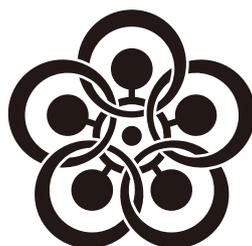


ANNUAL PUBLICATIONS

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

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Graduate School of Medical and Dental Sciences

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Life Science and Technology

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Oral Pathology

1. Staff and Students

Professor	Akira YAMAGUCHI	
Lecturer	Kei Sakamoto	
Assistant Professor	Kou Kayamori	
Technician	Miwako Hamagaki	
Graduate Students		
Ph.D. Course	Zhao Xin	Rumana Khanom
	Zayar Lin (Implant)	Rei Touyama
	Masita Mandasari	
	Ryousuke Nakamura (Maxillofacial Surgery)	
	Kenji Ogura (Maxillofacial Orthognathics)	
	Akane Yukimori	Wanlada Sawangarun
Secretary	Yumi Tanaka	

2. Purpose of Education

Oral Pathology section lectures the Module “Pathology” to 3rd grade students. This Module is comprised of two categories; General Pathology and Oral Pathology. Main objective of General Pathology is to provide students various opportunities and knowledge about general aspects of various diseases. Oral Pathology provides details of pathogenesis, pathophysiology and histopathological characteristics in various oral diseases.

3. Research Subjects

- 1) Clinico-patological research on oral and maxillofacial regions
- 2) Molecular mechanism of bone formation and bone regeneration
- 3) Roles of Notch signaling in skeletal formation and regeneration
- 4) Molecular mechanism of bone destruction by oral cancers
- 5) Evolutional changes in skeletal formation

4. Clinical Services

Our Dental Hospital has over 2,000 biopsy cases a year. Oral Pathology Section is involved in histopathological diagnosis of these biopsy cases.

5. Publications

Original Articles

1. Hoshino A, Ueha S, Hanada S, Imai T, Ito M, Yamamoto K, Matsushima K, Yamaguchi A, Iimura T: Roles of chemokine receptor CX3CR1 in maintaining murine bone homeostasis through the regulation of both osteoblasts and osteoclasts. *J Cell Sci* 126:1031-1045,2013
2. Tanabe R, Haraikawa M, Sogabe N, Sugimoto A, Kawamura Y, Takasugi S, Nagata M, Nakane A, Yamaguchi A, Iimura T, Masae Goseki-Sone : Retention of bone strength by feeding of milk and dairy products in ovariectomized rats; involvement of changes in serum levels of Ialpha, 25(OH)2D3 and FGF23. *J Nutr Biochem*. 24:1000-1007,2013
3. Makino Y, Takahashi Y, Tanabe R, Tamamura Y, Watanabe T, Haraikawa M, Hamagaki M, Hata K, Kanno J, Yoneda T, Saga Y, Goseki-Sone M, Kaneko K, Yamaguchi A, Iimura T: Spatiotemporal disorder in endochondral ossification during axial skeleton development in the Mesp2-null mouse: A developmental etiology of spondylocostal dysostosis and spondylothoracic dysostosis. *BONE* 53:248-258,2013
4. Matsumoto T, Iimura T, Ogura K, Moriyama K, Yamaguchi A: The role of osteocytes in bone resorption during orthodontic tooth movement. *J Dent Res* 92:340-345, 2013
5. Pal KS, Sakamoto K, Aragaki T, Akashi T, Yamaguchi A: The expression profiles of acidic epithelial keratins in Ameloblastoma. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* 115:523-531,2013
6. Sato K, Lee JW, Sakamoto K, Iimura T, Kayamori K, Yasuda H, Shindoh M, Ito M, Omura K, Yamaguchi A: RANKL synthesized by both stromal cells and cancer cells plays a crucial role in osteoclastic bone resorption induced by oral cancer. *Am J Pathol* 182:1890-1899,2013
7. Matsushita Y, Sakamoto K, Tamamura Y, Shibata Y, Minamizato T, Kihara T, Ito M, Katsube K, Hiraoka S, Koseki

H, Harada K, Yamaguchi A: CCN3 protein participates in bone regeneration as an inhibitory factor. *J Biol Chem* 288:19973-19985,2013

8. Shimada Y, Katsube K, Kabasawa Y, Morita K, Omura K, Yamaguchi A, Sakamoto K: Integrated genotypic analysis of hedgehog-related genes identifies subgroups of keratocystic odontogenic tumor with distinct clinicopathological features. *Plos One* 8:e70995, 2013

Review

1. Makino Y, Kaneko K, Yamaguchi A, Iimura T: Developmental biology and etiology of axial skeleton: Lessons from a mouse model of spondylocostal dysostosis and spondylothoracic dysostosis. *J Oral Biosci* 55:175-179,2013

Bacterial Pathogenesis

1. Staffs and Students (April 2013)

Professor	Ichiro Nakagawa
Associate Professor	Fumito Maruyama
Assistant Professor (Tenure Track)	Takashi Nozawa
Postdoctoral Student	Chihiro Aikawa Takayasu Watanabe
Graduate Student	Bijaya Haobam Amonrattana Roobthaisong Tejaswini Vaman Kulkarni (from Oct 2012) Shingo Hosomi Akiko Endo (Section of Periodontics) Noriko Maruyama (Section of Periodontics) Akira Goda (Section of Craniofacial Surgery) Ayako Kawabe (Section of Orthodontic Science) Seiichiro Oda (Section of Maxillofacial Surgery) Keiko Muramoto (Section of Maxillofacial Orthodontics) Yoshihiko Shiba (Section of Periodontics)

2. Education

Research education for postgraduate students

Our major research interests are to elucidate the bacterial evolution to escape from the host immune responses, and cellular defence mechanisms against bacterial infections. Especially, we focus (1) comparative genomics analysis of pathogenic bacterial evolution by acquisition of foreign genes, and the experimental demonstration of the unique hypothesis from bioinformatics information (2) analysis of molecular dynamics of recognition systems and inflammatory induction against bacterial pathogens. To achieve our mission, we are analyzing complete genomic sequences of various bacterial pathogens and comparative genomics, including genus streptococci (*Streptococcus pyogenes* and *S. mutans*), *Porphyromonas gingivalis*, etc., and cellular and molecular biological analyses for host responses.

These studies are collaborated not only with the other section of Tokyo Medical and Dental University, but also with Tokyo University, Tohoku University, Osaka University, and Nihon University.

Education for Undergraduate students

We took part in an education module "Infection and Host Defenses" for 3rd year students in School of Dentistry, and 1st and 2nd year students in School of Oral Health Care Sciences, and teaching pathogenic bacteriology and virology. In the dental field, infectious diseases such as dental caries and periodontitis are still major concerns. In addition, the prevention of iatrogenic infections such as HIV, Hepatitis B and C viruses are also important for dentistry. Therefore, our mission is not simply to give knowledge of microbiology but give talent to apply knowledge to lead appropriate diagnosis and treatment at the clinics. On this point of view, our lectures covered not only oral microbiology but also systemic microbiology and clinical microbiology to understand the variety of infectious diseases.

3. Research Subjects

1. Bacterial whole genome analysis.
2. Analysis of bacterial survival strategy based on bacterial whole genome gene expression.
3. Comparative genomics for bacterial gene acquisition and evolution systems.
4. Molecular analysis of recognition system and inflammation responses against bacterial infection.

4. Publications

Original articles

1. Sawabe T*, Ogura Y, Matsumura Y, Feng G, Amin AR, Mino S, Nakagawa S, Sawabe T, Kumar R, Fukui Y, Satomi M, Matsushima R, Thompson FL, Gomez-Gil B, Christen R, Maruyama F, Kurokawa K, Hayashi T "Updating the *Vibrio* clades defined by multilocus sequence phylogeny: proposal of eight new clades, and the description of *Vibrio tritonius* sp. nov." *frontiers in MICROBIOLOGY* 2013 Dec 27;4:414. doi: 10.3389/fmicb.2013.00414. eCollection 2013.

2. Nakagawa I "Streptococcus pyogenes Escapes from Autophagy" *Cell Host and Microbe* Volume 14, Issue 6, 604-606, 11 December 2013.
3. Ito C, Saito Y, Nozawa T, Fujii S, Sawa T, Inoue H, Matsunaga T, Khan S, Akashi S, Hashimoto R, Aikawa C, Takahashi E, Sagara H, Komatsu M, Tanaka K, Akaike T, Nakagawa I, Arimoto H "Endogenous Nitrated Nucleotide Is a Key Mediator of Autophagy and Innate Defense Against Bacteria" *Molecular Cell* 2013 Nov 19. pii: S1097-2765(13)00790-9. doi: 10.1016/j.molcel.2013.10.024.
4. Mori H*, Maruyama F*, Kato H*, Toyoda A, Dozono A, Ohtsubo Y, Nagata Y, Fujiyama A, Tsuda M**, Kurokawa K** "Design and Experimental Application of a Novel Non-Degenerate Universal Primer Set that Amplifies Prokaryotic 16S rRNA Genes with a Low Possibility to Amplify Eukaryotic rRNA Genes" *DNA Research* doi: 10.1093/dnares/dst052 (2013)
5. Goda A*, Maruyama F*, Michi Y**, Nakagawa I, Harada K "Analysis of the factors affecting the formation of the microbiome associated with chronic osteomyelitis of the jaw" *Clinical Microbiology and Infection* in press 2013.
6. Masuda S*, Hori K, Maruyama F, Ren S, Sugimoto S, Yamamoto N, Mori H, Yamada T, Sato S, Tabata S, Ohta H, Kurokawa K. "Whole-Genome Sequence of the Purple Photosynthetic Bacterium *Rhodovulum sulfidophilum* strain W4" *Genome Announcements* in press 2013.
7. Okada K*, Roobthaisong A, Swaddiwudhipong W, Hamada S, Chantaroj S. "Vibrio cholerae O1 Isolate with Novel Genetic Background, Thailand-Myanmar" *EMERGING INFECTIOUS DISEASES*. Volume 19, Number 6-June 2013.
8. Watanabe T*, Nozawa T, Aikawa C, Amano A, Maruyama F**, Nakagawa I. "CRISPR regulation of intraspecies diversification by limiting IS transposition and intercellular recombination." *GENOME BIOLOGY AND EVOLUTION*. 2013;5(6):1099-114. doi: 10.1093/gbe/evt075.
9. Takamatsu D*, Maruyama F*. "Diversity and Universality of Capsular Polysaccharide Synthesis Gene Clusters in *Streptococcus suis*." *Appl Environ Microbiol.* in press 2013.
10. Okura M*, Takamatsu D**, Maruyama F**, Nozawa T, Nakagawa I, Osaki M, Sekizaki T, Gottschalk M, Kumagai Y, Hamada S. "Genetic Analysis of Capsular Polysaccharide Synthesis Gene Clusters from All Serotypes of *Streptococcus suis*: Potential Mechanisms for the Generation of Capsular Variation." *Appl Environ Microbiol.* 79(8):2796-806 (2013)
11. Minegishi K*, Aikawa C*, Furukawa A, Watanabe T, Nakano T, Ogura Y, Ohtsubo Y, Kurokawa K, Hayashi T, Maruyama F**, Nakagawa I, Eishi Y. "Complete Genome Sequence of *Propionibacterium acnes* Isolate from sarcoidosis patient." *Genome Announc.* 1(1). pii: e00016-12. (2013)

Molecular Immunology

1. Staffs and Students

Professor	Miyuki AZUMA	
Associate Professor	Shigenori NAGAI (Sept.~)	
Assistant Professor	Tatsukuni OHNO	
Adjunct instructor	Hiroshi KIYONO	Masaaki HASHIGUCHI
	Yosuke KAMIMURA	Takeshi AZUMA (Oct.~)
Graduate Students (Doctor)	Chenyang ZHANG	Arundhati C. BHINGARE
	Siwen KANG	Syogo MAEKAWA
	Yuta KONDO	Hirunwidchayarat Worawalun (Oct.~)
Research Student	Doan Thi TOA (~Sept.)	Niken Adiba Nadya (Oct.~)
Secretary	Hatsue TADANO	

2. 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. Research Subjects

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

4. Publications

Original Article

1. Ueno T, Yeung MY, McGrath M, Yang S, Zaman N, Snawder B, Padera RF, Magee CN, Gorbato R, Hashiguchi M, Azuma M, Freeman GJ, Sayegh MH, Najafian N. Intact B7-H3 signaling promotes allograft proliferation through preferential suppression of Th1 effector responses. *Eur J Immunol* 42:2343-53, 2013.
2. Schmiedel BJ, Scheible CA, Neubling T, Kopp H, Wirths S, Azuma M, Schneider P, Jung G, Grosse-Hovest L, Salih HR. RANKL expression, function and therapeutic targeting in multiple myeloma and chronic lymphocytic leukemia. *Cancer Res* 73: 683-694, 2013.
3. Schmiedel BJ, Nuebling T, Steinbacher J, Malinowska A, Wende CM, Azuma M, Schneider P, Grosse-Hovest L, Salih HR. Rreceptor activator for NF-kB ligand in acute myeloid leukemia: expression, function and modulation of NK cell immunosurveillance. *J Immunol* 190:821-31, 2013.
4. Kamijo S, Takeda H, Tokura T, Suzuki M, Inui K, Hara M, Matsuda H, Matsuda A, Oboki K, Ohno T, Saito H, Nakae S, Sudo K, Suto H, Ichikawa S, Ogawa H, Okumura K, Takai T. IL-33-mediated innate response and adaptive immune cells contribute to maximum responses of protease allergen-induced allergic airway inflammation. *J Immunol* 190:4489-99, 2013.
5. Van der Werf N, Redpath SA, Azuma M, Yagita H, Taylor MD. Th2 cell-intrinsic hypo-responsiveness determines susceptibility to helminth infection. *PLOS Pathogens* 62:2859-60, 2013.
6. Pauken KE, Jenkins MK, Azuma M, Fife BT. PD-1, but not PD-L1, expressed by islet-reactive CD4+ T cells suppresses infiltration of the pancreas during type 1 diabetes. *Diabetes* 62:2859-60, 2013.
7. Saha A, Aoyama K, Taylor PA, Koehn BH, Vestrta RG, Panoskaltis-Mortari A, Munn DH, Murphy WJ, Azuma M, Yagita H, Fife B, Sayegh MH, Najafian N, Ahme R, Freeman GJ, Sharpe AH, Blazar BR. Host programmed death ligand-1 is dominant over programmed death ligand-2 expression in regulating graft-versus-host disease lethality *Blood* 122:3062-73, 2013.
8. Baghdadi M, Yoneda A, Yamashina T, Nagao H, Komohara Y, Nagai S, Akiba H, Foretz M, Yoshiyama H, Kinoshita I, Dosaka-Akita H, Takeya M, Viollet B, Yagita H, Jinushi M. TIM-4 glycoprotein-mediated degradation of dying tumor cells by autophagy leads to reduced antigen presentation and increased immune tolerance. *Immunity* 39:1070-81, 2013.
9. Murakami R, Denda-Nagai K, Hashimoto SI, Nagai S, Hattori M, Irimura T. A unique dermal dendritic cell subset that skews the immune response toward Th2. *PLoS One* 8:e73720, 2013.

10. Yoshida H, Kotani H, Kondo T, Tani I, Wei X, Tsuruta S, Kimura A, Asakawa M, Ito M, Nagai S, Yoshimura A. CDK inhibitors suppress Th17 and promote iTreg differentiation, and ameliorate experimental autoimmune encephalomyelitis in mice. *Biochem Biophys Res Commun* 435:378-84, 2013.

Review articles:

1. Nagai S, Kurebayashi Y, Koyasu S. Role of PI3K/Akt and mTOR complexes in Th17 differentiation. *Ann N Y Acad Sci* 280:30-34, 2013.
2. Kurebayashi Y, Nagai S, Ikejiri A, Koyasu S. Recent advances in understanding the molecular mechanisms of the development and function of Th17 cells. *Genes Cells* 18:247-65, 2013.
3. Nakae S, Morita H, Ohno T, Arae K, Matsumoto K, Saito H. Role of interleukin-33 in innate-type immune cells in allergy. *Allergol Int* 62:13-20, 2013.

Advanced Biomaterials

1. Staffs and Students

Professor	Motohiro Uo	
Associate Professor	Toshio Hongo	
Assistant Professor	Hideo Nakamura,	Takahiro Wada
Graduate Student	Maho Shiozawa,	Yuya Asakawa,
	Koottathape Natthavoot	
Special Non-matriculated Graduate Student		Tomoko Sugiyama

2. Purpose of 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. Research subjects:

1. 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. 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.

4. Publications

Original Articles

1. Uo M., Nakajima Y., Asakawa Y., Wada T., Hongo T., Soga K., Koga Y.: I Rare earth oxide containing filler for dental composite resin. *Key Engineering Materials*, 529, 512-515, 2013
2. Shiozawa M., Takahashi H., Finger W. J., Iwasaki N.: Effects of the space for wash materials on sulcus depth reproduction with addition-curing silicone using two-step putty-wash technique. *Dent Mater J.*, 32(1), 150-155, 2013
3. Shiozawa M., Takahashi H., Iwasaki N.: Fluoride release and mechanical properties after 1-year water storage of recent restorative glass ionomer cements. *Clin Oral Investig.*, 2013 Aug 22. [Epub ahead of print]
4. Shiozawa M., Takahashi H., Iwasaki N., Uo M.: Effect of calcium chloride solution immersion on surface hardness of restorative glass ionomer cements. *Dent Mater J.*, 32(5), 828-833, 2013
5. Asakawa Y., Takahashi H., Kobayashi M., Iwasaki N.: Effect of components and surface treatments of fiber-reinforced composite posts on bond strength to composite resin. *Journal of the Mechanical Behavior of Biomedical Materials*, 26, 23-33, 2013
6. Bando K. K., Wada T., Miyamoto T., Miyazaki K., Takakusagi S., Koike Y., Inada Y., Nomura M., Yamaguchi A., Gott T., Oyama S. T., Asakura K.: Combined in Situ QXAFS and FTIR Observation of a Ni Phosphide Catalyst - Determination of Active Species for a Hydrodesulfurization Reaction -, *Photon Factory Activity Report 2011 PART A*, 29, 32 - 33, 2013

Diagnostic Oral Pathology

1. Staffs and Students

Associate Professor	Toshiyuki IZUMO	
Visiting Lecturer	Norihiko OKADA	
Hospital Staff	Yuka HIROTA,	Yuuichi YAMADA,
	Kiyoko NAGUMO,	Kana NANBA,
	Kana ENDOU,	Akiko ASANO,
	Mayuko MINAMI,	Yukiko Kuroki

2. Purpose of Education

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

3. Research Subjects

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

4. Clinical Services

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

5. Publications

Original Article

1. Sakamoto K, Morita KI, Shimada Y, Omura K, Izumo T, Yamaguchi A. Peripheral odontogenic keratocyst associated with nevoid basal cell carcinoma syndrome: a case report. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2013 Dec 10. pii: S2212-4403(13)00523-3. doi: 10.1016/j.oooo.2013.09.015.
2. Kudo T, Shimazu Y, Yagishita H, Izumo T, Soeno Y, Sato K, Taya Y, Aoba T. Three-dimensional reconstruction of oral tongue squamous cell carcinoma at invasion front. *Int J Dent.* 2013;2013:482765. doi: 10.1155/2013/482765.

Organic Biomaterials

1. Staffs and Students

Professor	Nobuhiko YUI	
Assistant Professor	Ji-Hun SEO	
Assistant Professor	Atsushi TAMURA	
Secretary	Nanae NISHI	
Graduate Students	Nanako YOKOYAMA, Go IKEDA, Yuuki BABA, Kei NISHIDA,	Hajime TANAKA, Yasuaki OIKE, Hayato TONEGAWA, Mayu FUSHIMI

2. Purpose of Education

Training the synthetic route and evaluating method for preparing organic biomaterials, and its performance as a useful tool for regulating cellular responses

3. Research Subjects

1) Design of dynamic biomaterials surfaces

Biomaterials surfaces with dynamic properties are designed by utilizing a molecularly movable architecture of polyrotaxanes, and examined their effects on a variety of interactions such as protein adsorption, cell adhesion, proliferation, and differentiation.

2) Modulation of cellular function by dynamic ligand-polymers

Biomaterials and nanoparticles surfaces bearing biologically active ligands-introduced polyrotaxanes are designed, and examined the effects of the ligand movability in multivalent interactions with receptor proteins on cellular surfaces and the subsequent events such as intracellular signaling.

3) Induction of cellular function by intracellularly functionalizing supermolecule-biomolecule complexes.

Cytocleavable polyrotaxanes are designed by introducing intracellularly cleavable linkages into the polyrotaxanes, and investigated their degradable function in the intracellular delivery of nucleic acids and proteins.

4) Therapy of inherited metabolic disorders by biocleavable polyrotaxanes.

The function of intracellular release of threaded cyclodextrins from polyrotaxanes is utilized for the treatment of lysosomal storage diseases. To date, biocleavable polyrotaxanes are revealed to improve the abnormal cholesterol accumulation in Niemann-Pick type C disease.

4. Publications

Original Article

- 1) Yokoyama N., Seo J. H., Tamura A., Sasaki Y., Yui N. Tailoring the supramolecular structure of aminated polyrotaxanes toward enhanced cellular internalization. *Macromol. Biosci.* in press.
- 2) Fukumoto I., Tamura A., Matsumura M., Miura H., Yui N. Sensitization potential of dental resins: 2-hydroxyethyl methacrylate and its water-soluble oligomers have immunostimulatory effects. *PLoS ONE* 8(11): e82540, 2013.
- 3) Kakinoki S., Yui N., Yamaoka T. Platelet responses to dynamic biomaterial surfaces with different poly(ethylene glycol) and polyrotaxane molecular architectures constructed on gold substrates. *J. Biomater. Appl.* 28(4): 544-551, 2013.
- 4) Tamura A., Ikeda G., Seo J. H., Tsuchiya K., Yajima H., Sasaki Y., Akiyoshi K., Yui N. Molecular logistics using cytocleavable polyrotaxanes for the reactivation of enzymes delivered in living cells. *Sci. Rep.* 3: 2252, 2013.
- 5) Kakinoki S., Seo J. H., Inoue Y., Ishihara K., Yui N., Yamaoka T. A large mobility of hydrophilic molecules at the outmost layer controls the protein adsorption and adhering behavior with the actin fiber orientation of human umbilical vein endothelial cells. *J. Biomater. Sci. Polym. Ed.* 2(11): 1320-1332, 2013.
- 6) Tamura A., Yui N. A supramolecular endosomal escape approach for enhancing gene silencing of siRNA using acid-degradable cationic polyrotaxanes. *J. Mater. Chem. B* 1(29): 3535-3544, 2013.
- 7) Seo J. H., Kakinoki S., Inoue Y., Yamaoka T., Ishihara K., Yui N. Inducing rapid cellular response on RGD-binding

- threaded macromolecular surfaces. *J. Am. Chem. Soc.* 135(15): 5513-5516, 2013.
- 8) Seo J. H., Kakinoki S., Inoue Y., Nam K., Yamaoka T., Ishihara K., Kishida A., Yui N. The significance of hydrated surface molecular mobility in the control of the morphology of adhering fibroblasts. *Biomaterials* 34(13): 3260-3214, 2013.
 - 9) Seo J. H., Sakai K., Yui N. Adsorption state of fibronectin on poly(dimethylsiloxane) surfaces with varied stiffness can dominate adhesion density of fibroblasts. *Acta Biomater.* 9(3): 5493-5501, 2013.
 - 10) Tamura A., Yui N. Cellular internalization and gene silencing of siRNA polyplexes by cytoleavable cationic polyrotaxanes with tailored rigid backbones. *Biomaterials* 34(10): 2480-2491, 2013.
 - 11) Nagahama K., Aoki R., Saito T., Ouchi T., Ohya Y., Yui N. Enhanced stereocomplex formation of enantiomeric polylactides grafted on a polyrotaxane platform. *Polym. Chem.* 4(6): 1769-1773, 2013.
 - 12) Seo J. H., Yui N. The effect of molecular mobility of supramolecular polymer surfaces on fibroblast adhesion. *Biomaterials* 34(1): 55-63, 2013.
 - 13) Seo J. H., Kakinoki S., Yamaoka T., Yui N. Movable polyrotaxane surfaces for modulating cellular adhesion via specific RGD-integrin binding. *Adv. Sci. Tech.* 86: 59-62, 2013.

Books

- 1) Tamura A., Nagasaki Y. Environmentally-responsive nanogels for siRNA delivery. *Advanced Delivery and Therapeutic Application of RNAi*, Chang K, Mahato R. I. Ed., John Wiley & Sons, pp 207-224 (2013).

Functional Materials (Material-based Medical Engineering)

1. Staffs and Students

Associate Professor Tsuyoshi KIMURA
 Graduate Student Naoko NAKAMURA, PingLi WU,
 Mitsuki UEKI

2. Purpose of 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. Research Subjects

1) 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.

2) 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.

3) 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.

4. Clinical Services

The development of functional molecules can provide novel materials for the clinical application such as blood vessel, cornea, skin, or bone. Unlike the conventional materials which have been used in clinics so far, it would be possible to promote or suppress specific biological response using functionalized materials. Furthermore, the screening essential drug compound for certain purpose, it would help the patients to be treated with higher efficiency and less pain.

5. Publications

Original Article

- 1) Ji-HunSeo, S. Kakinoki, Y. Inoue, K. Nam, T. Yamaoka, K. Ishihara, A. Kishida, N. Yui, The significance of hydrated surface molecular mobility in the control of the morphology of adhering fibroblasts, *Biomaterials* 34(13):3206-3214, 2013.
- 2) N. Murakami, N. Wakabayashi, R. Matsushima, A. Kishida, Y. Igarashi, Effect of high-pressure polymerization on mechanical properties of PMMA denture base resin, *J. Mech. Behav. Biomed. Mater.*20:98-104, 2013.
- 3) N. Katoh, A. T. Kawaguchi, A. Kishida, T. Yamaoka, Static Cardiomyoplasty With Synthetic Elastic Net Suppresses Ventricular Dilatation and Dysfunction After Myocardial Infarction in the Rat: A Chronic Study, *Artif. Organs* 37(7):593-599, 2013.
- 4) T. Kimura, A. Sano, K. Nam, K. Akiyoshi, Y. Sasaki, A. Kishida, Improvement of Antisense Oligonucleotides Delivery Using High Hydrostatic Pressurized Lipoplex, *Proceedings of 2012 MRS fall meeting MRS Proceedings*, vol 1498
- 5) Y. Sawa, E. Tatsumi, T. Tsukiya, K. Matsuda, K. Fukunaga, A. Kishida, T. Masuzawa, G. Matsumiya, A. Myoui, M. Nishimura, T. Nishimura, T. Nishinaka, E. Okamoto, *Journal of Artificial Organs 2012: the year in review*, *Journal of Artificial Organs* 16(1): 1-8, 2013.

Oral Radiation Oncology

1. Staffs and Students

Professor	Masahiko MIURA	
Assistant Professor	Atsushi KAIDA	
Graduate Students(Doctor)	Tatsuki GOTOU,	Asumi HONDA
	Chisato YAMADA,	Eri TSUCHIDA
	Kouhei OKUYAMA,	Taito ASAHINA
Graduate Students(Mastor)	Shifumi DEGUCHI,	Itumi OOMORI
Research Associate	Rieko MATSUDA	
International Researcher	Lian XUE	

2. Purpose of 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.

3. Research Subjects

- 1) Visualization of tumor radioresponse by molecular imaging
- 2) Radiosensitization mechanism by novel anti- microtubule agents
- 3) Radioresistant signal transduction pathways
- 4) Radiotherapy for oral cancer

4. Clinical Services

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.

5. Publications

Original article

1. Kaida A, Miura M: Visualizing the effect fo tumor microenvironments on radiation-induced cell kinetics in multicellular spheroids consisting of HeLa cells. *Biochem Biophys Res Commun*. 439:453-458 (2013)
2. Yuasa-Nakagawa K, Shibuya H, Yoshimura R, Miura M, Watanabe H, Kishimoto S, Omura K. Cervical lymph node metastasis from early-stage squamous cell carcinoma of the oral tongue. *Acta Otolaryngol*. 133: 544-551 (2013)

Book

1. Miura M: Basic of radiation oncology, Stomatology. 4-10 Radiotherapy, Concept fo radiotherapy. p377-385, Asakura Publishing Co., Ltd. (2013)
2. Miura M: Radiation action to tumor. Radiation effect on human body. p395-402 Ishiyaku Publishers, Inc. (2013)
3. Miura M: Biology of tumor radiotherapy. Cutting edge of radiotherapy for gynecologic cancer. p889-895 Kanehara & Co., Ltd. (2013)

Oral and Maxillofacial Surgery

1. Staffs and Students (April, 2013)

Professor	Ken OMURA	
Associate Professor	Hiroyuki HARADA	
Junior Associate Professor	Yuji KABASAWA, Eriko MARUKAWA	
Assistant Professor	Minoru IKUTA,	Hiroaki SHIMAMOTO,
	Masaru SATO,	Fumihiko TSUSHIMA,
	Kae TANAKA,	Hirofumi TOMIOKA
Project Junior Associate Professor	Keiichi MORITA	
Graduate Student	Junpei SHIRAKAWA,	Atsushi KIMURA,
	Pradit RUSHATAMUKAYANUNT,	
	Namiaki TAKAHARA,	Aya NAKANO,
	Seiichiro ODA,	Dilruba AKTER,
	Yu OIKAWA,	Yusuke ONOZATO,
	Toru TAKEMOTO,	Yuko YAMAGATA

2. 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.

3. Research Subjects

- 1) Development of multidisciplinary treatment of oral cancer.
- 2) Clinical study on sentinel node navigation surgery for oral cancer.
- 3) Study on molecular markers for lymph node metastasis of oral cancer.
- 4) Clinical study on skeletal and dental changes after distraction osteogenesis in patients with cleft lip and palate.
- 5) Clinical study on maxillomandibular skeletal and dental changes after orthognatic surgery.
- 6) Study on neurosensory disturbances using the heat flux technique.
- 7) Clinical study on pre-surgical nasoalveolar molding in patients with cleft lip and palate.
- 8) Clinical study on alveolar bone grafting with platelet rich plasma.
- 9) Multidisciplinary treatment of temporomandibular disorders.
- 10) Clinical and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 11) Development of multidisciplinary treatment of oral mucosal diseases.

4. Clinical Services

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

5. Publications

Original Article

1. Yuasa-Nakagawa K, Shibuya H, Yoshimura R, Miura M, Watanabe H, Kishimoto S, Omura K: Cervical lymph node metastasis from early-stage squamous cell carcinoma of the oral tongue. *Acta Otolaryngol* 133(5):544-551, 2013.
2. Koizumi A, Matsushima E, Mochizuki Y, Omura K, Amagasa T: Changes in the psychological characteristics of oral cancer patients in the perioperative period: a quantitative evaluation. *J Med Dent Sci* 60(1):41-53 2013.

3. Kudoh M, Harada H, Omura K, Ishii Y: Epidermoid cyst arising in the submandibular region. *Case Rep Med.* 2013;419289, 2013.
4. Harada H, Omura K, Tomioka H, Nakayama H, Hiraki A, Shinohara M, Yoshihama Y, Shintani S: Multicenter phase II trial of preoperative chemoradiotherapy with S-1 for locally advanced oral squamous cell carcinoma. *Cancer Chemother Pharmacol.* 71(4): 1059-1064, 2013.
5. Mochizuki Y, Omura K, Tanaka K, Sakamoto K, Yamaguchi A: Myoepithelioma of the parotid gland presenting as a retroauricular cutaneous nodule: A case report. *J Clin Diagn Res* 7(6):1165-8, 2013.
6. Sato K, Lee JW, Sakamoto K, Iimura T, Kayamori K, Yasuda H, Shindoh M, Ito M, Omura K, Yamaguchi A: RANKL synthesized by both stromal cells and cancer cells plays a crucial role in osteoclastic bone resorption induced by oral cancer. *Am J Pathol.* 182(5): 1890-1899, 2013.
7. Shimada Y, Morita K, Kabasawa Y, Taguchi T, Omura K: Clinical manifestations and treatment for keratocystic odontogenic tumors associated with nevoid basal cell carcinoma syndrome: a study in 25 Japanese patients. *J Oral Pathol Med.* 42(3):275-80, 2013.
8. Shimada Y, Katsube K, Kabasawa Y, Morita K, Omura K, Yamaguchi A, Sakamoto K: Integrated genotypic analysis of hedgehog-related genes identifies subgroups of keratocystic odontogenic tumor with distinct clinicopathological features. *PLoS One.* 8(8): e70995, 2013.
9. Takahashi Y, Marukawa E, Omura K: Application of a new material (β -TCP/collagen composites) in extraction socket preservation: an experimental study in dogs. *Int J Oral Maxillofac Implants.* 28(2): 444-52, 2013.
10. Yoshida K, Sumita Y, Marukawa E, Harashima M, Asahina I: Effect of platelet-rich plasma on bone engineering with an alloplastic substitute containing BMP2. *Biomed Mater Eng.* 23(3): 163-172, 2013.

Oral and Maxillofacial Radiology

1. Staffs and Students (April, 2013)

Professor	Tohru KURABAYASHI	
Associate Professor	Hiroshi WATANABE	
Junior Associate Professor	Naoto OHBAYASHI,	Norio YOSHINO
Assistant Professor	Akemi TETSUMURA,	Shin NAKAMURA,
	Ami KURIBAYASHI,	Junichiro SAKAMOTO
Hospital Staff	Yoshikazu NOMURA,	Tadanobu ARAGAKI
Graduate Student	Kamrun NAHAR,	Kretapirom KORNKAMOL,
	Akira TAKAHASHI,	Madoka SUZUKI,
	Yoshihiro OZAKI,	Lam Dai PHONG,
	Shinya KOTAKI	
Secretary	Izumi MOTOHASHI	

2. Purpose of Education

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. Research Subjects

- 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.

4. Clinical Services

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.

5. Publications

Original Article

1. Hikita R, Miyamoto JJ, Ono T, Honda E, Kurabayashi T, Moriyama K. Activation patterns in the auditory association area involved in glottal stop perception. *J Oral Biosci* 55: 34-39, 2013.
2. Imaizumi A, Kodama S, Sakamoto J, Sasaki Y, Otonari-Yamamoto M, Kuribayashi A, Kurabayashi T, Sano T. Imaging findings of benign peripheral nerve sheath tumor in jaw. *Oral Surg Oral Med Oral Pathol Oral Radiol* 116: 369-76, 2013.
3. Kamrun N, Tetsumura A, Nomura Y, Yamaguchi S, Baba O, Nakamura S, Watanabe H, Kurabayashi T. Visualization of the superior and inferior borders of the mandibular canal: a comparative study using digital panoramic radiographs and cross-sectional computed tomography images. *Oral Surg Oral Med Oral Pathol Oral Radiol* 115: 550-7, 2013.
4. Kretapirom K, Okochi K, Nakamura S, Tetsumura A, Ohbayashi N, Yoshino N, Kurabayashi T. MRI characteristics of rheumatoid arthritis in the temporomandibular joint. *Dentomaxillofac Radiol* 42: 31627230, 2013.
5. Kuribayashi A, Imaizumi A, Tetsumura A, Yoshino N, Kurabayashi T. Magnetic resonance imaging of myoepithelioma in the salivary glands. *Oral Radiol* 29: 87-91, 2013.
6. Momin MA, Kurabayashi T, Yosue T. Quantitative and morphological evaluation of cancellous and cortical bone of the mandible by CT. *OMICS J Radiology* 3: 1000155, 2013.
7. Nakamura S, Toriihara A, Okochi K, Watanabe H, Shibuya H, Kurabayashi T. Optimal timing of post-treatment [¹⁸F]fluorodeoxyglucose (18F-FDG)-PET/computed tomography (CT) to identify tumor recurrence, nodal metastasis,

- and distant metastasis for surveillance and discuss the optimal timing of 18F-FDG-PET/CT examination after the completion of treatment for head and neck malignancy. *Nucl Med Commun* 34: 162-7, 2013.
8. Nomura Y, Watanabe H, Shirotzu K, Honda E, Sumi Y, Kurabayashi T. Stability of voxel values from cone-beam computed tomography for dental use in evaluating bone mineral content, *Clin Oral Implants Res* 24: 543-8, 2013.
 9. Ozaki Y, Watanabe H, Nomura Y, Honda E, Sumi Y, Kurabayashi T. Location dependency of the spatial resolution of cone-beam computed tomography for dental use. *Oral Surg Oral Med Oral Pathol Oral Radiol* 116: 648-655, 2013.
 10. Pal SK, Sakamoto K, Aragaki T, Akashi T, Yamaguchi A. The expression profiles of acidic epithelial keratins in ameloblastoma. *Oral Surg Oral Med Oral Pathol Oral Radiol* 115: 523-31, 2013.
 11. Sasaki Y, Sakamoto J, Otonari-Yamamoto M, Nishikawa K, Sano T. Potential of fluid-attenuated inversion recovery MRI as an alternative to contrast-enhanced MRI for oral and maxillofacial vascular malformations: experimental and clinical studies. *Oral Surg Oral Med Oral Pathol Oral Radiol* 116: 503-510, 2013.
 12. Takahashi A, Watanabe H, Honda E, Sumi Y, Kurabayashi T. Localizing the mandibular canal on dental CT reformatted images: usefulness of panoramic views. *Surg Radiol Anat* 35: 803-809, 2013.
 13. Toriihara A, Nakamura S, Kubota K, Makino T, Okochi K, Shibuya H. Can dual-time-point 18F-FDG PET/CT differentiate malignant salivary gland tumors from benign tumors? *AJR Am J Roentgenol* 201: 639-44, 2013.
 14. Yuasa-Nakagawa K, Shibuya H, Yoshimura R, Miura M, Watanabe H, Kishimoto S, Omura K. Cervical lymph node metastasis from early-stage squamous cell carcinoma of the oral tongue. *Acta Otolaryngol* 133: 544-51, 2013.

Anesthesiology and Clinical Physiology

1. Staffs and Students (April, 2013)

Professor	Haruhisa Fukayama	
Associate Professor	Hikaru Kohase	
Junior Associate Professor	Shigeharu Jinnō	
Assistant Professors	Fumihiko Yoshikawa, Ryo Wakita(OCT,1~),	Tomoyuki Miyamoto, Tomoka Matsumura(~SEP,30).
Hospital Staffs	Yuka Oono, Haruka Haida, Kanako Saji, Ayako Mizutani, Syuku Kumasaka.	Saori Oogami, Tomoka Matsumura(OCT,1~), Atsushi Nakajima, Hitomi Suzuki,
Graduate Students	Tomoko Ebisawa-Matsushita, Katsuhiko Matsumoto, Takutoshi Inoue.	Takuya Funayama, Yoko Sasaki,
Research Students	Tatsuya Harada	
Secretary	Natsu Sato	

2. Purpose of Education

The goal of the section is to give to the undergraduate students; the knowledge and techniques of general anesthesia, local anesthesia, systemic management of medically compromised patients, and pain management of clinic in the oral and maxillofacial regions. Within a fiscal year the lectures include 1) general and local anesthesia, 2) psychosedation, 3) cardiopulmonary resuscitation. General anesthesia is composed of physiology of respiration and circulation, pharmacodynamics of inhalation anesthetics, intravenous anesthetics, and muscle relaxants. Psychosedation includes theory and technique for dentally phobic patients and medically compromised patients. Since local anesthesia is often used in routine dental procedures, pharmacology of local anesthetics, techniques and complications are given to the undergraduate students. Cardiopulmonary resuscitation has principles of CPR, updated guidelines of CPR, in addition to simulated training. Out training systems also include infiltration anesthesia, conduction anesthesia, and nitrous oxide inhalation sedation.

3. Research Subjects

- 1) Noninvasive drug delivery system
- 2) Development of local anesthesia techniques for dentistry
- 3) Neuropathic pain in oral and maxillofacial regions
- 4) Diffuse noxious inhibitory control
- 5) Clinical applications of psychosedation and systemic management

4. Clinical Services

- 1) Systemic management of medically compromised patients using psychosedation
- 2) Ambulatory anesthesia service for disabled patients
- 3) Emergencies in the hospital
- 4) Low invasive local anesthesia

5. Publications

Original Article

1. Saji K, Ikeda Y, Kim W, Shingai Y, Tateno A, Takahashi H, Okubo Y, Fukayama H, and Suzuki H. Acute NK1 receptor antagonist administration affects reward incentive anticipation processing in healthy volunteers. *International Journal of Neuropsychopharmacology*, 2013 Aug;16(7):1461-71,2013.
2. Nakajima A, Wakita R, Haida H, Fukayama H: Efficacy of Lidocaine Iontophoresis Using Either Alternating or Direct Current in Hairless Rats. *J Med Dent Sci*. 2013 Sep 30;60(3):63-71, 2013.
3. Oono Y, Baad-Hansen L, Wang K, Arendt-Nielsen L, Svensson P. Effect of conditioned pain modulation on trigeminal somatosensory function evaluated by quantitative sensory testing. *Pain* 154: 2684-90, 2013.
4. Oono Y, Wang K, Atiş ES, Arendt-Nielsen L. Thermal application modulates orofacial somatosensory perception in

healthy men and women. *Clin Neurophysiol* 124: 581-588, 2013.

5. Fumihiko Yoshikawa, Yoh Tamaki, Hisa Okumura, Zenzo Miwa, Masaaki Ishikawa, Kazuhiro Shimoyama, Zenkou Nakamura, Hitomi Kunimori, Shigeharu Jinno, Hikaru Kohase, Haruhisa Fukayama. Risk Factors With Intravenous Sedation for Patients With Disabilities. *Anesth Prog.* 2013 Winter; 60(4): 153-161.
6. Townsend EA, Zhang Y, Xu C, Wakita R, Emala CW. Active Components of Ginger Potentiate β -Agonist-Induced Relaxation of Airway Smooth Muscle by Modulating Cytoskeletal Regulatory Proteins. *Am J Respir Cell Mol Biol.* 2014 Jan;50(1):115-24.

Congresses

1. Yoshikawa F, Sumi Y, Nishimura M, Togashi K, and Fukayama H : Anesthetic Effect of Water-Soluble Edible Film Containing Surface Anesthetics. IADR/AADR General Session. Seattle. March 21, 2013.
2. Tomoko Ebisawa, Katsuhiko Matsumoto, Atsushi Nakajima, Haruka Haida, Shizuka Ando, Tomohiko Yoshioka, Toshiyuki Ikoma, Junzo Tanaka, and Haruhisa Fukayama : Calcium Alginate gel as electrode material for iontophoresis of lidocaine. The 7th International Conference on the Science and Technology for Advanced Ceramics (STAC-7), Yokohama, Japan, 19-21 June, 2013.
3. Fukayama H: New devices for local anesthesia in dentistry. MANDALAY DENTAL CONFERENCE 2013, Myanmar, July, 2013.
4. Fukayama H: Painless local anesthesia. The 6th Annual Meeting of Federation of Asian Dental Anesthesiology Societies, The 13th Annual Meeting of the Korean Dental Society of Anesthesiology, Seoul Korea, July, 2013.
5. Oono Y, Wang K, Baad-Hansen L, Futarmal S, Ogami S, Matsumoto K, Fukayama H, Kohase H, Svensson P, Arendt-Nielsen L. Conditioned pain modulation in temporomandibular disorders patients. The 8th Congress of the European Federation of IASP Chapters (EFIC), Florence, Italy, October, 2013.
6. Atis ES, Wang K, Oono Y, Arendt-Nielsen L. Effect of local cooling on jaw-stretch reflex of masseter muscle of healthy human. In: Abstracts of the Annual Meeting of the Society for Neuroscience, Society for Neuroscience, Neuroscience, San Diego, CA, USA. 9-13 November, 2013.
7. Ebisawa T, Matsumoto K, Nakajima A, Haida H, Ando S, Yoshioka T, Ikoma T, Tanaka J, and Fukayama H : AC Iontophoresis of Lidocaine with Alginic-Acid Gel Electrodes, International Symposium on EcoTopia Science 2013 (SETS '13), Nagoya, Japan, 13-15 December, 2013.
8. T. Matsumura, Y. Ikeda, K. Kubota, S. Jinno, H. Fukayama. Intravenous Sedation for Dental Patients with Previous Methamphetamine Psychosis. IADR/AADR/CADR General Session & Exhibition - Seattle, Washington, USA, 2013.
9. Townsend EA, Zhang, Y, Xu C, Wakita R, Emala CW. Active Constituents Of Ginger Potentiate β -Agonist-Induced Relaxation of Airway Smooth Muscle. American Thoracic Society International Conference, Philadelphia USA, 5.13-22. 2013.

Orofacial Pain Management

1. Staffs and Students (April, 2013)

Professor	Masahiko SHIMADA	
Assistant Professor	Yoko YAMAZAKI	
Hospital Staff	Tomoko TAKAHASHI,	Yuko ANDOH,
	Daisuke TOMIZAWA	
Graduate Student	Akitoshi HOSODA,	Hiroko IMURA,
	Nguyen Ho QUYNH ANH	

2. Purpose and Education

Orofacial Pain Management is a branch of dental science which deals with dental anesthesiology. Main objective of orofacial pain management in the graduate course is to provide students opportunity to study the pain, abnormal sensation, sensory paralysis, abnormal movement and motor paralysis in the orofacial area and the treatment for the patients of orofacial pain.

