada, Tomohiro Morio, Kenjiro Kosaki, Yoshiro Maezawa, Koutaro Yokote, Takanobu Yoshimoto, Tetsuya Yamada. A case of generalized lipodystrophy-associated progeroid syndrome treated by leptin replacement with short and long-term monitoring of the metabolic and endocrine profiles. *Endocr. J.* 2020.02; 67(2); 211-218
2. Higashijima Y, Matsui Y, Shimamura T, Nakaki R, Nagai N, Tsutsumi S, Abe Y, Link VM, Osaka M, Yoshida M, Watanabe R, Tanaka T, Taguchi A, Miura M, Ruan X, Li G, Inoue T, Nangaku M, Kimura H, Furukawa T, Aburatani H, Wada Y, Ruan Y, Glass CK, Kanki Y. Coordinated demethylation of H3K9 and H3K27 is required for rapid inflammatory responses of endothelial cells. *The EMBO journal*. 2020.03; e103949
3. Terui-Kohbata Hiroko, Egawa Makiko, Yura Kei, Yoshida Masayuki. Knowledge and attitude of hereditary breast cancer among Japanese university female students *Journal of Human Genetics*. 2020.07; 65(7); 591-599
4. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a stimulation of differentiated HL60 induces THP-1 chemotaxis via MCP-1 dependent pathway(和訳中) *日本動脈硬化学会総会プログラム・抄録集*. 2020.07; 52 回; 268
5. Dewan Syed Masudur Rahman, Deushi Michiyo, Osaka Mizuko, Yoshida Masayuki. C5a Elevates MCP-1 Expression in Neutrophil-like Differentiated HL60 via NF- κ B Signaling Pathway(和訳中) *日本循環器学会学術集会抄録集*. 2020.07; 84 回; OE122-6

6. Tsuru Hiromi, Osaka Mizuko, Yoshida Masayuki. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver(和訳中) 日本循環器学会学術集会抄録集. 2020.07; 84回; PE28-2
7. Hiroko Terui-Kohbata, Masami Ikeda, Kei Yura. The reliability and validity of the Japanese version of Revised Illness Perception Questionnaires for Healthy people (IPQ-RH-J) British Journal of Cancer Research. 2020.08; 3(2); 341-348
8. Xiaoxi Yang, Tetsuo Sasano, Yusuke Ebana, Jun K Takeuchi, Kensuke Ihara, Masahiro Yamazoe, Tetsushi Furukawa. Functional Role of the L396R Mutation of Tks5 Identified by an Exome-Wide Association Study in Atrial Fibrillation. Circ J. 2020.10;
9. Tsuru H, Osaka M, Hiraoka Y, Yoshida M. HFD-induced hepatic lipid accumulation and inflammation are decreased in Factor D deficient mouse. Scientific reports. 2020.10; 10(1); 17593
10. Inoue Reiko, Nishi Hiroshi, Osaka Mizuko, Yoshida Masayuki, Nangaku Masaomi. NEUTROPHIL INTERFERON-INDUCED, DOUBLE-STRANDED RNA-ACTIVATED PROTEIN KINASE (EIF2AK2) PROMOTES ADHESION IN NON-VIRAL INFLAMMATORY KIDNEY DISEASE NEPHROLOGY. 2020.10; 25; 35

[Conference Activities & Talks]

1. Hiroko Terui-Kohbata. Genetic testing with a multi-gene hereditary cancer panel and genetic counseling. 2020.07.05 web
2. 大坂 瑞子、出牛 三千代、吉田 雅幸. 選択的 PPAR α アゴニスト、ペマフィブラートは LDL 受容体欠損マウス大腿動脈における高中性脂肪血症を改善し、白血球接着を抑制する. 第 52 回日本動脈硬化学会総会・学術集会 2020.07.17 名古屋
3. Syed Masudur Rahman Dewan, Michiyo Deushi, Mizuko Osaka, Masayuki Yoshida. C5a elevates MCP-1 expression in neutrophil-like differentiated HL60 via NF- κ B signaling pathway. 第 84 回日本循環器学会学術集会 2020.07.27 京都
4. Hiromi Tsuru, Mizuko Osaka, Masayuki Yoshida. Critical Role of Complement Factor D in the Development of High-fat Diet-induced Fatty Liver . 第 84 回日本循環器学会学術集会 2020.07.27 Kyoto
5. 大坂瑞子. 動脈硬化症関連血管炎症反応における好中球でのヒストンシトルリン化の重要性. 第 43 回日本分子生物学会年会 2020.12.02

[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

Center for Experimental Animals

(1) Publications

[Original Articles]

1. Ito H, Nozaki K, Sakimura K, Abe M, Yamawaki S, Aizawa H. Activation of proprotein convertase in the mouse habenula causes depressive-like behaviors through remodeling of extracellular matrix Neuropsychopharmacology. 2020;
2. Yamada, T, Takechi M (Co-first), Yokoyama N, Hiraoka Y, Ishikubo H, Usami T, Furutera T, Taga Y, Hirate Y, Kanai-Azuma M, Yoda T, Ogawa-Goto K, Iseki S. Heterozygous mutation of the splicing factor Sf3b4 affects development of the axial skeleton and forebrain in mouse. Developmental Dynamics. 2020.01;
3. Mami Uemura, Mayumi Higashi, Montri Pattarapanawan, Shohei Takami, Naoki Ichikawa, Hiroki Higashiyama, Taizo Furukawa, Jun Fujishiro, Yuki Fukumura, Takashi Yao, Tatsuro Tajiri, Masami Kanai-Azuma, Yoshiakira Kanai. Gallbladder wall abnormality in biliary atresia of mouse Sox17+/- neonates and human infants Disease Models & Mechanisms 2020. 2020.01;
4. Nozaki K, Ito H, Ohgidani M, Yamawaki Y, Sahin EH, Kitajima T, Katsumata S, Yamawaki S, Kato TA, Aizawa H. Antidepressant effect of the translocator protein antagonist ONO-2952 on mouse behaviors under chronic social defeat stress. Neuropharmacology. 2020.01; 162; 107835
5. Pattarapanawan M, Uemura M, Miyazaki N, Takami S, Tomiyasu H, Tsunekawa N, Hirate Y, Fujishiro J, Kurohmaru M, Kanai-Azuma M, Higashiyama H, Kanai Y. Anatomical and histological characteristics of the hepatobiliary system in adult Sox17 heterozygote mice. Anatomical record (Hoboken, N.J. : 2007). 2020.06;
6. Cui W, Aida T, Ito H, Kobayashi K, Wada Y, Kato S, Nakano T, Zhu M, Isa K, Kobayashi K, Isa T, Tanaka K, Aizawa H. . Dopaminergic signaling in the nucleus accumbens modulates stress-coping strategies during inescapable stress. Journal of Neuroscience. 2020.08;

[Books etc]

1. Veterinary Histology 8th Edition. 2020.03 (ISBN : 978-4-8736-2773-1)

[Conference Activities & Talks]

1. Hikaru Ito, Kanako Nozaki, Hidenori Aizawa. 細胞外基質分解酵素の不活性化によるうつ病モデルマウスの治療. 第43回日本神経科学大会 2020.07.29
2. Hiroshi Yomogita, Hikaru Ito, Yoshikazu Hirate, Naoyuki Miyasaka, Masami Kanai-Azuma. Comparative study of Nr1 gene expression in mice and humans. The 163rd Annual Meeting of the Japanese Society of Veterinary Medicine 2020.09.14