3. Research Subjects

- 1) New Treatment methods for neuropathic pain
- 2) Analyses of abnormal orofacila pain
- 3) Study on Biological Response to Dental Interventions
- 4) Analyses and new treatment of dysgeusia

4. Clinical Services

Orofacial Pain Clinic is concerned with the pain, abnormal sensation, sensory paralysis, abnormal movement and motor paralysis. Management of orofacial pain clinic is pharmacotherapy, nerve block, stimulation of the pheripheral nerves including acupuncture and psychotherapies.

5. Publication

Original Article & Clinical report

1. Yamazaki Y, Niimi T, Ando Y, Tomizawa D. and Shimada M. Necessity of Magnetic Resonance Imaging (MRI) using an appropriate sequence for diagnosis of trigeminal neuralgia associated with intracranial tumor. Open Journal of Stomatology, 3, 510-514, 2013 Dec.
2. Kohjitani, A. Miyawaki T., Shimada M., Sugiyama K.; Features of Lateral Cephalograms Associated With Difficult Laryngoscopy in Japanese Children Undergoing Oral and Maxillofacial Surgery, Pediatric Anesthesia, 23(11),994-1001, 2013.

Pediatric Dentistry

1. Staffs and Students (April, 2013)

Junior Associate Professor	Yoshiaki ONO,	Zenzo MIWA
Assistant Professor	Yoshiaki HASHIMOTO, Haruko FUJITA,	Michiyo MIYASHIN, Mizuho MOTEGI
Hospital Staff	Yuki IMAMURA(~March), Makiko TAKASHI, Atsushi OISHI, Naoko UEHARA(April~)	Satoko KAKINO, Yukie NAKAJIMA, Sachi GOTOH,
Graduate Student	Seiko OHBA(~March), Ayako NAKANE, Daiki HORIKAWA, Tomoki UEHARA, Ganbold KHONGORZUL(October~), Shen DONGHE(October~)	Kaori SHOI(~March), Taki SEKIYA, Sachiko ITOH, Kuniomi NAKAMURA(April~),
Part-time Lecturer	Youichiro SHIMADA, Nomutaka ISOKAWA, Mitsuro TANAKA,	Keiichi TAKEI, Hitoyata SHIMOKAWA, Yoshiharu MUKAI

2. Purpose of Education

Pediatric dentistry is a subject of clinical dentistry that deal with education and research of not only developmental oral health sciences but also prevention and treatment methods of the diseases which disturb oro-facial growth and development of children. The main objective of pediatric dentistry in this graduate course is to provide students an opportunity to study the theory and the method for the guidance of the oro-facial growth and development and for the diagnosis, prevention and treatment of diseases and malfunctions which disturb the oro-facial growth and development during the period of childhood.

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

3. Research Subjects

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

4. Clinical Services

The pediatric dentistry clinic in the department of oro-facial development and function provides the comprehensive dental treatment for a child while growing. The examination, diagnosis, and treatment of the oral diseases and the oral abnormalities are performed in the clinic. In addition, health guidance, preventive measures, and the long-term oral health management by the periodical checking system are carried out, in order to keep and promote oral health from infant to adult.

5. Publication

Original Article

1. Nassar M, Hiraishi N, Shimokawa H, Tamura Y, Otsuki M, Kasugai S, Ohya K, Tagami J. The inhibition effect of non-protein thiols on dentinal matrix metalloproteinase activity and HEMA cytotoxicity. *J Dent.* 2013 December 4. doi: 10.1016/j.jdent.2013.11.023. PMID: 24316344 [Epub ahead of print]
2. Sriarj W, Aoki K, Ohya K, Takahashi M, Takagi Y, Shimokawa H. TGF- beta in dentin matrix extract induces osteoclastogenesis in vitro. *Odontology* 2013 December 24. DOI 10.1007/s10266-013-0140-3 PMID: 24366403 [Epub ahead of print]
3. Pluemsakunthai P, Kuroda S, Shimokawa H, Kasugai S. A basic analysis of platelet-rich fibrin: distribution and release of platelet-derived growth factor-BB. *Inflammation and Regeneration.* 33 (3), 164-172, 2013.
4. Haga N, Kubota M, Miwa Z. Epidemiology of Hereditary Sensory and Autonomic Neuropathy Type IV and V in Japan. *American Journal of Medical Genetics Part A.* 161A:871-874, 2013.
5. Yoshikawa F, Tamaki Y, Okumura H, Miwa Z, Ishikawa M, Shimoyama K, Nakamura Z, Kunimori H, Jinno S, Kohase H, Fukayama H. Risk Factors with Intravenous Sedation for Patients with Disabilities. *Anesth Prog.* 60(4), 153-161, 2013.
6. Kakino S, Kushibiki S, Yamada A, Miwa Z, Takagi Y, Matsuura Y. Optical Measurement of Blood Oxygen Saturation of Dental Pulp. *ISRN Biomedical Engineering.* Vol. 2013, Article ID 502869, 2013.
7. Oishi A, Terashima T, Miyashin M, Takagi Y. Repair process of experimental root fractures in rat molars examined by histopathological techniques and 3D micro-CT imaging. *Pediatric Dental Journal,* 23, 8-15, 2013.

Orthodontic Science

1. Staffs and Students

Professor	Takashi ONO	
Associate Professor		
Junior Associate Professor	Yoshiro MATSUMOTO, Jun HOSOMICHI(Apr-)	Zuisei KANNO
Assistant Professor	Jun HOSOMICHI (-Mar), Ippei WATARI, Ikuo YONEMITSU,	Kazuo SHIMAZAKI, Satoshi KOKAI, Takayoshi ISHIDA (Apr-)
Graduate Students	Haruki IMAI (-Mar), Sarina KOIKE (-Mar), Takeru KYURAGI (-Mar), Yukiha FUNAKI, Hidemasa OKIHARA, Arisa SAWADA, Jutiporn PRIVATANANUPUNT, Jui-Chin HSU, Toshihiro IMAMURA, Mutsumi MIYAZAKI, Kulthida NUNTHAYANON, Souma KITA, Tomomi SAKAGUCHI, Hiroyuki YAMAGUCHI, Wei-Jen LAI, Yukano FUKUSHIMA (Apr-), Takuya OGAWA (Apr-), Karin Harumi UCHIMAKOECKLIN (Apr-), Akemi KANAGUCHI (Sep-),	Takako KANESHIMA (-Mar), Sachiko KOMORI (-Mar), Chisa SHITANO (-Mar), Ayako KAWABE, Rieko ONO, Emina WAKASUGI, Yuhei IKEDA, Minami MIYASAKA, Asuka OKITOU, Syuji OISHI, Yoichiro KUMA, Mio MAKIGUCHI, Jin-Gyu AN, Yasunori ABE (Apr-), Yuki KASAHARA (Apr-), Iku SHIBATA (Apr-), Velusamy PAVETHY NATH (Sep-)
Graduate School Research Students	Yukiko KURODA (-Mar), Maya HIRANUMA, Mariko MIZUMACHI (-Mar), Haruki IMAI (Apr-), Sarina KOIKE (Apr-), Chisa SHITANO (Apr-), Syusuke UESUGI, Junpei SUZUKI, Misako KOKETSU (Apr-), Katsuhiko SUZUKI (Apr-), Karin Harumi UCHIMA KOECKLIN (-Mar), Yusuke TAKATSU(-Sep), Daisuke TOMITA	Ikuko HATTORI (-Mar), Chiho KATO (-Mar), Keiichi SAKAI, Takako KANESHIMA (Apr-), Takeru KYURAGI (Apr-), Ayako KIRII, Tomonari MATSUMURA, Kyohei YAMADA, Takahiro SHIMAMINE (Apr-), Huan TANG (Sep-), Satoshi KURUSU,

2. Purpose of Education

Orthodontics 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.

Subjects of Education:

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.

3. 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

4. Clinical Service

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.

With the cooperation of related field, we also 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.

5. Publications

Original Articles

1. Usumi-Fujita R, Hosomichi J, Ono N, Shibutani N, Kaneko S, Shimizu Y, Ono T: Occlusal hypofunction causes periodontal atrophy and VEGF/VEGFR inhibition in tooth movement. *Angle Orthod* 83:48-56, 2013.
2. Shindoi JM, Matsumoto Y, Sato Y, Ono T, Harada K: Soft tissue cephalometric norms for orthognathic and cosmetic surgery. *J Oral Maxillofac Surg* 71:24-30, 2013.
3. Hikita R, Miyamoto JJ, Ono T, Honda E, Kurabayashi T, Moriyama K: Activation patterns in the auditory association area involved in glottal stop perception. *J Oral Biosci* 55:34-39, 2013.
4. Kapila S, Park Y, Ahmad N, Hosomichi J, Hayami T, Tacon C: Mechanisms for Relaxin's Modulation of MMPs and Matrix Loss in Fibrocartilages. *Ital J Anat Embryol* 118:62-65, 2013.
5. Ohmori H, Ono T: Unilateral scissors bite treated with a removable plate that incorporates a Ti-Ni wire. *Orthodontics* 14:222-226, 2013.
6. Koike S, Sujino T, Ohmori H, Shimazaki K, Fukuyama E, Kanai T, Hibi T, Ono T: Gastric emptying rate in subjects with malocclusion examined by [13C] breath test. *J Oral Rehabil* 40:574-581, 2013.
7. Shimizu Y, Ishida T, Hosomichi J, Kaneko S, Hatano K, Ono T: Soft diet causes greater alveolar osteopenia in the mandible than in the maxilla. *Arch Oral Biol* 58:907-911, 2013.

8. Imai H, Tanaka Y, Nomura N, Tsutsumi Y, Doi H, Kanno Z, Ohno K, Ono T, Hanawa T: Three-dimensional quantification of susceptibility artifacts from various metals in magnetic resonance images. *Acta Biomater* 9:8433-8439, 2013.
9. Ishida T, Yabushita T, Ono T: Functional reversibility of temporomandibular joint mechanoreceptors. *Arch Oral Biol* 58:1078-1083, 2013.
10. Hiranuma M, Kokai S, Fujita K, Ishida T, Shibata M, Naito S, Yabushita T, Ono T: Effects of a liquid diet on the response properties of temporomandibular joint nociceptive neurons in the trigeminal subnucleus caudalis of growing rats. *Orthod Craniofac Res* 16:214-222, 2013.
11. Ishida T, Yoon HS, Ono T: Asymmetrical distalization of maxillary molars with zygomatic anchorage, improved superelastic nickel-titanium alloy wires, and open-coil springs. *Am J Orthod Dentofacial Orthop* 144:583-593, 2013.
12. Shitano C, Baba O, Kaneko S, Hosomichi J, Shimizu Y, Shibutani N, Usumi R, Takano Y, Ono T: Alveolar bone loss induced by the orthodontic tooth movement under hypofunctional conditions in rats. *Orthod Waves* 72:148-155, 2013.

Books

1. Abbassy MA, Watari I, Bakry AS, Ono T. Chapter 15, The effect of type 1 Diabetes Mellitus on the dento-craniofacial complex. *Type 1 Diabetes*. (Eds. Escher AP, Li A), In Tech, pp.401-430, 2013.

Cariology and Operative Dentistry

1. Staffs and Students (April, 2013)

Professor	Junji Tagami	
Associate Professor	Masayuki Otsuki,	Yoshiyuki Sasaki
Junior Associate Professor	Toru Nikaido,	Masatoshi Nakajima
Assistant Professor	Takako Yoshikawa,	Yasushi Shimada,
	Yuichi Kitasako,	Go Inoue,
	Keiichi Hosaka,	Tomohiro Takagaki,
	Naoko Harada,	Rena Takahashi
Specially Appointed Junior Associate Professor	Syozi Nakashima,	Alireza Sadr
Specially Appointed Assistant Professor	Noriko Hiraishi,	NHM Khairul Matin
Hospital Staff	Masahiro Takahashi,	Oto Aramaki,
	Hidenori Hamba,	Tomoko Mizutani,
	Iori Sugita	
Foreign Researcher	Ilnaz Hariri,	Patricia Makishi
Secretary	Shiori Ogi,	Noriyo Yamada
Graduate Student	Gerardo Jose Joves Mendez,	Suppason Thittaweerat,
	Turki Abdulsam Bakhsh,	Azusa Tanaka,
	Kiminori Kainose,	Mona Mohammad Mandurah,
	Md. Sofiqul Islam,	Haidil Akmal Mahdan,
	Ena Lodha,	Upoma Guha,
	higeyuki Nagai,	Mohannad Nassar,
	Naoko Matsui,	Ikumi Wada,
	Yumiko Uesugi,	Nariaki Yoshimine,
	Megumi Oshima,	Ornnicha Thanatvarakorn,
	Alaa Turkistani,	Teerapong Mamanee,
	Sahar Jameel Khunkar,	Ka Kyou,
	Ehab Zaki Alsayed,	Junichi Shinagawa,
	Rena Oguro,	Takahide Ibusuki,
	Asami Aida,	Ayaka Chiba,
	Kei Horie,	Tomoka Ueno,
	Hiroki Tezuka,	Kento Sato,
	Takaaki Sato,	Masami Arai,
	Maria Nakamura,	Ritsuko Mashiko,
	Alaa Turkistani,	Teerapong Mamanee,
	Sahar Jameel Khunkar,	Kong Kalyan,
	Baba Bista,	Maria Jacinta Rosario Hernandez Romero,
	Patrycja Zakilna Majkut,	Rui Guan,
	Ayaka Kusanagi,	Yuka Tsuda,
	Takashi Hatayama,	Chihiro Matsuura,
	Yukinori Kano,	Yuuki Naruse,
	Juri Hayashi,	Miho Sugiura,
	Yuta Sumitani,	Atsuko Tagami,
	Keiki Nakamura,	Yukari Noda,
	Mari Okada,	Yuan Zhou,
	Keita Taguchi,	Jorge Espigares,
	Junji Atomura,	Thwe Zin Ei,
	Hamed Atrgiran Yazdi	
Research Student	Shinji Ogura,	Mineo Kijima,
	Yuichiro Mitsui	

2. Purpose of 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.

3. Research Subject

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) 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.

5) 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), which has shown a great potential for such assessment.

6) 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.

7) 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.

8) 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.

9) 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.

10) Characterization of polymerization characteristics of light-cured resin composites

Aiming to establish appropriate clinical techniques to overcome polymerization shrinkage stress of composite resins, we have investigated the influence of the adhesives, composite resins, light irradiation methods and cavity configuration (C-factor) on the development of polymerization shrinkage stress using various techniques such as optical coherence tomography (OCT) and micro-focus X-ray computed tomography (micro-CT).

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.

4. Clinical Service

Operative Dentistry clinic provide restoration of teeth with fillings for dental cavities, trauma and tooth wear, and root canal treatments.

5. Publications

Original Articles

1. Bakhsh TA, Sadr A, Shimada Y, Mandurah MM, Hariri I, Alsayed EZ, Tagami J, Sumi Y. (2013). Concurrent evaluation of composite internal adaptation and bond strength in a class-I cavity. *J Dent* 41(1), 60-70.
2. Bista B, Sadr A, Nanazri A, Shimada Y, Sumi Y, Tagami J. (2013). Non-destructive assessment of current one-step self-etch dental adhesives using optical coherence tomography. *J Biomed Opt* 18(7), 76020.
3. Chui C, Aoki A, Takeuchi Y, Sasaki Y, Hiratsuka K, Abiko Y, Izumi Y. (2013). Antimicrobial effect of a-PDT using high power blue LED and red dye agent on *Porphyromonas gingivalis*. *J Periodontal Res* 48(6), 696-705.
4. Emamieh S, Sadr A, Ghasemi A, Torabzadeh H, Akhavanzanjani V, Tagami J. (2013). Effects of solvent drying time on mass change of three adhesives. *J Conserv Dent* 16(5), 418-22.
5. Epasinghe DJ, Yiu CK, Burrow MF, Hiraishi N, Tay FR. (2013). The inhibitory effect of proanthocyanidin on soluble and collagen-bound proteases. *J Dent* 41(9), 832-9.
6. Gando I, Ariyoshi M, Ikeda M, Sadr A, Nikaido T, Tagami J. (2013). Resistance of dentin coating materials against abrasion by toothbrush. *Dent Mater J* 32(1), 68-74.
7. Hiraishi N, Tochio N, Kigawa T, Otsuki M, Tagami J. (2013). Monomer-collagen interactions studied by saturation transfer difference NMR. *J Dent Res* 92(3), 284-8.
8. Hiraishi N, Sono R, Sofiqul I, Yiu C, Nakamura H, Otsuki M, Takatsuka T, Tagami J. (2013). In vitro evaluation of plant-derived agents to preserve dentin collagen. *Dent Mater* 29(10),1048-54.
9. Hariri I, Sadr A, Nakashima S, Shimada Y, Tagami J, Sumi Y. (2013). Estimation of the enamel and dentin mineral content from the refractive index. *Caries Res* 47(1), 18-26.
10. Imamura Y, Otsuki M, Sadr A, Tagami J. (2013). Effect of CPP-ACP and sodium fluoride on prevention of re-staining after bleaching. *Asian Pac J Dent* 13(2), 47-55.
11. Joves GJ, Inoue G, Nakashima S, Sadr A, Nikaido T, Tagami J. (2013). Mineral density, morphology and bond strength of natural versus artificial caries-affected dentin. *Dent Mater J* 32(1), 138-43.

12. Kirihara M, Inoue G, Nikaido T, Ikeda M, Sadr A, Tagami J. (2013). Effect of fluoride concentration in adhesives on morphology of acid-base resistant zones. *Dent Mater J* 32(4), 578-84.
13. Li N, Nikaido T, Sadr A, Takagaki T, Chen J-H, Tagami J. (2013). Phosphoric acid-etching promotes bond strength and formation of ABRZ on enamel. *Oper Dent* 38(1), 82-90.
14. Mahdan MHA, Nakajima M, Foxton RM, Tagami J. (2013). Combined effect of smear layer characteristics with hydrostatic pulpal pressure on dentine bond strength of HEMA-free and -containing one-step adhesives. *J Dent* 41(10), 861-71.
15. Mandurah MM, Sadr A, Shimada Y, Kitasako Y, Nakashima S, Bakhsh TA, Tagami J, Sumi Y. (2013). Monitoring remineralization of enamel subsurface lesions by optical coherence tomography. *J Biomed Opt* 18(4), 046006.
16. Moosavi H, Hariri I, Sadr A, Thitthaweerat S, Tagami J. (2013). Effects of curing mode and moisture on nanoindentation mechanical properties and bonding of a self-adhesive resin cement to pulp chamber floor. *Dent Mater* 29(6), 708-17.
17. Mita H, Kitasako Y, Takagaki T, Sadr A, Tagami J. (2013). Development and evaluation of a low-erosive apple juice drink with Phosphoryl-Oligosaccharides of Calcium. *Dent Mater J* 32(2), 212-8.
18. Nakagawa H, Sadr A, Shimada Y, Tagami J, Sumi Y. (2013). Validation of swept source optical coherence tomography (SS-OCT) for the diagnosis of smooth surface caries in vitro. *J Dent* 41(1), 80-9.
19. Nassar M, Hiraishi N, Islam MS, Aizawa M, Tamura Y, Otsuki M, Kasugai S, Ohya K, Tagami J. (2013). Effect of phytic acid used as etchant on bond strength, smear layer, and pulpal cells. *Eur J Oral Sci* 121(5), 482-7.
20. Nazari A, Sadr A, Campillo-Funoller M, Nakashima S, Shimada Y, Tagami J, Sumi Y. (2013). Effect of hydration on assessment of early enamel lesion using swept-source optical coherence tomography. *J Biophotonics* 6(2), 171-7.
21. Nazari A, Sadr A, Saghiri MA, Campillo-Funollet M, Hamba H, Shimada Y, Tagami J, Sumi Y. (2013). Non-destructive characterization of voids in six flowable composites using swept-source optical coherence tomography. *Dent Mater* 29(3), 278-86.
22. Nazari A, Sadr A, Shimada Y, Tagami J, Sumi Y. (2013). 3D assessment of void and gap formation in flowable resin composites using optical coherence tomography. *J Adhes Dent* 15(3), 237-43.
23. Nishitani Y, Hosaka K, Hoshika T, Yoshiyama M, Pashley DH. (2013). Effects of chlorhexidine in self-etching adhesive: 24 hours results. *Dent Mater J* 32(3), 420-4.
24. Sadr A, Mandurah M, Nakashima S, Shimada Y, Kitasako Y, Tagami J, Sumi Y. (2013). Monitoring of enamel lesion remineralization by optical coherence tomography: an alternative approach towards signal analysis. *Proc SPIE*. 8566: 2-8.
25. Sakano W, Nakajima M, Prasansuttiorn T, Foxton RM, Tagami J. (2013). Polymerization behavior within adhesive layer of self-etch adhesives: A micro-Raman spectroscopic study. *Dent Mater J* 32(6), 992-8.
26. Shimizu A, Nakashima S, Nikaido T, Sugawara T, Yamamoto T, Momoi Y. (2013). Newly developed hardness testing system, "Cariotester": measurement principles and development of a program for measuring Knoop hardness of carious dentin. *Dent Mater J* 32(4), 643-7.
27. Takahashi M, Nakajima M, Tagami J, Scheffel DL, Carvalho RM, Mazzoni A, Cadenaro M, Tezvergil-Mutluay A, Breschi L, Tjäderhane L, Jang SS, Tay FR, Agee KA, Pashley DH. (2013). The importance of size-exclusion characteristics of type I collagen in bonding to dentin matrices. *Acta Biomater* 9(12), 9522-8.
28. Takahashi R, Jin J, Nikaido T, Tagami J, Hickel R, Kunzelmann KH. (2013). Surface characterization of current composites after toothbrush abrasion. *Dent Mater J* 32(1), 75-82.
29. Thanatvarakorn O, Nakashima S, Sadr A, Prasansuttiorn T, Thitthaweerat S, Tagami J. (2013). Effect of a calcium-phosphate based desensitizer on dentin surface characteristics. *Dent Mater J* 32(4), 615-21.
30. Thepyou R, Chanmitkul W, Thanatvarakorn O, Hamba H, Chob-Isara W, Trairatvorakul C, Tagami J. (2013). Casein phosphopeptide-amorphous calcium phosphate and glass ionomer show distinct effects in the remineralization of proximal artificial caries lesion in situ. *Dent Mater J* 32(4), 648-53.
31. Thitthaweerat S, Nakajima M, Foxton RM, Tagami J. (2013). Effect of solvent evaporation strategies on regional bond strength of one-step self-etch adhesives to root canal dentin. *Int Endod J* 46(11), 1023-31.
32. Yoshikawa T, Morigami M, Sadr A, Tagami J. (2013). Acceleration of curing of resin composite at the bottom surface using slowstart curing methods. *Dent Mater J* 32(6), 999-1004.
33. Utaka S, Nakashima S, Sadr A, Ikeda M, Nikaido T, Shimizu A, Tagami J. (2013). Cariotester, a new device for assessment of dentin lesion remineralization in vitro. *Dent Mater J* 32(2), 241-7.

Fixed Prosthodontics

1. Staffs and Students(April, 2013)

Professor	Hiroyuki MIURA	
Associate Professor	Keiichi YOSHIDA	
Junior Associate Professot	Daizo OKADA,	Wataru KOMADA
Assistant Professor	Chiharu SHIN,	Kumiko KAWASHIMA(to March),
	Shiho OTAKE,	Kenichi GOSHIMA,
	Koichiro YUSA,	Naosuke KUMAGAE,
	Reiko OGURA(from April)	
Graduate Student	Satoshi OMORI(to March),	Reina NEMOTO(to March),
	Sachi MAKINO(to March),	Ning XU,
	Yoji UEDA,	Izumi FUKUMOTO,
	Tasuku INAGAKI,	Rie FUJITA,
	Hiroyuki OKAMOTO,	Miho SATO,
	Fujino OSHIMA,	Kyoshi MATSUKAWA,
	Luo SIYANG,	Yoko ISHIKAWA,
	Natsuko IWATA,	Mariko KUBO,
	Kazuhisa FUJITA,	Hideto MATSUI,
	Risa YAMADA,	Paisankobrit Vibul(from October),
	Bakhit Mohammed Yassin M(from October)	

2. Purpose of Education

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

3. Research Subjects

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

4. Clinical Services

- 1) Clinic for prosthodontics (Prosthodontics practice clinic)

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

2) Clinic for dental allergy (Dental allergy clinic)

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

5. Publications

Original Article

1. Omori S, Komada W, Yoshida K, Miura H: Effect of thickness of zirconia-ceramic crown frameworks on strength and fracture pattern. *Dent Mater J.* 32(1), 189-194, 2013.
2. Nemoto R, Nozaki K, Fukui Y, Yamashita K, Miura H : Effect of framework design on surface strain of zirconia fixed partial dentures. *Dent Mater J*, 32(2), 289-295, 2013.
3. Makino S, Okada D, Shin C, Ogura R, Ikeda M and Miura H: Evaluation of the occlusal contact of crowns fabricated with the bite impression method. *J Med Dent Sci*, 60(3), 74-81, 2013.
4. Fukumoto I, Tamura A, Matsumura M, Miura H, Yui N: Sensitization potential of dental resins: 2-hydroxyethyl methacrylate and its water-soluble oligomers have immunostimulatory effects. *PLoS One*, Nov 29, 8(11), e82540, 2013.
5. Xu N, Shin C, Fukui Y, Omori S, Otake S, Nemoto R, Komada W, Kumagae N, Yoshida K, Miura H: The effect of prolonged holding time in firing schedules on the bond strength between the zirconia core and veneered porcelain. *Asian Pac J Dent*, 13, 19-25, 2013.

Pulp Biology and Endodontics

1. Staffs and Students (April 2013)

Professor	Hideaki SUDA	
Associate Professor	Mitsuhiro SUNAKAWA	
Junior Associate Professor	Atsushi TAKEDA,	Hideharu IKEDA
Assistant Professor	Arata EBIHARA,	Nobuyuki KAWASHIMA,
	Hiroyuki MATSUMOTO,	Reiko WADACHI,
	Noriyuki SUZUKI,	Sstoshi WATANABE,
	Jun KAWAMURA	
Graduate Student	Zhou MENGYU,	Kei KOMATSU,
	Kana MIYARA,	Mioko YAMAMOTO,
	Jindan PIAO,	Kazuto HURUHATA,
	Saliman AIERKIN,	Jie GU,
	Yoshiko IINO,	Shintaro URABA,
	Daisuke TOKITA,	Takeo TAZAWA,
	Kanako YAO,	Nami TAKASHINO,
	Alamuddin Bakhit	

2. Purpose of Education

The aim of the course is to train and educate graduate dental students so that they can act as leading clinical scientists, researchers or practitioners of endodontics in the world. 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 pulp biology, neuroscience, bacteriology, immunology and material 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. The graduates from this course are expected to disseminate new principles and techniques on endodontics among general dental practitioners and endodontic specialists.

3. Research Subjects

- 1) Defense systems in the dental pulp/periapical tissue
- 2) Regulation of periapical bone destruction in apical periodontitis
- 3) Dental pulp stem cells/ Differentiation of pulp cells/ Horizon of pulpal regeneration
- 4) Root canal irrigation
- 5) Development of new apex locators
- 6) Strain produced in the root canal wall dentin
- 7) Application of medicaments to endodontics
- 8) Evaluation of endodontic technique using computational fluid dynamics(CFD)
- 9) Histochemical study using cultured mandible tissue model
- 10) Application of laser to endodontics
- 11) Application of optical coherence tomography
- 12) Analysis of nickel-titanium endodontic instruments
- 13) Electrophysiological approach to cell-to-cell couplings between odontoblasts
- 14) Diffusion through enamel and dentin
- 15) Lymphangiogenesis in the dental pulp
- 16) Neuro-scientific research for dental pain
- 17) Diagnosis using CBCT
- 18) Logistic regression equation to screen for vertical root fractures using cone-beam CT (3DX)
- 19) Global Center of Excellence (GCOE) Program
“International Research Center for Molecular Science in Tooth and Bone Diseases”
- 20) Molecular biological approach to the alveolar bone resorption associated with pulpal diseases

4. Clinical Services

Pulp Biology and Endodontics is in charge of the Endodontic Clinic in our Dental Hospital, and offers the global standard

of endodontics to our patients. The representative treatments provided in our clinic are as follows:

- Diagnosis and treatment of pulpal and periapical diseases
- Protective procedures for the dental pulp
- Nonsurgical endodontic treatment
- Surgical endodontic treatment
- Bleaching discolored teeth
- Restoration of endodontically treated teeth

The latest development of endodontics is remarkable as seen in root canal instrumentation by super-elastic NiTi rotary files, root canal length measurement with newly developed electronic apex locators, diagnosis by cone beam computed tomography, and microendodontics by using a surgical microscope. Especially, microendodontics has dramatically changed conventional “blind” endodontics into more predictable endodontics by efficient and reliable procedures under a lightened and magnified view. Also, we seek to provide evidence-based endodontic treatment based on our clinical research.

5. Publications

Original articles

1. Hitoshi Sakaue, Kei Komatsu, Toshihiko Yoshioka, Hitomi Ishimura, Arata Ebihara, Hideaki Suda : Evaluation of coronal leakage and pathway of dye leakage after obturation with various materials for open apical foramina. *Dental Materials Journal*, 32(1):130-137, 2013.
2. Toshihiko Yoshioka, Hitoshi Sakaue, Hitomi Ishimura, Arata Ebihara, Hideaki Suda, Yasunori Sumi : Detection of root surface fractures with swept-source optical coherence tomography(SS-OCT). *Photomedicine and laser surgery*, 31(1):23-27, 2013.
3. Kana MIYARA, Yoshio YAHATA, Yohsuke HAYASHI, Yusuke TSUTSUMI, Arata EBIHARA, Takao HANAWA, Hideaki SUDA : The influence of heat treatment on the mechanical properties of Ni-Ti file materials. *Dental Materials Journal*, in press.
4. Wei S, Kawashima N, Suzuki N, Xu J, Takahashi S, Zhou M, Koizumi Y, Suda H : Kinetics of Th17-related cytokine expression in experimentally induced rat periapical lesions. *Aust Endod J*. 39(3):164-170, 2013.
5. Yu Koizumi, Kawashima N, Yamamoto M, Takimoto K, Zhou M, Suzuki N, Saito M, Harada H, Suda H : Wnt11 expression in rat dental pulp and promotional effects of Wnt signaling on odontoblast differentiation. *Congenital Anomalies*, 53:101-108. 2013.
6. Tomoatsu Kaneko, Uraivan Chokechanachaisakul, Jun Kawamura, Yusuke Yamanaka, Takafumi Ito, Mitsuhiro Sunakawa, Hideaki Suda, and Takashi Okiji : Up-regulation of p38 Mitogen-activated Protein Kinase during Pulp Injury-induced Glial Cell/Neuronal Interaction in the Rat Thalamus. *Journal of endodontics*, 39(4):488 – 492, 2013.
7. Ikeda H, Suda H : Odontoblastic syncytium through electrical coupling in the human dental pulp. *Journal of Dent Res*, 92(4):371-375, 2013.
8. Ikeda H, Suda H : Facilitatory Effect of AC-Iontophoresis of Lidocaine Hydrochloride on the Permeability of Human Enamel and Dentine in Extracted Teeth. *Archives of Oral Biology*, 58(4): 341-347, 2013.
9. Li Y, Ikeda H, Suda H : Measurement of the Functional Space for Hydrodynamic Fluid Movement in Rat Dentine Using Fluorescent Microspheres. *Archives of Oral Biology*, 58(7): 780-787, 2013.
10. Yamamoto M, Kawashima N, Takashino N, Koizumi Y, Takimoto K, Suzuki N, Saito M, Suda H: Three-dimensional spheroid culture promotes odonto/osteoblastic differentiation of dental pulp cells. *Archives of Oral Biology*, 59(3):310-317, 2014. *Arch Oral Biol*. 2014.

Removable Partial Prosthodontics

1. Staffs and Students (April, 2013)

Professor	Yoshimasa IGARASHI	
Associate Professor	Kenji FUEKI	
Junior Associate Professor	Takeshi UENO	
Assistant Professor	Masayuki SATO,	Ichirou MINAMI,
	Teruyasu NAKAMURA,	Jyuro WADACHI,
	Syusuke INUKAI,	Eiko YOSHIDA,
	Junnichirou WADA,	Natsuko MURAKAMI
Hospital Staff	Yuka ABE,	Kouta OKANO,
	Aiichirou AO,	Yuuki IWAKI,
	Kengo FUJIKI,	Atsushi TAKAICHI,
	Yasuhiro TSUBOTA,	Hironari HAYAMA
Secretary	Yoko FUKI	
Graduate Student	Kazuhito SHOUI, T	akashi SEKINISHI,
	Yuusuke TOYOSHIMA,	Ryo HAYASHI,
	Natsuki SUZUKI,	Ryousuke HARAKAWA,
	James LEE,	Yuuki ARAI,
	Hiroyuki ISHIYAMA,	Yuka KAJIMA,
	Hayato KUMAGAI,	Chiaki TSUTSUMI,
	Yasuha NOGAWA,	Kazuyuki HANNDA,
	Teisuke AKIMOTO,	Hideaki INAGAWA,
	Yuka INAMOCHI,	Naruyuki SUZUKI,
	Kensuke TAKAKUSAKI,	Chie YOSHIHARA,
	Chie WATANABE	

2. Purpose of Education

Removable Partial Prosthodontics is a section in the department of Oral Health Sciences specializing restoration of lost teeth, related oral structures, and oral functions with partial dentures designed and constructed to be removed. Our main educational goals are: (1) that dental students in the graduate courses learn the standard diagnostic procedures, technical skills, and basic clinical skills and knowledge related to removable partial dentures through lectures and practical training, and (2) that they acquire literacy to develop them in clinical situations.

3. Research Subjects

- 1) Association between occlusal curvature and masticatory function.
- 2) Exploration and evaluation of factors for jaw movement smoothness.
- 3) Genetic, psychological, and behavioral factors for sleep bruxism.
- 4) Influence of mechanical stimulation on osteoclast localization in the mouse maxilla.
- 5) Bone integration capability of surface-treated titanium implants.
- 6) Dimensional accuracy of optical bite registration in Cerec CAD/CAM system.
- 7) Application of finite element analysis to dental prosthesis design.
- 8) Improvement and clinical application of materials for removable partial dentures.

4. Clinical Services

National dental health surveys showed that the mean number of missing teeth is decreasing steadily and that the percentage of edentulous people is also declining. These findings suggest that management of partial edentulism in patients with compromised oral or general health status will be increasingly important in industrialized countries. The section of Removable Partial Prosthodontics specializes restoration of lost teeth, related oral structures, and oral functions with partial dentures designed and constructed to be removed. Our primary goal of treatment is to restore patients' quality of life by removable partial dentures designed for each individual patient.

5. Publications

Original Article

1. Ao A, Wakabayashi N, Nitta H, Igarashi Y. Clinical and microbiologic effects of lingual cervical coverage by removable partial dentures. *Int J Prosthodont.* 26: 45-50, 2013.
2. Fueki K, Yoshida E, Igarashi Y. Association between occlusal curvature and food comminution and mixing in human young adults with permanent dentitions. *Arch Oral Biol.* 58: 377-383, 2013.
3. Fueki K, Yoshida E, Okano K, Igarashi Y. Association between occlusal curvature and masticatory movements with different test foods in human young adults with permanent dentitions. *Arch Oral Biol.* 58: 674-580, 2013.
4. Fujiki K, Aoki K, Marcian P, Borak L, Hudieb M, Ohya K, et al. The influence of mechanical stimulation on osteoclast localization in the mouse maxilla: bone histomorphometry and finite element analysis. *Biomech Model Mechanobiol.* 12: 325-333, 2013.
5. Imakita C, Shiota M, Yamaguchi Y, Kasugai S, Wakabayashi N. Failure Analysis of an Abutment Fracture on Single Implant Restoration. *Implant Dent.* 22: 326-331, 2013.
6. Iwaki Y, Wakabayashi N, Igarashi Y. Dimensional Accuracy of Optical Bite Registration in Single and Multiple Unit Restorations. *Oper Dent.* 38: 309-315, 2013.
7. Minami I, Akhter R, Albersen I, Burger C, Whittle T, Lobbezoo F, Peck CC, Murray GM. Masseter Motor Unit Recruitment is Altered in Experimental Jaw Muscle Pain. *J Dent Res.* 92: 143-148, 2013.
8. Murakami N, Wakabayashi N, Matsushima R, Kishida A, Igarashi Y. Effect of high-pressure polymerization on mechanical properties of PMMA denture base resin. *J Mech Behav Biomed Mater.* 20: 98-104, 2013.
9. Ona M, Wakabayashi N, Yamazaki T, Takaichi A, Igarashi Y. The influence of elastic modulus mismatch between tooth and post and core restorations on root fracture. *Int Endod J.* 46: 47-52, 2013.
10. Takaichi A, Suyalatu, Nakamoto T, Joko N, Nomura N, Tsutsumi Y, et al. Microstructures and mechanical properties of Co-29Cr-6Mo alloy fabricated by selective laser melting process for dental applications. *J Mech Behav Biomed Mater.* 21: 67-76, 2013.
11. Wadachi J, Sato M, Igarashi Y. Evaluation of the rigidity of dentures made of injection-molded materials. *Dent Mater J.* 32: 508-511, 2013.
12. Wakabayashi N, Suzuki T. Patient-specific finite element analysis of viscoelastic masticatory mucosa. *J Dent Biomech.* 4: 1758736013483298, 2013 (doi: 10.1177/1758736013483298).
13. Weijnenberg RA, Scherder EJ, Visscher CM, Gorissen T, Yoshida E, Lobbezoo F. Two-color chewing gum mixing ability: digitalization and spatial heterogeneity analysis. *J Oral Rehabil.* 40: 737-743, 2013.
14. Yamada M, Ueno T, Minamikawa H, Ikeda T, Nakagawa K, Ogawa T. Early-stage osseointegration capability of a submicrofeatured titanium surface created by microroughening and anodic oxidation. *Clin Oral Implants Res.* 24: 991-1001, 2013.
15. Yamada M, Tsukimura N, Ikeda T, Sugita Y, Att W, Kojima N, Kubo K, Ueno T, Sakurai K, Ogawa T. N-acetyl cysteine as an osteogenesis-enhancing molecule for bone regeneration. *Biomaterials.* 34: 6147-6156, 2013.

Books

1. Minami I, Wirianski A. Chapter:9: Applications of the Accelerometer to The Human Jaw: The Assessment of Movement Smoothness. "Accelerometers: Principles, Structure and Applications." Editor: Paulo André and Humberto Varum. Nova Science Publishers, Inc. pp 215-244. 2013.

Oral Implantology and Regenerative Dental Medicine

1. Staffs and Students (April 2013)

Professor	Shohei KASUGAI	
Associate Professor	Makoto SHIOTA	
Associate Professor (Lecturer)	Noriko TACHIKAWA	
Assistant Professor	Shinji KURODA,	Motohiro MUNAKATA
Clinical Professor (Faculty of Dental)	Toshiro SUGAI	
Clinical Visiting Associate Professor	Kouji HAGINO	
Clinical Visiting Instructor	Tunezi OKADA	
Visiting Lecturer (Graduate School)	Hideaki KATSUYAMA,	Takashi OTSUKA,
	Yuzou TAKAHASHI,	
Visiting Lecturer (Faculty of Dental)	Sawako YOKOYAMA,	Tatsuya FUJIMORI,
	Nariyuki MAEZAWA,	Toru KANAI,
	Daisuke SATO,	Maho OZEKI,
	Yoko YAMAGUTI,	Hidemi NAKATA,
	Yuki SHIMIZU,	Hisatomo KONDO,
	Hidemichi KIHARA,	Yuki DATE
Dentists in Dental Implant Clinic	Aoi SAKUYAMA,	Takahiro NAKAMURA,
	Hiroshi KOBAYASHI,	Kazuhisa TSURUMI,
	Kei FUCHIGAMI,	Kazuhiro KON,
	Akiko FURUICHI,	Masaki FUJII,
	Tomoko NAGAYAMA,	
Graduate Students	Ken YUKAWA,	Maiko YAMAMOTO,
	Zayar LIN,	Miao YU,
	Pluemsakunthai WARUNEE,	Yu YAMASHITA,
	Yuki KUSUMOTO,	Minoru SANDA,
	Taiji HAMADA,	Hiroki MAEDA,
	Munemitsu MIYASAKA,	Kui ZHANG,
	You-kyoung KIM,	Kuppusamy MAHESWARI,
	Mizuki SATO,	Masaki SHIBASAKI,
	Tsuyoshi MATSUURA,	Songtao Wu, Xin WANG,
	Khaing Nyein Soe,	Moe Htet,
	Emi OKADA,	Masateru ADATI,
	DING Lin,	NGUYEN Vo Ngoc,
	BOOSANA Kaboosaya,	
Clinical research Student	Shuichi KOYAMA,	Takayuki KOMATSU,
	Hitoshi SAITO,	Tadamasa YOSHIDA,
	Toshimitu SHIGEMATSU,	Toshihiko MORIKAWA,
	Kazuhiko INOUE,	Takeshi WATANABE,
	Shuuko TAKEYAMA,	Hiroko HAYASHI,
	Arihiro IWATA,	Kilwoo AHN,
	Narumi SATO,	Yoshiko YOKOYAMA,
	Haruka KUBOTA,	Chiharu IMAKITA,
	Masahiro ISHIWATA,	Hidekazu KOTAKE,
	Haruka ITOH,	Gou INOUE,
	Seiji OHARA,	Akihiro SUZUKI,
	Tatsuya HOTTA,	Norio AKINO,
	Takayuki MIYAHARA,	Maho AKATSUKA,
	Shang GAO,	Masahiro SHIMOGISHI,
	Jyunya HAMAGUCHI,	Naoko KOBAYASHI,
	MULATI Aierken,	PHYO Thu Aung,
	TIN Htut Win Naing,	MYOE Kyaw Thet

Foreign research Student	Hao JIA,	Osama ZAKARIA
Specially Foreign research Student	Kang CHEN	
Registration Specialist Trainee	Hiroshi TURUBUTI, Tosho KOJIMA,	Ai YAMAMOTO, Kensuke FUKUTOMI,

2. Purpose of Education

Currently, oral rehabilitation with dental implant is very effective and predictable. It is absolutely important for the dental student to understand dental implant treatment compared to other modalities. Nine hours lectures for the 5th year dental students are the introduction part. Each of these students has a chance to see patient examination process and several steps of treatment planning for half a day in the dental implant clinic. Furthermore, each of the 6th year students have a chance to see surgical procedures, prosthodontic treatments and maintenance procedures. In the residential program, we accepted 9 dentists and teach them more advanced contents of dental implant treatment.

In the doctoral course of Implantology Biomaterial sciences, structural engineering, anatomical structures, diagnosis and technical innovations are overviewed. In the doctoral course of Regenerative Dental Medicine, tissue engineering concept, regeneration of soft tissue and bone and recent technological advancements in these field are overviewed.

3. Research Subjects

- Materials and structures of dental implant prostheses
- Implant design and surface modification of dental implant
- Dental implant and its surrounding tissues
- Regeneration of soft tissues
- Regeneration of bone

4. Clinical Services

In Dental Implant Clinic in the dental hospital, we treat partially or fully edentulous patients with dental implants. If soft tissue management and/or bone augmentation procedures are required, we also do these surgeries. Number of patients in Dental Implant Clinic is increasing every year and approximately 120 patients per day are treated, which is extremely over our capacities. Approximately 2,000 implants were installed in 2012. Patients with some clinical problems, who are treated in other clinics, are increasing and this is a great concern.

5. Publications

Original Articles

1. Ochi M, Kanazawa M, Sato D, Kasugai S, Hirano S, Minakuchi S. Factors affecting accuracy of implant placement with mucosa-supported stereolithographic surgical guides in edentulous mandibles. *Computer in Biology and Medicine* 43(11):1653-60, 2013.
2. Nassar M, Hiraishi N, Islam MS, Aizawa M, Tamura Y, Otsuki M, Kasugai S, Ohya K, Tagami J Effect of phytic acid used as etchant on bond strength, smear layer, and pulpal cells. *European Journal of Oral Science* 121(5):482-7, 2013.
3. Yukawa K, Tachikawa N, Munakara M, Akino N, Kasugai S. Long-term morphological evaluation of porous poly-DL-lactic acid for soft tissue augmentation. *Open Journal of Regenerative Medicine* 2 (4):106-111, 2013.
4. Gao S, Shiota M, Fujii M, Chen K, Shimogisi M, Sato M, Kasugai S. Combination of simvastatin and hydroxyapatite fiber induces bone augmentation. *Open Journal of Regenerative Medicine* 2 (3):53-60, 2013.
5. Chen K, Hao J, Noritake K, Yamashita Y, Kuroda S, Kasugai S. Effects of low intensity pulsed ultrasound stimulation on bone regeneration in rat parietal bone defect model. *Open Journal of Regenerative Medicine* 2 (1):8-14, 2013.
6. Imakita C, Shiota M, Yamaguchi Y, Kasugai S, Wakabayashi N. Failure Analysis of an Abutment Fracture on Single Implant Restoration. *Implant Dentistry* 22(4):326-331, 2013.
7. Nagayama T, Okuhara S, Ota MS, Tachikawa N, Kasugai S, Iseki S. FGF18 accelerates osteoblast differentiation by upregulating Bmp2 expression. *Congenital Anomalies* 53(2):83-8, 2013.
8. Madi M, Zakaria O, Noritake K, Fuji M, Kasugai S. Peri-implantitis progression around thin sputtered hydroxyapatite-coated implants: Clinical and radiographic evaluation in dogs. *International Journal of Oral and Maxillofacial Implants* 28(3):701-9, 2013.
9. Miyahara T, Dahlin C, Galli S, Parsafar S, Koizumi H, Kasugai S. A novel dual material mouthguard for patients

- with dental implants. *Dental Traumatology* 29(4):303-6, 2013.
10. Fujii M, Shiota M, Noritake K, Kon K, Sato H, Kasugai S. Effect of Density of Hydroxyapatite Fiber Material on Bone Regeneration in Vertical Bone Augmentation Model. *J Oral Tissue Engin* 10 (3) 115-122 2013.
 11. Chou J, Hao J, Kuroda S, Bishop D, Ben-Nissan B, Milthorpe B, Otsuka M. Bone Regeneration of Rat Tibial Defect by Zinc-Tricalcium Phosphate (Zn-TCP) Synthesized from Porous Foraminifera Carbonate Macrospheres. *Mar Drugs*. 2013 Dec 16;11(12):5148-58.
 12. Chou J, Hao J, Ben-Nissan B, Milthorpe B, Otsuka M. Coral Exoskeletons as a Precursor Material for the Development of Calcium Phosphate Drug Delivery System for Bone Tissue Engineering. *Biol Pharm Bull*. 2013;36(11):1662-5.
 13. Chou J, Hao J, Hatoyama H, Ben-Nissan B, Milthorpe B, Otsuka M. The therapeutic effect on bone mineral formation from biomimetic zinc containing tricalcium phosphate (ZnTCP) in zinc-deficient osteoporotic mice. *PLoS One*. 2013 Aug 13;8(8):e71821.
 14. Nassar M, Hiraishi N, Shimokawa H, Tamura Y, Otsuki M, Kasugai S, Ohya K, Tagami J. The inhibition effect of non-protein thiols on dentinal matrix metalloproteinase activity and HEMA cytotoxicity. *Journal of Dentistry* in press.
 15. Hao J, Acharya A, Chen K, Chou J, Kasugai S, Lang NP. Novel bioresorbable strontium hydroxyapatite membrane for guided bone regeneration. *Clinical Oral Implants Research* in press.
 16. Nassar M, Hiraishi N, Islam MS, Tamura Y, Otsuki M, Kasugai S, Ohya K, Tagami J, Tay FR. The effect of glutathione on 2-hydroxyethylmethacrylate cytotoxicity and on resin-dentine bond strength. *International Endodontic Journal* in press.
 17. Nyan M, Hao J, Miyahara T, Noritake K, Rodriguez R, Kasugai S. Accelerated and enhanced bone formation on novel simvastatin-loaded porous titanium oxide surfaces. *Clinical Implant Dentistry and Related Research* in press.
 18. Nyan M, Miyahara T, Noritake K, Hao J, Rodriguez R, Kasugai S. Feasibility of alpha tricalcium phosphate for vertical bone augmentation. *Journal of Investigative and Clinical Dentistry* in press.
 19. Madi M, Zakaria O, Kasugai S. Coated vs. uncoated implants: Bone defect configurations after progressive peri-implantitis in dogs. *Journal of Oral Implantology* in press.
 20. Gao S, Shiota M, Fujii M, Chen K, Shimogishi M, Sato M, Kasugai S. Combination of simvastatin and hydroxyapatite fiber induces bone augmentation. *Open Journal of Regenerative Medicine*. 2(3) 53-60 2013.

6. Conference Presentation

1. Kanai T, Munakata M, Okada T, Sato D, Kasugai S. A novel probing device measuring probing force to evaluate soft tissues around implants. *Academy of osseointegration 28th Annual meeting*. March 7-9, 2013, Tampa, FL.
2. Hao J, Chen K, Acharya A, Kuroda S, Kasugai S, Lang NP. Novel Bioresorbable Strontium Hydroxyapatite Membrane for Guided Bone Regeneration. *91st General Session of the IADR*, Seattle, USA, 2013 March 20-23.
3. Kasugai S. New strategy for effective, simple, less invasive and less costly bone augmentation. *The 54th Congress of the Korean Association of Oral and Maxillofacial Surgeons*. 2013.4.25-27 Hotel Inter-Burgo EXCO, Daegu, Korea.
4. Omar O, Miyahara T, Lennerås M, Palmquist A, Norlindh B, Shimoda A, Akiyoshi K, Kasugai S, Thomsen P. Cellular and Molecular Pattern of Bone Formation during Guided Bone Regeneration. *The European Chapter Meeting of the Tissue Engineering and Regenerative Medicine International Society (TERMIS-EU 2013)*, 2013. 6. 17-20, Istanbul, Turkey.
5. Yukawa K, Munakata M, Tachikawa N, Kasugai S. The attitude survey of smoking associated with periodontal and peri-implant disease. *The 10th Asia Pacific Conference on Tobacco or Health*. 2013.8.18.
6. Kasugai S. New strategy for bone augmentation: Encouraging endogenous key players and providing a space for bone regeneration. *The 2nd Meeting of International Association for Dental Research – Asia-Pacific Region* 2013.08.21-23 Plaza Athenee, Bangkok, Thailand.
7. Kasugai S. Prosthetic treatment with dental implants in posterior maxilla. *The 9th World Congress for Oral Implantology and American Academy of Implant Dentistry Global Conference* 2013.08-23-25 Millennium Seoul Hilton, Seoul, Korea.
8. Sanda M, Shiota M, Shang G, Fujii M, Kon K, Kasugai S. Capability of new bone formation in mixture of hydroxyapatite and beta-TCP granules. *Annual Scientific Meeting of the European Association of Osseointegration*. 17-19 October 2013, Dublin, Ireland.

Plastic and Reconstructive Surgery

1. Staffs and Students (April, 2013)

Professor:	Mutsumi Okazaki	
Junior Associate Professor:	Hiroki Mori	
Assistant Professor (Hospital Staff):	Satoshi Usami	
Graduate Student:	Tomoyuki Yano,	Noriko Uemura,
	Kentaro Tanaka,	Yuhki Wakimura,
	Makiko Inoue,	Takuya Higashino,
	Ktsuya Gorai,	Aki Takada,
	Hiroki Miyashita,	Yoko Maruyama

2. Purpose of Education

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

3. Research Subjects

Basic research

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

Clinical research

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

4. Clinical Services

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.

5. Publications

【Original article】

1. Tanaka K, Okazaki M. Visualization of blood supply to the 'vascularized nerve' with anterolateral thigh flap using indocyanine green fluorescence angiography. *J Plast Reconstr Aesthet Surg* 66: 146-147, 2013
2. Tanaka K, Mori H, Okazaki M, Nishizawa A, Yokozeki H. Long-term treatment outcome after only popliteal lymph node dissection for nodal metastasis in malignant melanoma of the heel: the only "interval node" dissection can be an adequate surgical treatment. *Case Reports in Oncological Medicine* 2013: 259326, 2013
3. Rodotheou P, Wang W, Itoh S, Okazaki M, Takakuda K. Laser-perforated porous nonwoven chitosan nerve conduit. *Journal of Biomechanical Science Engineering* 8: 139-151, 2013
4. Yano T, Okazaki M, Kawaguchi R, Suesada N, Tanaka K, Kishimoto S. Tongue reconstruction with minimal donor site morbidity using a deep inferior epigastric perforator (DIEP) free flap in a 6-year-old girl. *Microsurgery* 33:487-90, 2013
5. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y, Tanaka K, Okazaki M. Combined arterial reconstruction and free tissue transfer for patients with critical limb ischemia. *Ann Vasc Dis.* 6:706-10, 2013

Head and Neck Surgery

1. Staff s and Students

Professor	Seiji Kishimoto	
Junior Associate Professor	Takuro Sumi	
Senior Resident	Takao Tokumaru (~March), Fuminori Nomura, Yasuhiro Inayoshi (April~)	
Secretary	Mariko Tosa	
Graduate Student	Masakazu Miyazaki, Toru Sasaki, Tatsuo Masubuchi, Takao Tokumaru(April~)	Sadamoto Zenda, Fuminori Nomura, Yosifumi Fukushima,
Foreign student	Paiboon Sureepong(~March)	

2. Purpose of Education

In the Department of Head and Neck Surgery, our goal is to deliver the highest possible clinical care for patients with benign and malignant tumors of the head and neck.

Postgraduate residents participate in a variety of head and neck surgeries. Weekly clinical rounds help to extend the experience beyond the operating room. Tumor conferences are held weekly with a lively interdisciplinary discussion including otolaryngology, plastic surgery. They are also offered opportunity to participate in various clinical research projects.

3. Research subjects

- 1) Anatomy of the skull base.
- 2) Development of new surgical techniques in cancer treatment.
- 3) Clinical application of new device of endoscopic examination.
- 4) Surgical treatment of pediatric head and neck tumors.
- 5) Human papilloma virus infection and head and neck cancer.

4. Clinical Services

Our team treats patients with tumors of the thyroid gland, salivary glands, oral cavity, larynx, pharynx, paranasal sinus, and skull base, and sarcomas of the soft tissue and bone.

5. Publication

Original Article

1. Nakagawa K, Shibuya H, Yoshimura R, Miura M, Watanabe H, Kishimoto S, Nomura F: Cervical lymph node metastasis from early-stage squamous cell carcinoma of the oral tongue. *Acta Oto-Laryngologica*, 2013; Early Online, 1-8
2. Zenda S, Ishi S, Ichihashi T, et al. A Dermatitis Control Program (DeCoP) for head and neck cancer patients receiving radiotherapy: a prospective phase II study. *Int J Clin Oncol* 2013 Apr; 18(2): 350-55
3. Zenda S, Nakagami Y, Akimoto T, et al.: Strontium-89 (Sr-89) chloride in the treatment of various cancer patients with multiple bone metastases. *Int J Clin Oncol* 2013, in-press.
4. Yoshida K, Yamaguchi T, Natsume T, Kufe D, Miki Y.: JNK phosphorylation of 14-3-3 regulates nuclear targeting of c-Abl in the apoptotic response
5. Kishimoto S: Technique for excision of cervical schwannoma. *Masters Techniques in Otolaryngology-Head and Neck Surgery: Head and neck surgery Vol.2 Ed.P81-91*

International Congress

1. Y. Yoshino, S. Nemoto, T. Tomori, K. Miki, M. Inoue, K. Arimura, A. Tsunoda, S. Kishimoto, K. Kitamura : Endoscopically assisted direct intratumoral embolization of juvenile nasopharyngeal angiofibroma. 2nd Meeting of European Academy of ORL-HNS and CE ORL-HNS, Nice, 2013. 4.27
2. T. Homma, T. Yano, K. Tanaka, N. Suesada, M. Aoyagi, S. Kishimoto, M. Okazaki : Free flap reconstruction of huge and invasive craniofacial nasopharyngeal angiofibroma involving skull base region. 7th World Society for Reconstructive Microsurgery 2013 Congress, Chicago, July, 2013

3. T Yano, M Okazaki, N Suesada, T Honma, K Tanaka, M Aoyagi, S Kishimoto : An impact of standardization of reconstructive procedure in skull base reconstruction using free flaps, 7th World Society for Reconstructive Microsurgery 2013 Congress, Chicago, July, 2013
4. S. Kishimoto: Moderator:Panel Discussion "Management of Advanced Oropharyngeal Cancer". 20th IFOS World Congress 2013 (Seoul) June 2013
5. S Kishimoto : Chairman:Symposium-Oncology, The 8th International Symposium on Tonsils and Mucosal Barriers of the Upper Airways (ISTMB), Zurich, July 2013
6. T Sugimoto, S Kishimoto, K Kawada, Y Kiyokawa, T Okada, J Swangsri, T Sumi, T Tokumaru, F Nomura. Symposium: Hypopharyngeal cancer "Transoral Resection of Hypopharyngeal Cancer". The 3rd ASHNO Congress (Cebu, Philippines), 2013.3.21
7. S Kishimoto, T Sugimoto, A Tsunoda, T Sumi, M Aoyagi, Y Kawano, T Yano, K Tanaka : Symposium: Paranasal sinuses & Skull Base Surgery "Skull Base Surgery for Sinonasal Malignant Tumor". The 3rd ASHNO Congress (Cebu, Philippines), 2013.3.21
8. S Kishimoto, T Sugimoto, A Tsunoda, M Aoyagi, Y Kawano, T Yano, K Tanaka : Symposium: Other Head & Neck Cancers "Pediatric Head and Neck Malignancy with Skull Base Invasion". The 3rd ASHNO Congress (Cebu, Philippines), 2013.3.21
9. A Tsunoda, S Kishimoto. Symposium: Temporal Bone Cancer "Surgical Treatment for Ear Cancer". The 3rd ASHNO Congress (Cebu, Philippines),2013.3.21
10. S. Kishimoto : Keynote Lecture : Historical and current concepts of neck management in head and neck cancer. 20th IFOS World Congress 2013 (Seoul) June 2013
11. S. Kishimoto: Symposium "Management of Sinonasal Tumors" : Craniofacial resection and reconstruction for sinonasal tumors involving the skull base. 20th IFOS World Congress 2013 (Seoul) June 2013
12. Sugimoto, S Kishimoto, K Kawada, Y Kiyokawa, T Okada, H Fujiwara, T Kawano, T Sumi, F Nomura, Y Inayoshi, T Ito, H Kawachi : Symposium: Early Detection and Organ Preservation Surgery of the Pharyngeal Cancer in Japan "Endoscopic laryngo-pharyngeal surgery using curved distending laryngoscope. UAE Cancer Congress 2013, Dobai, October2013

Radiation Therapeutics and Oncology

1. Staff and Students (2013)

Radiation Therapeutics and Oncology

Professor	Hitoshi Shibuya(~Mar.)	
Research Associates	Keiji Hayashi,	Keiko Nakagawa(Apr.~)
Hospital Staff members	Keiko Nakagawa(~Mar.), Rikiya Sato(Jul.~)	Naoki Harata(~Sep.),

Diagnostic Radiology and Nuclear Medicine

Associate Professors	Isamu Ohashi and Ichiro Yamada	
Lecturers	Kaoru Hanafusa and Mitsuhiro Kishino,	
Research Associates	Tomoko Makino(~Mar.), Akira Toriihara, Kaori Okazawa, Akiyuki Matsuhisa(Nov.~)	Yoshio Kitazume, Youichi Machida (Apr.~), Masashi Nakadate(Apr.~Sep.),
Hospital Staff members	Masashi Nakadate(~Mar, Oct.~)	Tomoyuki Fujioka(Apr.~), Runa Kakubari(~Mar.), Wataru Yamashita(Apr.~Oct.)
Resudent	Tomoyuki Fujioka(~Mar.),	
Graduate Students	Youichi Machida(~Mar.), Mais M Abd-Alamear(~Mar.)	Satoko Hayashi(~Mar.),
Research Students	Syuichi Yanai(~Mar.)	

2. Purpose of Education

In the new training system of the certified radiologists, eligibility for admission to the certified radiologist exam can be obtained (6 years after graduation) after the comprehensive training of three years in Japan Radiological Society certified training facility following the post-graduate clinical training of two years. The further specialized training of two years (8 years after graduation) after passing the certification exam is necessary to obtain the certified diagnostic radiologists or the certified radiation oncologists.

From July 2013, the Radiology department was divided into the two departments, the Radiation Therapeutics and Oncology, and the Diagnostic Radiology and Nuclear Medicine. However, since the certified radiologist exam is common, the comprehensive training of three years is carried out without having to be divided into the two departments. It is common that two-years training in the off-campus affiliated hospitals is done following one-year training in the campus, in compliance with the certified radiologist training curriculum guidelines established by the Japan Radiological Society. Currently, there are off-campus affiliated hospitals (5 Tokyo, Kanto 6) of 11 as a training institution of the Japan Radiological Society certification. It would be belonging to each department (Radiation Therapeutics and Oncology or Diagnostic Radiology and Nuclear Medicine) at the time of entering the specialized training. Everyone aims to the certified diagnostic radiologists or the certified radiation oncologists after two years. In addition, nearly all aim at the medical PhD, enrolled in graduate school.

3. Clinical Services and Research Subjects

A. Diagnostic Radiology

CT section:

The diagnostic radiology department has a total of three MDCT- equipments in the Radiology Center and ER. We performed CT examination of 30415 in 2013. Interpretation of consecutive 1mm-thick images and MPR (multi-planar reconstruction) images have improved the diagnostic ability.

MRI section:

The diagnostic radiology department has a total of three MRI-units in the Radiology Center (one 3-Tesla system and two 1.5-Tesla system). Inspection number has increased significantly (12505 examinations in 2013). Further one 3-Tesla system will be introduced during the current fiscal year. One of the theme of clinical research is a clinical application and development of diagnostic imaging methods using a diffusion-weighted images.

Interventional Radiology:

In vascular fields, we perform TAE for hepatocellular carcinoma, PTA and intra-arterial stent placement for occlusive arterial disease, arterial infusion therapy for pelvic tumors, and emergency hemostasis from the ER (401 exams in 2013). In non-vascular fields, CT-guided biopsy for thoracic areas mainly (14 exams in 2013) and US-guided biopsy for lymph nodes and mammary gland tumors mainly (221 exams in 2013).

Ultrasonography and Mammography section:

With the cooperation of the breast surgery, we are responsible for the breast diagnostic imaging in the hospital. We perform the high-quality diagnosis with combined with mammography, ultrasonography, MRI, and FDG-PET/CT. One of the theme of clinical research is the development of breast diagnostic methods with combined using of breast imaging and image-guided biopsy.

B. Nuclear Medicine

On Nov. 2006, two sets of PET/CT examination have been introduced and started operation. About 15 patients a day are examined using ¹⁸F-FDG/CT. SPECT examinations have been performed in about 10 cases of disease every day. Clinical data obtained in the diagnosis of head and neck and breast cancer have offered the chance to study pathology of head/neck cancer and breast cancer.

C. Radiation Oncology

Low-dose rate brachytherapy for head/neck as well as prostate cancer is a unique character of the radiation oncology section. The 720 new patients referred for radiotherapy in 2010 included 250 cases of head and neck cancer patients, 120 prostate cancer patients and 110 breast cancer patients. Over 160 oral/oropharynx cancer patients were treated by brachytherapy in 2009. The results of brachytherapy were compatible to the results obtained by surgery, and post-treatment quality of life was better than after surgery.

We have renewed Linear accelerating machines in 2010, and we had three Linear accelerating machines equipped IMRT (intensity-modulated radiation therapy) and IGRT (image-guided radiation therapy).

4. Manuscript

1. Yamada I, Hikishima K, Miyasaka N, Tokairin Y, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H, Shibuya H. Diffusion-tensor MRI and tractography of the esophageal wall ex vivo. *J Magn Reson Imaging* 2013, doi:10.1002/jmri.24411.
2. Yamada I, Hikishima K, Miyasaka N, Kawano T, Tokairin Y, Ito E, Kobayashi D, Eishi Y, Okano H. Esophageal carcinoma: ex vivo evaluation with diffusion-tensor MR imaging and tractography at 7 T. *Radiology* (in press).
3. Toriihara A, Nakamura S, Kubota K, Makino T, Okochi K, Shibuya H. Can dual-time-point (18)F-FDG PET/CT differentiate malignant salivary gland tumors from benign tumors? *Am J Roentgenol* 2013;201:639-44
4. Nakamura S, Toriihara A, Okochi K, Watanabe H, Shibuya H, Kurabayashi T. Optimal timing of post-treatment [18F]fluorodeoxyglucose-PET/CT for patients with head and neck malignancy. *Nucl Med Commun* 2013;34:162-167
5. Umezaki Y, Katagiri A, Watanabe M, Takenoshita M, Sakuma T, Sako E, Sato Y, Toriihara A, Uezato A, Shibuya H, Nishikawa T, Motomura H, Toyofuku A. Brain perfusion asymmetry in patients with oral somatic delusions. *Eur Arch Psychiatry Clin Neurosci* 2013;263:315-323
6. Takagi Y, Toriihara A, Nakahara Y, Yomota M, Okuma Y, Hosomi Y, Shibuya M, Okamura T. Eligibility for bevacizumab as an independent prognostic factor for patients with advanced non-squamous non-small cell lung cancer: a retrospective cohort study. *PLoS One* 2013;8:e59700(Epub 2013 Mar.26)
7. Machida Y, Takemoto A, Ban D, Yoshimoto T, Mihara M, Shibuya H. Adrenal cortical adenoma arising from an adrenohepatic union. *Jpn J Radiol.* 2013 Sep;31(9):623-6. doi: 10.1007/s11604-013-0211-y. Epub 2013 May 18.
8. Nakadate M, Yoshida K, Ishii A, Koizumi M, Tochigi N, Suzuki Y, Ryu Y, Nakagawa T, Umehara I, Shibuya H. Is 18F-FDG PET/CT useful for distinguishing between primary thyroid lymphoma and chronic thyroiditis? *Clin Nucl Med.* 2013;38: 709-714
9. Kojima M, Shibuya H, Hayashi K, Yuasa - Nakagawa K, Harata N. Steady decrease of the time interval between the occurrence of the primary and subsequent primary early (stage I-II) head and neck cancers. *World Journal of Epidemiology and Cancer Prevention* 2013; 2: 1-7.

5. Congress

1. Yamada I, Hikishima K, Miyasaka N, Tokairin Y, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H, Shibuya H. Esophageal Carcinoma: evaluation with diffusion-tensor MR imaging and tractography ex vivo. The 99th Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, USA, December, 2013.
2. Yamada I, Miyasaka N, Hikishima K, Tokairin Y, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H, Shibuya H. Ultra-

high-field (7.0-T) MR imaging of esophageal carcinoma ex vivo: correlation of high-spatial-resolution MR images and histopathologic findings. The 99th Scientific Assembly and Annual Meeting of the Radiological Society of North America, Chicago, USA, December, 2013.

3. Kubota K, Machida Y, Katayama T, Okazawa K, Fujioka T, Toriihara A, Ohashi I. How to Use Multiple Modalities for Diagnosis of Axillary Lymph Node and Other Axillary Diseases? RSNA 2013 annual meeting, Dec 2013, Chicago, USA
4. J. Isogai, M. Miyazaki, T. Yamada, T. Miyata. Non-contrast high resolution MR venography of lower extremity perforating veins. 21th ISMRM, April 2013, Salt Lake City, US
5. Toriihara A, Kitazume Y, Kubota K, Machida Y, Nakadate K, Okazawa K, Makino T, Shibuya H. Comparison of FDG-PET/CT images between chronic renal failure patients on hemodialysis and controls with normal renal function. SNNMI 60th Annual Meeting, June 8-12, 2013, Vancouver, BC, Canada

Maxillofacial Anatomy

1. Staffs and Students (April, 2013)

Professor	Shunichi SHIBATA	
Associate Professor	Tatsuo TERASHIMA	
Assistant Professor	Shun-ichi SHIKANO,	Tatsuhiko ABE(~March)
Graduate Students	Tsuyoshi MORITA(April~),	Kaoru FUJIKAWA(April~)

2. Purpose of Education

Main educational purpose of maxillofacial anatomy in graduate course is to provide students opportunity to understand the function of various oral organs in a morphological viewpoint and ability to evaluate various vital phenomenon encountered in medical practice.

3. Research Subjects

- 1) Structural features of mandibular condylar cartilage.
- 2) Mechanism of epithelial attachment of junctional epithelium in human gingiva.
- 3) Comparative histology and embryology of teeth.
- 4) Observation on the structural features of oral mucous
- 5) Anatomical names of the structures of human skeletal system.
- 6) Biological analysis of root formation of mouse molars by long-term organ culture method.
- 7) Mechanisms of enamel formation in amelogenesis imperfecta rat (ami).
- 8) Role of the dental sac in the formation and the development of the dental and periodontal tissues.
- 9) Hyaluronan synthesis in tooth germ.
- 10) Studies on regeneration of jaw bone.

4. Publications

Original Article

1. Baba O, Ota MS, Terashima T, Tabata MJ, Takano Y: Expression of transcripts for fibroblast growth factor 18 and its possible receptors during postnatal dentin formation in rat molars. *Odontology*. 2013 Dec 28. [Epub ahead of print]
2. Hinata N, Murakami G, Abe S, Shibata S, Morizane S, Honda M, Isoyama T, Sejima T, Takenaka A: Coexistence of elastic fibers with hyaluronic acid in the human urethral sphincter complex: A histological study. *J Urol*, 190: 1313-1319, 2013.
3. Kakhlon O, Glickstein H, Feinstein N, Liu Y, Baba O, Terashima T, Akman HO, Dimauro S, Lossos A: Polyglucosan neurotoxicity caused by glycogen branching enzyme deficiency can be reversed by inhibition of glycogen synthase. *J Neurochem*, 127(1):101-113, 2013 Oct.
4. Kim JH, Parkkila S, Shibata S, Fujimiya M, Murakami G, Cho BH: Expression of carbonic anhydrase IX in human fetal joints, ligaments and tendons: a potential marker of mechanical stress in fetal development? *Anat Cell Biol*: 46(4): 272-284, 2013 Dec.
5. Oishi A, Terashima T, Miyashin M, Takagi Y: Repair processes of experimental root fractures in rat molars examined by histopathological techniques and 3D micro-CT imaging. *Pediatr Dent J*, 23: 8-15, 2013.
6. Shibata S, Cho KH, Kim JH, Abe H, Murakami G, Cho BH: Expression of hyaluronan (hyaluronic acid) in the developing laminar architecture of the human fetal brain. *Ann Anat*, 195(5):424-430, 2013 Oct.
7. Shibata S, Sato R, Murakami G, Fukuoka H, Rodríguez-Vázquez JF: Origin of mandibular condylar cartilage in mice, rats, and humans: Periosteum or separate blastema? *J Oral Biosci*, 55: 208-216, 2013.
8. Shibata S, Sakamoto Y, Baba O, Qin C, Murakami G, Cho BH: An immunohistochemical study of matrix proteins in the craniofacial cartilage in midterm human fetuses. *Eur J Histochem*, 57, No. 4: e.39, 2013.

Review Article

Book

Cognitive Neurobiology

1. Staffs and Students

Professor	Masato Taira	
Junior Associate Professor	Hisayuki Ojima	
Assistant Professor	Narumi Katsuyama	
Research Associate	Nobuo Usui	
Part-time Instructor	Mari Kumashiro	
Post-doctoral fellow	Juri Fujiwara	
Graduate Student	Eriko Tachi,	Saneyuki Mizutani,
	Yuko Imai,	Youko Kohno,
	Chisato Yamate,	Mayumi Yamamoto

2. Purpose of Education

1. Lectures of unit “Functions of Nervous Systems I (Introduction to Neurophysiology, Motor Functions)”

Basic knowledge of neurophysiology will be lectured as an introduction together with the motor functions.

2. Lectures of unit “Functions of Nervous Systems II (Perception, Emotion, Instinct, Sleep, Higher functions)”

A series of lectures will be taught on functions of the sensation, perception, and motion as well as the neural mechanisms of higher brain functions.

3. Lectures of unit “Homeostatic Functions for Life Support”

Lectures will be taught on the structure of the autonomic nervous system and its regulatory mechanisms in the circulation, respiration, digestion/absorption, humor/body temperature, metabolism, excretion, and internal secretion/reproduction.

4. Lectures of unit “Oral Physiology”

Lectures will be taught on the structure and function of various somatosensory organs in the oral cavity. Neural regulations of mastication and deglutition as well as the secretion mechanism of saliva will also be learned.

5. Unit of “Practice in Physiological Functions”

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.

3. Research Subjects

1. Neural Mechanisms of control of motor behavior.

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

2. Neuronal mechanisms for perception and cognition.

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

3. Processing of natural sounds in auditory cortex

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

4. Publications

Original Article

1. Fujiwara, J., Usui, N., Park, S.Q., Williams, T., Iijima, T., Taira, M., Tsutsui, K., Tobler, P.N. (2013): Value of freedom to choose encoded by the human brain. *J Neurophysiol.* 110:1915-1929.
2. Kawakubo, N., Miyamoto, JJ, Katsuyama N., Ono, T., Honda, E.I., Kurabayashi, T., Taira, M., Moriyama, K. (2013): Effects of cortical activations on enhancement of handgrip force during teeth clenching: An fMRI study. *Neuroscience Research*, in press.
3. Murakami, T., Matsukawa, M., Katsuyama, N., Imada, M., Aizawa, S., Sato, T. (2013). Stress-related activities induced by predator odor may become indistinguishable by hinokitiol odor. *Neuroreport* 23:1071-1076.
4. Takarada, Y., Ohki, Y., Taira, M. (2013) : Effect of transient vascular occlusion of the upper arm on motor evoked potentials during force exertion. *Neurosci Res.* 76:224-229.
5. Yamaoka, A., Koike, H., Sato, T., Kanayama, K., Taira, M. (2013): Standard electrocardiographic data of young

Japanese monkeys (*Macaca fusucata*). *J Am Assoc Lab Anim Sci.* 52:491-494.

Molecular Craniofacial Embryology

1. Staffs and Students

Professor	Sachiko Iseki
Associate Professor	Masa-Aki Ikeda
Lecturer	Masato Ota (until March)
Part-time lecturers	Hirofumi Doi, Shumpei Yamada, Shigeru Okuhara
Visiting Researcher	Yoichiro Ninomiya
Graduate Students	Akihiko Machida (Maxillofacial Surgery)(until March), Prasitsak Thanit, Endrawan Pratama, Zhang Kui (Oral Implantology and Regenerative Dental Medicine), Toshiko Furutera (from April), Charoenlarp Ponkawee (from October), Yuki Kasahara (Orthodontic Science)(from October)
Research Student	Toshiko Furutera (until March), Mya Nandar (from April), Akihiko Machida (Maxillofacial Surgery)(from April)
Foreign Researcher	Khandakar Abu Shameem MD. Saadat (until March)
Secretary	Kaori Morinaka

2. Research subjects

- 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 their stemness
- 4) Regulation of gene expression in cell growth and stress response
- 5) Nuclear architecture and function in regulating gene expression

3. Publications

Original articles

1. Nagayama T., Okuhara S., Ota M.S., Tachikawa N., Kasugai S., Iseki S. (2013) FGF18 accelerates osteoblast differentiation by upregulating Bmp2 expression. *Congenit. Anom.* 53(2): 83-88.
2. Kameda Y., Saitoh T., Nemoto N., Katoh T., Iseki S., Fujimura T. (2013) Hes1 is required for the development of pharyngeal organs and survival of neural crest-derived mesenchymal cells in pharyngeal arches. *Cell Tissue Res.* 353: 9-25.
3. Khandakar A. S. M. Saadat. (2013) Role of ARID3A in E2F target gene expression and cell growth. *J. Stomatol. Soc.* 80 (1): 15-20.

Review Articles

(1 Japanese article)

Cellular Physiological Chemistry

1. Staffs and Students (April, 2013)

Professor	Ikuro Morita	
Associate Professor	Ken-ichi Nakahama	
Junior Associate Professor	Hiroshi Fujita,	Mayumi Abe,
	Chieko Yokoyama	
Tokuninn Assistant Professor	Masako Akiyama,	Olga Safronova
Graduate Student	Takeshi Watanabe	
Research Student	Yukihiko Hashida,	Kaori Shimizu,
	Yu Hatano,	Izumi Honda,
	Bowen Xu,	Chikako Morioka,
	Keiko Akasawa,	Masayuki Tooi,
	Mizuki Nagata,	Asuka Okitoh,
	Takeshi Matsuura,	Yuri Numata,
	Mami Ikeda	
Associate Professor (Nano Medicine DNP)	Motohiro Komaki	
Assistant Professor (Nano Medicine DNP)	Kengo Iwasaki	
Visiting Researcher (Nano Medicine DNP)	Naoyuki Yokoyama, Hirohito Ayame	
Research Student (Nano Medicine DNP)	Yasuyuki Kimura	

2. Purpose of Education

For undergraduate students. We have some classes in biological chemistry for the third grader. In these classes, the students should understand basic biochemistry and physiology under healthy/diseased conditions.

For graduate students. These students can choose the one of themes in our lab. These students are expected to solve the problems by themselves. However, appropriate suggestions will be given by at least three supervisors whenever you want.

3. Research Subjects

1. Regulatory mechanism of angiogenesis and application to regenerative medicine
2. Bone remodeling and cell communication
3. Inflammation under hypoxic conditions (epigenetic control of gene expression)
4. Life of gap junction

4. Publications

Original Article

1. Akiyama M, Nakahama K, Morita I. Impact of docosahexaenoic acid on gene expression during osteoclastogenesis in vitro-comprehensive analysis. *Nutrients*, 2013 Aug, 13:5(8):3151-62
2. Sawabe M, Aoki A, Komaki M, Iwasaki K, Ogita M, Izumi Y. Gingival tissue healing following Er:YAG laser ablation compared to electrosurgery in rats. *Lasers Med Sci*. 2013 Nov 16. [Epub ahead of print]
3. Iwasaki K, Komaki M, Yokoyama N, Tanaka Y, Taki A, Honda I, Kimura Y, Takeda M, Akazawa K, Oda S, Izumi Y, Morita I. Periodontal Regeneration Using Periodontal Ligament Stem Cell-Transferred Amnion. *Tissue Eng Part A*. 2013 Dec 9. [Epub ahead of print]
4. Iwasaki K, Komaki M, Yokoyama N, Tanaka Y, Taki A, Kimura Y, Takeda M, Oda S, Izumi Y, Morita I. Periodontal Ligament Stem Cells Possess the Characteristics of Pericytes. *J Periodontol*. 2013 Oct;84(10):1425-33
5. Fujita H, Ohwada A, Handa N and Nishimura S. Relative monocytosis in patients with erythrocytosis. *Open J Blood Diseases*. 3:21-24. 2013
6. Fujita H, Sakuma R and Nishimura A. Possible red blood cell damage due to iatrogenic transfusion filter-related mistakes during blood transfusion. *Medical Instrumentation*. doi: 10.7243/2052-6962-1-4. 2013
7. Kato H, Uruma M, Okuyama Y, Fujita H, Handa M, Tomiyama Y, Shimodaira S, Kurata Y and Takamoto S. Incidence of transfusion-related adverse reactions per patient reflects the potential risk of transfusion therapy in Japan. *Am J Clin Pathol*. 140:219-224. 2013
8. Kato K, Morita I. Promotion of osteoclast differentiation and activation in spite of impeded osteoblast-lineage differentiation under acidosis: Effect of acidosis on bone metabolism. *Biosci Trends*, 2013, 7(1):33-41

Metals

1. Staffs and Students

Professor	Takao HANAWA	
Associate Professor	Yusuke TSUTSUMI	
Assistant Professor	Hisashi DOI,	Maki ASHIDA
Research Assistant	Osamu FUKUSHIMA	
Project Assistant Professor	Peng CHEN	
Secretary	Toshie NAKANISHI,	Yasuko SEKI
Graduate Student	Takeru NISHISAKA	

2. Purpose of Education

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. Research Subjects

1) Bio-functionalization of metals with electrochemical 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 artifacts 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.

4. Publications

Original Articles

1. Imai H, Tanaka Y, Nomura N, Tsutsumi Y, Doi H, Kanno Z, Ohno K, Ono T, Hanawa T. Three-dimensional quantification of susceptibility artifacts from various metals in magnetic resonance images. *Acta Biomaterialia* 9: 8433-8439, 2013.
2. Zhu S, Xie G, Qin F, Wang X, Hanawa T. Ti particles dispersed Ti-based metallic glass matrix composite prepared by spark plasma sintering. *Materials Transactions* 54: 1335-1338, 2013.
3. Seki I, Umetsu R, Xie G, Nomura N, Wang X, Hanawa T. Cooling rate and composition dependences of magnetic susceptibility for $Zr_{54-x}Cu_{30+x}Al_8Ag_8$ glassy alloys. *Materials Transactions* 54: 1356-1360, 2013.
4. Hieda J, Niinomi M, Nakai M, Kamura H, Tsutsumi H, Hanawa T. Improvement of adhesive strength of segmented polyurethane on Ti-29Nb-13Ta-4.6Zr alloy through H_2O_2 treatment for biomedical application. *Journal of Biomedical Materials Research* 101B: 776-783, 2013.
5. Takaichi A, Suyalatu, Nakamoto T, Joko N, Nomura N, Tsutsumi Y, Migita S, Doi H, Kurosu S, Chiba A, Wakabayashi N, Igarashi Y, Hanawa T. Microstructures and mechanical properties of Co-29Cr-6Mo alloy fabricated by selected laser melting. *The Journal of the Mechanical Behavior of Biomedical Materials* 21: 67-79, 2013.
6. Kaneto M, Namura Y, Tamura T, Shimizu N, Tsutsumi Y, Hanawa T, Yoneyama T. Influence of electrolytic treatment time on the corrosion resistance of Ni-Ti orthodontic wire. *Dental Materials Journal* 32: 305-310, 2013.

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7. Kondo R, Shimizu R, Nomura N, Doi H, Suyalatu, Tsutsumi Y, Mitsuishi K, Shimojo M, Noda K, Hanawa T. Effect of cold rolling on the magnetic susceptibility of the Zr-14Nb alloy. *Acta Biomaterialia* 9: 5795-5801, 2013.
8. Tsutsumi Y, Kobayashi E, Ogo M, Suyalatu, Migita S, Doi H, Nomura N, Noda K, Hanawa T. Accelerated calcium phosphate formation on titanium utilizing galvanic current between titanium and gold in Hanks' solution. *Materials Transactions* 54: 149-155, 2013.

Review Articles

1. Hanawa T. Research and development of metals for medical devices based on clinical needs. *Science and Technology of Advanced Materials* 13: 064102, 2013.

Books

1. Hanawa T. Metal-polymer composite biomaterial, *Polymeric Biomaterials. Structure and Function, Volume 1*, (S. Dumitriu, V. Popa Eds.) , CRC Press, Boca Raton, FL, USA, 2013.

Biodesign

1. Staffs and Students

Professor	Kazuo TAKAKUDA	
Assistant Professor	Wei WANG	
Research Assistants	Shukan OKANO	
Graduate Students	Hazuki KOSHITOMAE,	Ryo KOKUBUN,
	Yutaka FUKUDA,	Masahiro WATANABE,
	Tetsuro WATANABE,	Kimihiro OKANO,
	Ryoichi SUZUKI,	Katsunari MURAKAMI,
	Hiroki IKEDA,	Tarou KIMURA,
	Hiroyuki KUSABA,	Hisaya NOMATA,
	Eiko MARUKAWA	

2. Purpose of Education

Biodesign. The class is for the understanding of fundamental concepts of mechanics, and introduction to the advanced studies including the biomechanics of living bodies, tissues, and cells. Some applications to the basics design of medical devices with mechanical functions are also discussed.

3. Research Subjects

1. Remodeling of structural and supporting tissues under mechanical stimuli

Biomechanical studies on structural/supporting tissues such as bones, ligaments and tendons are carried out. In particular, to elucidate the adaptation mechanism of these tissues, the effects of controlled mechanical stimuli applied to living cells and tissues are investigated.

2. Development of Bone Regeneration Device with Bioabsorbable Organic/Inorganic Composite Materials

Devices for bone regeneration with the use of bioabsorbable Organic/Inorganic Composite materials are developing. In vitro and animal experiments are carrying out for pre-clinical experiments. Furthermore, bone regeneration mechanism when implanting Organic/Inorganic composite materials is examined by in vitro and in vivo tests.

3. Development of Regeneration Devices for Soft Tissues with the use of bioabsorbable materials

Regeneration technology for structural/supporting tissues such as ligaments, tendons, dura mater, peripheral nerves and small blood vessels are investigated utilizing bioabsorbable polymers. Our strategy is based on the regeneration by the self-healing mechanism achieved through the optimum milieu provided by biomaterials. We already have promising results in the animal experiments for the cases of dura mater and peripheral nerves.

4. Publications

Original Articles

1. Nozaki K, Wang W, Horiuchi N, Nakamura M, Takakuda K, Yamashita K, Nagai A. Enhanced osteoconductivity of titanium implant by polarization-induced surface charges. *J Biomed Mater Res A*. 2013 Oct 7;
2. Rodotheou P, Wang W, Itoh S, Okazaki M, Takakuda K. Laser-Perforated Porous Nonwoven Chitosan Nerve Conduit. *Journal of Biomechanical Science and Engineering*. 2013;8(2):139-151.
3. Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama K. Hydroxyapatite/collagen nanocomposite-coated titanium rod for achieving rapid osseointegration onto bone surface. *J Biomed Mater Res Part B Appl Biomater*. 2013 Aug;101(6):1031-1038.
4. Asoda S, Arita T, Takakuda K. Mechanical attachment of soft tissue to dental and maxillofacial implants with mesh structures: an experiment in percutaneous model. *J Biomed Mater Res Part B Appl Biomater*. 2013 May;101(4):553-559.
5. Kimura T, Yokoyama Y, Sakota D, Nagaoka E, Kitao T, Takakuda K, Takatani S. Evaluation of platelet aggregability during left ventricular bypass using a MedTech MagLev VAD in a series of chronic calf experiments. *J Artif Organs*. 2013 Mar;16(1):34-41.

Presentations

1. Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama. Optimum Thickness of Hydroxyapatite/Collagen Nano Composite Coating for Subperiosteal Devices. The 7th International Conference on the Science and Technology for

Advanced Ceramics. Jun 2013, Yokohama, Japan.

2. Takakuda K. Biomaterials: From Basics To Clinics. 5th International Summer Program of TMDU. Aug. 2013, Tokyo, Japan.
3. Wang W, Itoh S, Takakuda K. Decellularized Nerve for Peripheral Nerve Repairing. TERMS-AP 2013 Annual Conference. Oct, 2013. Shanghai, China.

Maxillofacial Surgery

1. Staffs and Students (2013)

Professor	Kiyoshi HARADA(from April)	
Junior Associate Professor	Masashi YAMASHIRO(until March, from April Clinical Professor) Satoshi YAMAGUCHI(from April), Narikazu UZAWA	
Assistant Professor	Yutaka SATO, Yasuyuki MICHI, Kouichi NAKAKUKI,	Hiroyuki YOSHITAKE, Kazuto KUROHARA, Yoshio OHYAMA(from April)
Hospital Staff	Itaru SONODA, Miho SUZUKI(MIZUTANI), Nobuyoshi TOMOMATSU, Chieko MICHIKAWA(from April), Jun SUMINO,	Kunihiro MYO, Ken-Ichiro TAKAHASHI, Hiroyuki NAKACHI, Erika OUE, Chika MIURA
Graduate Student	Akira GOUDA, Yujiro MORIYA, Eri TSUCHIDA, Takayuki YAMADA, Uyanga ENKHBOLD, Chihiro YOSHIDA, Masahiko TERAUCHI, Kouhei OKUYAMA, Yuuta KONDOU, Tomoki KANEMARU(from April), Yusuke KASAHARA(from April), Sakie KATSUMURA(from April),	Yukihiko HASHIDA, Chisato YAMADA, Ryosuke NAKAMURA, Li KEI, Takuma MORITA, Takeshi OKAMURA, Hirokazu KACHI, Sou WAKE, Reiko HOSHI(from April),
Student	Yumi SANO(from April),	Syun NISHIHARA(from April)

2. Purpose of Education

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. 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.

4. 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.

Total number of new patients was 7,194 for 2013. Number of In-patients was 589 and 457 operations were performed.

5. Publication

Original Article

1. Kamrun N, Tetsumura A, Nomura Y, Yamaguchi S, Baba O, Nakamura S, Watanabe H, Kurabayashi T Visualization of the superior and inferior borders of the mandibular canal: a comparative study using digital panoramic radiographs and cross-sectional CT images. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 115(4):550-557, 2013
2. Yagihara K, Okabe S, Ishii J, Amagasa T, Yamashiro M, Yamaguchi S, Yokoya S, Yamazaki T, Kinoshita Y Mandibular reconstruction using a poly(l-lactide) mesh combined with autogenous particulate cancellous bone and marrow: a prospective clinical study. *Int J Oral Maxillofac Surg.* 42(8):962-969, 2013
3. Takayuki Yamada, Masashi Yamashiro, Aya Kawamata, Yuko Katsuki, Asumi Uezono-Honda, Kou Kayamori, Kiyoshi Harada: Transparotid excision of rhabdomyosarcoma in masseter muscle: A case report. *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology* In press
4. Goda A, Maruyama F, Michi Y, Nakagawa I, Harada K Analysis of the factors affecting the formation of the microbiome associated with chronic osteomyelitis of the jaw. *Clin Microbiol Infect.* DOI: 10.1111/1469-0691.12400 (2013)
5. Yukihiko Hashida, Ken-ichi Nakahama, Kaori Shimizu, Masako Akiyama, Kiyoshi Harada, Ikuo Morita Communication-dependent mineralization of osteoblasts via gap junctions. *BONE* Volume 61 page19-26 April, 2014
6. Shindoi JM, Matsumoto, Y, Sato Y, Ono T, Harada K Soft tissue cephalometric norms for orthognathic and cosmetic surgery. *J Oral Maxillofac Surg.* 71(1) 24-30, 2013.
7. Aya Kawamata, Masashi Yamane, Yoshimasa Nakazato A rare case of aggressive fibromatosis in the maxillary sinus *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology, In Press, Corrected Proof, Available online 10 July 2013*
8. Matsushita Y, Sakamoto K, Tamamura Y, Shibata Y, Minamizato T, Kihara T, Ito M, Katsube K, Hiraoka S, Koseki H, Harada K, Yamaguchi A CCN3 Protein Participates in Bone Regeneration as an Inhibitory Factor. *J Biol Chem* 288(27):19973-85, 2013
9. Harazono Y, Muramatsu T, Endo H, Uzawa N, Kawano T, Harada K, Inazawa J, Kozaki K miR-655 is an EMT-suppressive microRNA targeting ZEB1 and TGFBR2 *PLoS One* 14:8(5):e62757, 2013
10. Harazono Y, Yamashiro M, Yoshitake H, Kayamori K, Izumo T, Harada K A case of highly suspected small cell osteosarcoma in the mandible *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology.* 462(6)665, 2013
11. Shang Gao, Makoto Shiota, Masaki Fujii, Kang Chen, Masahiro Shimogishi, Masashi Sato, Shohei Kasugai Combination of simvastatin and hydroxyapatite fiber induces bone augmentation. *Open Journal of Regenerative Medicine.* 2(3):53-60, 2013
12. Michi Y, Suzuki M, Kurohara K, Harada K. A case of hemangiopericytoma of the soft palate with articulate disorder and dysphagia. *Int J Oral Sci.* 5(2):111-4, 2013

Conference Presentations

1. Yosuke Harazono, Ken-ichi Kozaki, Tomoki Muramatsu, Hironori Endo, Narikazu Uzawa, Tatsuyuki Kawano, KiyoshiHarada, Johji Inazawa: miR-655 is an EMT-suppressive microRNA targeting ZEB1 and TGFBR2 *AACR/JCA Joint Conference, February 21-25, 2013 Maui, HI USA*
2. Motoko Okamitsu, Taiko Hirose, Taeko Teramoto, Noriko Okubo, Hidemi Yoshimasu, Yutaka Sato, Kei-ichi Morita, Ken Omura: Factors related to social support of mothers of infants with cleft lip and/or palate. *International Collaboration for Community Health Nursing Research Conference 2013,(March 11-13, Edinburgh, Scotland)*
3. Harriman E.J, Ohyama Y, and Mochida Y: Characterization of Wdr72 Knockout Rats, Causative Gene for Amelogenesis Imperfecta. *International Association for Dental Research. March 20-23, 2013, Seattle USA.*
4. Venkitapathi S, Ohyama Y, Jaha H.S, Almahmadi A, Aljamaan R, and, Mochida Y: Ciliary Colocalization and Interaction of Evc & Evc2 Proteins. *International Association for Dental Research. March 20-23, 2013, Seattle USA.*

5. Nagaoka R, Torikai T, Fukawa T, Kijima T, Misawa T, Naganisi H, Omura S: Le Fort II distraction osteogenesis using original distractor in a patient with Apert syndrome. 12th International Congress on Cleft Lip/Palate and Related Craniofacial Anomalies May 5-10, 2013, Florida
6. Yuki Matsushita, Kei Sakamoto, Ken-ichi Katsube, Kiyoshi Harada, Akira Yamaguchi: Role of CCN3/NOV in bone regeneration. 2nd Joint Meeting of the International Bone and Mineral Society and The Japanese Society for Bone and Mineral Research (IBMS-JSBMR) May 28-June 1, 2013, Kobe
7. Goda A, Maruyama F, Michi Y, Ichiro N, Harada K: Analysis of the factors affecting the formation of the microbiome associated with chronic osteomyelitis of the jaw. FEMS 2013 5th congress of European microbiologists July 21-25, 2013, Leipzig, Germany
8. Yuki Matsushita, Kei Sakamoto, Tokutarou Minamizato, Kiyoshi Harada, Akira Yamaguchi: CCN3 participates in bone regeneration as an inhibitory factor. The American Society for Bone and Mineral Research 2013 Annual Meeting (ASBMR) Oct 3-7, 2013, Baltimore
9. Narikazu Uzawa, Miho Suzuki, Yasuyuki M Ichi, Masashi Yamashiro, Kiyoshi Harada: Microsurgical Free Flap Reconstructions of Head and Neck Region in 401 cases: A 25-Year Experience. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona
10. Yuki Matsushita, Kei Sakamoto, Yoshihiro Tamamura, Ken-ichi Katsube, Kiyoshi Harada, Akira Yamaguchi: CCN3 inhibits bone regeneration via BMP signaling pathway. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona
11. Chieko Michikawa, Narikazu Uzawa, Toshiyuki Izumo, Akira Yamaguchi, Kiyoshi Harada: Classification of extracapsular spread of the lymph node metastasis in oral cancer. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona
12. SONODA Itaru, UZAWA Narikazu, SAKAMOTO Kei, HARADA Kiyoshi: Two cases of Plasmocytosis Circumorficialis. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona
13. Hidemi Yoshimasu, Yutaka Sato, Takashi Mishimagi, Yuko Katsuki, Kiyoshi Harada: Long-term results following the pharyngeal flap operation in patients with cleft palate and congenital velopharyngeal. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona
14. Tomomatsu N, Uzawa N, Aragaki T, Yoshitake H, Suzuki M, Watanabe Y, Harada K: A prognostic factor of the odontogenic maxillary sinusitis. 21st International Conference on Oral and Maxillofacial Surgery Oct 21-24, 2013, Barcelona

Maxillofacial Orthognathics

1. Staffs and Students (April, 2013)

Professor	Keiji MORIYAMA	
Associate Professor	Shoichi SUZUKI	
Junior Associate Professor	Tatsuo KAWAMOTO,	Takuya OGAWA
Assistant Professor	Michiko TSUJI,	Norihisa HIGASHIHORI,
	Jun MIYAMOTO,	Yukiho KOBAYASHI
Hard Tissue Genome Research Center, Research Assistant Professor	Hiroyuki Suzuki	
Graduate Student	Masayoshi UEZONO,	Ryo MARUOKA,
	Masako YOSHIZAKI,	Carolina DUARTE,
	Paveenarat AUKKARASONGSUP,	
	Takayuki UMEZAWA,	Kenji OGURA,
	Keiko MURAMOTO,	Naomi YAMAMOTO,
	Thunyaporn SURAPORNSAWASD,	
	Shiyong LIU,	Kouhei YAHIRO,
	Maki MORISHITA,	Naoki KOUDA,
	Akitsu IKEDA,	Tsasan TUMURKHUU,
	Ayumi SHOUJI,	Taizou HIRATSUKA,
	Wanting LING	

2. Purpose of 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. Research Subjects

- 1) Research on etiology, diagnosis, and treatment for developmental and congenital anomalies in the craniofacial region
- 2) Biomaterials research for the development of new orthodontic appliances
- 3) Epidemiological research related to dentofacial growth and malocclusion
- 4) Research on mechanical stress and bone metabolism
- 5) Research on stomatognathic function and central nervous system

4. Clinical Services

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.

5. Publications

Original Article

1. Honda A, Baba Y, Ogawa T, Suzuki S, Moriyama K. Long-term maxillomandibular changes after maxillary distraction osteogenesis in growing children with cleft lip with or without palate. *Cleft Palate Craniofac J.* 50(2):168-73, 2013.
2. Okamura E, Suda N, Baba Y, Fukuoka H, Ogawa T, Ohkuma M, Ahiko N, Yasue A, Tengan T, Shiga M, Tsuji M, Moriyama K. Dental and maxillofacial characteristics of six Japanese individuals with ectrodactyly-ectodermal

- dysplasia-clefting syndrome. *Cleft Palate Craniofac J.* 50(2):192-200, 2013.
3. Hikita R, Miyamoto JJ, Ono T, Honda E, Kurabayashi T, Moriyama K. Activation patterns in the auditory association area involved in glottal stop perception. *J Oral Biosci.* 55: 34-39, 2013.
 4. Matsumoto T, Iimura T, Ogura K, Moriyama K, Yamaguchi A. The role of osteocytes in bone resorption during orthodontic tooth movement. *J Dent Res.* 92:340-5 2013.
 5. Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama K. Hydroxyapatite/collagen nanocomposite-coated titanium rod for achieving rapid osseointegration onto bone surface. *J Biomed Mater Res B Appl Biomater.* 101:1031-8, 2013.
 6. Aukkarasongsup P, Haruyama N, Matsumoto T, Shiga M, Moriyama K. Periostin inhibits hypoxia-induced apoptosis in human periodontal ligament cells via TGF- β signaling. *Biochem Biophys Res Commun.* 441:126-32, 2013.
 7. Cho A, Haruyama N, Hall B, Danton MJS, Zhang L, Arany P, Mooney DJ, Harichane Y, Goldberg M, Gibson CW, Kulkarni AB. TGF- β regulates enamel mineralization and maturation through KLK4 expression. *PLoS One.* 2013 Nov;8(11): e82267.
 8. Kawakubo N, Miyamoto JJ, Katsuyama N, Ono T, Honda E, Kurabayashi T, Taira M, Moriyama K. Effects of cortical activations on enhancement of handgrip force during teeth clenching: an fMRI study. *Neurosci Res.* 2013 Dec 8. pii: S0168-0102(13)00263-0.
 9. Watanabe C, Morita M, Hayata T, Nakamoto T, Kikuguchi C, Li X, Kobayashi Y, Takahashi N, Notomi T, Moriyama K, Yamamoto T, Ezura Y, Noda M. The stability of mRNA influences osteoporotic bone mass via Cnot3. *Proc Natl Acad Sci USA.* (in press)
 10. Miyamoto JJ, Yabunaka T, Moriyama K. Cervical characteristics of Noonan syndrome. *Eur J Orthod.* (in press)
 11. Ito Y, Kawamoto T, Moriyama K. The orthopaedic effects of bone-anchored maxillary protraction in a beagle model. *Eur J Orthod.* (in press)
 12. Morita J, Nakamura M, Kobayashi Y, Deng CX, Funato N, Moriyama K. Soluble form of FGFR2 with S252W partially prevents craniosynostosis of the apert mouse model. *Dev Dyn.* (in press)
 13. Ogawa T, Sato C, Kawakubo N, Moriyama K. Orthodontic treatment of a patient with hypoglossia. *Cleft Palate Craniofac J.* (in press)
 14. Hikita R, Kobayashi Y, Tsuji M, Kawamoto T, Moriyama K. Long-term orthodontic and surgical treatment and stability of a patient with Beckwith–Wiedemann syndrome. *Am J Orthod Dentofacial Orthop.* (in press)
 15. Ahiko N, Baba Y, Tsuji M, Suzuki S, Kaneko T, Kinndaicji J, Moriyama K. Investigation of maxillofacial morphology and dental development in hemifacial microsomia. *Cleft Palate Craniofac J.* (in press)

Maxillofacial Prosthetics

1. Staffs and Students (April, 2013)

Professor	Hisashi TANIGUCHI	
Junior Associate Professor	Yuka SUMITA	
Assistant Professor	Mariko HATTORI,	Takafumi OTOMARU
Hospital Staff	Mihoko HARAGUCHI,	Mai MURASE,
	Moe KOSAKA	
Secretary	Ikuko ICHINOHE	
Graduate Student	Yiliyaer AIMAIJIANG,	Shigen YOSHI,
	Ayako KANAZAKI	

2. Purpose of Education

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.

3. Research Subjects

1. Diagnosis of functional impairment in patients with a maxillofacial defect
2. Treatments for functional rehabilitation of patients with a maxillofacial defect
3. Evaluation on masticatory function in patients with a maxillofacial defect
4. Speech evaluation in patients with a maxillofacial defect
5. Development of new materials for facial prosthesis

4. Clinical Services

Maxillofacial Prosthetic clinic provides the restoration of functional and esthetic disorders of maxillofacial areas that are caused by congenital developmental or acquired diseases by means of the high-advanced dental and medical cares.

5. Publications

Original Article

1. Hattori M, Sumita YI, Taniguchi H: Automatic evaluation of speech impairment caused by wearing a dental appliance. *Open Journal of Stomatology* 3, 365-369, 2013.

Books

1. Sumita YI, Inohara K, Sakurai R, Hattori M, Ino S, Ifukube T, Taniguchi H: Chapter 4 Development of articulation simulation system using vocal tract Model. *Selected Topics on Computed Tomography* edited by Dongqing Wang, ISBN 978-953-51-1102-3, InTech, May 5, 2013.

Cell biology

1. Staffs and students (April 2013)

Professor	Takao NAKATA	
Associate Professor	Akihiro INOUE	
Assistant Professor	Tomohiro ISHII,	Toshiyuki KAKUMOTO
Research Technician	Satoko NAKAMURA	

2. Purpose of Education

We teach histology 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.

3. Research Subject

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.

4. Presentation

Original Article

1. T. Kakumoto, T. Nakata. Optogenetic Control of PIP3: PIP3 Is Sufficient to Induce the Actin-Based Active Part of Growth Cones and Is Regulated via Endocytosis. PLOS ONE 8(8): e70861. 2013.

Books

1. Ishii, T. Genetic manipulation to analyze pheromone responses: knockouts of multiple receptor genes. Methods in Molecular Biology (2013)1068:133-154.

Medical Biochemistry

1. Staffs and Students (April, 2013)

Professor	Yutaka Hata
Junior Associate Professor	Kentaro Nakagawa
Assistant Professor	Hiroaki Iwasa
Assistant Professor	Junichi Maruyama
Other two staffs and twelve students	

2. Purpose of Education

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 cell adhesion-related signaling pathway which is involved in the regulation of cell proliferation, cell polarity, and apoptosis. This pathway is well conserved from fly to human. The mutations of some 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.

3. Research Subjects

- 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 suppressive 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

4. Clinical Services

N/A

5. Publications

1. Iwasa H, Kudo T, Maimaiti S, Ikeda M, Maruyama J, Nakagawa K, Hata Y. RASSF6 tumor suppressor regulates apoptosis and cell cycle via MDM2 and p53. *J. Biol. Chem.* 288(42):30320-30329
2. Yang Z, Hata Y. What is the Hippo pathway?: Is the Hippo pathway conserved in *Caenorhabditis elegans*? *J. Biochem.* 154(3):207-209 J. Biochem. (2013)
3. Hata Y, Timalisina S, Maimaiti S. Okadaic acid: a tool to study the Hippo pathway. *Marine Drugs* 11(3):896-902 (2013)
4. Sanada Y, Kumoto T, Suehiro H, Nishimura F, Kato N, Hata Y, Sorisky A, Yanaka N. RASSF6 expression in adipocytes down-regulated by interaction with macrophages. *PLoS One* 8(4):e61931 (2013)
5. Iwasa H, Maimaiti S, Kuroyanagi H, Kawano S, Inami K, Timalisina S, Ikeda M, Nakagawa K, Hata Y. Yes-associated protein homolog, YAP-1, is involved in the thermotolerance and aging in the nematode *Caenorhabditis elegans*. *Exp. Cell Res.* 319(7):931-945 (2013)
6. Iwasa H, Kuroyanagi H, Maimaiti S, Ikeda M, Nakagawa K, Hata Y. Characterization of RSF-1, the *Caenorhabditis elegans* homolog of the Ras-association domain family protein 1. *Exp. Cell Res.* 319(3):1-11 (2013)

Joint Surgery and Sports Medicine

1. Staffs and Students

Professor	Takeshi MUNETA	
Associate Professor	Kunikazu TSUJI (Department of Cartilage Regeneration) Tomoyuki MOCHIZUKI (Department of Joint Reconstruction)	
Junior Associate Professor	Tetsuya JINNO,	Toshifumi WATANABE
Assistant Professor	Hideyuki KOGA	
Graduate Student	Kazumasa MIYATAKE,	Daisuke HATSUSHIKA,
	Hiroki KATAGIRI,	Koji OTABE,
	Jun YAMADA,	Arata YUKI,
	Yusuke NAKAGAWA,	Yu MATSUKURA,
	Mio UDO,	Shinpei KONDO,
	Ryusuke SAITO,	Katsuaki YANAGISAWA,
	Mikio SHIODA,	Kaori NAKAMURA,
	Kanehiro HIYAMA	

2. Purpose of Education

We are operating at the “department of orthopaedic surgery in the medical university” in corporation with section of orthopaedic surgery in the graduate school. After postgraduate training, students are given opportunity for basic education and acquire the comprehensive knowledge of the orthopaedic surgery and traumatology in the associated hospitals. In concretely terms, students mainly take traumatology training as a basis for clinical medicine for 2 years. Training also includes anesthesiology, emergency medicine, rehabilitation, and neurology. Subsequently, students will take training of joint surgery and neurosurgery in the specialized hospitals for at least 2 years. After basic training of 6 years, students are required to be an orthopaedic specialist which was certificated by Japan Orthopaedic Association. As for an admission to a graduate school, students will be allowed depending on the personal desire and individual achievements after 4 years' education.

We also accept extramural and international students, doctors, and veterinarians who are interested in the research at our graduate school.

3. Research Subjects

Following studies have been extensively carried out in our laboratory with various biological and molecular biological techniques:

- Establishment of separation and proliferation of mesenchymal stem cells
- Elucidation of biological properties of mesenchymal stem cells
- Development of treatment of joint cartilage injury using mesenchymal stem cells
- Mechanism and treatment of joint pain
- Development of knee and hip arthroplasty which accommodates Japanese
- Promotion of anatomical knee anterior cruciate ligament reconstruction

4. Clinical Services

- Promotion of treatment about diseases of lower extremity from children to elderly people
- Development of program for early social recovery after total hip and knee arthroplasty patients
- Development and education of treatment which accommodates sports fields
- Regenerative medicine for cartilage disease

5. Publications

Original articles

1. Matsukura Y, Muneta T, Tsuji K, Koga H, Sekiya I. Erratum to: Mesenchymal Stem Cells in Synovial Fluid Increase After Meniscus Injury. Clin Orthop Relat Res. 2014 Jan 3. [Epub ahead of print] No abstract available. PMID:24385041
2. Matsukura Y, Muneta T, Tsuji K, Koga H, Sekiya I. Mesenchymal Stem Cells in Synovial Fluid Increase After Meniscus Injury. Clin Orthop Relat Res. 2013 Dec 13. [Epub ahead of print] PMID:24338094

3. Nakamura T, Sekiya I, Muneta T, Kobayashi E. [Bone and Cartilage Diseases and Regeneration. Articular cartilage regenerative therapy with synovial mesenchymal stem cells in a pig model]. *Clin Calcium*. 2013;23(12):1741-9. doi: [10.1007/s12121-013-1741-9](https://doi.org/10.1007/s12121-013-1741-9). Japanese. PMID:24292528
4. Horie M, Muneta T, Yamazaki J, Nakamura T, Koga H, Watanabe T, Sekiya I. A modified quadrant method for describing the femoral tunnel aperture positions in ACL reconstruction using two-view plain radiographs. *Knee Surg Sports Traumatol Arthrosc*. 2013 Nov 28. [Epub ahead of print] PMID:24288076
5. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Sekiya I. Effect of femoral tunnel position on graft tension curves and knee stability in anatomic double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2013 Sep 24. [Epub ahead of print] PMID:24061720
6. Ozeki N, Muneta T, Koga H, Katagiri H, Otabe K, Okuno M, Tsuji K, Kobayashi E, Matsumoto K, Saito H, Saito T, Sekiya I. Transplantation of Achilles tendon treated with bone morphogenetic protein 7 promotes meniscus regeneration in a rat model of massive meniscal defect. *Arthritis Rheum*. 2013 Nov;65(11):2876-86. doi: [10.1002/art.38099](https://doi.org/10.1002/art.38099). PMID:23897174
7. Katagiri H, Muneta T, Tsuji K, Horie M, Koga H, Ozeki N, Kobayashi E, Sekiya I. Transplantation of aggregates of synovial mesenchymal stem cells regenerates meniscus more effectively in a rat massive meniscal defect. *Biochem Biophys Res Commun*. 2013 Jun 14;435(4):603-9. doi: [10.1016/j.bbrc.2013.05.026](https://doi.org/10.1016/j.bbrc.2013.05.026). Epub 2013 May 16. PMID:23685144
8. Hatsushika D, Muneta T, Horie M, Koga H, Tsuji K, Sekiya I. Intraarticular injection of synovial stem cells promotes meniscal regeneration in a rabbit massive meniscal defect model. *J Orthop Res*. 2013 Sep;31(9):1354-9. doi: [10.1002/jor.22370](https://doi.org/10.1002/jor.22370). Epub 2013 Apr 17. PMID:23595964
9. Mochizuki T, Fujishiro H, Nimura A, Mahakkanukrauh P, Yasuda K, Muneta T, Akita K. Anatomic and histologic analysis of the mid-substance and fan-like extension fibres of the anterior cruciate ligament during knee motion, with special reference to the femoral attachment. *Knee Surg Sports Traumatol Arthrosc*. 2014 Feb;22(2):336-44. doi: [10.1007/s00167-013-2404-4](https://doi.org/10.1007/s00167-013-2404-4). Epub 2013 Jan 24. PMID:23344119
10. Koga H, Muneta T, Yagishita K, Ju YJ, Mochizuki T, Horie M, Nakamura T, Okawa A, Sekiya I. Effect of posterolateral bundle graft fixation angles on graft tension curves and load sharing in double-bundle anterior cruciate ligament reconstruction using a transtibial drilling technique. *Arthroscopy*. 2013 Mar;29(3):529-38. doi: [10.1016/j.arthro.2012.10.018](https://doi.org/10.1016/j.arthro.2012.10.018). Epub 2013 Jan 20. PMID:23343714
11. Yamazaki J, Muneta T, Ju YJ, Koga H, Morito T, Sekiya I. The kinematic analysis of female subjects after double-bundle anterior cruciate ligament reconstruction during single-leg squatting. *J Orthop Sci*. 2013 Mar;18(2):284-9. doi: [10.1007/s00776-012-0350-5](https://doi.org/10.1007/s00776-012-0350-5). Epub 2013 Jan 18. PMID:23329075
12. Ichinose S, Tagami M, Muneta T, Mukohyama H, Sekiya I. Comparative sequential morphological analyses during in vitro chondrogenesis and osteogenesis of mesenchymal stem cells embedded in collagen gels. *Med Mol Morphol*. 2013 Mar;46(1):24-33. doi: [10.1007/s00795-012-0005-9](https://doi.org/10.1007/s00795-012-0005-9). Epub 2013 Jan 17. PMID:23325551
13. Miyatake K, Tsuji K, Yamaga M, Yamada J, Matsukura Y, Abula K, Sekiya I, Muneta T. Human YKL39 (chitinase 3-like protein 2), an osteoarthritis-associated gene, enhances proliferation and type II collagen expression in ATDC5 cells. *Biochem Biophys Res Commun*. 2013 Feb 1;431(1):52-7. doi: [10.1016/j.bbrc.2012.12.094](https://doi.org/10.1016/j.bbrc.2012.12.094). Epub 2013 Jan 3. PMID:23291184
14. Watanabe T, Muneta T, Sekiya I, Banks SA. Intraoperative joint gaps affect postoperative range of motion in TKAs with posterior-stabilized prostheses. *Clin Orthop Relat Res*. 2013 Apr;471(4):1326-33. doi: [10.1007/s11999-012-2755-z](https://doi.org/10.1007/s11999-012-2755-z). Epub 2012 Dec 19. PMID:23250854
15. Watanabe T, Ishizuki M, Muneta T, Banks SA. Knee kinematics in anterior cruciate ligament-substituting arthroplasty with or without the posterior cruciate ligament. *J Arthroplasty*. 2013 Apr;28(4):548-52. doi: [10.1016/j.arth.2012.06.030](https://doi.org/10.1016/j.arth.2012.06.030). Epub 2012 Oct 31. PMID:23122654
16. Hatsushika D, Nimura A, Mochizuki T, Yamaguchi K, Muneta T, Akita K. Attachments of separate small bundles of human posterior cruciate ligament: an anatomic study. *Knee Surg Sports Traumatol Arthrosc*. 2013 May;21(5):998-1004. doi: [10.1007/s00167-012-2224-y](https://doi.org/10.1007/s00167-012-2224-y). Epub 2012 Sep 29. PMID:23052116
17. Muneta T, Koga H, Ju YJ, Horie M, Nakamura T, Sekiya I. Remnant volume of anterior cruciate ligament correlates preoperative patients' status and postoperative outcome. Muneta T, Koga H, Ju YJ, Horie M, Nakamura T, Sekiya I. *Knee Surg Sports Traumatol Arthrosc*. 2013 Apr;21(4):906-13. doi: [10.1007/s00167-012-2023-5](https://doi.org/10.1007/s00167-012-2023-5). Epub 2012 Apr 28. PMID:22543472
18. Atesok K, Doral MN, Bilge O, Sekiya I. Synovial stem cells in musculoskeletal regeneration. *J Am Acad Orthop Surg*. 2013 Apr;21(4):258-9. doi: [10.5435/JAAOS-21-04-258](https://doi.org/10.5435/JAAOS-21-04-258). No abstract available. PMID:23545732
19. Matsukura Y, Muneta T, Tsuji K, Koga H, Sekiya I. Mesenchymal Stem Cells in Synovial Fluid Increase After

Meniscus Injury. Clin Orthop Relat Res. 2013 Dec 13. [Epub ahead of print] PMID:24338094

20. Piao J, Tsuji K, Ochi H, Iwata M, Koga D, Okawa A, Morita S, Takeda S, Asou Y. Sirt6 regulates postnatal growth plate differentiation and proliferation via Ihh signaling. Sci Rep. 2013 Oct 23;3:3022. doi: 10.1038/srep03022.

Biostructural Science

1. Staffs and Students (as of April, 2013)

Professor	Yoshiro TAKANO
Associate Professor	Makoto J TABATA
Technician	Hachiro ISEKI (~ March)
Technician	Makoto Sugiura (May ~)
Secretary	Haruno Kuroda (April ~)
Graduate Student	Ravindra Kumar RATNAYAKE (~ March), Dawud ABDUWELI

2. Purpose of Education

[Undergraduate Education]

Provide dental students with the essential knowledge and methods of studies necessary to understand fundamentals of structure and function of the human body, based primarily on macroscopic- and microscopic anatomy (Histology), including dissection lab works which lasts nearly 3 months. Emphasis is placed on the structure and function of oral and maxillofacial regions including teeth, periodontal tissues, salivary glands and temporomandibular joints, as well as muscles and nerves related to these structures. These comprise major part of the largest teaching module of the 2nd-year dental education curriculum and are expected to build solid basis for future studies of advanced dental science and clinical dental medicine. Importantly, dental students learn part of these studies with medical students in the same class in the 2nd year.

[Graduate School]

Provide graduate students with updated information of mechanisms of biological mineralization, structural features, as well as ontogenic and evolutionary aspects of the development of biological hard tissues, and give a lab course of essential methods for structural analyses of hard tissues, particularly of teeth and periodontal tissues.

3. Research Subjects

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

- 1) Biological mineralization.
- 2) Induction and/or regeneration of dental and periodontal tissues.
- 3) Reaction-diffusion phenomenon in biological systems
- 4) Origin and evolution of tooth
- 5) Molecular mechanisms of tooth development
- 6) Role of dentin matrix proteins in the development of root and periodontal tissues
- 7) Sensory apparatus in masticatory systems.

4. Publications

Original Article

- 1) Ratnayake A.R.K. Ratnayake, Dawud Abduweli, Seong-Suk Jue, Otto Baba, Makoto J. Tabata, Kaj Josephsen, Ole Fejerskov, Yoshiro Takano: Organic Anion Transport in during Rat Enamel Formation. *J Oral Biosci* (2013) 55: 40-46.
- 2) Chisa Shitano, Otto Baba, Sawa Kaneko, Jun Hosomichi, Yasuhiro Shimizu, Naoki Shibutani, Risa Usumi-Fujita, Yoshiro Takano, Takashi Ono: Alveolar bone loss induced by the orthodontic tooth movement under hypofunctional conditions in rats. *Orthodontic Waves* 01/2013; 72(4):148-155.
- 3) Helle Damkier; Kaj Josephsen; Yoshiro Takano; Dirk Zahn; Ole Fejerskov; Sebastian Frische: Fluctuations in surface pH of maturing rat incisor enamel are a result of cycles of H⁺ secretion by ameloblasts and variations in enamel buffer characteristics, *Bone*. 2013 Dec 25;60C:227-234. doi: 10.1016/j.bone.2013.12.018. [Epub ahead of print]
- 4) Nahar Kamrun, Akemi Tetsumura, Yoshikazu Nomura, Satoshi Yamaguchi, Otto Baba, Shin Nakamura, Hiroshi Watanabe, Tohru Kurabayashi. Visualization of the superior and inferior borders of the mandibular canal: a comparative study using digital panoramic radiographs and cross-sectional CT images. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 115:550-557, 2013.
- 5) Yin Wang, Keli Ma, Peixiang Wang, Otto Baba, Helen Zhang, Jack M Parent, Pan Zheng, Yang Liu, Berge A

Minassian, Yan Liu: Laforin Prevents Stress-Induced Polyglucosan Body Formation and Lafora Disease Progression in Neurons. *Mol Neurobiol* 48:49-61, 2013.

- 6) Clara Prats, Alba Gomez-Cabello, Pernille Nordby, Jesper L Andersen, Jørn W Helge, Flemming Dela, Otto Baba, Thorkil Ploug: An optimized histochemical method to assess skeletal muscle glycogen and lipid stores reveals two metabolically distinct populations of type I muscle fibers. *PLoS One* 8(10):e77774, 2013.
- 7) Otto Baba, Masato S Ota, Tatsuo Terashima, Makoto J Tabata, Yoshiro Takano: Expression of transcripts for fibroblast growth factor 18 and its possible receptors during postnatal dentin formation in rat molars. *Odontology*. 2013 Dec 28. [Epub ahead of print]
- 8) Chunlin Chen, Zhongchang Wang, Mitsuhiro Saito, Tetsuya Tohei, Yoshiro Takano & Yuichi Ikuhara: Fluorine in Shark Teeth: Its Direct Atomic-Resolution Imaging and Strengthening Function. *Angew Chem Int Ed Engl* (DOI: 10.1002/anie.201307689)

Abstracts

- 1) Y. Takano, S. Jue, R. Ratnayake, D. Abduweli T. Uchida: Co-Localization of Amelogenin and Ubiquitin/Proteasome in the Cytosol of Ameloblasts. 91st IADR/AADR General Session, Seattle, USA, March 20-23, 2013.
- 2) Yoshiro Takano: Ameloblast cell modulation during enamel maturation – why and how?” Ole Fejerskov Memorial Symposium, Oral Biology 1967-2013, Aarhus, Denmark May 3, 2013.
- 3) Donacian M. Lyaruul, Jing Guo1, Carolyn W. Gibson, Yoshiro Takano, Pamela DenBesten, Antonius LJJ Bronckers: Quantitative X-ray microprobe analysis of fluorotic amelogenin-null enamel. 11th International Conference on Tooth Morphogenesis and Differentiation, La Londo, France, May 27-31, 2013.
- 4) Dawud Abduweli, Otto Baba, Yoshiro Takano: Teleost Fish Medaka- A New Experimental Modal for Tooth Regeneration. IADR-APR, JADR General Session 2013 Bangkok, Thailand, Aug 21-23, 2013.
- 5) Y. Takano and D. Abduweli: Enamel pH affects calcium acquisition, crystal growth and dissolution. IADR-APR, JADR General Session 2013 Bangkok, Thailand, Aug 21-23, 2013.
- 6) Chisa Shitano, Otto Baba, Sawa Kaneko, Jun Hosomichi, Yasuhiro Shimizu, Naoki Shibusaki, Risa Usumi-Fujita, Yoshiro Takano, Takashi Ono: Alveolar bone loss induced by hypofunctional tooth movement in rats. IADR-APR, JADR General Session 2013 Bangkok, Thailand, Aug 21-23, 2013.
- 7) ChunLin Chen, Susumu Tsukimoto, Yuichi Ikuhara, Tetsuya Tohei, YoshiroTakano: Microstructural Characterization of the Enameloid of Shark teeth. Japan ceramic society meeting. Tokyo Institute of Technology March 17-19, 2013.
- 8) Yoshiro Takano, Jue Seong-Suk ², Ratnayake R ¹, Abduweli Dawud ¹, Takashi Uchida: Cytosolic Processing of Enamel Matrix Proteins in Rat Incisors. 118th Annual Meeting of Japanese Association for Anatomists , Takamatsu, Kagawa, March 28-30, 2013.
- 9) Hiroyuki Mishima, Akiko Inoue, Atsuhiko Hattori, Nobuo Suzuki, Makoto Tabata, Mitsuo Kakei, Kei Matsumoto, Kazuto Satomura, Yasuo Miake: Relation between the dentin growth lines and secretion of signaling molecule of internal clock, melatonin. 118th Annual Meeting of Japanese Association for Anatomists, Takamatsu, Kagawa, March 28-30, 2013.
- 10) ChunLin Chen, Mitsuhiro Saito, Zhongchang Wang, Tetsuya Tohei, Yoshiro Takano, Yuichi Ikuhara: Atomic-Level Characterization of the Enameloid of Shark teeth, 69th Annual Meeting of Japanese Society of Microscopy, Senri, Osaka, May 20-22, 2013.
- 11) Yoshiro Takano, Dawud Abduweli: Propagating Waves of Ameloblast Modulation Affect Enamel pH, Mineral Acquisition, and Crystal Growth in Maturing Enamel. 57th Symposium of Japanese Society of Microscopy, Nagoya, November 15-16, 2013.

5. Invited Lectures

- 1) Yoshiro Takano: Ameloblast cell modulation during enamel maturation – why and how?” Ole Fejerskov Memorial Symposium, Oral Biology 1967-2013, Aarhus, Denmark May 3, 2013.
- 2) Yoshiro Takano: Regulatory mechanisms of hard tissue formation and biological mineralization. Tsurumi University Dental Society Lecture Series. Tsurumi, Yokohama, November 7, 2013.
- 3) Yoshiro Takano: Enamel maturation -Cellular regulation for the induction of gigantic enamel apatite crystals- Matsumoto Dental College Seminar for Graduate Students, Matsumoto, December 12, 2013.

Pharmacology

1. Staffs and Students (2013)

Professor	Keiichi OHYA
Associate Professor	Kazuhiro AOKI
Assistant Professor	Yukihiko TAMURA
Technologist	Mariko TAKAHASHI
Researcher	Nobuyoshi TOMOMATSU (Maxillofacial Surgery), Kengo FUJIKI (Removable Prosthodontics), Yasuhiro SHIMIZU (Orthodontic Science)
Researcher (JSPS)	Atsushi KAIDA (~Aug)
Graduate Student	Toshimi SATO, Md. Abdulla Al Masud KHAN (~Mar), Md. Abdullah Al MAMUN (~Sept), Atsushi KIMURA (Oral and Maxillofacial Surgery), Genki KATO, Yasutaka SUGAMORI, Natsuki SUZUKI (Removable Prosthodontics), Tomoki UEHARA (Pediatric Dentistry Jul~), Yuki ARAI (Removable Prosthodontics Jul~), Md. Zahirul Haque BHUYAN (Oct~)

2. 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. Research Subjects

- 1) Pharmacological analysis of the formation and resorption mechanisms of teeth and bone
- 2) Drug effects on the differentiation of the cells that participate formation and resorption process of the hard tissues
- 3) Identification of the new drug targets for hard tissue diseases
- 4) Translational research for the hard tissue regeneration
- 5) Analysis of side effects of the drug that appear in oral tissues

4. Publications

Original Article

1. Khan, M. Alles, N. Soysa, N. Mamun, A. Nagano, K. Mikami, R. Furuya, Y. Yasuda, H. Ohya, K. Aoki, K.: The local administration of TNF- α and RANKL antagonist peptide promotes BMP-2-induced bone formation. *J Oral Biosciences* 55:47-54 DOI: 10. 1016/j.job. 2012. 12. 006 2013
2. Mamun, A. Khan, M. Alles, N. Matsui, M. Tabata, Y. Ohya, K. Aoki, K.: Gelatin hydrogel carrier with the W9-peptide elicits synergistic effects on BMP-2-induced bone regeneration. *J Oral Biosciences* 55:217-223 DOI: 10. 1016/j.job. 2013. 06. 008 2013
3. Furuya, Y. Inagaki, A. Khan, M. Mori, K. Penninger, J.M. Nakamura, M. Udagawa, N. Aoki, K. Ohya, K. Uchida, K. Yasuda, H.: Stimulation of bone formation in cortical bone of mice treated with a receptor activator of nuclear factor- κ B ligand (RANKL)-binding peptide that possesses osteoclastogenesis inhibitory activity. *J Biol Chem* 288(8): 5562-5571 DOI: 10. 1074/jbc.M112. 426080 2013
4. Nagai, Y. Osawa, K. Fukushima, H. Tamura, Y. Aoki, K. Ohya, K. Yasuda, H. Hikiji, H. Takahashi, M. Seta, Y. Seo. S. Kurokawa, M. Kato, S. Honda, H. Nakamura, I. Maki, K. Jimi, E.: p130Cas, Crk-associated substrate, plays important roles in osteoclastic bone resorption. *J Bone and Mineral Res* 28(12): 2449-2462 DOI: 10. 1002/jbmr. 1936 2013
5. Sriarj, W. Aoki, K. Ohya, K. Takahashi, M. Takagi, Y. Shimokawa, H.: TGF- β in dentin matrix extract induces osteoclastogenesis in vitro. *Odontology* 12 DOI:10.1007/s10266-013-0140-3 2013

6. Nassar, M. Hiraishi, N. Islam, MS. Aizawa, M. Tamura, Y. Otsuki, M. Kasugai, S. Ohya, K. Tagami, J.: Effect of phytic acid used as etchant on bond strength, smear layer, and pulpal cells. *Eur J Oral Science* 121(5):482-487 DOI: 10.1111/eos.12064 2013
7. Nakamura, H. Aoki, K. Masuda, W. Alles, N. Nagano, K. Fukushima, H. Osawa, K. Yasuda, H. Nakamura, I. Mikuni-Takagaki, Y . Ohya, K. Maki, K. Jimi, E.: Disruption of NF- κ B1 prevents bone loss caused by mechanical unloading. *J Bone and Mineral Res* 28(6):1457-1467 DOI: 10.1002/jbmr.1866 2013
8. Fujiki, K. Aoki, K. Marcian, P. Borak, L. Hudieb, M. Ohya, K. Igarashi, Y. Wakabayashi, N.: The influence of mechanical stimulation on osteoclast localization in the mouse maxilla: bone histomorphometry and finite element analysis. *Biomechanics and Modeling in Mechanobiology* 12(2): 325-333 DOI: 10.1007/s10237-012-0401-z 2013

Connective Tissue Regeneration

1. Staff (April, 2013)

Associate Professor

Tamayuki SHINOMURA

2. Purpose of Education

Our laboratory is interested in the molecular mechanisms underlying the formation and maintenance of connective tissues including cartilage and periodontal tissues. Our goal is to control the restoration and regeneration of the tissues. To achieve this goal, we are focusing on extracellular matrix molecules specifically expressed in the tissues and transcription factors regulating their expressions. Therefore, in our graduate course, we provide students opportunity to study molecular biology and extracellular matrix biology.

3. Research Subjects

- 1) Study on transcription factors necessary for the maintenance of chondrogenic phenotype.
- 2) Study on the molecular dynamics of extracellular matrix in connective tissues.
- 3) Study on novel genes actively expressed in periodontal tissues.

4. Publications

Original Articles

1. Takahashi S, Fukuda M, Mitani A, Fujimura T, Iwamura Y, Sato S, Kubo T, Sugita Y, Maeda H, Shinomura T, Noguchi T Follicular dendritic cell-secreted protein is decreased in experimental periodontitis concurrently with the increase of interleukin-17 expression and the Rankl/Opg mRNA ratio J Periodontal Res. (2013)

Biochemistry

1. Staffs and student (April, 2013)

Professor	Masaki Yanagishita
Associate Professor	Miki Yokoyama
Junior Associate Professor	Yasuhiro Kumei
Assistant Professor	Katarzyna Anna Podyma-Inoue
Technical staff	Kazue Terasawa
Part-time instructure	Zeredo, Jorge Luis Lopes Akira Asari
Graduate student	Hiroko Yamanokuchi, Rajapakshe Mudiyanseelage Anupama Rasadari Rajapakshe

2. Purpose of education

Intracellular transport of lysosome/endosome system is an underlying mechanism of cellular homeostasis and thus its disfunction is related to etiology of various diseases. Our section focuses on the research and education on molecular composition, biological functions and pathological processes involving intracellular transport of lysosomes/endosomes.

3. Research subjects

- Role of heparan sulfate proteoglycans in etiology of neurodegenerative disease
- Structural and functional aspects of intracellular transport-machinery of lysosomes
- Regulation of membrane dynamics by sphingolipids
- Mechanism of sensation and response to low gravity

4. Publications

Original Article

- Hara-Yokoyama, M., Terasawa K., Ichinose S., Watanabe, A., Podyma-Inoue, K.A., Akiyoshi K., Igarashi, Y. and Yanagishita M. (2013) Sphingosine kinase 2 inhibitor SG-12 induces apoptosis via phosphorylation by sphingosine kinase 2. *Bioorganic & Medicinal Chemistry Letters* 23: 2220-2224.
- Takehara S., Yanagishita M., Podyma-Inoue, K.A. and Kawaguchi Y. (2013) Degradation of MUC7 and MUC5B in human saliva. (2013) *PLoS One* 8(7): e69059.
- Kasekarn Kasevayuth, Katarzyna Anna Podyma-Inoue, Masaki Yanagishita (2013) Effect of lipopolysaccharede from *Porphyromonas gingivalis* on expression of heparanase in human gingival epithelial cell line, Ca9-22, Chulalongkorn University Dental Journal, 36, 143-152.

Review Articles

- Hara-Yokoyama, M. (2013) Glycosylation Regulates CD38 Assembly on the Cell Surface. *Trends In Glycoscience and Glycobiology (TIGG)* 25(146): 215-225.
- Ebe, N., Hara-Yokoyama, M., and Izumi Y. (2013) Role of HMGB1 in Periodontal Disease. in "Studies on Periodontal Disease" edited by Ekuni etal., Humana Press.

Cell Signaling

1. Staffs and Students

Associate Professor (Principal Investigator)

Tomoki NAKASHIMA (April~)

Assistant Professor

Mikihito HAYASHI (June~)

2. 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. 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

4. Publications

【Original Article】

1. Komatsu N, Okamoto K, Sawa S, Nakashima T, Oh-hora M, Kodama T, Tanaka S, Bluestone JA, Takayanagi H. Pathogenic conversion of Foxp3⁺ T cells into T_H17 cells in autoimmune arthritis. *Nat Med* 20, 62-68 (2013).

【Review Article】

1. O'Brien CA, Nakashima T, Takayanagi H.: Osteocyte control of osteoclastogenesis. *Bone* 54, 258-263 (2013).

【Presentation】

1. IBMS-JSBMR 2013 Kobe, Young investigator workshop1:Experience of doing a postdoc. Tomoki Nakashima, May 28 2013
2. The 22nd International Rheumatology Symposium Kyoto, Regulation of bone remodeling by osteocytes. Tomoki Nakashima April 19 2013

【Award】

1. Tomoki Nakashima: TMDU Research Award 2013.Oct
2. Mikihito Hayashi: The Japanese Society of Inflammation and Regeneration. Young Investigator Award 2013.July

Institute of Biomaterials and bioengineering (Inorganic Biomaterials) (Inorganic Materials)

1. Staffs and Students

Professor	Kimihiro Yamashita	
Associate Professor	Miho Nakamura	
Assistant Professor	Nahohiro Horiuchi	
Project Assistant Professor	Noriko Ebe	
Graduate Students	Yu Tsuchiya,	Nanba Saki
	Kazuhiro Kohata,	Shen Dongbe

2. Education

Biomaterial engineering

3. Research Subjects

(1) Development of Electrovector ceramics

Some ceramics, such as a hydroxyapatite, are able to be ionically polarized by thermoelectrical treatments. Consequently, the polarized ceramics have large and time-durable induced electrostatic charges on their surfaces. The effects of the induced charges profoundly dominate the proximate few millimeter regions. We named the effects "Electrovector effects" and develop "Electrovector ceramics" defined as ceramics emitting the Electrovector Effects.

(2) Control of electrical space on Electrovector ceramic

To translate the Electrovector ceramics into practical applications for medical devices, electrical space on Electrovector ceramics should be suitably controlled under the poling process. We are evaluating the poling mechanisms of some bioceramics, based on the various disciplines. In particular, we are putting emphasis on the relationship between the origin of electrical space and the crystal structure on the surface of the polarized bio-ceramics. The crystal defect, crystal distortion and fine change of ion composition of Electrovector ceramics polarized under various conditions are systematically investigated.

(3) Manipulation of biological responses by Electrovector ceramics

The electrostatic energies of the Electrovector effects aforementioned dominate the limited proximate areas and can control reactions locally. Therefore, the Electrovector ceramics can manipulate biological responses in a target space by both of the surface character and the electrostatic energies of the Electrovector ceramics at ion and tissue levels. We have demonstrated that the Electrovector ceramics enhanced protein adsorption, proliferation, adhesion, and differentiation of cultured cells on the ceramics as well as osteoconductivities in vivo by molecular biological and immunological detections.

(4) Development of applicable devices by ceramic technologies

We apply the Electrovector ceramics aforementioned to implant systems, such as artificial bones, bone joints, tooth roots, and are developing implantable devices with autograft-like osteoconductivities. We are undergoing improvements of sol-gel method for hydroxyapatite thin film coating and materials for vascular regeneration. We are extending our researches based on ceramic technologies farther, such as a control of oral environment, an improvement of oral esthetics, more effective and precise diagnosis systems for clinical laboratory medicine.

4. Publications

Original Article

1. Wada N, Mukougawa K, Horiuchi N, Wei W, Hiyama T, Nakamura M, Nagai A, Okura T, Yamashita K. Fundamental Electrical Properties of Ceramic Electrets. *Mater. Res. Bull.*, 48; 3854-3859, 2013.
2. S. Ohba, W. Wei, S. Itoh, A. Nagai, K. Yamashita, Enhanced Effects of New Bone Formation by an Electrically Polarized Hydroxyapatite Microgranule/Platelet-rich Plasma Composite Gel, *Key Eng. Mater.*, 529-539; 82-87, 2013.
3. M. Nakamura, A. Nagai, K. Yamashita, Surface Electric Fields of Apatite Electret Promote Osteoblastic Responses, *Key Eng. Mater.*, 529-539; 357-360, 2013.
4. Y. Tsuchiya, N. Horiuchi, M. Nakamura, K. Nozaki, A. Nagai, K. Hashimoto, K. Yamashita, Effect of Polarization Treatment Time on Inhibition of Low Temperature Degradation in Y-Doped ZrO₂, *Key Eng. Mater.*, 529-539; 601-

604, 2013.

5. R. Nemoto, K. Nozaki, K. Yamashita, H. Miura, Effect of Framework Design on the Surface Strain of Zirconia Fixed Partial Dentures, *Dent. Mater. J.*, 32; 289-295, 2013.
6. Wada N, Horiuchi N, Nakamura M, Hiyama T, Nagai A, Okura T, Yamashita K. Effect of Poly(acrylic acid) and Polarization on the Controlled Crystallization of Calcium Carbonate on Single-Phase Calcite Substrates. *Cryst. Growth Des.* 13; 2928-2937, 2013.
7. Nakamura M, Toyama T, Morita A, Horiuchi N, Nozaki K, Nagai A, Yamashita K. Electric poling of cement composites of hydroxyapatite whiskers with chitosan and their chemical properties in simulated body fluid. *J Ceram Soc Japan.*, 121; 895-900, 2013.
8. Nakamura M, Hentunen T, Salonen J, Nagai A, Yamashita K. Characterization of bone mineral-resembling biomaterials for optimizing human osteoclast differentiation and resorption. *J Biomed Mater Res A.*, 101A; 3141-3151, 2013.
9. Horiuchi N, Nakamura M, Nagai A, Yamashita K. Drug Adsorption Property of Surfaces of Polarized Calcium Phosphate Powders. *Key Eng. Mater.*, 566; 302-305, 2013.
10. Horiuchi N, Endo J, Nozaki K, Nakamura M, Nagai A, Katayama K, Yamashita K. Dielectric evaluation of fluorine substituted hydroxyapatite. *J. Ceram. Soc. Jpn.*, 121; 770-774, 2013.
11. Horiuchi N, Endo J, Wada N, Nozaki K, Nakamura M, Nagai A, Katayama K, Yamashita K. Dielectric properties of stoichiometric and defect-induced hydroxyapatite. *J. Appl. Phys.*, 113; 134905, 2013.
12. K. Kohata, S. Itoh, S. Takeda, M. Kanai, T. Yoshioka, H. Suzuki, K. Yamashita, Enhancement of Fracture Healing by Electrical Stimulation in the Comminuted Intraarticular Fracture Treatment, *Bio-Med. Mater. Eng.*, 23; 485-493, 2013.
13. A. Nagai, N. Horiuchi, K. Nozaki, M. Nakamura, K. Yamashita, Quantitative Evaluation of the Hydrophilic Properties of Polarized Hydroxyapatite, *Ceram. Trans.*, 242; 103-112, 2013.
14. M. Nakamura, A. Kobayashi, K. Nozaki, N. Horiuchi, A. Nagai, K. Yamashita, Improvement of Osteoblast Adhesion through Polarization of Plasma-Sprayed Hydroxyapatite Coatings on Metal, *J. Med. Biol. Eng.*(in press)

Conferences

■Invited

1. Horiuchi N, Nozaki K, Nakamura M, Nagai A, and Yamashita K, Electric characterization in hydroxyapatite for understanding biointerfaces, the International Union of Materials Research Society - the International Conference in Asia - 2013 (IUMRS-ICA 2013), Bangalore, India, Dec. 2013.
2. Nagai A, Yamashita K. Recent advances of carbonated apatite. 2013 Asian Bioceramics symposium, Kyoto, Japan, Dec., 2013.
3. Nakamura M, Horiuchi N, Nozaki K, Nagai A, Yamashita K. Improved osteogenic cell behaviors by surface electric fields of polarized apatite. International Symposium on EcoTopia Science 2013, Nagoya, Dec., 2013.

■General

1. Nakamura M, Hentunen T, Salonen J, Nakahama K, Morita I, Yamashita K. Osteoclast differentiation and activation from bone marrow cells through the stimulation of osteocytes on surface-charged calcium apatite. 2nd Joint Meeting of the International Bone and Mineral Society and the Japanese Society for Bone and Mineral Research. Kobe, May 2013.
2. Horiuchi N, Tsuchiya Y, Nakamura M, Nozaki K, Nagai A, and Yamashita K, Thermally Stimulated Depolarization Current in YSZ Ceramics, the 19th International Conference on Solid State Ionics (SSI-19), Kyoto, Japan, June 2013.
3. Nozaki K., Nagai A., Yamashita K. Effect of surface charges on early osseointegration of polarized Ti implant. 13th International Conference of the European Ceramic Society. Limoges, France, Jun., 2013.
4. Nagai A, Hattori T, Nozaki K, Aizawa M, Yamashita K. Electric Fields Induced by Electric Polarization Reduce Proliferation Rates of Tumor Cell through Cell Cycle Modulation. The 4th International symposium of Surface and Interface of Biomaterials, Roma, Italy, Sep.,2013
5. Nakamura M, Hentunen T, Salonen J, Nakahama K, Morita I, Nagai A, Yamashita K. Cell-mediated Stimulation of Osteoclast Differentiation without Any Differentiation Factors on Carbonated Apatite. 25th European Conference on Biomaterials. Madrid, Spain, Sep.,2013.
6. Horiuchi N, Nakamura M, Nozaki K, Ebe N, Nagai A, and Yamashita K, Evaluation of Electric Field on Polarized Hydroxyapatite Using Vibrating Electrode, International Conference on BioSensors, BioElectronics, BioMedical Devices, BioMEMS/NEMS and Applications 2013 (Bio4Apps 2013), Tokyo, Japan, Oct. 2013.

7. Koizumi H., Nozaki K., Nagai A., Okura T., Yamashita K. Effect of electrical polarization on the adhesion of streptococcus mutans to the dental porcelain. 2nd International Symposium on Inorganic and Environmental Materials, Rennes, France, Oct., 2013.
8. Nozaki K., Horiuchi N., Nakamura M., Nagai A., Yamashita K. Enhanced osteoinductivity of titanium implant with controlled surface charge. International Conference on BioSensors, BioElectronics, BioMedecal Devices, BioMEMS / NEMS and Applications 2013 & 5th Sensing Biology Symposium. Tokyo, Japan, Oct., 2013.
9. Tsuchiya Y, Horiuchi N, Nozaki K, Nakamura M, Nagai A, Hashimoto K, and Yamashita K, Polarization effect on phase stability in yttria stabilized zirconia ceramics, the 13th Asian BioCeramics Symposium (ABC2013), Kyoto, Japan, Dec. 2013.
10. Namba S, Nakamura M, Toyama T, Nishimiya N, Yamashita K. Surface free energy of poalrized hydroxyapatite affects osteocyte behaviors. Asian BioCeramics Symposium 2013, Kyoto, Dec., 2013.
11. Nozaki K., Ebe N., Nakamura M., Horiuchi N., Nagai A., Yamashita K. Effect of estrogen deficiency on osseointegration around surface charged titanium implant. International Symposium on EcoTopia Science 2013 & The 4th International Symposium on Advanced Materials Development and Integration of Novel Structured Metallic and Inorganic Materials. Dec., 2013.

Periodontology

1. Staffs and Students

Professor	Yuichi IZUMI	
Associate Professor	Hisashi WATANABE	
Lecturer	Satsuki HAGIWARA,	Akira AOKI
Research Associate	Hiroaki KOBAYASHI, Tatsuya AKIZUKI, Tomonari SUDA	Yasuo TAKEUCHI, Koji MIZUTANI
Graduate Students	Kaori FUJIWARA, Ye CHANGCHANG, Mayumi OGITA, Yuichi IKEDA, Akiko ENDO, Akiko TSUNO, Supreda SUPHANANTACHAT, Kuniha KONUMA, Takanori MATSUURA, Keiko AKAZAWA, Masahiro NODA, Ayano UEKUBU, Makoto KANEKO, Yuka SHIHEIDO, Wataru ONO(April~), Takeaki SUDO(April~), Kiichi MARUYAMA(April~),	Yasuo ITO, Asuka SEKINISHI, Norihiko ASHIGAKI, Yasuyuki KIMURA, Noriko MARUYAMA, Takahiko SHIBA, Shogo MAEKAWA, Takashi HOSHI, Masayuki TOI, Takahiro IKAWA, Masaru ONIZUKA, Misa GOKYU, Taicheng Lin, Hiroki SATO(April~), Mizuki NAGATA(April~), Kosei NANO(April~)

Hospital Staff: 7, Research Student: 20, Registered dentist: 46

2. Purpose of Education

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.

3. Research Subjects

- 1) Periodontopathic bacteria and their pathogenicity
- 2) Inflammatory and immunological factors in periodontal disease
- 3) Analyses of growth factors and bio materials in periodontal regeneration
- 4) Clinical applications of laser in periodontics
- 5) Influence of periodontal disease on general health

4. Clinical Services

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

5. Publications

Original Article

1. Almehti A, Aoki A, Ichinose S, Taniguchi Y, Sasaki KM, Ejiri K, Sawabe M, Chui C, Katagiri S, Izumi Y. Histological and SEM analysis of root cementum following irradiation with Er:YAG and CO₂lasers. *Lasers Med Sci* 28: 203-213, 2013.
2. Aoyama N, Suzuki J, Ogawa M, Watanabe R, Kobayashi N, Hanatani T, Ashigaki N, Sekinishi A, Izumi Y, Isobe M. Toll-like receptor-2 plays a fundamental role in periodontal bacteria-accelerated abdominal aortic aneurysms. *Circ J* 77: 1565-1573, 2013.
3. Ashigaki N, Suzuki J, Ogawa M, Watanabe R, Aoyama N, Kobayashi N, Hanatani T, Sekinishi A, Zempo H, Tada Y,

- Takamura C, Wakayama K, Hirata Y, Nagai R, Izumi Y, Isobe M. Periodontal Bacteria Aggravate Experimental Autoimmune Myocarditis in Mice. *Am J Physiol-Heart Circul Physiol* 304: 740-748, 2013.
4. Ashigaki N, Suzuki J, Ogawa M, Watanabe R, Aoyama N, Kobayashi N, Hirata Y, Komuro I, Izumi Y, Isobe M. Periodontal bacteria aggravate chronic renal failure induced by subtotal nephrectomy in mice. *Immunology, Endocrine & Metabolic Agents in Medicinal Chemistry* 13(3): 206-213, 2013.
 5. Ashigaki N, Suzuki J, Aoyama N, Ogawa M, Watanabe R, Kobayashi N, Komuro I, Izumi Y, Isobe M. The periodontal pathogen *Aggregatibacter actinomycetemcomitans* affects experimental autoimmune myocarditis in mice. *Int Heart J* 54(6):412-416, 2013.
 6. Bharti P, Katagiri S, Nitta H, Nagasawa T, Kobayashi H, Takeuchi Y, Izumiyama H, Uchiyama I, Inoue S, Izumi Y. Periodontal treatment with topical antibiotics improves glycemic control in association with elevated serum adiponectin in patients with type 2 diabetes mellitus. *Obes Res Clin Pract* 7:e129-e138, 2013.
 7. Chui C, Aoki A, Takeuchi Y, Sasaki K, Hiratsuka K, Abiko Y, Izumi Y. Antimicrobial effect of photodynamic therapy using high-power blue light-emitting diode and red-dye agent on *Porphyromonas gingivalis*. *J Periodontal Res* 48: 696-705, 2013.
 8. Ejiri K, Aoki A, Yamaguchi Y, Ohshima M, Izumi Y. High-frequency low-level diode laser irradiation promotes proliferation and migration of primary cultured human gingival epithelial cells. *Lasers Med Sci* DOI 10.1007/s10103-1292-7.
 9. Etemadi A, Sadeghi M, Abbas FM, Razavi F, Aoki A, Azad RF, Chiniforush N. Comparing Efficiency and Root Surface Morphology After Scaling with Er:YAG and Er,Cr:YSGG Lasers. *Int J Periodontics Restorative Dent* 2013;33:e140-e144
 10. Hamaya R, Ogawa M, Suzuki J, Kobayashi N, Hirata Y, Nagai R, Komuro I, Isobe M. A selective peroxisome proliferator-activated receptor- β / δ agonist attenuates neointimal hyperplasia after wire-mediated arterial injury. *Expert Opin Investig Drugs* 22(9):1095-106, 2013.
 11. Hayakumo S, Arakawa S, Mano Y, Izumi Y. Clinical and microbiological effects of ozone nano-bubble water irrigations as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. *Clin Oral Invest* 17:379-388, 2013.
 12. Ito H, Numabe Y, Sekino S, Murakami E, Iguchi H, Hashimoto S, Sasaki D, Yaegashi T, Kunimatsu K, Takai H, Mezawa M, Ogata Y, Watanabe H, Hagiwara S, Izumi Y, Hiroshima Y, Kido J, Nagata T. Evaluation of bleeding on probing and gingival crevicular fluid enzyme activity for detection of periodontally active sites during supportive periodontal therapy. *Odontology* in press.
 13. Iwasaki K, Komaki M, Yokoyama N, Tanaka Y, Taki A, Kimura Y, Takeda M, Oda S, Izumi Y, Morita I. Periodontal Ligament Stem Cells Possess the Characteristics of Pericytes. *J Periodontol* 84: 1425-1433, 2013.
 14. Katagiri S, Nitta H, Nagasawa T, Izumi Y, Kanazawa M, Matsuo A, Chiba H, Fukui M, Nakamura N, Oseko F, Kanamura N, Inagaki K, Noguchi T, Naruse K, Matsubara T, Miyazaki S, Miyauchi T, Ando Y, Hanada N, Inoue S. Effect of glycemic control on periodontitis in type 2 diabetic patients with periodontal disease. *J Diabetes Invest* 4: 320-325, 2013.
 15. Kobayashi N, Suzuki J, Ogawa M, Aoyama N, Komuro I, Izumi Y, Isobe M. *Porphyromonas gingivalis* promotes neointimal formation after arterial injury through toll-like receptor 2 signaling. *Heart Vessels* in press.
 16. Koyanagi T, Sakamoto M, Takeuchi Y, Maruyama N, Ohkuma M, Izumi Y. Comprehensive microbiological findings in peri-implantitis and periodontitis. *J Clin Periodontol* 40: 218-226, 2013.
 17. Li Q, Park K, Li C, Rask-Madsen C, Mima A, Qi W, Mizutani K, Huang PL, King GL. Induction of vascular insulin resistance, endothelin-1 expression, and acceleration of atherosclerosis by the over expression of protein kinase C β isoform in the endothelium. *Circ Res* 113(4):418-27, 2013.
 18. Miyazaki H, Oshiro T, Watanabe H, Kakizaki H, Makiguchi T, Kim M, Negishi A, Yokoo S. Ultrasound-guided intralesional laser treatment of voluminous venous malformation in the oral cavity. *Int J Oral Maxillofac Surg* 42:281-287, 2013.
 19. Murakami M, Suzuki J, Yamazaki S, Ikezoe M, Matsushima R, Ashigaki N, Aoyama N, Kobayashi N, Wakayama K, Akazawa H, Komuro I, Izumi Y, Isobe M. High incidence of *Aggregatibacter actinomycetemcomitans* infection in patients with cerebral infarction and diabetic renal failure: a cross-sectional study. *BMC Infect Dis* in press.
 20. Okamoto T, Ishikawa I, Kumasaka A, Morita S, Katagiri S, Okano T, Ando T. Blue-violet light emitting diode (LED) irradiation in combination with hemostatic gelatin sponge (Spongel®) application ameliorates immediate socket bleeding in patients taking warfarin. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* in press.
 21. Onishi H, Ro M, Hayashi J, Tatsumi J, Satomi N, Yatabe K, Arakawa S, Izumi Y, Shin K. Modification of forsythia

- detaching factor by gingival crevicular fluid in periodontitis. *Arch Oral Biol* 58:1007-1013, 2013.
22. Park K, Li Q, Rask-Madsen C, Mima A, Mizutani K, Winnay J, Maeda Y, D'Aquino K, White MF, Feener EP, King GL. Serine phosphorylation sites on IRS2 activated by angiotensin II and protein kinase C to induce selective insulin resistance in endothelial cells. *Mol Cell Biol* 33(16):3227-41, 2013.
 23. Sawabe M, Aoki A, Komaki M, Iwasaki K, Ogita M, Izumi Y. Gingival tissue healing following Er:YAG laser ablation compared to electrosurgery in rats. *Lasers Med Sci* Nov 16 (e-pub), 2013.
 24. Suzuki J, Aoyama N, Aoki M, Tada Y, Wakayama K, Akazawa H, Shigematsu K, Hoshina K, Izumi Y, Komuro I, Miyata T, Hirata Y, Isobe M. High incidence of periodontitis in Japanese patients with abdominal aortic aneurysm. *Int Heart J* in press.
 25. Suzuki T, Notomi T, Miyajima D, Mizoguchi F, Hayata T, Nakamoto T, Hanyu R, Kamolratanakul P, Mizuno A, Suzuki M, Ezura Y, Izumi Y, Noda M. Osteoblastic differentiation enhances expression of TRPV4 that is required for calcium oscillation induced by mechanical force. *Bone* 54:172-178, 2013.
 26. Taniguchi Y, Aoki A, Mizutani K, Takeuchi Y, Ichinose S, Takasaki A, Schwarz F, Izumi Y. Optimal Er:YAG laser irradiation parameters for debridement of microstructured fixture surfaces of titanium dental implants. *Lasers Med Sci* 28: 1057-1068, 2013.
 27. Thanakun S, Watanabe H, Thaweboon S, Izumi Y. An effective technique for the processing of saliva for the analysis of leptin and adiponectin. *Peptides* 47: 60-65, 2013.
 28. Tsuchida S, Satoh M, Kawashima Y, Sogawa K, Kado S, Sawai S, Nishimura M, Ogita M, Takeuchi Y, Kobayashi H, Aoki A, Kodera Y, Matsushita K, Izumi Y, Nomura F. Application of quantitative proteomic analysis using tandem mass tags for discovery and identification of novel biomarkers in periodontal disease. *Proteomics* 13: 2339-2350, 2013.
 29. Wara-aswapati N, Chayasodom A, Surarit R, Pitiphat W, Boch JA, Nagasawa T, Ishikawa I, Izumi Y. Induction of Toll-Like Receptor Expression by *Porphyromonas gingivalis*. *J Periodontol* 84: 1010-1018, 2013.
 30. Yamada A, Iwata T, Yamato M, Okano T, Izumi Y. Diverse functions of secreted frizzled-related proteins in the osteoblastogenesis of human multipotent mesenchymal stromal cells. *Biomaterials* 34: 3270-3278, 2013.
 31. Yamada Y, Nakamura S, Ito K, Umemura E, Hara K, Nagasaka T, Abe A, Baba S, Furuichi Y, Izumi Y, Klein OD, Wakabayashi T. Injectable Bone Tissue Engineering Using Expanded Mesenchymal Stem Cells. *Stem Cells* 31: 572-580, 2013.
 32. Ye C, Katagiri S, Miyasaka N, Bharti P, Kobayashi H, Takeuchi Y, Momohara Y, Sekiguchi M, Takamine S, Nagasawa T, Izumi Y. The anti-phospholipid antibody-dependent and independent effects of periodontopathic bacteria on threatened preterm labor and preterm birth. *Arc Gynecol Obstet* 288:65-72, 2013.

Health Promotion

1. Staffs and Students

Professor	Takehito Takano
Lecturer	Masashi Kizuki
Assistant Professor	Ayako Morita (from August)
Graduate Student	Mari Uchimura, Aya Anzai, Yoshiko Shimosawa (from April), Chau Darapheak (till September), Satoshi Suyama (till March), Miho Ito (till March), Azusa Okada (till March)

2. Purpose of Education

Graduate School Programs

The objective of postgraduate education in the field of public health is to pursue professional qualifications of high caliber who exhibit leadership in the advancement of public health and promotion of health on an international scale. The department helps students attain knowledge, skills, attitude, and experiences that are necessary to become a competent public health specialist. With the expansion of the new graduate programs in the university, greater attention is now given to making commitments and contributions in the international arena. Presently, the phrase “think globally and act locally” has become a global movement. The advancement of public health demands an increase in professionals who possess a global perspective yet appreciate the importance of local activities.

[Master Programs]: Masters degree students receive a systematic intensive training that leads to the acquisitions of broad expertise in the fields of public health, immunology, and medicine of health promotion. This program now consists of students with backgrounds in various majors.

[Doctoral 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. A rich variety of educational activities are arranged in the course of the program. These include, among others, individual discussion sessions with professors and other faculty members, field investigations, 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 research and confirmation on each of their progress.

[Public Health Leaders (PHL) Program]: Students in the PHL program achieve in attaining the skills required for public health professionals with an international perspective, particularly 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.

Public Health Education Program for Medical School Student

The Graduate School of Medicine aims to prepare its medical students for future careers as physicians who will recognize the societal importance of their medical services and have the ability to fulfill both the scientific and social roles of their professions.

[Social Medicine] The Medical Education at Tokyo Medical and Dental University can be broken down into three fields. They are 1) experimental, 2) clinical, and 3) social medicine. Social medicine emphasizes on the social aspects of medicine, which primarily has to do with the mechanisms of health, the occurrences of diseases, prevention methods, and the role of healthcare. It strives to identify the causes and mechanisms underlying the health problems confronting society, as well as to engineer solutions backed by a systematic and organized approach. Changes in the modern social atmosphere of medicine and healthcare are closely linked to several changes within the international society. The Social Medicine department follows the Medical Education Core Curriculum as its base, and also uses it as a benchmark study for the national examination for medical practitioners. Studies covered in this curriculum include critical issues that may or may not be new, but are relevant to the field of social medicine.

[Public Health] The Public Health education program is comprised of courses in public health, researches on public health related topics, off-campus internships pertaining to public health, and small group seminars. The topics in the Public Health education are the following:

I. Healthcare doctrine; 1. The history of public health 2. Health concepts and awareness 3. Synergies of health and the environment 4. Health determinants 5. Human living environments 6. International healthcare 7. Regional healthcare and medical practice 8. Urban healthcare 9. The coordination of healthcare, medical practice, and welfare 10. Administrative

frameworks and resources for healthcare, medical practice, and welfare 11. Social insurance frameworks and medical economics 12. Laws relation to healthcare, medical practice, and welfare.

II. Preventive medicine and health promotion; 1. Public health statistics and multivariate analysis 2. Epidemiology 3. Health promotion 4. Health education 5. Health management 6. Lifestyles and health 7. Maternal healthcare 8. Adult and elderly healthcare 9. School healthcare 10. Mental healthcare 11. Industrial medicine and healthcare 12. Environmental toxicology 13. Environmental pollution and its impact on health 14. Environmental health and global environmental problems 15. Food health and the impact of diet on health 16. Measures against infectious disease

The courses in the Public Health education program are limited in time, and thus, cannot cover all the topics listed above in full detail. Nonetheless, in demands presented by the national exam for medical practitioners, their post-graduate research, and for their future roles as physicians, students will need to thoroughly study the subjects on their own. In addition to these and counting, there is close to one hundred different topics that can be considered as topics for student's research papers. In this paper, each student will be expected to develop and analyze an in-depth understanding about the subject they choose from the list. As part of the research, students will gather requisite materials and documentation, conduct surveys, analyze data, and prepare reports based on their topic. Internships and participation in small group seminars involve students working in small teams to investigate common subject matters. These programs are designed to help students reinforce their ability to engage in multifaceted investigations concerning with specific problems in the field of public health. Furthermore, students are to actively pursue in independent study, apply scientific reasoning, and be able to present their reasoning and conclusions to a broader audience in a structure that is comprehensive and explicit. Classes are taught by Tokyo Medical and Dental University Graduate School professors in the field of environmental, social, and clinical medicine.

3. Research Subjects

- Urban environments, lifestyles, and health
- Urbanization and its impact on health in developing countries
- Socioeconomic conditions, social inequalities, and health
- Standards and determinants of health
- Monitoring and evaluation of healthy cities development
- Information technology applications in Public Health
- The utilization of geographic information systems for Public Healthy policies
- The measurement of disease infection risks in urban societies
- The lifestyles and growth of children in urban areas
- Globalization of health care service and migration of medical professionals
- End of Life in the community healthcare system
- Working conditions of medical doctors
- Reconstruction support of disaster-affected areas

4. Publications

Original Article

1. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate Partner Violence and Symptoms of Sexually Transmitted Infections: Are the Women from Low Socio-economic Strata in Bangladesh at Increased Risk. *Int J Behav Med.* 2014 Apr;21(2):348-57.
2. Rahman M, Nakamura K, Seino K, Kizuki M. Do Tobacco Smoking and Illicit Drug/Alcohol Dependence Increase the Risk of Mental Disorders Among Men? Evidence from a National Urban Bangladeshi Sample. *Perspect Psychiatr Care.* 2014 Jan 17.
3. Rahman M, Nakamura K, Seino K, Kizuki M. Does gender inequity increase the risk of intimate partner violence among women? Evidence from a national Bangladeshi sample. *PLoS One.* 2013 Dec 23;8(12):e82423.
4. Al-Khulaidi GA, Nakamura K, Seino K, Kizuki M. Decline of supportive attitudes among husbands toward female genital mutilation and its association to those practices in Yemen. *PLoS One.* 2013 Dec 18;8(12):e83140.
5. Soli KW, Kas M, Maure T, Umezaki M, Morita A, Siba PM, Greenhill AR, Horwood PF. Evaluation of colorimetric detection methods for *Shigella*, *Salmonella*, and *Vibrio cholerae* by loop-mediated isothermal amplification. *Diagn Microbiol Infect Dis.* 2013 Dec;77(4):321-3.
6. Pham HL, Kizuki M, Takano T, Seino K, Watanabe M. Out-of-pocket costs of disabilities and its association with household socio-economic status among school-aged children in Vietnam. *J Rural Med.* 2013 Nov;8(2):205-11.

7. Kibusi SM, Ohnishi M, Outwater A, Seino K, Kizuki M, Takano T. Sociocultural factors that reduce risks of homicide in Dar es Salaam: a case control study. *Inj Prev*. 2013 Oct;19(5):320-5.
8. Keoprasith B, Kizuki M, Watanabe M, Takano T. The impact of community-based, workshop activities in multiple local dialects on the vaccination coverage, sanitary living and the health status of multiethnic populations in Lao PDR. *Health Promot Int*. 2013 Sep;28(3):453-65.
9. Darapheak C, Takano T, Kizuki M, Nakamura K, Seino K. Consumption of animal source foods and dietary diversity reduce stunting in children in Cambodia. *Int Arch Med*. 2013 Jul 17;6(1):29.
10. Molina HF, Nakamura K, Kizuki M, Seino K. Reduction in inequality in antenatal-care use and persistence of inequality in skilled birth attendance in the Philippines from 1993 to 2008. *BMJ Open*. 2013 Jun 20;3(6).
11. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and chronic undernutrition among married Bangladeshi women of reproductive age: are the poor uniquely disadvantaged? *Eur J Clin Nutr*. 2013 Mar;67(3):301-7.
12. Rahman M, Nakamura K, Seino K, Kizuki M. Are survivors of intimate partner violence more likely to experience complications around delivery? Evidence from a national Bangladeshi sample. *Eur J Contracept Reprod Health Care*. 2013 Feb;18(1):49-60.

Environmental Parasitology

1. Staffs and Students

Professor	Nobuo Ohta	
Associate Professor	Nobuaki Akao	
Lecturer	Takashi Kumagai,	
Assistant Professor	Takenori Seki,	Mitsuko Suzuki (Dispatched as a JICA expert)
Project Professor	Takashi Suzuki	
Senior Technical staff	Misato Tomoda	
Graduate Student (PhD)	Toshihiro Tokiwa (-March), Katarina Macuhova (-March), Nobuhide Hata, Wataru Kagaya	Yuki Miyazawa (-March), Katsumi Maezawa, Toshio Arai, Francis Ekow Dennis,
Graduate Student (Master)	Masafumi Yamabe, Emi Wada	Daisuke Kobayashi,

2. Purpose of Education

Because of the recent development and the global changes in social system and life style, parasitic infections are becoming more heterogeneous. When we consider about factors promoting spreading parasitic diseases, multidisciplinary approaches are needed: medical, zoological and sociological.

Our laboratory mainly deals with pathophysiology and epidemiology of parasitic infections. Immunology, molecular biology and clinico-pathology are approaches employed. Main subjects in our laboratory are schistosomiasis, zoonotic helminthiasis, malaria and trypanosomiasis, all of which include laboratory and field investigations. In the schistosomiasis research, we focus on developing new diagnostic method by DNA detection in the sample, and uncovering immunopathogenesis of the typical hepatic inflammation. For zoonotic helminthiasis, developments of diagnostic tools are urgent matters to be studied. Our laboratory is one of the reference stations for the diagnosis in Japan.

Since 2008, TMDU started collaboration project on research on infectious diseases at Noguchi Memorial Institute for Medical Research. At the collaboration center at NMIMR, molecular approaches to discover new drug targets for African trypanosomiasis are underway.

3. Research Subjects

- (1) Pathological Research on zoonotic parasitoses: Toxocariasis, Dilofilariasis
- (2) Epidemiological survey of parasitic diseases: Toxocariasis, Angiostrongyloidiasis, Spirurine larva, Schistosomiasis
- (3) Molecular epidemiology of tropical diseases: Drug resistance of malaria parasites, Drug resistance of anopheline mosquitoes, Molecular detection of Trypanosomes in Tsetse fly.
- (4) Immunopathology of schistosomiasis: Regulation of egg-granuloma formation in schistosomiasis japonica.
- (5) Drug development against parasitic infection: New drug candidates for schistosomiasis
- (6) Regulation of gene expression in parasitic helminthes: RNAi and parasitism in schistosome parasites.
- (7) Molecular and epidemiological research on parasitic infections in West African sub-region.

4. Clinical Services

Clinical services for the diagnosis of parasitic infections are our routine activities.

5. Publications

Original articles

1. Shimogawara R, Hata N, Schuster A, Lesshafft H, Guedes de Oliveira S, Ignatius R, Akao N, Ohta N, Feldmeier H. Hookworm-related cutaneous larva migrans in patients living in an endemic community in Brazil: immunological patterns before and after ivermectin treatment. *Eur J Microbiol Immunol*, 3:258-66, 2013.
2. Obata-Ninomiya K, Ishiwata K, Tsutsui H, Nei Y, Yoshikawa S, Kawano Y, Minegishi Y, Ohta N, Watanabe N, Kanuka H, Karasuyama H. The skin is an important bulwark of acquired immunity against intestinal helminths. *J Exp Med*, 210:2583-95, 2013.
3. Tokiwa T, Hashimoto T, Yabe T, Komatsu N, Akao N, Ohta N. First report of *Angiostrongylus cantonensis* (Nematoda: Angiostrongylidae) infections in invasive rodents from five islands of the Ogasawara Archipelago, Japan.

PLOS ONE 2013 Aug 7, 8(8):e70729.

4. Tokiwa T, Ueda W, Takatsuka S, Okawa K, Onodera M, Ohta N, Akao N. The first genetically confirmed case of *Diocotophyme renale* (Nematoda: Diocotophymatida) in a patient with a subcutaneous nodule. *Parasitol Int*, doi: 10.1016/j.parint.2013.09.015.
5. Anyan WK, Seki T, Kumagai T, Obata-Ninomiya K, Furushima-Shimogawara R, Kwansa-Bentum B, Akao N, Bosompem KM, Boakye DA, Wilson MD, Karasuyama H, Ohta N. Basophil depletion downregulates *Schistosoma mansoni* egg-induced granuloma formation. *Parasitol Int*, 62:508-13, 2013.
6. El-Malky MA, Maruyama H, Al-Harhi SA, El-Beshbishi SN, Ohta N. The role of B-cells in immunity against adult *Strongyloides venezuelensis*. *Parasit Vectors*, 24:148, 2013.
7. Okumura-Noji K, Miura Y, Lu R, Asai K, Ohta N, Brindley PJ, Yokoyama S. CD36-related protein in *Schistosoma japonicum*: candidate mediator of selective cholesteryl ester uptake from high-density lipoprotein for egg maturation. *FASEB J*, 27:1236-44, 2013.
8. El-Malky MA, Lu SH, El-Beshbishi SN, Saudy NS, Ohta N. Effect of Mirazid in *Schistosoma japonicum*-infected mice: parasitological and pathological assessment. *Parasitol Res*, 112:373-7, 2013.
9. Macuhova K, Akao N, Fujinami Y, Kumagai T, Ohta N. Contamination, distribution and pathogenicity of *Toxocara canis* and *T. cati* eggs from sandpits in Tokyo, Japan. *J Helminthol*. 87:271-276. 2013.

Review Article

(None)

Book

(None)

International Conference

1. Kumagai T, Seki T, Yamabe M, Shimogawara R, Ohta N. Gene-knockdown by RNAi at the sporocyst stage of *Schistosoma japonicum*. 16th Folum Cheju International Parasitologist' Seminar, Aug 30-31, 2013, Seoul, Korea.
2. Takenori Seki, Mitsuko Suzuki, Takashi Suzuki, Wataru Kagaya, Mei Ikenori, Kofi D. Kwofie, Naa Ammah, Daniel A. Boakye, Kwadwo A. Koram, Frederic Aboagye, Dominic Edoh, Shoji Yamaoka, Yukihiro Shoyama and Nobuo Ohta Anti-trypanosomal activity of compound from *Alnus japonicain* vivo and in vitro. Establishment of Effective Research Network for Infectious Diseases and Medical Plants in GHANA. 19 September, 2013, Legon, Ghana.

Forensic Medicine

1. Staff and Students

Professor	Koichi UEMURA	
Junior Associate Professor	Toshihiko AKI	
Junior Associate Professor	Kana UNUMA	
Assistant Professor	Takeshi FUNAKOSHI	
Graduate Student	Kyoko UCHIDA,	Mayumi WATANABE,
	Kanako NORITAKE,	Naho HIRAYAMA,
	Izumi FUNAKOSHI,	Atsushi YAMADA,
	Marie BESSYO,	Yusuke FUJII,
	Haruka KOJIMA,	Yo AIHARA

2. 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. Research Subjects

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

4. 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.

5. Publications

Original Article

1. Unuma K, Aki T, Matsuda S, Funakoshi T, Yoshida K, Uemura K. Inducer of heme oxygenase-1 cobalt protoporphyrin accelerates autophagy and suppresses oxidative damages during lipopolysaccharide treatment in rat liver. *Hepato Res.* 2013;43(1):91-6.
2. Funakoshi T, Aki T, Unuma K, Uemura K. Lysosome vacuolation disrupts the completion of autophagy during norephedrine exposure in SH-SY5Y human neuroblastoma cells. *Brain Res.* 2013;1490:9-22.
3. Hirose I, Harada K, Kuroda R, Ishii Y, Nakajima M, Kamei Y, Takazawa Y, Yoshida KI. An autopsy report on a ruptured rudimentary horn (uterine anomaly) with ectopic pregnancy. *Forensic Sci Int.* 2013;224(1-3):e4-6.
4. Unuma K, Aki T, Funakoshi T, Yoshida K, Uemura K. Cobalt Protoporphyrin Accelerates TFEB Activation and Lysosome Reformation during LPS-Induced Septic Insults in the Rat Heart. *PLoS One.* 2013;8(2):e56526. doi: 10.1371/journal.pone.0056526.
5. Sugihara M, Odagiri F, Suzuki T, Murayama T, Nakazato Y, Unuma K, Yoshida K, Daida H, Sakurai T, Morimoto S, Kurebayashi N. Usefulness of running wheel for detection of congestive heart failure in dilated cardiomyopathy mouse model. *PLoS One.* 2013;8(1):e55514.
6. Unuma K, Harada K, Oka T, Uemura K. Starch accumulation in the lungs of two infants following positive ventilation. *Forensic Sci Med Pathol.* 2013;9(4):554-7.
7. Fujii Y, Funakoshi T, Uchida K, Watanabe M, Saka K, Uemura K. An autopsy case of acute carbon monoxide poisoning with fatal hypnotic drugs in the blood. *Int Med J.* 2013;20(5):587-588.
8. Bessho M, Aki T, Funakoshi T, Unuma K, Noritake K, Kato C, Uemura K. Rho-Kinase Inhibitor Y-27632 Attenuates Arsenic Trioxide Toxicity in H9c2 Cardiomyoblastoma Cells. *Cardiovasc Toxicol.* 2013;13(3):267-77.
9. Aki T, Funakoshi T, Unuma K, Uemura K. Impairment of autophagy: From hereditary disorder to drug intoxication. *Toxicology.* 2013;311(3):205-215.
10. Funakoshi-Hirose I, Aki T, Unuma K, Funakoshi T, Noritake K, Uemura K. Distinct effects of methamphetamine on

autophagy-lysosome and ubiquitin-proteasome systems in HL-1 cultured mouse atrial cardiomyocytes. *Toxicology*. 2013;312(4):74-82.

International Health and Medicine

1. Staffs and Students

Associate Professor	Keiko Nakamura, MD, PhD
Junior Associate Professor	Kaoruko Seino, MMs, PhD
RONPAKU (Dissertation PhD)	Tayphasavanh Fengthong, MD, MPH
Program Fellow	
Graduate Student	Honeyfaith Molina Alteza, MPH; Rami Hani Al- Rifai, DVM; Adam Izzeldin Fadl, MSc; Ghada Alkhulaidi, MA; Mosiur Rahman, MSc; Nguen Huu Chau Duc, MD; Rakprasit Jutarat, MPH; Shagdarsuren Tserendulam. MA; Saber Al-Sobaihi, MPH; Omar Mohammad Mashal, MD

2. Purpose of Education

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.

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

- Access 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 academic, public health research
- Facilitate learning of staff, students, and colleagues, and
- Practice and respect professional ethics in a socio-culturally diverse environment.

Master Programs

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

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. A rich variety of educational activities are 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.

Public Health Leaders (PHL) Program

Students in the PHL program 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.

3. Research

The department's major research interest is to elucidate physical, social, economic and cultural factors determining inequity in health. Our research investigates local, national and international policies and programs to redress health inequalities. The department works closely with WHO and other international agencies to help develop guidelines of scientific evaluation and recommended practices.

Major Research Topics:

- 1) Measuring population health to identify inequity in health and determinants thereof
- 2) Use of geographic information systems for evaluation of public health
- 3) Transfiguration of the ecosystem and its interaction with human health
- 4) Socio-cultural factors determining health
- 5) Outcome and process evaluation of health-development programs
- 6) Use of information technology to improve public health

4. Publications**[Original Articles]**

1. Al-Khulaidi GA, Nakamura K, Seino K, Kizuki M. Decline of supportive attitudes among husbands toward female genital mutilation and its association to those practices in Yemen. *PLoS One*. 8(12):e83140, 2013.
2. Molina HF, Nakamura K, Kizuki M, Seino K. Reduction in inequality in antenatal care use and persistence of inequality in skilled birth attendance in the Philippines from 1993 to 2008. *BMJ Open*. 3: e002507. doi:10.1136/bmjopen-2012-002507, 2013.
3. Rahman M, Nakamura K, Seino K, Kizuki M. Does gender inequity increase the risk of intimate partner violence among women? Evidence from a national Bangladeshi sample. *PLoS One*. 8(12):e82423, 2013.
4. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate Partner Violence and Symptoms of Sexually Transmitted Infections: Are the Women from Low Socio-economic Strata in Bangladesh at Increased Risk. *Int J Behav Med*. 2013
5. Rahman M, Nakamura K, Seino K, Kizuki M. Are survivors of intimate partner violence more likely to experience complications around delivery? Evidence from a national Bangladeshi sample. *Eur J Contracept Reprod Health Care*. 18(1):49-6, 2013.
6. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and symptoms of sexually transmitted infections: Are the women from low socio-economic strata in Bangladesh at increased risk. *Int J Behav Med*. Mar 21, 2013.
7. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and chronic undernutrition among married Bangladeshi women of reproductive age: are the poor uniquely disadvantaged? *Eur J Clin Nutr*. 67(3):301-7, 2013.
8. Rahman M, Nakamura K, Seino K, Kizuki M. Do Tobacco Smoking and Illicit Drug/Alcohol Dependence Increase the Risk of Mental Disorders Among Men? Evidence from a National Urban Bangladeshi Sample. *Perspect Psychiatr Care*. 2014 Jan 17.
9. Kibusi SM, Ohnishi M, Outwater A, Seino K, Kizuki M, Takano T. Sociocultural factors that reduce risks of homicide in Dar es Salaam: a case control study. *Inj Prev*. 19(5):320-5, 2013.
10. Darapheak C, Takano T, Kizuki M, Nakamura K, Seino K. Consumption of animal source foods and dietary diversity reduce stunting children in Cambodia. *Int Arch Med*. 6 (1):29, 2013.

[Review Articles]

1. Nakamura K. Health centered city planning. *Health of Cities*. The 75th Meeting on Urban Issues in Japan. 2013; 36-41.

[Conferences]

1. Nakamura K. Health Promotion and Urban Planning. 8th Global Conference on Health Promotion, Helsinki, June 2013.
2. Nakamura K. Adherence to mass drug administration against lymphatic filariasis through traditional village forums in Fiji. The 85th Annual Meeting of Japanese Association of Hygiene, Kanazawa, March 2013.
3. Al-Khulaidi G. Maternal mortality associated with age and education of women in Yemen. The 72th Annual Meeting of the Japan Association of Public Health, Mie, October 2013.
4. Al-Rifai R. Psychological distress and associated factors among male workers in Jordan. The 72th Annual Meeting of the Japan Association of Public Health, Mie, October 2013.
5. Duc C. Associated factors with under five child mortality in Vietnam. The 72th Annual Meeting of the Japan Association of Public Health, Mie, October 2013.
6. Rahman M. Tobacco smoking and the risk of mental disorders among urban Bangladeshi men. The 72th Annual Meeting of the Japan Association of Public Health, Mie, October 2013.

[International collaboration in research/education]

1. Nakamura K. Meeting for Collaboration in Research on Health Policy between Tokyo Medical and Dental

Public Health

University and Naresuan University. February 2013.

2. Nakamura K. Research Meeting on Healthy Cities Research, Taiwan Healthy City Association, July 2013.
3. Nakamura K. Socio-cultural determinants influencing knowledge, attitude, and practice of contraception among currently married child bearing aged women in Afghanistan. Collaborative Research. July-October 2013.

[Collaboration with international organizations]

1. Nakamura K. 15th Steering Committee Meeting of the Alliance for Healthy Cities. Wonju, Republic of Korea, October 2013.
2. Nakamura K. Secretariat of the Alliance for Healthy Cities. January - December 2013.

[Collaboration with local and national public health programs]

1. Nakamura K. Commission on optimal application of Healthy Cities in Owariasahi City, Owariasahi City, 2013.
2. Nakamura K. Healthy Cities in the world. Ichikawa WHO Wayo Group, January 2013.
3. Nakamura K. Promotion of Healthy Cities: Role of health professionals, governments, and community members. Katsuura-Isumi Medical Association, February 2013.
4. Nakamura K. Healthy Eating and Healthy Cities. The First Healthy Cities Network Convention. Yawatahama, February 2013.
5. Nakamura K. Progress of Healthy Cities. Ichikawa, Ichikawa Citizens Lecture, March 2013.
6. Nakamura K. Japan Chapter of the Alliance for Healthy Cities, Kita-Nagoya, July 2013.

[JSPS program]

1. Fengthong T. Spatial environmental health monitoring model by using interactive associations among various health determinants and health status in Lao PDR.

Health Care Management and Planning

1. Staffs and Students (April, 2013)

Professor	Kazuo KAWAHARA	
Assistant Professor	Makiko SUGAWA	
Graduate Student	Hidehito TAKENAKA,	Daiske IKEDA
	Youichi SHIMA,	Eiko SHIMIZU,
	Takeo NIGA,	Kenjiro IDE,
	Sawako OKAMOTO,	Keiko YOSHIDA,
	Md. Ismail Tareque,	Taro TOMIZUKA,
	Towfiqua Mahfuza Islam,	Woonkwan Hyun,
	Masakazu KIKUCHI,	Yoko KOMURA,
	Jian CHEN,	Masao MURATA,
	Takamichi KOGURE,	Daisuke MUMAZAWA,
Hisashi OMOTE		

2. Purpose of Education

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

3. Research Subjects

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

- 1) The significance of public healthcare planning, its challenges, and influences on the healthcare system
We conduct research on issues related to new healthcare policies including planning, analysis, issue resolution, and making positive changes to the healthcare plan. This research area includes the Japanese emergency medical service and the impartial evaluation of the travel distance of aid agents and the time required for them to reach their destination.
- 2) Structural analyses and policy choices concerning national blood services
In Japan, we experienced HIV infection from tainted blood products. There were various causes for this event, and improvements are required in all processes: collecting blood, screening blood, manufacturing blood products, and following-up on the usage of these products. By analyzing background information related to the adverse events and their causes, we can propose the most appropriate policies related to blood services, thus ensuring safety, and securing a stable supply. To achieve a stable supply of blood products, we also conduct epidemiological studies to review guidelines on collecting blood.
- 3) The government role in preventing medical errors
Issues related to medical errors and adverse events have recently attracted a great deal of attention in Japan. We study the role that the government should play regarding various medical errors and their prevention as well as review and address the financial loss caused by blood-related adverse events and policies on prevention.
- 4) Structural analyses of healthcare system in the community
By reviewing and analyzing activities related to disease prevention and health promotion conducted by local healthcare centers, we research the role of the local healthcare system and its effectiveness and efficiency.
- 5) Systemizing and evaluating public health policies
We review the processes of creating public health policies and systems, address the association with the creating processes and stakeholders such as political parties and lobby groups, evaluate their policies, and then suggest improvements to these policies and systems.
- 6) The role of healthcare communication to fill in gaps between medical providers and patients, and to share the uncertainties related to medicine and healthcare

- 7) The influence of healthcare communication on patient and medial safety
- 8) Reviewing communication tools and skills, and their systematic introduction into the healthcare system in order to realize patient participation and proactive involvement in treatment processes

4. Clinical Services

None

5. Publications

Original Article

1. Tomoko FUJIMOTO, Kazuo KAWAHARA, Hiroo YOKOZEKI. Epidemiological study and considerations of primary focal hyperhidrosis in Japan : From questionnaire analysis. *Journal of dermatology* 2013; 40: 1-5
2. Tareque MI, Hoque N, Islam TM, Kawahara K, Sugawa, M.: Relationships between the active aging index and disability-free life expectancy: A case study in the Rajshahi district of Bangladesh. *Canadian Journal on Aging*. S. Okamoto, K. Kawahara, A. Okawa, and Y. Tanaka. Values and risks of second opinion in Japan's universal health care system. *Health Policy* in publication, January 2013.
3. S. Okamoto, K. Kawahara, A. Okawa, & Y. Tanaka. "Values and risks of second opinion in Japan's universal health care system," accepted by *Health Expectation*, online published on February, 2013.

International conference

1. Takamichi Kogure, Masahiko Sumitani, Kenji Azuma, Hiroshi Sekiyama, Kazuo Kawahara, Yoshitsugu Yamada. CHRONIC PAIN PATIENTS WITH THE TRANSDERMAL FENTANYL GET ADEQUATE SLEEP, COMPARED BY THOSE WITHOUT OPIOID ANALGESICS: AN OBJECTIVE ASSESSMENT OF THE SLEEP ARCHITECTURE. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
2. Maria Bito, Masahiko Sumitan, Takuya Ohata, Takamichi Kogure, Kenji Azuma, Maiko Obuchi,, Hiroshi Sekiyama, Yoshitsugu Yamada. CARE BURDEN TO MALE PATIENTS WITH CHRONIC PAIN IS GREATER THAN THAT TO FEMALE PATIENTS. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
3. Kenji Azuma, Masahiko Sumitani, Takamichi Kogure, Mizuho Yagisawa-Sumitani, Hiroshi Sekiyama, Syuichi Katano, Yoshitsugu Yamada. MRI examinations in supine and prone positions: A novel diagnostic test of the lumbar adhesive arachnoiditis. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
4. Kaou Sugiura, Masahiko Sumitani, Maiko Obuchi, Kenji Azuma, Takamichi Kogure, Hiroshi Sekiyama, Yoshitsugu Yamada. Health literacy of chronic pain patients indicates necessity of different pain management and education. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
5. Maiko Obuchi, Masahiko Sumitani, Takamichi Kogure, Kenji Azuma, Hiroshi Sekiyama, Katsushi Takeshita, Yoshitsugu Yamada. Obese Neuropathic Pain Patients Complain of More Severe Pain than Normal-weighted Neuropathic Pain Patients. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
6. Ai Furuta, Masahiko Sumitani, Takamichi Kogure, Kenji Azuma, Hironobu Uematsu, Hiroshi Sekiyama, Yoshitsugu Yamada. Classification of the pain nature of CRPS type 1, based on patients' complaint, into neuropathic pain and nociceptive/inflammatory pain using the McGill Pain Questionnaire. presented in the 5th Association of South-East Asian Pain Societies Conference, Singapore, 2-5 May 2013
7. Tareque MD Ismail Kawahara K, Sugawa, M, Hoque N.: Healthy Life Expectancy and the Correlates of Self-rated Health for the Elderly in Rajshahi District of Bangladesh International Union for the Scientific Study of Population (IUSSP), Venue: BEXCO Convention Hall Lobby, Busan, South Korea, August 28th 2013
8. Tareque MD Ismail Kawahara K, Sugawa, M, Hoque, Changes in Healthy Life Expectancy and the Correlates of Self-rated Health in Bangladesh between 1996 and 2002 Wednesday, International Union for the Scientific Study of Population (IUSSP), Venue: BEXCO Convention Hall Lobby, Busan, South Korea, August 28th 2013
9. Islam TM, Tareque MI, Kawahara K, Sugawa, M, Hoque N.: *The most important factor needs attention in intimate partner violence: A case of Bangladesh*. Presented in Session 233: Intimate partner violence, organized by International Union for the Scientific Study of Population (IUSSP), Venue: BEXCO Convention Hall Lobby, Busan, South Korea, August 31, 2013.

10. Islam TM, Tareque MI, Rahman KMM, Sugawa M, Kawahara K.: Violence against women. In Titumir RAM (ed.) *Institutions Matter: State of Women in Bangladesh 2013*. The Unnayan Onneshan, Dhaka-1215, Bangladesh.

Review Article

None

Book

1. Tareque MI, Hoque N, Islam TM, Kawahara K, Sugawa M.: Active aging index and healthy life expectancy in Bangladesh. In N. Hoque, M. McGeHee, B. Bradshaw (eds.), *Applied Demography and Public Health*. NY: Springer. 2013.

Molecular Epidemiology

1. Staffs and Students (April, 2013)

Professor	Masaaki MURAMATSU	
Associate Professor	Noriko SATO	
Assistant Professor	Shinobu IKEDA	
Adjunct Instructor	Katsuko SUDO,	Fumihiko SATA
Graduate Student	Nay Chi Htun,	Cuneyd Palrayan,
	Atsuko Hiraishi,	Zhao Chen-xi,
	Sariya Dechamethakun,	Mia Sawabe,
	Kaung Si Thu,	Khin Thet Thet Zaw
Research Students	Tay Zar Kyaw,	Yumie Hiraoka

2. Education

Many common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis are caused by multiple genetic and environmental factors. We 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. The effects of intrauterine environment on fetal epigenome are investigated using mouse model.

3. Research Subjects

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Responder vs non-responder of prodrugs and polymorphisms of drug metabolizing enzymes.
4. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
5. The role of epigenetic regulation and fetal programming in common diseases.
6. Likelihood ratio based integrated personal risk assessment of type 2 diabetes.

4. Publications

1. Kengia JT, Ko KC, Ikeda S, Hiraishi A, Mieno-Naka M, Arai T, Sato N, Muramatsu M, Sawabe M. A gene variant in the *Atp10d* gene associates with atherosclerotic indices in Japanese elderly population. *Atherosclerosis*. 231:158-62. 2013
2. Daimon M, Sato H, Kaino W, Tada K, Takase K, Karasawa S, Wada K, Kameda W, Susa S, Oizumi T, Kayama T, Muramatsu M, Kato T. Association of the G-protein $\beta 3$ subunit gene polymorphism with the incidence of cardiovascular disease independent of hypertension: the Funagata study. *J Hum Hypertens*. 27:612-6. 2013
3. Honma N, Mori S, Zhou H, Ikeda S, Mieno MN, Tanaka N, Takubo K, Arai T, Sawabe M, Muramatsu M, Ito H. Association between estrogen receptor- β dinucleotide repeat polymorphism and incidence of femoral fracture. *J Bone Miner Metab*. 31:96-101.2013
4. Honma N, Yamamoto K, Ohnaka K, Morita M, Toyomura K, Kono S, Muramatsu M, Arai T, Ueki T, Tanaka M, Kakeji Y, Maehara Y, Okamura T, Ikejiri K, Futami K, Maekawa T, Yasunami Y, Takenaka K, Ichimiya H, Terasaka R. Estrogen receptor- β gene polymorphism and colorectal cancer risk: effect modified by body mass index and isoflavone intake. *Int J Cancer*. 132:951-8. 2013
5. Yatsuga C, Toyohisa D, Fujisawa TX, Nishitani S, Shinohara K, Matsuura N, Ikeda S, Muramatsu M, Hamada A, Tomoda A. No association between COMT genotype and attention deficit hyperactivity disorder (ADHD) in Japanese children. *Brain Dev*. S0387-7604(13)00258-1 2013
6. Kaniwa N, Sugiyama E, Saito Y, Kurose K, Maekawa K, Hasegawa R, Furuya H, Ikeda H, Takahashi Y, Muramatsu M, Tohkin M, Ozeki T, Mushiroda T, Kubo M, Kamatani N, Abe M, Yagami A, Ueta M, Sotozono C, Kinoshita S, Ikezawa Z, Matsunaga K, Aihara M; Japan Pharmacogenomics Data Science Consortium. Specific HLA types are associated with antiepileptic drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Japanese subjects. *Pharmacogenomics*. 14:1821-31. 2013

Research Development

1. Staffs and Students (April, 2013)

Professor	Kozo TAKASE	
Graduate Students		
Doctor course	Yuko OJIRO, Naoko MIAKE, Akemi HIRABAYASHI, Kiyoshi KOMIYA, Hidehiro ANDO, Hideki TERUYA,	Yuji HIGASIDE, Keisuke YOSIHARA, Tomoko IZUGAMI, Akira MIURA, Yasumasa OOSHIRO, Masakazu HARAMO
Master course (Master of Medical Administration)	Namiko IOKA, Keiji SADA, Masataka YANO,	Rie Ishii, Junko NAKATANI, Tetsuya YUKINO

2. Education

- 1) Hospital Information Management
- 2) Medical Informatics, statistics
- 3) TQM in medicine
- 4) Biological bias and data management
- 5) Medical Law and Ethics
- 6) Medical induction course for Judges and Prosecutors (collaborated with the Supreme Court and Department of Justice)
- 7) Medical Engineering special program with Tokyo Institute of Technology
- 8) Health Promotion Policy program (General Medicine, Risk Management in Medicine) with Hitotsubashi University

3. Research Subjects

- 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) Development of medical engineering apparatus

4. Publications etc.

1) Original Papers

Kozo Takase, Kiyoshi Komiyama

Kiyoshi Komiyama, Momoko Saito, Yuika Sakurai, Hiromi Kojima and Kozo Takase. Effectiveness of setting numerical targets in the surgical training of residents: A trial to achieve an optimal balance. J Med Dent Sci. 2013;60(4):93-101.

Kozo Takase, Keisuke Yoshihara :

Keisuke Yoshihara, Kozo Takase. Correlation between doctor's belief on the patient's self-determination and medical outcomes in obtaining informed consent. J Med Dent Sci. 2013;60(1):23-40.

Health Policy and Informatics

1. Staffs and Students (April, 2013)

Professor	Kiyohide FUSHIMI	
Graduate Student	Ayako ODA,	Takahiro INOUE,
	Kenjiro MATSUFUJI,	Asako TUKASAKI,
	Tsuyoshi KANEKO,	Kyoko SHINODA,
	Ayako MATSUO,	Motoko SANO,
	Toshihiro TAMAKI,	Yuya MIZUNO,
	Daisuke SHINJO,	Hiroki AIZAWA

2. Purposes of Education

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

3. Research Subjects

- 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.

4. Publications

Original Article

1. Inoue, T., Fushimi, K. Stroke Care Units Versus General Medical Wards for Acute Management of Stroke in Japan. *Stroke*. 2013; 44(11): 3142-7.
2. Hamada, T., Yasunaga, H., Nakai, Y., Isayama, H., Horiguchi, H., Matsuda, S., Fushimi, K., Koike, K. Continuous regional arterial infusion for acute pancreatitis: a propensity score analysis using a nationwide administrative database. *Crit Care*. 2013; Oct 2;17(5): R214.
3. Kunisawa, S., Morishima, T., Ukawa, N., Ikai, H., Otsubo, T., Ishikawa, KB., Yokota, C., Minematsu, K., Fushimi, K., Imanaka, Y. Association of geographical factors with administration of tissue plasminogen activator for acute ischemic stroke. *J Am Heart Assoc*. 2013; Sep 17: 2(5):e000336. doi: 10.1161/JAHA.113.000336.
4. Yasunaga, H., Horiguchi, H., Matsuda, S., Fushimi, K., Hashimoto, H., Ayanian, JZ. Body mass index and outcomes following gastrointestinal cancer surgery in Japan. *Br J Surg*. 2013; Sep;100(10): 1335-43. doi: 10.1002/bjs.9221.
5. Nakamura, M., Yasunaga, H., Shimada, T., Horiguchi, H., Matsuda, S., Fushimi, K. Body mass index and in-hospital mortality in anorexia nervosa: data from the Japanese Diagnosis Procedure Combination Database. *Eat Weight Disord*. 2013; Dec;18(4): 437-9. doi: 10.1007/s40519-013-0051-x.
6. Sugihara, T., Yasunaga, H., Horiguchi, H., Fujimura, T., Nishimatsu, H., Kume, H., Ohe, K., Matsuda, S., Fushimi, K., Homma, Y. Is mechanical bowel preparation in laparoscopic radical prostatectomy beneficial? An analysis of a Japanese national database. *BJU Int*. 2013; Jul;112(2): E76-81. doi: 10.1111/j.1464-410X.2012.11725.x.
7. Chikuda, H., Yasunaga, H., Horiguchi, H., Takeshita, K., Sugita, S., Taketomi, S., Fushimi, K., Tanaka, S. Impact of age and comorbidity burden on mortality and major complications in older adults undergoing orthopaedic surgery: an analysis using the Japanese diagnosis procedure combination database. *BMC Musculoskelet Disord*. 2013; May 28;14(1):173.
8. Hamada, T., Yasunaga, H., Nakai, Y., Isayama, H., Horiguchi, H., Matsuda, S., Fushimi, K., Koike, K. Rarity of severe bleeding and perforation in endoscopic ultrasound-guided fine needle aspiration for submucosal tumors. *Dig Dis Sci*. 2013; Sep;58(9): 2634-8. doi: 10.1007/s10620-013-2717-7.
9. Miyata, K., Konno, Y., Nakanishi, T., Kobayashi, A., Kato, M., Fushimi, K., Hasegawa, Y. Chameleon luminophore for sensing temperatures: control of metal-to-metal and energy back transfer in lanthanide coordination polymers. *Angew Chem Int Ed Engl*. 2013; Jun 17;52(25): 6413-6. doi: 10.1002/anie.201301448.
10. Sugihara, T., Yasunaga, H., Horiguchi, H., Fujimura, T., Nishimatsu, H., Kume, H., Ohe, K., Matsuda, S., Fushimi, K., Homma, Y. Longer operative time is associated with higher risk of severe complications after percutaneous nephrolithotomy: Analysis of 1511 cases from a Japanese nationwide database. *Int J Urol*. 2013; Dec;20(12): 1193-8. doi: 10.1111/iju.12157.

11. Yasunaga, H., Horiguchi, H., Kuwabara, K., Matsuda, S., Fushimi, K., Hashimoto, H., Ayanian, JZ. Outcomes Following Laparoscopic or Open Distal Gastrectomy for Early-stage Gastric Cancer: A Propensity-matched Analysis. *Annals of Surgery*. 2013; 257(4): 640–646.
12. Akiyama, T., Chikuda, H., Yasunaga, H., Horiguchi, H., Fushimi, K., Saita, K. Incidence and risk factors for mortality of vertebral osteomyelitis: a retrospective analysis using the Japanese diagnosis procedure combination database. *BMJ Open*. 2013; 3(3). pii: e002412. doi: 10.1136/bmjopen-2012-002412.
13. Hamada, T., Yasunaga, H., Nakai, Y., Isayama, H., Horiguchi, H., Fushimi, K., Koike, K. Japanese severity score for acute pancreatitis well predicts in-hospital mortality: a nationwide survey of 17,901 cases. *Journal of Gastroenterology*. 2013; 48(12): 1384-1391.
14. Fukuda, T., Yasunaga, H., Horiguchi, H., Ohe, K., Fushimi, K., Matsubara, T., Yahagi, N. Health care costs related to out-of-hospital cardiopulmonary arrest in Japan. *Resuscitation*. 2013; 84(7): 964-969.
15. Nakamura, M., Yasunaga, H., Haraguchi, T., Ando, S., Sugihara, T., Horiguchi, H., Ohe, K., Matsuda, S., Fushimi, K. Length of mechanical restraint following haloperidol injections versus oral atypical antipsychotics for the initial treatment of acute schizophrenia: A propensity-matched analysis from the Japanese diagnosis procedure combination database. *Psychiatry Research*. 2013; 209(3): 412-416.
16. Takeuchi, M., Yasunaga, H., Horiguchi, H., Fushimi, K. The burden of epiglottitis among Japanese children before the Haemophilus influenzae type b vaccination era: an analysis using a nationwide administrative database. *Journal of Infection and Chemotherapy*. 2013; 19(5): 876-879.
17. Kuwabara, K., Matsuda, S., Fushimi, K., Ishikawa, K.B., Horiguchi, H., Fujimori, K. Comparative study of functional outcomes of three laparoscopic intestinal surgical procedures. *Health Policy and Technology*. 2013; 2(2): 94-109.
18. Kuwabara, K., Matsuda, S., Fushimi, K., Ishikawa, K.B., Horiguchi, H., Fujimori, K. Coronary artery bypass graft and lung lobectomy: Functional outcome at discharge. *Journal of Clinical Medicine and Research*. 2013; 5(3): 29-39.
19. Yasunaga, H., Horiguchi, H., Kuwabara, K., Matsuda, S., Fushimi, K., Hashimoto, H., Ayanian, JZ. Outcomes After Laparoscopic or Open Distal Gastrectomy for Early-stage Gastric Cancer: A Propensity-matched Analysis. *Ann Surg*. 2013; 257(4): 640-6. IF 6.329
20. Umegaki, T., Nishimura, M., Tajimi, K., Fushimi, K., Ikai, H., Imanaka, Y. An In-Hospital Mortality Equation for Mechanically Ventilated Patients in Intensive Care Units. *Journal of Anesthesia*. 2013; 27: 541-549. DOI 10.1007/s00540-013-1557-0. IF 0.831
21. Sugihara, T., Yasunaga, H., Horiguchi, H., Tsuru, N., Fujimura, T., Nishimatsu, H., Kume, H., Ohe, K., Matsuda, S., Fushimi, K., Homma, Y. Wide range and variation in minimally invasive surgery for renal malignancy in Japan: a population-based analysis. *International Journal of Clinical Oncology*. 2013; 18(6): 1070-1077. PMID:23179640. IF 1.727
22. Sugihara, T., Yasunaga, H., Horiguchi, H., Fujimura, T., Nishimatsu, H., Ohe, K., Matsuda, S., Fushimi, K., Kattan, MW., Homma, Y. Does Mechanical Bowel Preparation Improve Quality of Laparoscopic Nephrectomy? Propensity Score-matched Analysis in Japanese Series. *Urology* 2013; 81(1): 74-9. IF 2.424
23. Sugihara, T., Yasunaga, H., Horiguchi, H., Tsuru, N., Ihara, H., Fujimura, T., Nishimatsu, H., Ohe, K., Fushimi, K., Homma, Y. Comparisons of perioperative outcomes and costs between open and laparoscopic radical prostatectomy: a propensity-score matching analysis based on the Japanese Diagnosis Procedure Combination database. *Int J Urol*. 2013; 20(3): 349-53. IF 1.734
24. Yamashita, K., Ikai, H., Nishimura, M., Fushimi, K., Imanaka, Y. Effect of certified training facilities for intensive care specialists on mortality in Japan. *Critical Care and Resuscitation*. 2013 Mar;15(1): 28-32. IF 1.67
25. Yasunaga, H., Horiguchi, H., Hashimoto, H., Matsuda, S., Fushimi, K. Effect and Cost of Treatment for Acute Pancreatitis With or Without Gabexate Mesylate: A Propensity Score Analysis Using a Nationwide Administrative Database. *Pancreas*. 2013 Mar;42(2): 260-4. IF 2.953
26. Sugihara, T., Yasunaga, H., Horiguchi, H., Nishimatsu, H., Kume, H., Ohe, K., Matsuda, S., Fushimi, K., Homma, Y. A Nomogram Predicting Severe Adverse Events after Ureteroscopic Lithotripsy: 12,372 Patients in Japanese National Series. *BJU Int*. 2013 Mar;111(3): 459-66. IF 3.046
27. Kuwabara, K., Fushimi, K., Matsuda, S., Ishikawa, K.B., Horiguchi, H., Fujimori, K. Association of early post-procedure hemodynamic management with the outcomes of subarachnoid hemorrhage patients. *Journal of neurology*. 2013; 260(3): 820-831. IF 3.578
28. Kuwabara, K., Hagiwara, A., Matsuda, S., Fushimi, K., Ishikawa, K.B., Horiguchi, H., Fujimori, K. A community-based comparison of trauma patient outcomes between d- and l-lactate fluids. *The American Journal of Emergency Medicine*. 2013; 31(1): 206–214. IF 1.704
29. Sugihara, T., Yasunaga, H., Horiguchi, H., Fujimura, T., Nishimatsu, H., Tsuru, N., Kazuo, S., Ohe, K., Fushimi, K.,

Homma, Y. Regional, institutional and individual factors affecting selection of minimally invasive nephroureterectomy in Japan: A national database analysis. *Int J Urol.* 2013; 81(1): 74-79.

Life Sciences and Bioethics (Life Sciences and Bioethics Research Center)

1. Staffs and Students (April, 2013)

Director & Professor	Masayuki YOSHIDA	
Junior Associate Professor	Masumi AI,	Yuka OZASA
Assistant Professor	Mizuko OSAKA,	Hitoshi Kuwana
Tokunin Assistant Professor	Miwa SUZUKI	
Visiting Associate Professor	Hideto ISHII	
Visiting Junior Associate Professor	Eiichiro KANDA	
Nurse	Naoko NII	
Research Associate	Michiyo DEUSHI	
Doctoral student	Kôtarô AIHARA,	Katsuhiko HAMADA,
	Shunsuke ITO,	Yûya MATSUE,
	Hakubun KYO,	Midori SHUHARA

2. Purpose of Education

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.

3. Research Subjects

Department of Life Sciences and Bioethics actively conduct biomedical basic research described below:

- 1) MCP-1/CCR2 signals in vascular inflammation
- 2) Vascular inflammation in immature endothelium.
- 3) Mechanism of indoxyl-sulfate -triggered vascular inflammation .
- 4) Anti-atherosclerotic effect of lactotripeptide
- 5) Influence of high-fat diet-feeding on intestinal lymph

4. Clinical Services

Department of Life Sciences and Bioethics is responsible for Department of Clinical Genetics Division at the Medical Hospital of TMDU. Our clinical department provides counseling to individuals and families regarding actual and/or potential genetic concerns. We also offer laboratory services including cytogenetic testing and molecular genetic testing. Our Genetic Medicine department is approved by the Japanese Medical Genetics Society for the Genetics Board.

5. Publications

Original Article

1. Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yamazaki T, Yokoi H, **Yoshida M** Effect of Long-Term Intensive Lipid-Lowering Therapy With Rosuvastatin on Progression of Carotid Intima-Media Thickness. *Circ J* 77:1526-33 (2013)
2. Yamazaki T, Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yokoi H, **Yoshida M** Justification for Atherosclerosis Regression Treatment (JART) Investigators. Intensive lipid-lowering therapy for slowing progression as well as inducing regression of atherosclerosis in Japanese patients. *Int Heart J* 54(1):33-39. (2013)
3. **Osaka M**, Hagita S, **Yoshida M**. In vivo imaging of leukocyte recruitment to the atheroprone femoral artery reveals anti-inflammatory effects of rosuvastatin. *Biomed Res Int*. 2013;962369. 2013

4. **Toyozaki M, Osaka M**, Kondo K, **Yoshida M**. High fat and high cholesterol diet induces DPP-IV activity in intestinal lymph. *J Oleo Sci.* 62(4):201-5. 2013
5. **Ito S**, Higuchi Y, Yagi Y, Nishijima F, Yamato H, Ishii H, **Osaka M, Yoshida M**. Reduction of indoxyl sulfate by AST-120 attenuates monocyte inflammation related to chronic kidney disease. *J Leukoc Biol.* 93(6):837-45. 2013
6. **Matsue Y**, Suzuki M, Nagahori W, Ohno M, Matsumura A, Hashimoto Y. Beta-blocker prevent sudden cardiac death in patients with hemodialysis. *Int J Cardiol* 2013; 165: 519-522.
7. **Matsue Y**, Suzuki M, Nagahori W, Ohno M, Matsumura A, Hashimoto A, Yoshida K, **Yoshida M**. Endothelial dysfunction measured by peripheral arterial tonometry predicts prognosis in patients with heart failure with preserved ejection fraction. *Int J Cardiol* 2013; 168: 36-40.
8. **Matsue Y**, Matsumura A, Abe M, Ono M, Seya M, Nakamura T, Iwatsuka R, Mizukami A, Setoguchi M, Nagahori W, Ohno M, Suzuki M, Hashimoto Y. Prognostic implications of chronic kidney disease and anemia after percutaneous coronary intervention in acute myocardial infarction patients. *Heart Vessels.* 2013; 28: 19-26.
9. **Matsue Y**, Suzuki M, Seya M, Iwatsuka R, Mizukami A, Nagahori W, Ohno M, Matsumura A, Hashimoto Y. Tolvaptan Reduces the Risk of Worsening Renal Function in Patients with Acute Decompensated Heart Failure in High-Risk Population. *J Cardiol.* 2013; 61: 169-174.
10. **Matsue Y**, Matsumura A, Suzuki M, Hashimoto Y, **Yoshida M**. Discrepancy of atorvastatin and ezetimibe between lowering effect of low-density lipoprotein cholesterol and effect on endothelial function: a randomized controlled trial. *Circ J.* 2013; 77: 1791-1798.
11. Furusyo N, Koga T, Ai M, Otokozawa S, Kohzuma T, Ikezaki H, Schaefer EJ, Hayashi J. Plasma glycated albumin level and at herosclerosis: results from the Kyushu and Okinawa Population Study (KOPS). *Int J Cardiol.* 167:2066-72, 2013
12. Furusyo N, Ai M, Okazaki M, Ikezaki H, Ihara T, Hayashi T, Hiramine S, Ura K, Kohzuma T, Schaefer EJ, Hayashi J. Serum cholesterol and triglyceride reference ranges of twenty lipoprotein subclasses for healthy Japanese men and women. *Atherosclerosis* 231: 238-45, 2013.
13. **Kanda E**, Ai M, Iwamoto A, Okazaki M, Maeda Y, Sasaki S, Yoshida M. Relationship between Icodextrin use and decreased level of small low-density lipoprotein cholesterol fractioned by high-performance gel permeation chromatography. *BMC Nephrol.* 14:234, 2013.
14. **Kanda E**, Ai M, Okazaki M, Maeda Y, Sasaki S, Yoshida M. The association of very-low-density lipoprotein with ankle-brachial index in peritoneal dialysis patients with controlled serum low-density lipoprotein cholesterol level. *BMC Nephrol.* 14:212, 2013.
15. Iimori S, Noda Y, Okado T, Naito S, Toda T, Chida Y, Kuwahara M, Ando R, Nishio Y, Maeda Y, Tanaka H, Tamura T, Kimoto S, **Kanda E**, Inoshita S, Yoshikawa M, Okutsu R, Tajima M, Kusaura T, Kobayashi K, Rai T, Uchida S, Sasaki S. Baseline characteristics and prevalence of cardiovascular disease in newly visiting or referred chronic kidney disease patients to nephrology centers in Japan: a prospective cohort study. *BMC Nephrol.* 14:152, 2013.
16. **Kanda E**, Ai M, Yoshida M, Kuriyama R, Shiigai T. High serum bicarbonate level within the normal range prevents the progression of chronic kidney disease in elderly chronic kidney disease patients. *BMC Nephrol.* 14:4, 2013.
17. Beaubrun AC, **Kanda E**, Bond TC, McClellan WM. Form CMS-2728 Data Versus Erythropoietin Claims Data: Implications for Quality of Care Studies. *Ren Fail.* 35:320-6, 2013.
18. Mandai S, **Kanda E**, Arai Y, Hirasawa S, Hirai T, Aki S, Inaba N, Aoyagi M, Tanaka H, Ikeda T, Tamura T, Sasaki S. Anti-centromere antibody is an independent risk factor for chronic kidney disease in patients with primary biliary cirrhosis. *Clin Exp Nephrol.* 17:405-10, 2013.
19. Muneyuki T, Suwa K, Oshida H, Takaoka T, Kutsuma A, Yoshida T, Saito M, Hori Y, Kannno Y, **Kanda E**, Kakei M, Momomura S, Nakajima K. Design of the Saitama Cardiometabolic Disease and Organ Impairment Study (SCDOIS): A Multidisciplinary Observational Epidemiological Study. *Open Journal of Endocrine and Metabolic Diseases.* 3: 144-156, 2013.

Oral/Poster Presentation

1. Ito S, Hamada K, Edamatsu T, Ito Y, Osaka M, Yoshida M. Uremic toxin-induced endothelial E-selectin gene expression involves aryl hydrocarbon receptor-dependent activation of AP-1. American Heart Association 2013. Dallas, USA. 2013
2. Ito S, Aoki R, Hamada K, Edamatsu T, Ito Y, Osaka M, Yoshida M., UREMIC TOXIN TRANSCRIPTIONALLY UP-REGURATES ENDOTHELIAL E-SELECTIN VIA ARYL HYDROCARBON RECEPTOR. ERA-EDTA.

Istanbul, Turkey. 2013

3. Ito S, Hamada K, Edamatsu T, Ito Y, Osaka M, Yoshida M. Aryl Hydrocarbon Receptor Plays a Crucial Role for Uremic Toxin-induced Vascular Inflammation. *Kidney week 2013*. Atlanta, USA. 2013
4. Matsue Y, Abe M, Suzuki M, Matsumura A, Hashimoto Y. CLINICAL IMPLICATION FOR PROGNOSIS OF CHRONOTROPIC INCOMPETENCE IN HEART FAILURE. *American College of Cardiology 62th Annual Scientific Session San Francisco, CA , 2013*.
5. Matsue Y, Suzuki M, Matsumura A, Hashimoto Y. IMPACT OF BODY MASS INDEX ON PROGNOSTIC PREDICTION BY CREATININE-BASED ESTIMATED GLOMERULAR FILTRATION RATE AND CYSTATIN C IN HEART FAILURE. *American College of Cardiology 62th Annual Scientific Session San Francisco, CA , 2013*.
6. Matsue Y, Ninomiya R, Abe M, Suzuki M, Matsumura A, Hashimoto Y. COMPARISON OF HAS-BLED SCORE TO ATRIA SCORE IN PREDICTING ABILITY FOR BLEEDING EVENTS IN JAPANESE ATRIAL FIBRILLATION PATIENTS UNDER ANTICOAGULATION. *American College of Cardiology 62th Annual Scientific Session San Francisco, CA , 2013*.
7. Y. Matsue; A. Mizukami; W. Nagahori; M. Ohno; M. Suzuki; A. Matsumura; Y. Hashimoto; M. Yoshida. Endothelial dysfunction is an independent predictor of new-onset heart failure in coronary artery disease patients. *European Society of Cardiology Congress 2013*. Amsterdam, Netherland. 2013.
8. K. Yoshida, W. Nagahori, M. Ohno, M. Suzuki, A. Matsumura, Y. Hashimoto M. Yoshida. Endothelial dysfunction predicts residual risk in coronary artery disease patients with statin therapy. *European Society of Cardiology Congress 2013*. Amsterdam, Netherland. 2013.
9. Matsue Y, Suzuki M, Matsumura A, Hashimoto Y. High-Sensitive Cardiac Troponin-I and NT-proBNP Improve Predictive Ability of Risk Stratification Model for Sudden Cardiac Death in End-Stage Renal Disease. *American Heart Association Scientific Session 2013*. Dallas. 2013.
10. Ozasa Y. Considering of the education programs for midwives about genetic counseling for prenatal diagnosis in Japan. *International Society Of Nurses in Genetics 25th anniversary conference, Bethesda, October 2013*.
11. Suzuki M, Ozasa Y, Nii N, Ai M, Yoshida M. Roles of genetic nurses for the molecular genetics predictive test of neurology in Japan. *International Society Of Nurses in Genetics 25th anniversary conference, Bethesda, October 2013*.
12. Suzuki M, Ozasa Y, Nii N, Ai M, Yoshida M. Judgment of the ethical committee for the molecular genetics predictive test of neurology at Tokyo Medical and Dental University in Japan. *Public Responsibility in Medicine & Research, Boston, November 2013*.
13. Ai M, Suzuki M, Nii N, Ozasa Y, Abe Y, Kanda E, Yoshida M. A Workshop for IRB Chairs and Members in Japan. *Public Responsibility in Medicine & Research, Boston, November 2013*.
14. Abe Y, Izumimoto N, Hakamada T, Toyoshima K, Yamauchi M, Kaneko E, Shimokado K. Long distance evacuation was wholesome for refugees of the 2011 Tohoku Earthquake. *The 20th IAGG World Congress of Gerontology and Geriatrics, Seoul, June 2013*.
15. Ishii H., Asano H. Combination therapy with insulin plus sitagliptin in Japanese type 2 diabetic patients. *WORLD DIABETES CONGRESS 2013, Melbourne, December 2013*.
16. Kanda E, Ai M, Kuriyama R, Yoshida M, Shiigai T. Dietary Acid Load Is Associated with Chronic Kidney Disease Progression in Elderly Patients. *The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013*.
17. Iseki K, Tsuruya K, Kanda E, Nomura T, Hirakata H. Effects of Sleepiness on Survival in Japanese Hemodialysis Patients:J-DOPPS-Q. *The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013*.
18. Kanda E, Muneyuki T, Sakamoto K, Hirayama T, Nakajima K, Matsumoto Y, Watanabe S, Kanno Y. Does a Low Salt Diet Affect Protein Intake in Chronic Kidney Disease Patients? *The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013*.
19. Kanda E, Ai M, Kuriyama R, Yoshida M, Shiigai T. Fluctuating Protein Intake Is an Independent Risk Factor for the Progression of Chronic Kidney Disease. *The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013*.
20. Kanda E, Ai M, Okazaki M, Maeda Y, Sasaki S, Yoshida M. Very-Low-Density Lipoprotein Affects Atherosclerosis of Peripheral Artery in Peritoneal Dialysis Patients. *The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013*.

Invited Speaker

Public Health

1. Yoshida M: Dynamic Imaging system reveals pathophysiology of atherosclerosis and vascular inflammation IEEE Conference Osaka, 2013 July
2. Yoshida M: A Comparison of Japan and US bioethical principles, Advancing Ethical Reserch Conference 2013, Boston USA

Health Care Economics

1. Staffs and Students (April, 2013)

Professor	Koichi KAWABUCHI
Assistant Professor	Isao IGARASHI
Graduate Students	James Tumaini KENGIA,
Research Student	Sadao WATANABE

2. Purpose of Education

The purpose is to provide students with education and training in theoretical as well as practical approaches necessary in conducting economical analysis of various phenomena and reality found in healthcare field.

3. Research Subjects

- 1) Study on measuring output from industry in non-market service (healthcare)
- 2) Study on analysis of big-data in healthcare and its implications to policy evaluation
- 3) Research on cost-effectiveness analysis of proton radiotherapy for pediatric tumor such as medulloblastoma
- 4) Study on lifestyle diseases and healthcare cost control
- 5) Study on dental economics

4. Publications

Original Articles

1. James Tumaini Kengia, Isao Igarashi, Koichi Kawabuchi: Effectiveness of Health Sector Reforms in Reducing Disparities in Utilization of Skilled Birth Attendants in Tanzania. *The Tohoku Journal of Experimental Medicine*, 230(4), 241-253, 2013.
2. James Tumaini Kengia, Kyi Chan Ko, Shinobu Ikeda, Atsuko Hiraishi, Makiko Mieno-Naka, Tomio Arai, Noriko Sato, Masaaki Muramatsu, Motoji Sawabe: A gene variant in the *Atp10d* gene associates with atherosclerotic indices in Japanese elderly population. *Atherosclerosis*, 231(1), 158-162, 2013.

Review Article

1. Koichi Kawabuchi, Keiko Kajitani: Evidence-based Policy Making for Sustainable Healthcare in Japan: 2025 and beyond. *Japan Hospitals*, 32: 29-37, 2013.

Book

1. Koichi Kawabuchi: The Status Quo and Issues of Health Care Insurance and Long-Term Care Insurance for the Old-Old in Japan. In Fanny M. Cheung, Jean Woo, Chi-kin Law (editors): *Health Systems: Challenges, Visions, and Reforms from a Comparative Global Perspective*, p.p.65-82, The Chinese University Press, 2013, Hong Kong.

Dental Education Development

1. Staff and Students

Professor	Ikuko MORIO
Junior Associate Professor	Jun TSURUTA(~ 2013. 3)
Assistant Professor	Naoko SEKI (2013. 6~)
Graduate Students	Rei MUROGA, Akira TAKINAGA, Chinatsu MATSUKAWA

2. Purpose of 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. Research Subjects

- 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

4. Clinical Services

5. Publications

6. Others

[International Congresses]

1. Tsuruta J: Curriculum Design - Ethics and Professionalism. 16th Scientific Meeting & Refresher Course in Dentistry (KPPIKG2013), Jakarta, Indonesia, 28 February.
2. Muroga R, Matsukawa C, Tsuruta J, Morio I: Educational environment concerning four-handed dentistry of Japanese dental hygiene schools. 19th International Symposium on Dental Hygiene, Cape Town, South Africa, 14-17 August.

[Coordination for International Seminar, Symposium, Workshop or Other Events]

1. TMDU exhibition at the 2nd meeting of International Association Dental Research-Asia Pacific Region (IADR-APR) in Bangkok, Thailand, 21-23 August.
2. Development of Dental Education in Asia 2013 -Symposium and Exchange-, Tokyo, 29 October.
3. The Third Tri-University Consortium, Tokyo, 6-7 November.

Oral Health Promotion

1. Staffs and Students

Professor	Yoko Kawaguchi	
Associate Professor	Masayuki Ueno	
Assistant Professor	Sayaka Furukawa	
Hospital Staff	Mari Ohnuki	
Part-time Lecturer	Akiko Ohshiro,	Takashi Zaitso, Sachiko Takehara (International Exchange Center)
Registered Resident	Hiromi Nishiyama	
Graduate Student	Haslina Binti Rani, Yuri Uraoka, Anastasiya Blizniuk, Nguyen Thi Hoang Yen(October~)	Ei Ei Aung, Marie Sato(~March), Sachiko Komori(April~),
Research Student	Motoko Ariake(~March)	

2. Purpose of Education

1) Graduate School, Oral Health Promotion

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

2) Undergraduate Education

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

3. Research Subjects

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

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

4. 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.

5. Publications

Original article

1. S.Takeuchi,M.Ueno,S.Takehara,T.A.V.Pham,C.Hakuta,S.Morishima,K.Shinada,Y. Kawaguchi:The relationship between

- turbidity of mouth – rinsed water and oral health status, *Acta Odontologica Scandinavica*, 2013 ; 71:183-188
2. Ueno M, Takeuchi S, Samnieng P, Morishima S, Shinada K, Kawaguchi Y: Turbidity of mouthrinsed water as a screening index for oral malodor, *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2013 Aug;116(2):203-9.
 3. M.Ueno, S.Takeuchi, A.Oshiro, Y.Kawaguchi:Relationship between oral health literacy and oral health behaviors and clinical status in Japanese adults, *Journal of Dental Sciences*, 2013;8,170-176
 4. M.Ueno, S.Ohara, M.Inoue, S.Tsugane, Y.Kawaguchi:Association between parity and dentition status among Japanese women: Japan public health center-based oral health study, *BMC Public health*, 2013; 13:993.
 5. M.Ueno, A.Takayama, M.Adiatman, M.Ohnuki, T.Zaitso, Y.Kawaguchi : Application of visual oral health literacy instrument in health education for senior high school students, *International Journal of Health Promotion and Education*, 2013, DOI:10.1080/14635240.2013.845412

Sports Medicine/Dentistry

1. Staffs and Students (April. 2013)

Associate Professor	Toshiaki Ueno	
Assistant Professor	Toshiyuki Takahashi,	Hiroshi Churei
Hospital Staff	Katsuhide Kurokawa	
Graduate Student	Sharika Shahrin,	Ruman Uddin Chowdhury,
	Takayuki Ishigami,	Kairi Hayashi,
	Mai Tanabe,	Akihiro Mitsuyama,
	Sintaro Fukasawa,	Abhishekhi Shrestha,
	Takahiro Sirako	

2. Purpose of Education

Sport medicine/dentistry is a branch of medical and dental sciences which deals with the clinical management of oral health of athletes and sports-active people and the safety measures of sports-related traumatic injuries and disorders. Main objective of sports medicine/dentistry in graduate course 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.

3. Research Subjects

- 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
- 5) Relations between mastication and occlusion and brain functions
- 6) Application of HBO therapy to sports-related dental diseases and traumatic injury

4. Clinical services

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.

5. Publications

Original Articles

- 1) Abe K, Takahashi H, Churei H, Iwasaki N, Ueno T: Flexural properties and shock absorbing capabilities of new face guard materials reinforced with fiberglass cloth. *Dent Traumatol* 29: 23-28, 2013.
- 2) Reza F, Churei H, Takahashi H, Iwasaki N, Ueno T: Flexural impact force absorption of mouthguard materials using film sensor system. *Dent Traumatol*, Online published, 18 Sep 2013.
- 3) Shahrin S, Takahashi T, Chowdhury RU, Chowdhury NU, Toyoshima Y, Ueno T: General and oral injuries of the cricketers and field hockey players in Bangladesh. *Int J Sports Dent* 6: 13-23, 2013.

Public Health

- 4) Tanabe M, Takahashi T, Shimoyama K, Toyoshima Y, Ueno T: Effects of rehydration and food consumption on salivary flow, pH and buffering capacity in young adult volunteers during ergometer exercise. *J Int Soc Sports Nutr* 10: 49-54, 2013.

Invited article

- 1) Maeda Y, Yasui T, Tanaka Y, Ando T, Ishigami K, Ueno T, Matsumoto M, Matsuda N: Is mouthguard effective for preventing traumatic injuries during sports event?: A strategic protocol formulated by the Japanese Academy of Sports Dentistry (JASD) to accumulate scientific evidence. *Int J Sports Dent* 6: 7-11, 2013.

6. Presentations

- 1) Fukasawa S, Churei H, Chowdhury RU, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T: Application of dental silicone rubber material for repairing mouthguard. 2nd IADR Asia Pacific Resion Meeting, Bangkok, Thailand, Aug 21-23, 2013.
- 1) Fukasawa S, Churei H, Chowdhury RU, Shrestha A, Wada T, Uo M, Takahashi H, Ueno T: Application of dental silicone rubber material for repairing mouthguard. 5th TMDU International Summer Program (ISP2013), Tokyo, Aug 27-29, 2013.
- 3) Mitsuyama A, Takahashi T, Tanabe M, Ueno T: Dental injury incidence and prevalence of mouthguard in Japanese ice hockey players. 101th FDI Annual World Dental Congress, Istanbul, Turkey, Aug 28-31, 2013.
- 4) Ishigami T, Takahashi T, Fujino S, Ueno T: Effect of change in occlusal supporting zone on the stabilization of posture stance disturbed by electrical stimulation. 15th Biennial Meeting of the International College of Prosthodontists, Torino, Italy, Sep 18-21, 2013.

7. Grants and Fellowships

- 1) JSPS Grant-in-Aid for Scientific Research (Japan Society for the Promotion of Science, 2011.4-14.3). Takahashi T, Kato G, Ueno T.
- 2) Research Grant for Special Project (MEXT, 5 years from 2011). Yagishita K, Enomoto M, Ueno T, Takahashi T, et al.
- 3) Project Research Grant (Japanese Association for Dental Science, 2012.4-14.3). Yasui T, Maeda Y, Ishigami K, Ueno T, Takamata T, Koide K, Matsumoto M, Kawara M.
- 4) Research Grant (The Descent and Ishimoto Memorial Foundation of the Promotion of Sports Science, 2013.4-14.3). Churei H, Fukasawa S, Takahashi H, Uo M, Ueno T:
- 5) JSPS Grant-in-Aid for Scientific Research (Japan Society for the Promotion of Science, 2013.4-16.3). Kurokawa K, Takahashi T, Ueno T.

8. Awards and Honors

N/A

9. Volunteer activities and International exchange, etc

- 1) Shrestha A: Country introduction of Nepal. Bunkyo-ku International Cultural Exchange Seminar. Bunkyo Civic Center, Tokyo, Feb 15, 2013.
- 2) Ueno T, Churei H, Sharika S, Chowdhury RU, Shrestha A, Mitsuyama A, Kurokawa K: Information of dental injury prevention, mouthguard and oral health care. 6th Rugby festival in Ichikawa city with Kubota Spears and NTT communications ShiningArcs, Ichikawa/Chiba, March 24, 2013.

Educational System in Dentistry

1. Staffs and Students

Professor	Kouji ARAKI	
Junior Associate Professor (non-full time)	Yukio NAKAMURA,	Hiroki KATAOKA
Secretary	Satomi ITOH	
Graduate Student	Michiyo KUROSA	

2. Purpose of Education

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.

3. Research Subjects

- 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

4. Clinical Services

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

5. Publication

- 1) Hirono Kikuchi, Masaomi Ikeda, Koji Araki : Evaluation of a Virtual Reality Simulation System for Porcelain Fused to Metal Crown Preparation at Tokyo Medical and Dental University, Journal of Dental Education Vol.77(No.6), p782~792, 2013

Educational Media Development

1. Staffs and Students

Professor Astuhiro KINOSHITA

Assistant Professor Masayo SUNAGA

2. Purpose of Education

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

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

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

3. Research Subjects

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 Computerized Dental Simulator for Training of Dental Cavity Preparation and Prosthodontic Tooth Preparation practices:

We plan to develop a new computerized dental simulator and evaluate its effectiveness for training in dental cavity preparation and prosthodontic tooth preparation.

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

Dental and dental hygiene students must acquire skills for measuring periodontal pockets and must learn to identify the base of the pocket. However, few dental models are commercially available, and students cannot measure deep periodontal pockets by practicing on one another. Thus, we developed a new dental model with

which the students can practice the probing of deep periodontal pockets, and plan to evaluate its effectiveness in training and evaluation of examiners.

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

If students can experience and recognize three-dimensional space from the operator's (instructor's) viewpoint during their practice sessions and lectures, it would have educational benefits. Thus, we plan to develop a Composing and Screening System for Original 3D Movies from an Operator's Viewpoint. Furthermore, we will improve the quality of distance learning and remotely operated instruction using the superimposing method.

- Development of Dental Handpiece System with CCD camera:

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

4. Publications

Original Article

1. Sunaga M, Kondo K, Adachi T, Miura Y, Kinoshita A. Development and evaluation of a new dental model at Tokyo Medical and Dental University for the practice of periodontal pocket probing. *J Dent Educ.* 2013 Sep;77(9):1185-1192.
2. Iwaki M, Kanazawa M, Sunaga M, Kinoshita A, Minakuchi S. Live broadcast lectures on complete denture prosthodontics at Tokyo Medical and Dental University: comparison of two years. *J Dent Educ.* 2013 Mar;77(3):323-330.

Insured Medical Care Management

Our department has been established since October 1st, 2013.

1. Staffs and Students

Professor Masumi AI (October 1st~)

2. Purpose of 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.

3. Research Subjects

- 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, and laboratory medicine.

4. Clinical Services

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

5. Publication

Original Articles

1. Miida T, Nishimura K, Okamura T, Hirayama S, Ohmura H, Yoshida H, Miyashita Y, **Ai M**, Tanaka A, Sumino H, Murakami M, Inoue I, Kayamori Y, Nakamura M, Nobori T, Miyazawa Y, Teramoto T, Yokoyama S. Validation of homogeneous assays for HDL-cholesterol using fresh samples from healthy and diseased subjects. *Atherosclerosis* (in press).
2. Kanda E, **Ai M**, Kuriyama R, Yoshida M, Shiigai T. Dietary acid intake and kidney disease progression in the elderly. *Am J Nephrol* (in press).
3. Furusyo N, **Ai M**, Okazaki M, Ikezaki H, Ihara T, Hayashi T, Hiramane S, Ura K, Kohzuma T, Schaefer EJ, Hayashi J. Serum cholesterol and triglyceride reference ranges of twenty lipoprotein subclasses for healthy Japanese men and women. *Atherosclerosis*.231(2):238-45,2013.
4. Kanda E, **Ai M**, Iwamoto A, Okazaki M, Maeda Y, Sasaki S, Yoshida M. Relationship between icodextrin use and decreased level of small low-density lipoprotein cholesterol fractioned by high-performance gel permeation chromatography. *BMC Nephrol*. 2013 Oct 26;14:234.
5. Kanda E, **Ai M**, Okazaki M, Maeda Y, Sasaki S, Yoshida M. The association of very low-density lipoprotein with ankle-brachial index in peritoneal dialysis patients with controlled serum low-density lipoprotein cholesterol level. *BMC Nephrol*. 2013 Oct 7;14:212.

Geriatrics and Vascular Medicine

1. Staffs and Students

Professor	Kentaro SHIMOKADO, MD	
Associate Professor	Eiji KANEKO, MD	
Assistant Professor	Yasuko ABE, MD	Shohei SHINOZAKI, PhD
	Kenji TOYOSIMA, MD	
Graduate Student	Haruko USHIO, MD	Norihiko IZUMIMOTO, MD
	Ayumi TOBA, MD	Kae ITO, MD
	Tomomi HAKAMADA, MD	Yuki KISHIMOTO, MS
	Marie NAKAMURA, MD	Taku Mabuchi, MD
	Mari Sasaki, MD	Keita TAKAHASHI, MS

2. Purpose of Education

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

3. Research Subjects

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

4. Clinical Services

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

5. Publications (Original articles)

1. Shohei Shinozaki, Tsuyoshi Chiba, Koichi Kokame, Toshiyuki Miyata, Eiji Kaneko, Kentaro Shimokado. A Deficiency of Herp, an Endoplasmic Reticulum Stress Protein, Suppresses Atherosclerosis in ApoE Knockout Mice by Attenuating Inflammatory Responses. *PlosOne* 2013 ; 8 : e75249
2. Yuki Kishimoto, Takao Kanai, Kayoko Sato, Jaewon Lee, Kyu-Shik Jeong, Kentaro Shimokado, Naoki Maruyama, Akihito Ishigami. Insufficient ascorbic acid intake during gestation induces abnormal cardiac dilation in fetal and neonatal SMP30/GNL knockout mice *Pediatric Research* 2013; 73:578
3. Kae Ito, Hiroki Inagaki, Mika Sugiyama, Tsuyoshi Okamura,3 Kentaro Shimokado, Shuichi Awata1 Association between subjective memory complaints and mental health well-being in urban community-dwelling elderly in Japan.. *iGeriatrics and Geront Int* 2013;234
4. Yuki Kishimoto, Norikatsu Saito, Katsumi Kurita, Kentaro Shimokado, Naoki Maruyama, Akihito Ishigami. Ascorbic acid enhances the expression of type 1 and type 4 collagen and SVCT2 in cultured human skin fibroblasts. *Biochemical and Biophysical Research Communications* 2013;430: 579-584

Rehabilitation Medicine

1. Staffs and Students (April, 2013)

Associate Professor	Sadao MORITA	
Graduate Student	Kazuhisa INOUE,	Akihito KUBOTA,
	Tomoko ARAKI,	Keisuke KAJI,
	Kashitarou HYOUDOU,	Junying PIAO,
	Tomokazu MASAOKA,	Chisato TAKADA,
	Maierhaba AILIXIDING,	Kazuko KATSUKI,
	Takanori KOKUBUN,	Takashi IKEDA,
	Masayuki HIRAO,	Ryohei TAKADA

2. 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. Research Subjects

- 1) 3-dimension motion analysis in activities of daily living
- 2) Balance and occlusion
- 3) Biomechanical analysis of artificial limb
- 4) Prevention of dislocation after total hip arthroplasty
- 5) Prevention of disuse bone atrophy

4. Publications

Original Article

1. Piao J, Tsuji K, Ochi H, Iwata M, Koga D, Okawa A, Morita S, Takeda S, Asou Y. Sirt6 regulates postnatal growth plate differentiation and proliferation via Ihh signaling. *Sci Rep.* Oct 23; 3:3022, 2013.
2. Aizawa J, Masuda T, Hyodo K, Jinno T, Yagishita K, Nakamaru K, Koyama T, Morita S. Ranges of active joint motion for the shoulder, elbow, and wrist in healthy adults. *Disabil Rehabil.* Aug; 35(16):1342-9, 2013
3. Inoue K, Uematsu M, Maruoka H, hara K, Kanemura N, Masuda T, Morita S. Influence of Lower Limb Muscle Fatigue on Balance Function. *Journal of Physical Therapy Science* Vol.25 No.3 331-335, 2013.
4. Maruoka H, Hujii T, Inoue K. Effect of Ubiquinol on Exercise and the Oxidative Stress Regulation System in SMAP1 Mice. *Journal of Physical Therapy Science* Vol.25 No.3, 345-348, 2013.

Gerodontology and Oral Rehabilitation

1. Staffs and Students

Professor	Shunsuke MINAKUCHI	
Associate Professor	Tsuneto OHWATARI,	Haruka TOHARA
Junior Associate Professor	Ken'ichi KOBAYASHI,	Toshiaki SEKITA
Assistant Professor	Kazuo MOTOMURA,	Ayako NAKANE,
	Shino MURATA,	Shinya MIKUSHI,
	Syuuhei TAKEUCHI,	Norihisa AKIBA,
	Manabu KANAZAWA,	Yusuke SATO,
	Maiko IWAKI,	Mai OKUBO
Graduate Student	Bai Doug Ying,	Yu YOSHIZUMI,
	Hiroataka SHOJI,	Nami OGAWA,
	Eji Yoshii,	Marie SATO,
	Hikomichi SHINOZAKI,	Tomonori KAGAWA,
	Minoru INOUE,	Yoshihito HOSHINO,
	Takeshi HORIE,	Keisuke KIKUCHI,
	Shinta YAMAMOTO,	Mariko TANOUE,
	Yuri OMURA,	Ayami JO,
	Daisuke HIRAYAMA,	Ayako FUJIMOTO,
	Toshinari Nakamura,	Hiroyuki TANIMOTO,
	Ken ODA,	Taro YOSHIZAKI,
	Yui FUJIMOTO,	Gaku OWADA,
	Go KAMOCHI,	Keisuke SUZUKI,
	Hitomi SOEDA,	Akane MIZUNO,
	Hideo SAKAGUCHI,	Hiroshi MAEDA,
	Sachiko OBA,	Akemi HOSODA,
	Hiroko AKABANE,	Ai OOSHIMA

2. Purpose of Education

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

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

3. Research Subjects

- 1) Medical management of Elderly Patients During Dental Treatment
- 2) New Examination Method for Dry Mouth
- 3) Oral Stereognosis Ability in the Elderly
- 4) Threshold of Mucous Membrane under Denture Base in Elderly Oral Mucosa Patients
- 5) State of the art Lasers in Zirconia Prosthetic Processing and Pain-free Treatment
- 6) Denture Mobility
- 7) Deglutition in Elderly Patients Requiring Nursing Care
- 8) Eating and Swallowing Rehabilitation in Post-Oral Tumor Surgery Patients
- 9) Dysphagia of Medullary Infarction Patients
- 10) Dental Approaches to Dysphagia
- 11) Screening Methods of Silent Aspiration
- 12) Swallowing Dynamics and Brain Activity
- 13) Stress analyses of implant overdenture

- 14) Factorial analysis of complete denture prosthesis
- 15) Resilient denture lining material
- 16) CAD/CAM system for fabricating complete dentures
- 17) Evaluations of masticatory performance using color-changeable chewing gum

4. Clinical Services

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

5. Publications

- 1) Arakawa T, Ando E, Xin Wang, Miyajima K, Takeuchi S, Kudo H, Saito H, Takahashi M, Mitani T, Mitsubayashi K. Chemiluminescent Visualization for Evaluation of Gaseous Ethanol Distribution During 'La France' Pear Maturation, *IEEE Sensors Journal*, 13(8): 2842-2848, 2013.
- 2) Iida T, Tohara H, Wada S, Nakane A, Sanpei R, Ueda K. Aging decreases the strength of suprahyoid muscles involved in swallowing movements. *Tohoku J Exp Med*. 2013;231(3):223-8.
- 3) Hara K, Tohara H, Wada S, Iida T, Ueda K, Ansai T. Jaw-Opening Force Test to Screen for Dysphagia: Preliminary Results. *Arch Phys Med Rehabil*. 2013 Sep 19.
- 4) Nakayama E, Kagaya H, Saitoh E, Inamoto Y, Hashimoto S, Fujii N, Katada K, Kanamori D, Tohara H, Ueda K. Changes in pyriform sinus morphology in the head rotated position as assessed by 320-row area detector CT. *Dysphagia*. 2013 Jun;28(2):199-204.
- 5) Inokoshi M, Kameyama A, De Munck J, Minakuchi S, Van Meerbeek B. Durable bonding to mechanically and/or chemically pre-treated dental zirconia. *J Dent*. 2013 Feb;41(2):170-9.
- 6) Inokoshi M, Poitevin A, De Munck J, Minakuchi S, Van Meerbeek B. Bonding effectiveness to different chemically pre-treated dental zirconia. *Clin Oral Investig*. 2013 Nov 27.
- 7) Iwaki M, Kanazawa M, Sunaga M, Kinoshita A, Minakuchi S. Live broadcast lectures on complete denture prosthodontics at Tokyo Medical and Dental University: comparison of two years. *J Dent Educ*. 2013 Mar;77(3):323-30.
- 8) Yamaga E, Sato Y, Minakuchi S. A structural equation model relating oral condition, denture quality, chewing ability, satisfaction, and oral health-related quality of life in complete denture wearers. *J Dent*. 2013 Aug;41(8):710-7.
- 9) Katase H, Kanazawa M, Inokoshi M, Minakuchi S. Face simulation system for complete dentures by applying rapid prototyping. *J Prosthet Dent*. 2013 Jun;109(6):353-60.
- 10) Ochi M, Kanazawa M, Sato D, Kasugai S, Hirano S, Minakuchi S. Factors affecting accuracy of implant placement with mucosa-supported stereolithographic surgical guides in edentulous mandibles. *Comput Biol Med*. 2013 Nov;43(11):1653-60.
- 11) Umezaki Y, Katagiri A, Watanabe M, Takenoshita M, Sakuma T, Sako E, Sato Y, Toriihara A, Uezato A, Shibuya H, Nishikawa T, Motomura H, Toyofuku A. Brain perfusion asymmetry in patients with oral somatic delusions. *Eur Arch Psychiatry Clin Neurosci*. 2013 Jun;263(4):315-23.

Laboratory Medicine

1. Staffs and Students

Professor	Nobuo NARA	
Associate Professor	Shuji TOHDA	
Research Associate	Mai ITOH	
Graduate Students	Yuki OKUHASHI,	Yusuke TAKAHASHI,
	Mika Ohtaka	

2. Purpose of Education

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.

3. Research Subjects

- 1) Mechanism of abnormal growth of acute leukemia cells
- 2) Molecular diagnostic tests for cancer and infectious diseases
- 3) Mechanism of abnormal growth of lymphoma cells
- 4) Detection of minimal residual leukemia or lymphoma cells

4. Clinical Services

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

5. Publications

Original Article

1. Ono A, Oike R, Okuhashi Y, Takahashi Y, Itoh M, Nara N, Tohda S. Comparative effects of PP242 and rapamycin on mTOR signalling and NOTCH signalling in Leukemia cells. *Anticancer Res.* 2013; 33: 809-814.
2. Yonekura S, Itoh M, Okuhashi Y, Takahashi Y, Ono A, Nara N, Tohda S. Effects of the HIF1 inhibitor, echinomycin, on growth and NOTCH signalling in leukaemia cells. *Anticancer Res.* 2013; 33: 3099-3103.
3. Okuhashi Y, Itoh M, Nara N, Tohda S. *NOTCH* knockdown affects the proliferation and mTOR signaling of leukemia cells. *Anticancer Res.* 2013; 33: 4293-4298.

Critical Care Medicine

1. Staffs and Students (January 2012~December 2012)

Associate Professor	Chieko MITAKA
Lecturer	Go Haraguchi (Intensive Care Unit) (2011.4.1~)
Assistant Professor	Mamoru Yamamoto (Intensive Care Medicine) (2012.6.1~) Masatoshi Jibiki (Critical Care Meedicine) (2012.4.1~2013.9.30) Takahiro Toyofuku (Critical Care Medicine) (2011.4.1~)
Hospital Staff	Naoto Fujiwara (Intensive Care Unit) (2012.4.1~) Masato Nishizawa (Intensive Care Unit) (2013.10.1~)
Postgraduate students	May Khin Hnin Si (2010.4.1~) Miniwan Tulafu (2010.4.1~)

2. Purpose of Education

Undergraduate education

Lectures: Fourth-year medical students

- 1) Acute respiratory failure and mechanical ventilation (Mitaka)
- 2) Sepsis and multiple organ dysfunction syndrome (Mitaka)
- 3) Examination of critical care medicine

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 check clinical data every morning and evening and make system-oriented presentation at ICU rounds.

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

3. Research Subjects

- 1) Treatment and prevention of ischemia/reperfusion injury of lung
- 2) High tidal volume ventilation and remote organ injury
- 3) A selective inhibitor for inducible NO synthase in endotoxic shock
- 4) Blockade of NF- κ B activation in endotoxic shock
- 5) Treatment for septic shock by poly (ADP-ribose) synthetase inhibitor
- 6) Clinical study of atrial natriuretic peptide
- 7) Effects of atrial natriuretic peptide on acute kidney injury

4. Clinical Services

Critical care medicine provides intensive care and treatment of critically ill patients. The role of intensivists take charge treatment of critically ill patients in the ICU. 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 attending physician. The purpose of critical care medicine is to treat and improve the serious condition by maintaining the patients' hemodynamics to be stable.

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, abnormal electrolyte, acute kidney injury, central nervous system dysfunction, and hospital-acquired infection, mechanical ventilation, pharmacological support, cardiopulmonary support system, blood purification, and nutrition support.

5. Publications

【Original Article】

1. Hnin Si MK, Mitaka C, Tulafu S, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M, Inhibition of poly

(adenosine diphosphate-ribose) polymerase attenuates lung-kidney crosstalk induced by intratracheal lipopolysaccharide instillation in rats. *Respir Res* 2013;14:126-133

2. Tulafu M, Mitaka C, Hnin Si MH, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M, Atrial natriuretic peptide attenuates kidney-lung crosstalk in kidney injury. *J Surg Res* 2014;186:217-225
3. Takashi Ishihara, MD, PhD; Go Haraguchi, MD, PhD; Daisuke Tezuka, MD; Tetsuo Kamiishi, MD; Hiroshi Inagaki, MD, PhD; Mitsuaki Isobe, MD, PhD, Diagnosis and Assessment of Takayasu Arteritis by Multiple Biomarkers. *Circ J* 2013; 77: 477-483
4. Susumu Hosokawa, Go Haraguchi, Akihito Sasaki, Hirokuni Arai, Susumu Muto, Akiko Itai, Shozaburo Doi, Shuki Mizutani, and Mitsuaki Isobe, Pathophysiological roles of nuclear factor kappaB (NF- κ B) in pulmonary arterial hypertension: effects of synthetic selective NF- κ B inhibitor IMD-0354. *Cardiovascular Research* 2013; 99: 35-43
5. Daisuke Tezuka, Go Haraguchi, Hiroshi Inagaki, Mitsuaki Isobe, Progression of thrombogenesis in large coronary aneurysms during anticoagulant therapy in a Buerger's disease patient. *BMJ Case Rep* 2013. doi:10.1136/bcr-2013-009945

【Conference】

1. Hnin Si MK; Mitaka C; Tulafu M; Abe S; Ikeda S, Atrial natriuretic peptide attenuates metabolic acidosis and inflammation of kidney, lung and heart in a rat model of renal ischemia-reperfusion injury, The 33rd International Symposium on Intensive Care and Emergency Medicine, March 20, 2013, Brussels, Belgium
2. Mitaka C, Dong Z, Haraguchi G, The value of serum procalcitonin level for differentiation of infectious from noninfectious systemic inflammatory response syndrome after cardiac surgery. European Society of Intensive Care Medicine, The 26th Annual Congress of the European Society of Intensive Care Medicine, October 8, 2013

【Research grant】

1. Chieko Mitaka, Grants-in Aid for Scientific Research from the Ministry of Education, Science and Culture. Basic research (C) 22592010 Renal protective effects of atrial natriuretic peptide in acute kidney injury

Liaison Psychiatry and Palliative Medicine

1. Staffs and Students (April, 2013)

Associate Professor	Eisuke MATSUSHIMA	
Junior Associate Professor	Miho MIYAJIMA	
Tokunin Assistant Professor		
Hospital Staff		
Secretary	Kyoko NAKAGAWA	
Graduate Student	Aya KOIZUMI,	Motonori KIMURA,
	Hirofumi NAKAMURA,	Makiko KOIKE,
	Ako HANEKAWA,	Mare NISHIURA,
	Mariko KOBAYASHI,	Yuhko KOHNO,
	Nao NAKAYAMA,	Satsuki WATANABE,
	Aya YAMASITA,	Kanako ICHIKURA,
	Rie OMOYA,	Takamasa NODA,
	Toshimi TAKANO,	Noriko ISHIDUKA,
	Saho WADA,	Noriko YOSHIDA,
	Toshi KURIYAMA,	Shino UMEZAWA,
	Hiroshi KOBO,	Yoko SUZUKI,
	Ayasa MATSUDA,	Natsumi NAKAMURA
Research Student	Okihiko AIHARA,	Ryuhō IBARAKI

2. Purpose of Education

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

3. Research Subjects

- 1) Assessment of mental state in cancer and other physical patients using written questionnaire
- 2) Research on quality of life (QOL) in cancer patients and their families
- 3) Investigation cognitive function of patients with organic disorders (SLE, diabetics, and so on) undergoing a battery of psychometry tests and neuroimaging examinations
- 4) Explanation for the relationship between physical symptoms and mental states in patients with psychosomatic diseases including chronic pain and irritable bowel syndrome (IBS)
- 5) Examination for physiological phenomenon of psychiatric patients using eye mark recorder, electroencephalogram (EEG) and functional MRI (fMRI)

4. Clinical Services

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

5. Publications

Original Article

1. Iwatani T, Matsuda A, Kawabata H, Miura D, Matsushima E. Predictive factors for psychological distress related to diagnosis of breast cancer. *Psycho-Oncol* 22(3): 523-529, 2013.
2. Watanabe S, Hara K, Ohta K, Ino H, Miyajima M, Matsuda A, Hara M, Maehara T, Matsuura M, Matsushima M. Aroma helps to preserve information processing resources of the brain in healthy subjects but not in temporal lobe epilepsy. *Seizure* 22(1): 59-63, 2013.
3. Koizumi A, Matsushima E, Mochizuki Y, Omura K, Amagasa T. Changes in the psychological characteristics of oral cancer patients in the perioperative period: a quantitative evaluation. *J Med Dent Sci* 60(1): 41-53, 2013.
4. Terauchi M, Hiramitsu S, Akiyoshi M, Owa Y, Kato K, Obayashi S, Matsushima E, Kubota T. Associations among

- depression, anxiety and somatic symptoms in peri- and postmenopausal women. *J Obstet Gynaecol Res* 39(5): 1007-1013, 2013.
5. Hara K, Maehara T, Miyajima M, Ohta K, Iino H, Inaji M, Matsuda A, Matsushima E, Hara M, Matsuura M. Post-operative mismatch negativity recovery in a temporal lobe epilepsy patient with cavernous angioma. *Clin Neurol Neurosurg* 115(6): 756-759, 2013.
 6. Matsuda A, Hara K, Miyajima M, Matsushima E, Ohta K, Matsuura M. Distinct pre-attentive responses to non-scale notes: An auditory mismatchnegativity (MMN) study. *Clin Neurophysiol* 124(6): 1115-1121, 2013.
 7. S. Watanabe, K. Hara, A. Matsuda et al., Aroma helps to preserve information processing resources of the brain in healthy subjects but not in temporal lobe epilepsy. *Seizure*, 2013; 22(1):59-63.
 8. Matsuda A, Hara K, Watanabe S, Matsuura M, Ohta K, Matsushima E. Pre-attentive auditory processing of non-scale pitch in absolute pitch possessors. *Neurosci Lett.* 26;548:155-158, 2013.
 9. Kobayashi M, Kobayashi M, Suwa H, Matsushima E. The Validity and Usefulness of the Japanese Version of the Calgary Sleep Apnea Quality of Life Index in Patients with Obstructive Sleep Apnea Hypopnea Syndrome. *Internal Medicine.* 2013; 52(3): 309-15.
 10. Nakanishi H, Kurosaki M, Nakanishi K, Tsuchiya K, Noda T, Tamaki N, *et al.* Impaired brain activity in cirrhotic patients with minimal hepatic encephalopathy: Evaluation by near-infrared spectroscopy. *Hepato Res.* 2013 Apr 5. doi: 10.1111/hepr.12127. [Epub ahead of print]
 11. Kunugi H, Koga N, Hashikura M, Noda T, Shimizu Y, Kobayashi T, *et al.* Validation of computer-administered clinical rating scale: Hamilton Depression Rating Scale assessment with Interactive Voice Response technology--Japanese version. *Psychiatry Clin Neurosci.* 2013 May;67(4):253-8.
 12. Ota M, Sato N, Nakata Y, Ito K, Kamiya K, Maikusa N, Ogawa M, Okamoto T, Obu S, Noda T, Araki M, Yamamura T, Kunugi H. Abnormalities of cerebral blood flow in multiple sclerosis: a pseudocontinuous arterial spin labeling MRI study. *Magn Reson Imaging.* 2013 Jul;31(6):990-5.
 13. Ota M, Ishikawa M, Sato N, Hori H, Sasayama D, Hattori K, Teraishi T, Noda T, Obu S, Nakata Y, Higuchi T, Kunugi H. Discrimination between schizophrenia and major depressive disorder by magnetic resonance imaging of the female brain. *J Psychiatr Res.* 2013 Oct;47(10):1383-8.
 14. Koseki S, Noda T, Yokoyama S, Kunisato Y, Ito D, Suyama H, *et al.* The relationship between positive and negative automatic thought and activity in the prefrontal and temporal cortices: a multi-channel near-infrared spectroscopy (NIRS) study. *J Affect Disord.* 2013 Oct;151(1):352-9.
 15. Kono Y, Matsushima E, Uji M: Psychometric properties of the 25-Item work limitations questionnaire in Japan factor structure, validity, and reliability in information and communication technology company employees. *Journal of Occupational and Environmental Medicine* 56(2), 2014.

Pharmacokinetics and Pharmacodynamics

1. Staffs and Students (April, 2013)

Professor Masato Yasuhara

Associate Professor Masashi Nagata

2. Purpose of Education

Department of Hospital Pharmacy, University Hospital of Medicine, 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 and drug transport will be given. Students will have the practice of pharmacokinetic analysis and animal experiments.

3. Research Subjects

- 1) Investigation on the membrane transport of drugs
- 2) Kinetics of drug action in disease states
- 3) Therapeutic drug monitoring and clinical pharmacokinetics
- 4) Development of new drug delivery systems

4. Clinical Services

Department of Hospital Pharmacy provides all services about the pharmacotherapy, including dispensing, formulation, preparation of injections and infusion solutions, drug information, and therapeutic drug monitoring.

5. Publications

Original Article

1. Ishiwata Y, Takahashi Y, Nagata M, Yasuhara M.: Effects of moxifloxacin on serum glucose concentrations in rats
Biol. Pharm. Bull., 36, 686-690 (2013).

Medical Education Research and Development

1. Staffs and Students

Professor	Yujiro TANAKA	
Junior Associate Professor	Makoto TAKAHASHI,	Shinya OOKA (to March 2013), Yasuhiro ITSUI (from April 2013)
Associate Professor	Yuki SUMI	
Project Junior Associate Professor	Toru SUGIYAMA (to March 2013)	
Attending Staff	Akiko KITAZUME (to March 2013)	Takako WATANABE (from April 2013)

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

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

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

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

2. Education

Undergraduate Education

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

Postgraduate Education (Clinical Training)

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

Postgraduate Education (Master's degree courses)

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

3. Research

Research on continuing education in clinical EBM (Tanaka)

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

Medical risk education using the HAZOP method-through analyzing basic surgical procedure (Takahashi)

Structured risk analysis methods, HAZOP, are applied for medical risk management. We have also developed computer software for risk analysis with HAZOP. As a method of medical education for medical risk as well, HAZOP is a comprehensive method that is effective in reducing medical errors.

Review of clinical training in postgraduate clinical education (Tanaka, Takahashi)

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

General research on medical education (Tanaka, Takahashi, Ooka, Sugiyama, Sumi, Itsui)

We are developing a comprehensive research project regarding postgraduate medical education, primary care in rural regions, development of clinical competence, and a new PBL system.

4. Clinical Practice

Second Opinion (Ooka, Itsui)

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

Patient Safety (Ooka)

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

5. Original Article

1. Okamoto S, Kawahara K, Okawa A, Tanaka Y. Values and risks of second opinion in Japan's universal health-care system. *Health Expect.* 2013 Feb 14.

Acute Critical Care and Disaster Medicine

1. Staffs and Students (April, 2013)

Professor	Yasuhiro OTOMO	
Junior Associate Professor	Masahito KAJI,	Junichi AIBOSHI
Assistant Professor	Atsushi SHIRAISHI,	Kiyoshi MURATA,
	Junji YASUIKE,	Hiroto USHIZAWA,
	Kenichi HONDO,	Akira ENDO,
	Marie TAKAHASHI,	Atsushi SENDA
Hospital Staff	Minoru UEKI,	Kanae OCHIAI,
	Mitsuaki KOJIMA,	Tomohiko Ai,
	Sayuri INAGAKI	
Graduate Student	Junichi INOUE,	Saori MIKAMI,
	Hideaki ANAN,	Shino Miwa,
	Shinya ENOMOTO,	Yousuke TAKADA
Resident	Fumitaka SAIDA,	Ayako YOSHIYUKI,
	Keita NAKAZUTSUMI,	Tomonori TOMISHIGE

2. Purpose of Education

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

3. Research Subjects

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

4. Clinical Services

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

Publications

Original Article

1. Ushizawa H, Foxwell AR, Bice S, Matsui T, Ueki Y, Tosaka N, Shoko T, Aiboshi J, Otomo Y.: Needs for disaster medicine: lessons from the field of the Great East Japan Earthquake. *Western Pacific Surveillance and Response Journal*. 4(1):51-55, 2013
2. Morishita K, Aiboshi J, Kobayashi T, Yokoyama Y, Mikami S, Kumagai J, Onisawa K, Otomo Y.: Group VIB Ca²⁺-independent phospholipase A2F is associated with acute lung injury following trauma and hemorrhagic shock. *J Trauma Acute Care Surg*. 75: 767-774, 2013
3. Gando S, Saitoh D, Ishikura H, Ueyama M, Otomo Y, Oda S, Kushimoto S, Tanjoh K, Mayumi T, Ikeda T, Toshiaki Iba, Eguchi Y, Okamoto K, Ogura H, Koseki K, Sakamoto Y, Takayama Y, Shirai K, Takasu O, Inoue Y, Mashiko K, Tsubota T, Endo S. : A randomized, controlled, multicenter trial of the effects of antithrombin on disseminated intravascular coagulation in patients with sepsis. *Critical Care* 2013, 17:R297 doi:10.1186/cc13163
4. Hondo K, Shiraishi A, Fujie S, Saitoh D, Otomo Y : In-hospital trauma mortality has decreased in Japan possibly due to trauma education. *J Am Coll Surg*. 217(5):850-857, Nov. 2013

5. Akira Endo, Atsushi Shiraishi, Junichi Aiboshi, Yoshiro Hayashi, and Yasuhiro Otomo : A case of purpura fulminans caused by *Hemophilus influenzae* complicated by reversible cardiomyopathy. *Journal of Intensive Care* In press.
6. Chang PC, Turker I, Lopshire JC, Masroor S, Nguyen BL, Tao W, Rubart M, Chen PS, Chen Z, Ai T. Heterogeneous Upregulation of Apamin-Sensitive Potassium Currents in Failing Human Ventricles. *J Am Heart Assoc* 2013; 2:e004713
7. Hsieh YC, Chang PC, Lee YS, Weiss JN, Chen Z, Ai T, Lin SF, Chen PS. Inhibition of small conductance Ca-activated K⁺ channels flattens the action potential duration restitution and hinders the maintenance of ventricular fibrillation in failing rabbit ventricles. *Circ Arrhythmia Electrophysiol* 6:410-8, 2013
8. Turker I, Chang PC, Chen Z, Sohma Y, Chen PC, Ai T. Amiodarone inhibits small conductance Ca²⁺-activated K⁺ (SK2) channel expressed in HEK-293 cells. *PLoS ONE* 2013;8:e70450
9. Xi Y, Wu G, Ai T, Cheng N, Kalisnik JM, Sun J, Abbasi S, Yang D, Fan C, Yuan X, Wang S, Elayda M, Gregoric ID, Kantharia BK, Lin SF, Cheng J. Ionic mechanisms underlying the effects of vasoactive intestinal polypeptide on canine atrial myocardium. *Circ Arrhythm Electrophysiol* 6:976-83, 2013
10. Maruyama, M, Ai T, Chua SK, Park HW, Lee YS, Shen MJ, Chang PC, Lin SF, Chen PS. Hypokalemia Promotes Late Phase 3 Early Afterdepolarization and Recurrent Ventricular Fibrillation During Isoproterenol Infusion in Langendorff Perfused Rabbit Ventricles. *Heart Rhythm* 2013. In press
11. Turker I, Ai T. Editorial Commentary: "Cervical sympathetic denervation: the last resort?" *Heart Rhythm* 2013. In press.
12. Katayama, Yoichi; Hifumi, Toru; Inoue, Junichi; Koido, Yuichi: A case of Takotsubo cardiomyopathy induced by accidental hypothermia and diabetic ketoacidosis. *BMJ Case Reports* . p1-3. Apr2013
13. Hifumi T, Kiri N, Kato H, Inoue J, Koido Y: Survival after prolonged resuscitation from cardiac arrest due to diabetic ketoacidosis using extracorporeal life support. *Am J Emerg Med* 31(5):892.e1-2, 2013

Clinical Oncology

1. Staffs and Students (April, 2013)

Professor	Satoshi MIYAKE
Associate Professor	Shinya OOKA
Assistant Professor	Hiroyuki SAKASHITA
Assistant Professor	Chiharu KAWAKAMI

2. Purpose of Education

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

3. Research Subjects

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

4. Clinical Services

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

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

5. Publications

Original Article

1. Sakashita H, Inoue H, Akamine S, Ishida T, Inase N, Shirao K, Mori M, Mimori K. Identification of the NEDD4L gene as a prognostic marker by integrated microarray analysis of copy number and gene expression profiling in non-small cell lung cancer. *Ann Surg Oncol*. 2013;20 Suppl 3:S590-8.
2. Komazaki Y, Sakashita H, Furuiye M, Fujie T, Tamaoka M, Sumi Y, Miyazaki Y, Kojima K, Jin Y, Inase N: Feasibility study of adjuvant chemotherapy of S-1 and carboplatin for completely resected non-small cell Lung cancer. *Chemotherapy* 59: 35-41, 2013
3. Chiba S, Tsuchiya K, Sakashita H, Ito E, Inase N: Rifampicin-induced acute kidney injury during the initial treatment for pulmonary tuberculosis: A case report and literature review. *Intern Med* 52:2457-2460, 2013

Dentistry for Persons with Disabilities

1. Staffs and Students(April, 2013)

Junior Associate Professor	Osamu SHINOZUKA	
Junior Associate Professor(Part-time)	Sadamu HAGA,	Minoru INADA,
	Goro SEKIGUCHI,	Hiroyuki ISHIKAWA,
	Yohei TAKEUCHI,	Syohei TAMURA,
	Moriyuki NAKAMURA	
Assistant Professor	Yasuka KUSUMOTO	
Hospital Staff	Tomo SUZUKI,	Naoki HAYASHI,
	Taiji HOSHIAI,	Yousuke KINOSHITA
Graduate International Research Student		
	Hirotoishi YAMAWAKI	
Visiting Clinical		
Junior Associate Professor	Seiji SAKURAI	

2. Purpose of Education

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

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

3. Research Subjects

- 1) Formation of oral biofilm
- 2) Elimination of oral biofilm of persons with disabilities
- 3) Drug induced gingival overgrowth
- 4) Oral health status of the medically compromised patient
- 5) Oral management of genetic syndrome

4. Clinical Services

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

For example,

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

General Dentistry (Oral Diagnosis and General Dentistry)

1. Staffs and Students (April, 2013)

Chief	Shiro MATAKI	
Associate Professor	Shigeru ODA	
Junior Associate Professor	Masayuki HIDESHIMA,	Satoko OHARA,
	Ken-ichi TONAMI	
Assistant Professor	Sachi UMEMORI,	Kanako NORITAKE
Hospital Staff	Ayaka INAKAZU,	Yuko MITSUMA,
	Hirono KIKUCHI,	Akina ADACHI,
	Takahumi SUZUKI,	Azusa YAMADA,
	Mina GOTO	

2. Purpose of Education

General Dentistry is a branch of dental science which deals with oral diagnosis and general dentistry. Education objective of General Dentistry is to acquire comprehensive patient care methods from medical interview to periodic maintenance after dental treatment. Therefore, General dentistry provides practical training course of medical interview, oral examination, oral diagnosis, writing dental records, and simulation education.

3. Research Subjects

- 1) Study on Implementation and assessment of new dental clinical education systems
- 2) Study on development of the training method to improve the ability of diagnosis of dental students and residents
- 3) Study on variety of diagnosis and treatment planning of the patient appealing for several symptoms
- 4) Study on analysis of various factors necessary to be diagnosed correctly
- 5) Study on development of a new oral diagnosis method (ex. Caries diagnosis using digital imaging)
- 6) Study on new dental treatment based on concept of minimal intervention (ex. Selective caries removal using ArF excimer laser/ chemical solvent)
- 7) Study on patients-friendly environment for dental treatment (ex. Sterilization of water line of dental chair unit using small electronic current. Stress monitoring during dental treatment using physiological parameter)

4. Clinical Services

In our dental hospital, most new patients consult dentists in our clinic of general dentistry and oral diagnosis to receive suitable treatment for their chief complaints. Dentists of our clinic decide where to refer each case for the optimal clinic in our hospital for their needs. If new patient is suitable for treatment in general dentistry, dentists of our clinic ask them to receive treatments from students or residents.

Clinic of general dentistry and oral diagnosis also provides patient-centered general practice and oral care by dental hygienists.

5. Publications

- 1) Marwa Madi, Osama Zakaria, Kanako Noritake, Masaki Fuji, Shohei Kasugai. Peri-implantitis Progression Around Thin Sputtered Hydroxyapatite-Coated Implants: Clinical and Radiographic Evaluation in Dogs. *J Oral and Maxillofacial Implants*. 28(3) 701-709, 2013.
- 2) Nyan M, Hao J, Miyahara T, Noritake K, Rodriguez R, Kasugai S. Accelerated and Enhanced Bone Formation on Novel Simvastatin-Loaded Porous Titanium Oxide Surfaces. *Clin Implant Dent Relat Res*. 2013.
- 3) Masaki Fujii, Makoto Shiota, Kanako Noritake, Kazuhiro Kon, Hitoshi Sato, and Shohei Kasugai. Effect of Density of Hydroxyapatite Fiber material on Bone Regeneration in Vertical Bone Augmentation Model. *J Oral Tissue Engin* 10(3) 115-122, 2013
- 4) Kang Chen, Jia Hao, Kanako Noritake, Yu Yamashita, Shinji Kuroda, Shohei Kasugai. Effects of low intensity pulsed ultrasound stimulation on bone regeneration in rat parietal bone defect model. *Open Journal of Regenerative Medicine*. 2(1), 8-14 2013
- 5) Sorasun Rungsiyanont, Kanako Noritake, Warunee Pluemsakunthai, Somchai Yodsanga, Somporn Swasdison and

- Shohei Kasugai. In vivo biocompatibility evaluation of gelatin-hydroxyapatitecrosslink biomimetic scaffolds for bone regeneration. *J Nanomater Mol Nanotechnol* 26, 2013
- 6) Ken-ichi Tonami, Shiro Mataka. Students'perception of clinical attire compared with those of patients and dentists. Jun 5. 2013, MedEdPublish (<http://www.mededworld.org/MedEdWorld-Papers.aspx>), Oct 9. 2013.
 - 7) Yuki Ohara, Hirohiko Hirano, Yutaka Watanabe, Ayako Edahiro, Emiko Sato, Shoji Shinkai, Hiroto Yoshida and Shiro Mataka. Masseter muscle tension and chewing ability in older persons. *Geriatrics Gerontology International* 13:372-377, 2013
 - 8) Ohara Y, Hirano H, Yoshida H, Obuchi S, Ihara K, Fujiwara Y, Mataka S. Prevalence and factors associated with xerostomia and hyposalivation among community-dwelling older people in Japan. *Gerodontology*. 2013 Dec 4. doi: 10.1111/ger.12101. [Epub ahead of print]
 - 9) Kengo Iwasaki, Motohiro Komaki, Naoki Yokoyama, Yuichi Tanaka, Atsuko Taki, Yasuyuki Kimura, Masaki Takeda, Shigeru Oda, Yuichi Izumi, Ikuo Morita, Periodontal ligament stem cells possess the characteristics of pericytes, *Journal of Periodontology*, Vol.84, No.10, 1425-1433, 2013.

Psychosomatic Dentistry

1. Staffs and Students (April, 2013)

Professor	Akira Toyofuku	
Assistant Professor	Miho Takenoshita	
Hospital Staff	Tatsuya Yoshikawa,	Emi Sakou,
	Tomomi Sakuma Kurasawa	
Graduate Student	Yojiro Umezaki,	Motoko Watanabe,
	Spica Suzuki	
Lecturer (part-time)	Haruhiko Motomura,	Ayano Katagiri

2. Purpose of 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.

3. Research Subjects

- 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

4. Clinical Services

We take charge of “Head and Neck Psychosomatic Medicine 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 400 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. Publications

Original Article

- 1) Yojiro Umezaki, Ayano Katagiri, Motoko Watanabe, Miho Takenoshita, Tomomi Sakuma, Emi Sako, Yusuke Sato, Akira Toriihara, Akihito Uezato, Hitoshi Shibuya, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku : Brain perfusion asymmetry in patients with oral somatic delusions. *Eur Arch of Psychiatry Clin Neurosci.* 263(4)315-323, 2013. (IF : 3.362)
- 2) Katagiri A, Okamoto K, Thompson R, Bereiter DA. : Posterior hypothalamic modulation of light-evoked trigeminal neural activity and lacrimation. *Neuroscience.* 2013 Aug 29; 246:133-41. (IF : 3.122)
- 3) Okamoto K, Thompson R, Katagiri A, Bereiter DA. : Estrogen status and psychophysical stress modify temporomandibular joint input to medullary dorsal horn neurons in a lamina-specific manner in female rats. *Pain.* 2013 Jul;154(7):1057-64. (IF : 5.644)

Abstract

- 1) Yojiro Umezaki, Ayano Katagiri, Motoko Watanabe, Miho Takenoshita, Tomomi Sakuma, Emi Sako, Yusuke Sato, Akira Toriihara, Akihito Uezato, Hitoshi Shibuya, Toru Nishikawa, Haruhiko Motomura, Akira Toyofuku : Brain perfusion asymmetry in patients with oral somatic delusions. 11th World Congress of Biological Psychiatry, 23-27 June 2013, Kyoto, Japan.
- 2) Motoko Watanabe, Yojiro Umezaki, Ayano Katagiri, Tomomi Sakuma, Emi Sako, Miho Takenoshita, Akira Toyofuku : Phantom bite syndrome : comorbid psychiatric disorders and psychopharmacological efficacy: 11th World Congress of Biological Psychiatry, 23-27 June 2013, Kyoto, Japan.
- 3) Miho TAKENOSHITA, Ayano KATAGIRI, Yojiro UMEZAKI, Motoko WATANABE, Emi SAKO, Tomomi SAKUMA, Tatsuya YOSHIKAWA, Akira TOYOFUKU : Psychiatric comorbidity and treatment on patients with Atypical Odontalgia. 23rd world congress of psychosomatic medicine, Lisbon, 12-14 September 2013.
- 4) Motoko Watanabe, Yojiro Umezaki, Supika Suzuki, Ayano Katagiri, Tomomi Sakuma, Emi Sako, Miho Takenoshita, Akira Toyofuku : Phantom Bite Syndrome: Comorbid psychiatric disorders and psychopharmacological efficacy. 23rd world congress of psychosomatic medicine, Lisbon, 12-14 September 2013.
- 5) Ayano Katagiri, Randall Thompson, Keiichiro Okamoto, Mostafeezur Rahman and David A. Bereiter : Evidence for central sensitization in a rat model of Dry Eye. *Neuroscience 2013 (Society for Neuroscience) Sun Diego Nov. 9 – 13 2013.*
- 6) Mostafeezur Rahman, Keiichiro Okamoto, Ayano Katagiri, Randall Thompson and David A. Bereiter : Physiological stimulation of eye blink electromyographic activity in a rat model for dry eye. *Neuroscience 2013 (Society for Neuroscience) Sun Diego Nov. 9 – 13 2013.*
- 7) Khasabov, S., K. Okamoto, A. Katagiri, D. Simone and DA Bereiter : Activation of “NEUTRAL” cells in the RVM by noxious craniofacial stimulation. *Neuroscience 2013 (Society for Neuroscience) Sun Diego Nov. 9 – 13 2013.*

Behavioral Dentistry

1. Staffs and Students (April, 2013)

Professor	Shiro Mataka
Associate Professor	Hiroshi Nitta
Graduate Student	Yuki Ohara

2. Purpose of Education

Topic of Behavioral Dentistry included characteristics of human behavior, especially of relationship between patients and dental staff based on the informed consent. Main objective of behavioral dentistry in the graduate course is to provide students opportunity to study application of behavioral science to deal with dental patients showing various perception and behavior in clinic.

3. Research Subjects

- 1) Construction of educational system of behavioral dentistry for dental students
- 2) Application of behavioral science to development of dental educational curriculum
- 3) Patients' evaluation of the dental hospital and the dental educational system
- 4) Application of behavioral science to dental clinic

4. Clinical Services

Behavioral Dentistry provides medical interview for preliminary diagnosis and general dental practice at the clinic of oral diagnosis and general dentist cooperating with General Dentistry.

5. Publications

Original Article

- 1) Ao A, Wakabayashi N, Nitta H, Igarashi Y. Clinical and microbiologic effects of lingual cervical coverage by removable partial dentures. *Int J Prosthodont.* 26:45-50, 2013.
- 2) Pariksha Bharti, Sayaka Katagiri, Hiroshi Nitta, Toshiyuki Nagasawa, Hiroaki Kobayashi, Yasuo Takeuchi, Hajime Izumiyama, Isao Uchimura, Shuji Inoue, Yuichi Izumi. Periodontal treatment with topical antibiotics improves glycemic control in association with elevated serum adiponectin in patients with type 2 diabetes mellitus. *Obesity Research & Clinical Practice* 7:e129-e138, 2013.
- 3) Katagiri S, Nitta H, Nagasawa T, Izumi Y, Kanazawa M, Matsuo A, Chiba H, Fukui M, Nakamura N, Oseko F, Kanamura N, Inagaki K, Noguchi T, Naruse K, Matsubara T, Miyazaki S, Miyauchi T, Ando Y, Hanada N, Inoue S. Effect of glycemic control on periodontitis in type 2 diabetic patients with periodontal disease. *J Diabetes Investig.* 4:320-325, 2013.
- 4) Yuki Ohara, Hirohiko Hirano, Yutaka Watanabe, Ayako Edahiro, Emiko Sato, Shoji Shinkai, Hiroto Yoshida and Shiro Mataka. Masseter muscle tension and chewing ability in older persons. *Geriatrics Gerontology International* 13:372-377, 2013
- 5) Ohara Y, Hirano H, Yoshida H, Obuchi S, Ihara K, Fujiwara Y, Mataka S. Prevalence and factors associated with xerostomia and hyposalivation among community-dwelling older people in Japan. *Gerodontology.* 2013 Dec 4. doi: 10.1111/ger.12101. [Epub ahead of print]
- 6) Ken-ichi Tonami, Shiro Mataka. Students' perception of clinical attire compared with those of patients and dentists. Jun 5. 2013, *MedEdPublish* (<http://www.mededworld.org/MedEdWorld-Papers.aspx>), Oct 9. 2013.

Abstracted Papers Presented at Scientific Meeting

- 1) Ito Y, Tonami K, Sasaki Y, Mataka S, What is behavior Science? Our investigation and study as one example, 33rd Myanmar Dental Conference & 14th FDI-MDA Joint Educational Meeting, Yangon, Myanmar, 2013, 1月.

Temporomandibular Joint and Oral Function

1. Staffs (April, 2013)

Associate Professor	Koji KINO	
Assistant Professor	Akira NISHIYAMA	
Hospital Staff	Hiroko KIMURA,	Shoko TOBE,
	Natsuko OTOMO	
Graduate Student	Kaori TUKAGOSHI	

2. Purpose of Education

Purpose of education for students and residents in this course is to provide an opportunity to learn basic knowledge on diagnostic and therapeutic procedures for temporomandibular diseases. In special course for graduate students and undergraduate students, we instruct statistical techniques especially with the multi variate analysis by using clinical data acquired from patients with temporomandibular disorders (TMD).

3. Research Subjects

- 1) Development of multidimensional evaluation system for etiological factors of TMD
- 2) Influence of patients' psychosomatic factors for TMD
- 3) Sleep bruxism: its etiology, influence and treatment
- 4) Effectiveness of physiological therapy for TMD
- 5) Mechanisms of occlusal discomfort

4. Clinical Services

Temporomandibular joint clinic provides diagnosis and treatment for diseases and dysfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

Professional Development in Health Sciences

1. Staffs and Students

Professor	Kazuki TAKADA	
Associate Professor	Jun TSURUTA,	Mina NAKAGAWA
Junior Associate Professor	Kumiko YAMAGUCHI	

2. Purpose of Education

Worldwide, accelerated aging and the shift in disease burdens have created a demand for innovations in health sciences, healthcare, and the healthcare delivery system. Innovation requires not only a vast amount of knowledge and superior skills, but also critical and creative thinking skills. Innovation concerning new drugs and medical devices further requires understanding of the entire flow and process of research and development. In our department, we provides educational opportunities for learners to acquire high-level and practical knowledge of the followings: history of medical and dental education in Japan, professional education/development/certification in Japan and North American/European countries, key pedagogical theories and learning methods, process-based approach and logic models in curriculum development, and competencies and their assessment/evaluation.

3. Research Subjects

- Needs assessment in health care and in professional development in health science fields
- Curriculum development for professionals of the future needs in health sciences
- Interprofessional education curriculum development

4. Clinical Services

Medical Hospital	Kazuki TAKADA : Rheumatology
	Mina NAKAGAWA : Gastroenterology and Hepatology
Dental Hospital	Jun TSURUTA : Oral Diagnosis and General Dentistry

5. Publications

Original Article

1. Muro S, Yamaguchi K, Nakajima Y, Watanabe K, Harada M, Nimura A, Akita K. Dynamic intersection of the longitudinal muscle and external anal sphincter in the layered structure of the anal canal posterior wall. *Surg Radiol Anat.* 2013 Nov 21.

Neuroanatomy and Cellular Neurobiology

1. Staffs and Students

Professor	TERADA Sumio
Assistant Professor	KAWAGISHI Masahiko, SAITO Kenta SATO Keisuke
Graduate Student	TERAISHI Toshiya (-March), SATO Fumiya (April-)
Technician	TAGUCHI Mie

2. Purpose of 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. Research Subjects

- 1) Molecular mechanism of intracellular transport, quality control of transporting cargos, and their interrelation (Slow axonal transport and neurodegeneration)
- 2) Development of the real-time detection system of the biomolecular network in vivo and its application to cell biology
- 3) Molecular and cellular biological analysis of neuron-specific small G proteins
- 4) Development of new spectroscopic methods to visualize the localization of biomolecules without fluorescence labeling
- 5) Search for new cellular morphological regulatory factors on cytoskeletal dynamics

4. Publications

1. T. Matsuda, K. Horikawa, K. Saito, and T. Nagai: Highlighted Ca²⁺ imaging with a genetically encoded 'caged' indicator. *Scientific Report*, 3: 1398 (2013).
2. M. Yamanaka, K. Saito, N.I. Smith, S. Kawata, T. Nagai, and K. Fujita: Saturated excitation (SAX) of fluorescent proteins for sub-diffraction-limited imaging of living cells in three dimensions. *Interface Focus*, 3: 20130007 (2013).
3. K. Saito, Y. Higuchi, Y. Arai, and T. Nagai: Video-rate imaging of luminescent tumour cells in freely moving unshaved mice. *Protocol Exchange*, (2013).

Systems Neurophysiology

1. Staff and Students

Professor	Izumi Sugihara	
Associate Professor	Yuriko Sugiuchi	
Lecturer	Yoshiko Izawa	
Assistant Professor	Mayu Takahashi	
Postdoctoral fellow (JSPS PD)	Hirofumi Fujita	
Students	Suteera Vibulyaseck,	Yuanjun Luo

2. 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. They 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 cellular through the organismic levels. For students to gain first-hand experience in basic matters such as generation and propagation of excitation in nerve cells, we have developed a computer simulation program for a part of the laboratory course.

3. Research Subjects

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.

2) Neural mechanism of eye movement control

An animal fixates on a target of interest by moving its eyes and head. This eye-head coordination system is an important model of motor control in the central nervous system of higher mammals. To understand the mechanism of the visuo-motor transformation in eye movement system, we analyze neural mechanisms of signal transformation from the superior colliculus (center for rapid gaze shifts) to the brainstem, the midbrain, and the spinal cord using electrophysiological and morphological methods. Furthermore, we analyze the mechanisms for the control of eye movements and visual fixation in the systems from the frontal and parietal cortices to the superior colliculus and the brainstem.

4. Publications

Original Articles

1. Sasamura K, Ohki-Hamazaki H, Sugihara I (2013) Morphology of the olivocerebellar projection of the chick: an

axonal reconstruction study. *J Comp Neurol*; **521**:3321-3339.

2. Cerminara N, Aoki H, Loft M, Sugihara I, Apps R (2013) Structural basis of cerebellar microcircuits in the rat. *J Neurosci*; **33**:16427-16442.
3. Sugiuchi Y, Takahashi M, Shinoda Y (2013) Input-output organization of inhibitory neurons in the interstitial nucleus of Cajal projecting to the contralateral trochlear and oculomotor nucleus. *J Neurophysiol* **110**: 640-657.

Book Chapters

1. Voogd J, Shinoda Y, Ruigrok TJ, Sugihara I (2013) Cerebellar Nuclei and the Inferior Olivary Nuclei: Organization and Connections In: Ed. M. Manto, D. Gruol, J. Schmammann, N Koibuchi, F. Rossi eds, Handbook of the Cerebellum and Cerebellar Disorders, Part 2, Pages 377-436. New York, Springer.
2. Shinoda Y, Sugihara I (2013) Axonal Trajectories of Single Climbing and Mossy Fiber Neurons in the Cerebellar Cortex and Nucleus In: Ed. M. Manto, D. Gruol, J. Schmammann, N Koibuchi, F. Rossi eds, Handbook of the Cerebellum and Cerebellar Disorders, Part 2, Pages 437-467. New York, Springer.

Reviews

1. Fujita H, Sugihara I (2013) Branching patterns of olivocerebellar axons in relation to the compartmental organization of the cerebellum. *Front. Neural Circuits* **7**:3.
2. Sugihara I, Fujita H (2013) Peri- and postnatal development of cerebellar compartments in the mouse. *Cerebellum* **12**:325-327.
3. Sugihara I, Brown KM, Ascoli GA (2013) New insights on vertebrate olivo-cerebellar climbing fibers from computerized morphological reconstructions. *BioArchitecture* **3**: 38-41.

Pharmacology and Neurobiology

1. Staffs and Students (April, 2013)

Professor	Tsutomu TANABE	
Assistant Professor	Hironao SAEGUSA,	Shuqin ZONG
Graduate Student		

2. Purpose of Education

2-1

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.

2-2

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.

3. Research Subject

1. Regulation of Microglial function in Neuroinflammation/Neurodegenerative diseases
2. Regulation of Macrophage function in Inflammatory bowel disease and Rheumatoid arthritis
3. Molecular basis of Calcium channelopathy
4. miRNAs in neuronal function and dysfunction
5. Alteration of Neuron-Glia interaction in Neurological disorders

4. Publications

Meetings:

Tsutomu Tanabe, Hironao Saegusa and Shuqin Zong: Activation of N-type Calcium channel in microglia induces neuropathic pain, 4th International Congress on Neuropathic Pain, Toronto Canada 5.23-26, 2013.

Molecular Neuroscience

1. Staffs and Students (April, 2013)

Professor	Kohichi Tanaka	
Associate Professor	Hidenori Aizawa	
Assistant Professor	Tomomi Aida	
Project Assistant Professor	Miho Soma	
Project Assistant Professor	Yukiko Ito	
Project Assistant Professor	Ning Bai	
Project Assistant Professor	Michiko Yanagisawa	
Graduate Student	Junya Sugimoto,	Cui Wanpeng,
	Risa Imahashi,	Takaya Katsurayama,
	Kaori Sugiyama	

2. Purpose of Education

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

3. Research Subjects

- 1) Role of glutamate transporters in the neuropsychiatric disorders.
- 2) Role of the lateral habenula in the psychiatric disorders
- 3) Highly efficient and ultra-rapid in vivo genome editing in mice

4. Publications

Original Article

1. Bai, N., Aida, T., Yanagisawa, M., Katou, S., Sakimura, K., Mishina, M., Tanaka K. NMDA receptor subunits have differential roles in NMDA-induced neurotoxicity in the retina. *Mol Brain* 6. 34, 2013.
2. Namekata, K., Kimura, A., Kawamura, K., Guo, X., Harada, C., Tanaka, K., Harada, T. Dock3 attenuates neural cell death due to NMDA neurotoxicity and oxidative stress in a mouse model of normal tension glaucoma. *Cell Death Differ* 20. 1250-1256, 2013.
3. Hiraoka, Y., Komine, O., Nagaoka, M., Bai, N., Hozumi, K., Tanaka, K. Delta like 1 regulates Bergmann glial differentiation during cerebellar development. *Mol Brain* 6. 25, 2013.
4. Bai, N., Hayashi, H., Aida, T., Namekata, K., Harada, T., Mishina, M., Tanaka, K. Dock3 interaction with a glutamate-receptor NR2D subunit preprotects neurons from excitotoxicity. *Mol Brain* 6. 22, 2013.
5. Aizawa H, Yanagihara S, Kobayashi M, Niisato K, Takekawa T, Harukuni R, McHugh TJ, Fukai T, Isomura Y, Okamoto H. The synchronous activity of lateral habenular neurons is essential for regulating hippocampal theta oscillation. *J Neurosci*. 33. 8909-21, 2013.
6. Isomura Y, Takekawa T, Harukuni R, Handa T, Aizawa H, Takada M, Fukai T. Reward-modulated motor information in identified striatum neurons. *J Neurosci*. 33. 10209-20, 2013.
7. Aoki T, Kinoshita M, Aoki R, Agetsuma M, Aizawa H, Yamazaki M, Takahoko M, Amo R, Arata A, Higashijima S-I, Tsuboi T, Okamoto H. Imaging of neural ensemble for the retrieval of a learned behavioral program. *Neuron* 78. 881-894, 2013.

Reviews

1. Aizawa, H., Cui, W., Tanaka, K., Okamoto, H. Hyperactivation of the habenula as a link between depression and sleep disturbance. *Front Hum Neurosci* 7. 826, 2013.
2. Aizawa H. Habenula and the asymmetric development of the vertebrate brain. *Anat Sci Int*. 88. 1-9, 2013.
3. Okamoto H and Aizawa H. Fear and anxiety regulation by conserved affective circuits. *Neuron* 78. 411-413, 2013.

Neuropathology

1. Staff and Students (April 2013)

Professor:	Hitoshi Okazawa	
Associate Professor:	Kazuhiko Tagawa	
Adjunct Lecturer:	Nobuyuki Nukina,	Masaki Sone,
	Toshiki Uchihara	
Assistant Professor:	Takuya Tamura	
Project Assistant Professor:	Toshikazu Sasabe	
Project Assistant Professor:	Chisato Yoshida	
Project Assistant Professor:	Kyota Fujita	
Project Assistant Professor:	Kazumi Motoki	
Project Assistant Professor:	Xigui Chen	
Project Assistant Professor:	Hidenori Honma	
Technicians:	Tayoko Tajima,	Chiharu Mizoi,
	Yuko Uyama,	Kimiko Ibagawa
Secretary:	Asami Ohashi	
Graduate Students:	Ying Mao,	Shigenori Uchida,
	Kanou Kondo	
Research Trainees:	Juliana Bosso Taniguchi	

2. Purpose of 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. We also guide practical research techniques on neuropathology especially neurodegenerative diseases.

3. Research Subjects

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

- 1) Investigation of molecular pathologies of neurodegenerative diseases.
- 2) Studies on impairment of DNA-repair in polyglutamine diseases.
- 3) Development of new seed drugs for neurodegeneration.
- 4) Development of new seed drug for mental retardation.
- 5) Investigation of molecular functions of Oct-3/4

4. Clinical Services

DNA sequence based diagnosis of PQBP1-related mental retardation.

Publications

Original Articles

1. Fujita, K., Nakamura, Y., Oka, T., Ito, H., Tamura, T., Tagawa, K., Sasabe, T., Katsuta, A., Motoki, K., Shiwaku, H., Sone, M., Yoshida, C., Katsuno, M., Eishi, Y., Murata, M., Taylor, JP., Wanker, EE., Kono, K., Tashiro, S., Sobue, G., La Spada, AR., and Okazawa, H. (2013) A functional deficiency of TERA/VCP/p97 contributes to impaired DNA damage repair in multiple polyglutamine diseases. *Nature Commun.* 4:1816. doi: 10.1038/ncomms2828
2. Ikeuchi, Y., de la Torre, L., Matsuda, T., Steen, H., Okazawa, H., Bonni, A. (2013) The XLID protein PQBP1 and the GTPase dynamin 2 define a signaling link that orchestrates ciliary morphogenesis in postmitotic neurons. *Cell Reports* 4, 1–11. doi:10.1016/j.celrep.2013.07.042
3. Li, C., Ito, H., Fujita, K., Shiwaku, H., Yunlong Qi, Y., Tagawa, K., Tamura, T., Okazawa, H. (2013) Sox2 transcriptionally regulates Pqbp1, an Intellectual Disability-Microcephaly causative gene, in neural stem progenitor cells. *PLOS ONE* 8, e68627. doi: 10.1371/journal.pone.0068627
4. Shiwaku, H., Yagishita S., Eishi Y., Okazawa, H. (2013) Bergmann glia are reduced in spinocerebellar ataxia type 1. *Neuroreport*. 24, 620-625. doi: 10.1097/WNR.0b013e32836347b7.

5. Barclay, S.S., Tamura, T., Ito H., Fujita, K., Tagawa, K., Shimamura, T., Katsuta, A., Shiwaku, H., Sone, M., Imoto, S., Miyano, S. and Okazawa, H. (2013) Systems biology analysis of *Drosophila in vivo* screen data elucidates core networks for DNA damage repair in SCA1. *Hum Mol Genet* 2013 Nov 6. [Epub ahead of print]. doi: 10.1093/hmg/ddt524

Ophthalmology and Visual Science

1. Staff and students (April, 2013)

Associate Professor;	Kyoko Ohno-Matsui	
Junior Associate Professor;	Hiroshi Takase,	Koju Kamoi
Assistant Professor:	Shintaro Horie,	Manabu Ogawa,
	Hideki Murai,	Kengo Hayashi
Graduate student;	Tomoka Ishida,	Yuko Iwasaki,
	Ayano Imai,	Kosei Shinohara

2. Purpose of education

Ophthalmology and Visual Science deal with the eye. 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. 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.

3. Research subjects

- 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.
- 5) 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
- 6) Mechanism of visual pathway in normal conditions as well as in the patients with amblyopia.
- 7) Development of a novel treatment for vitreoretinal disorders like retinal detachment, diabetic retinopathy, and macular holes.
- 8) Analysis of retinochoroidal complications in high myopia (choroidal neovascularization, myopic tractional retinopathy)
- 9) 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)
- 10) Gene analysis of highly myopic patients (collaborator project with Kyoto University)
- 11) Establishment of a novel therapy to prevent an axial elongation or the formation of posterior staphyloma
- 12) Development of new materials for contact lens, the development of a novel drug delivery system using contact lens
- 13) Effect of the visual background on binocular vision as well as the influence of strabismus on dynamic visual acuity.

4. Clinical services

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 uveitis clinic, retinal detachment clinic, diabetic retinopathy clinic, neuro-ophthalmology clinic, high myopia clinic, and medical retina clinic.

Approximately, 1,100 surgeries are performed per year (e.g., cataract surgery, vitreoretinal surgery, glaucoma surgery, strabismus surgery).

5. Publications

[Original Article]

1. Wolf S, Balciuniene VJ, Laganovska G, Menchini U, Ohno-Matsui K, Sharma T, Wong TY, Silva R, Pilz S, Gekkieva M; RADIANCE Study Group. RADIANCE: A Randomized Controlled Study of Ranibizumab in Patients with Choroidal Neovascularization Secondary to Pathologic Myopia. *Ophthalmology*, (in press)
2. Takahashi H, Ishizuka A, Miyanaga M, Kawaguchi T, Ohno-Matsui K, Mochizuki M. Choroidal Thickness in Convalescent Vogt-Koyanagi-Harada Disease. *RETINA* (in press)
3. Shinohara K, Moriyama M, Shimada N, Tanaka Y, Ohno-Matsui K. Myopic stretch lines: linear lesions in fundus of

- eyes with pathologic myopia that differ from lacquer cracks. *RETINA* (in press)
4. Yokoi T, Moriyama M, Hayashi K, Shimada N, Tomita M, Yamamoto N, Nishikawa T, Ohno-Matsui K. Predictive factors for comorbid psychiatric disorders and their impact on vision-related quality of life in patients with high myopia. *Int Ophthalmol.* (in press)
 5. Nagata K, Maruyama K, Sugita S, Fukuchi U, Terada Y, Ishizuka A, Nakazawa T, Mochizuki M, Kinoshita S. Age Differences in Sarcoidosis Patients with Posterior Ocular Lesions. *NOcul Immunol Inflamm.* (in press)
 6. Ohno-Matsui K, Hirakata A, Inoue M, Akiba M, Ishibashi T. Evaluation of congenital optic disc pits and optic disc colobomas by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci.* 54:7769-7778, 2013
 7. Khor CC, Miyake M, Chen LJ, Shi Y, Barathi VA, Qiao F, Nakata I, Yamashiro K, Zhou X, Tam PO, Cheng CY, Tai ES, Vithana EN, Aung T, Teo YY, Wong TY, Moriyama M, Ohno-Matsui K, Mochizuki M, Matsuda F; Nagahama Study Group, Yong RY, Yap EP, Yang Z, Pang CP, Saw SM, Yoshimura N. Genome-wide association study identifies ZFH1B as a susceptibility locus for severe myopia. *Hum Mol Genet.* 22: 5288-5294, 2013
 8. Koh VT, Nah GK, Chang L, Yang AH, Lin ST, Ohno-Matsui K, Wong TY, Saw SM. Pathologic changes in highly myopic eyes of young males in singapore. *Ann Acad Med Singapore.* 42:216-224, 2013
 9. Miyake M, Yamashiro K, Nakanishi H, Nakata I, Akagi-Kurashige Y, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yamada R, Matsuda F, Yoshimura N. Insulin-like growth factor 1 is not associated with high myopia in a large Japanese cohort. *Mol Vis.* 19:1074-1081, 2013
 10. Miyake M, Yamashiro K, Nakanishi H, Nakata I, Akagi-Kurashige Y, Kumagai K, Oishi M, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yoshimura N. Evaluation of Pigment Epithelium-derived Factor and Complement Factor I Polymorphisms as a Cause of Choroidal Neovascularization in Highly Myopic Eyes. *Invest Ophthalmol Vis Sci.* 54:4208-4212, 2013
 11. Shinohara K, Moriyama M, Shimada N, Nagaoka N, Ishibashi T, Tokoro T, Ohno-Matsui K. Analyses of Shape of Eyes and Structure of Optic Nerves in eyes with Tilted Disc Syndrome by Swept-source Optical Coherence Tomography and Three Dimensional Magnetic Resonance Imaging. *Eye.* 27:1233-1241, 2013
 12. Chang L, Pan CW, Ohno-Matsui K, Lin X, Cheung GC, Gazzard G, Koh V, Hamzah H, Tai ES, Lim SC, Mitchell P, Young TL, Aung T, Wong TY, Saw SM. Myopia-Related Fundus Changes in Singapore Adults With High Myopia. *Am J Ophthalmol.* 155: 991-999, 2013
 13. Ohno-Matsui K, Akiba M, Moriyama M. Macular pits and scleral dehiscence in highly myopic eyes with macular chorioretinal atrophy. *Retinal Cases Brief Rep.* 7: 334-337, 2013
 14. Ohno-Matsui K, Kasahara K, Moriyama M. Characteristics of intrachoroidal cavitation located temporal to optic disc in highly myopic eyes. *Eye.* 27:630-638, 2013
 15. Ohno-Matsui K. Complicated mechanism for axial elongation in eyes with pathologic myopia accompanying scleral thinning and deformity. *Graefes Arch Clin Exp Ophthalmol.* 251:2279, 2013
 16. Jonas JB, Spaide RF, Ohno-Matsui K. Macular Bruch's membrane defects and axial length: association with gamma zone and delta zone in peripapillary region. *Invest Ophthalmol Vis Sci* 54:1295-1302, 2013
 17. Ohno-Matsui K, Kasahara K, Moriyama M. Detection of Zinn-Haller arterial ring in highly myopic eyes by simultaneous indocyanine green angiography and optical coherence tomography. *Am J Ophthalmol* 155:920-926, 2013
 18. Ishida T, Ohno-Matsui K, Mochizuki M. Polypoidal choroidal vasculopathy in a case with retinitis pigmentosa. *Int Ophthalmol.* 33:305-308, 2013
 19. Saka N, Moriyama M, Shimada N, Nagaoka N, Fukuda K, Hayashi K, Yoshida T, Tokoro T, Ohno-Matsui K. Changes of axial length measured by IOL master during two years in eyes of adults with pathologic myopia. *Graefes Arch Clin Exp Ophthalmol.* 251:495-499, 2013
 20. Yokoi T, Moriyama M, Hayashi K, Shimada N, Ohno-Matsui K. Evaluation of refractive error after cataract surgery in highly myopic eyes. *Int Ophthalmol.* 33:343-348, 2013
 21. Shimada N, Tanaka Y, Tokoro T, Ohno-Matsui K. Natural course of myopic traction maculopathy and factors associated with progression or resolution. *Am J Ophthalmol.* 56 :948-957, 2013
 22. Iwasaki Y, Yamamoto N, Kawaguchi T, Ozaki N, Tomita M, Ajisawa A, Mochizuki M, Murakami K. Human Fytomegalovirus disease association. *Jpn J Ophthalmol.* 57:372-378, 2013
 23. Hayashi K, Katori N, Kasai K, Kamisanuki T, Kokubo K, Ohno-Matsui K. Comparison of Nylon Monofilament Suture and Polytetrafluoroethylene Sheet for Frontalis Suspension Surgery in Eyes with Congenital Ptosis. *Am J Ophthalmol.* 155:654-663, 2013
 24. Liu J, Copland DA, Horie S, Wu WK, Chen M, Xu Y, Paul Morgan B, Mack M, Xu H, Nicholson LB, Dick AD. Myeloid Cells Expressing VEGF and Arginase-1 Following Uptake of Damaged Retinal Pigment Epithelium

Suggests Potential Mechanism That Drives the Onset of Choroidal Angiogenesis in Mice. *PLoS ONE*. 16:8(8):e72935, 2013

25. Sugita S, Kawazoe Y, Imai A, Kawaguchi T, Horie S, Keino H, Takahashi M, Mochizuki M. Role of IL-22- and TNF- α -producing Th22 cells in uveitis patients with Behcet's disease. *J Immunol*. 190:5799-5808, 2013
26. Horie S, Robbie SJ, Liu J, Wu WK, Ali RR, Bainbridge JW, Nicholson LB, Mochizuki M, Dick AD, Copland DA. CD200R signaling inhibits pro-angiogenic gene expression by macrophages and suppresses choroidal neovascularization. *Sci. Rep*. 3:3072, 2013
27. Sugita S, Ogawa M, Shimizu N, Morio T, Ohguro N, Nakai K, Maruyama K, Nagata K, Takeda A, Usui Y, Sonoda KH, Takeuchi M, Mochizuki M. Use of a comprehensive polymerase chain reaction system for diagnosis of ocular infectious diseases. *Ophthalmology*. 120:1761-1768, 2013
28. Maruyama K, Nagata K, Kojima K, Inaba T, Sugita S, Mochizuki M, Kinoshita S. Intraocular Invasion of Adult T-Cell Leukemia Cells without Systemic Symptoms after Cataract Surgery. *Case Rep Ophthalmol*. 4:252-256, 2013
29. Sugita S, Kawazoe Y, Imai A, Usui Y, Takahashi M, Mochizuki M. Suppression of IL-22-producing T helper 22 cells by RPE cells via PD-L1/PD-1 interactions. *Invest Ophthalmol Vis Sci*. 54:6926-6933, 2013
30. Sugita S, Kawazoe Y, Imai A, Usui Y, Iwakura Y, Isoda K, Ito M, Mochizuki M. Mature dendritic cell suppression by IL-1 receptor antagonist on retinal pigment epithelium cells. *Invest Ophthalmol Vis Sci*. 54:3240-3249, 2013
31. Kawazoe Y, Sugita S, Yamada Y, Akino A, Miura K, Mochizuki M. Psoriasis triggered by infliximab in a patient with Behçet's disease. *Jpn J Ophthalmol*. 57:95-7, 2013
32. Iwahashi-Shima C, Azumi A, Ohguro N, Okada AA, Kaburaki T, Goto H, Sonoda KH, Namba K, Mizuki N, Mochizuki M. Acute retinal necrosis: factors associated with anatomic and visual outcomes. *Jpn J Ophthalmol*. 57:98-103, 2013

[Review Article]

1. Mochizuki M, Sugita S, Kamoi K. Immunological homeostasis of the eye. *Prog Retin Eye Res*. 33:10-27, 2013

[Presentation]

1. Yokoi T, Moriyama M, Shimada N, Nagaoka N, Kasahara K, Shinohara K, Tanaka Y, Kaneko Y, Tokoro T, Ohno-Matsui K. Prognostic factors associated with pathological myopia in young patients with high myopia. The Association for Research in Vision and Ophthalmology Annual Meeting. 2013.5.5. Seattle, USA
2. Kaneko Y, Moriyama M, Shimada N, Nagaoka N, Shinohara K, Tanaka Y, Yokoi T, Kasahara K, Tokoro T, Ohno-Matsui K, Hirahara S, Ogura Y. Retinal vascular abnormalities in the far periphery of pathologic myopic eyes imaged by ultra wide-field fluorescein angiography. The Association for Research in Vision and Ophthalmology. 2013.5.5-9. Seattle, USA
3. Horie S, Copland DA, Liu J, Wu W-K, Nicholson LB, Mochizuki M, Dick AD. CD200 Receptor Signaling subverts pro-angiogenic macrophage phenotype generation and experimental chorioretinal neovascularization. The Association for Research in Vision and Ophthalmology Annual Meeting. 2013.5.5. Seattle, USA
4. Takahashi H, Ohno-Matsui K, Takase H, Shimada N, Mochizuki M. Myopia progression accompanying with myopic disc change at the convalescent stage of Vogt-Koyanagi-Harada disease. The association for research in vision and ophthalmology. 2013.5.6. Seattle, USA
5. Shimada M. Natural Course and Treatment of Myopic Traction Maculopathy. The 8th APVRS congress. 2013.12.6-8. Nagoya, Japan
6. Moriyama M. Multimodal Imaging of Pathologic Myopia. The 8th APVRS congress. 2013.12.6-8. Nagoya, Japan
7. Tan N, Wong TY, Ishibashi T, Ohno-Matsui K, Petrillo J, Leteneux C, Bressler N. Impact of Ranibizumab on Patient-Reported Visual Function in Choroidal Neovascularization secondary to Pathologic Myopia: 12 Month Results from RADIANCE. The 13th EURETINA Annual Congress. 2013.9.26-29. Hamburg, Germany

[Symposium, Special lecture]

1. Takase H. Prevalence of ocular sarcoidosis in Japan. International workshops on granulomatous uveitis and ocular Behçet's disease and Asia-Pacific intraocular inflammation study group. 2013.4.12. Taiwan
2. Ohno-Matsui K. Novel surgical technique: Fovea-sparing ILM peeling. Symposium on Imaging & Management advices in Retinal Diseases. 2013.5.11. Singapore
3. Ohno-Matsui K. Novel OCT entities. Symposium on Imaging & Management advices in Retinal Diseases. 2013.5.11. Singapore
4. Ide M, Kubono R, Miyayama M, Kamoi K, Takase H, Mochizuki M. A case of idiopathic uveal effusion accompanied

- with systemic lymphadenopathy and leg edema. Fluorescein Conference in Tokyo. 2013.7.21. Tokyo, Japan
5. Ohno-Matsui K. Wide-field retinal imaging of the eyes with pathologic myopia. Annual meeting of Taiwan Retina Society. 2013.11.9-10. Taipei, Taiwan
 6. Ohno-Matsui K. Retina Subspecialty day: Choroidal Neovascularization Secondary to Pathologic Myopia. The American Academy of Ophthalmology. 2013.11.16. New Orleans, USA.
 7. Ohno-Matsui K. A proposal of new classification of posterior staphyloma. 2013 International Congress of the Korean Retina Society. 2013.11.29. Seoul, South Korea.
 8. Ohno-Matsui K. Wide-field retinal imaging of pathologic myopia. 2013 International Congress of the Korean Retina Society. 2013.11.29. Seoul, South Korea.

Otorhinolaryngology

1. Staffs and Students

Professor	Ken KITAMURA	
Associate Professor	Atsunobu TSUNODA	
Junior Associate Professor	Taro SUGIMOTO,	Yoshihiro NOGUCHI,
Assistant Professor	Hisashi TOKANO,	Yasuhiro SUZUKI,
	Masatoki TAKAHASHI,	Yoshiyuki KAWASHIMA (Aug 2013~)
Hospital Staff	Yusuke KIYOKAWA,	Yuichiro INABA,
	Midori NAGAOKA,	Yoko YAMAMOTO
Graduate Student	Yoshimi TAMEKUCHI,	Katsura YAMAMOTO,
	Ayako NISHIO,	Keiji HONDA,
	Palida AIHAITI,	Naoto TAKAHASHI,
	Ryoichi YOSHIMOTO	

2. Purpose of Education

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. Research Subjects

- 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

4. Clinical Services

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.

5. Publications

Original Articles

1. Kimura Y, Kubo S, Koda H, Shigemoto K, Sawabe M, Kitamura K: RNA analysis of inner ear cells from formalin fixed paraffin embedded (FFPE) archival human temporal bone section using laser microdissection –A technical report. *Hear Res* 302: 26-31, 2013.
2. Nishio A, Noguchi Y, Sato T, Naruse T, Kimura A, Takagi A, Kitamura K: A DFNA5 mutation identified in

Japanese families with autosomal dominant hereditary hearing loss. *Ann Hum Genet* (in press).

3. Honda K, Noguchi Y, Kawashima Y, Takahashi M, Nishio A, Kitamura K: Ex vivo visualization of the mouse otoconial layer compared to micro-computed tomography. *Otol Neurotol*. (accepted)
4. Pan B, Geleoc GS, Asai Y, Horwitz GC, Kurima K, Ishikawa K, Kawashima Y, Griffith AJ, Holt JR: TMC1 and TMC2 are components of the mechanotransduction channel in hair cells of the mammalian inner ear. *Neuron* 79: 504-515, 2013.
5. Rehman AU, Santos-Cortez RL, Morell RJ, Drummond MC, Ito T, Lee K, Khan AA, Basra MA, Wasif N, Ayub M, Ali RA, Raza SI; University of Washington Center for Mendelian Genomics, Nickerson DA, Shendure J, Bamshad M, Riazuddin S, Billington N, Khan SN, Friedman PL, Griffith AJ, Ahmad W, Riazuddin S, Leal SM, Friedman TB: Mutations in TBC1D24, a gene associated with epilepsy, also cause nonsyndromic deafness DFNB86. *Am J Hum Genet*: Dec 2013 [Epub ahead of print].
6. Li X, Sanneman JD, Harbidge DG, Zhou F, Ito T, Nelson R, Picard N, Chambrey R, Eladari D, Miesner T, Griffith AJ, Marcus DC, Wangemann P: SLC26A4 targeted to the endolymphatic sac rescues hearing and balance in Slc26a4 mutant mice. *Plos Genet* 9; e1003641, 2013.
7. Okada R, Suzuki M, Takeuchi K, Horikoshi H, Tsunoda A: Measurement of shear wave velocities coupled with an evaluation of elasticity using ARFI elastography in diagnosis of papillary thyroid carcinoma. *OJCD* 3: 178-182, 2013.
8. Suzuki M, Tsunoda A, Kudo T, Okada R, Toyoda M: Successful management of hypoparathyroidism following total thyroidectomy with vitamin D3 alone. *Auris Nasus Larynx* 41: 53-55, 2013.
9. Yan D, Zhu Y, Walsh T, Xie D, Yuan H, Sirmaci A, Fujikawa T, Wong AC, Loh TL, Du L, Grati M, Vljakovic SM, Blanton S, Ryan AF, Chen ZY, Thorne PR, Kachar B, Tekin M, Zhao HB, Housley GD, King MC, Liu XZ: Mutation of the ATP-gated P2X(2) receptor leads to progressive hearing loss and increased susceptibility to noise. *Proc Natl Acad Sci USA* 110: 2228-2233, 2013.
10. Shepard K, Ito T, Griffith AJ: Extracting energy from the inner ear. *Nat Biotechnol*: 1204-1205, 2012.
11. Ito T, Muskett J, Chattaraj P, Choi BY, Lee KY, Zalewski CK, King KA, Li X, Wangemann P, Shawker T, Brewer CC, Alper SL, Griffith AJ: *SLC26A4* mutation testing for hearing loss associated with enlargement of the vestibular aqueduct. *World J Otorhinolaryngol* 3: 26-34, 2013.

Conference Presentations

1. Kitamura K: Panel discussion, Active middle ear implant, Baha experience: A note on complications. 20th IFOS World Congress. Seoul Korea, June 2013.
2. Kitamura K, Takahashi N, Tsunoda A, Shirakura S: Anatomical feature of the middle cranial fossa in fetal periods causes superior canal dehiscence. 29th Politzer Society Meeting, Antalya Turkey, Nov 2013.
3. Kitamura K, Sato T, Noguchi Y, Nishio A, Naruse T, Kimura A, Takagi A: A DFNA5 mutation in two Japanese families with autosomal dominant hereditary hearing loss. 29th Politzer Society Meeting, Antalya Turkey, Nov 2013.
4. Noguchi Y, Nishio A, Takeda N, Shimada A, Chida I, Naruse T, Kimura A, Kitamura K: A Japanese family with autosomal dominant auditory neuropathy spectrum disorder. 36th Annual Midwinter Meeting of the Association for Research in Otolaryngology, Baltimore USA, February 2013.
5. Noguchi Y, Takahashi M, Ito T, Tokano H, Nishio A, Yamamoto K, Kitamura K: Delayed restoration of speech discrimination score in sudden sensorineural hearing loss. 20th World Congress of the international Federation of Oto-Rhino-Laryngological Society (IFOS), Seoul Korea, June 2013.
6. Suzuki Y, Tokano H, Inaba Y, Iwasaki A, Kitamura K: The relationship between basophil and eosinophil in eosinophilic chronic sinusitis patients. EAACI and WAO World Allergy and Asthma Congress 2013. Milan Italy, June 2013.
7. Kimura Y, Koda H, Kubo S, Shigemoto K, Arai T, Kitamura K: A case of mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS); histopathology and mutational analysis of the temporal bone. 13th Triennial Meeting of the International Otopathology Society. Boston USA, June 2013.
8. Ito T, Choi BY, Wangemann P, Griffith AJ: Mouse model of the fluctuating hearing loss associated with enlargement of the vestibular aqueduct in Pendred syndrome. 36th ARO meeting, Baltimore USA, February 2013.
9. Ito T, Li X, Kurima K, Choi BY, Wangemann P, Griffith AJ: Fluctuating hearing loss associated with stria vascularis intermediate layer pathology in a mouse model of Pendred syndrome. Second Biannual Meeting of the Pendrin Consortium. Jamestown USA, June 2013.
10. Rehman AU, Lee K, Morell RJ, Ito T, Drummond MC, Griffith AJ, Riazuddin S, Leal SM, Friedman TB: Identification of mutations of the gene causing DFNB86 deafness. American Society of Human Genetics. Boston

USA, October 2013.

11. Ito M, Takahashi H, Kitamura K, Kobayashi T, Yamanaka N, Harabuchi Y, Watanabe Y, Origasa H, Yoshizaki T: Efficacy of herbal medicine, Juzen-Taiho-To (JTT) in children with recurrent acute otitis media – a randomized controlled trial. 20th IFOS World Congress. Seoul Korea, June 2013.
12. Kato T, Noguchi Y, Kimura Y, Kitamura K: Comprehensive analyses for mitochondrial DNA in patients with hereditary hearing loss. 13th Triennial Meeting of the International Otopathology Society. Boston USA, June 2013.
13. Fujikawa T, Petralia RS, Fitzgerald TS, Wang YX, KacharB: Localization of kainate receptors in inner and outer hair cell synapses. 36th Mid Winter Meeting of Association for Research in Otolaryngology. Baltimore USA, February 2013.
14. Yamamoto K, Tabei K, Katsuyama N, Taira M, Kitamura K: Functional MRI study of speech recognition in noise for patients with profound unilateral hearing loss. 13th Triennial Meeting of the International Otopathology Society. Boston USA, June 2013.
15. Inaba Y, Suzuki Y, Tokano H, Iwasaki A, Kitamura K: Allergic reaction in Japanese patients with obstructive sleep apnea syndrome (OSAS) and upper airway resistance syndrome (UARS). EAACI and WAO World Allergy and Asthma Congress 2013. Milan Italy, June 2013.
16. Okada R, Yagi K, Ibuki K, Yamaguchi K, Tsunoda K, Akita K: Positional relationships between the tensor velipalatini and the superior constrictor. European Joint Congress of Clinical Anatomy 2013. Lisbon Portugal, June 2013.
17. Takeda T, Kawashima Y, Kamada T, Kishine N, Hatanaka A, Kitamura K: Risk factors for the development of descending necrotizing mediastinitis in patients with cervical necrotizing fasciitis. The 12th Taiwan-Japan Conference on Otolaryngology-Head and Neck surgery. Taipei Taiwan, Dec 2013.

Neurology and Neurological Science

1. Staffs and Students (April, 2013)

Professor, Chairman	Hidehiro Mizusawa	
Professor	Takanori Yokota	
Junior Associate Professor	Kinya Ishikawa,	Nobuo Sanjo
Assistant Professor	Satoru Ishibashi,	Takuya Ohkubo,
	Shoichiro Ishihara	
Hospital Staff	Keiko Ichinose,	Fumiko Furukawa,
	Yurie Nose,	Satoko Kina,
	Hiroyuki Maruoka,	Kyohei Fujita,
	Shinichi Otsu	
Senior Resident	Rieko Nishi,	Akiko Miyashita
Post-doctorial Fellow	Kazutaka Nishina,	Nozomu Sato,
	Taro Ishiguro,	Hiroya Kuwahara
	Daishi Yui	
Graduate Students (Doctoral course)	Tomoko Nishina,	Yuji Hashimoto,
	Kiyobumi Ota,	Teruhiko Sekiguchi,
	Kokoro Ozaki,	Maya Higuma,
	Saneyuki Mizutani,	Masahiko Ichijo,
	Kazumasa Soga,	Yoshiyuki Numasawa,
	Keisuke Abe,	Kotaro Yoshioka,
	Nobutaka Ishizu,	Temuqina,
	Yoko Ito,	Yosuke Yagi

2. Purpose of Education

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 an unique “clinical neurological training for specialist” in a four-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, neuroimaging, or neurogenetics and so on. The faculty and staff are committed to facilitate resident education and training.

After completion of their training for four 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. Research Subjects

- 1) Gene identification and investigation of its pathomechanism for hereditary diseases such as spinocerebellar ataxias, especially for SCA6 and SCA31
- 2) Development of gene therapies using RNAi and other techniques
- 3) Development of ALS animal model
- 4) Basic and clinical researches for neurodegenerative diseases such as spinocerebellar ataxia, amyotrophic lateral sclerosis, and Alzheimer disease
- 5) Development of neuroregenerative therapy using stem cells for cerebrovascular and neurodegenerative disorders
- 6) Basic and clinical researches of neurological autoimmune diseases
- 7) Electrophysiological studies using electric and magnetic stimulation
- 8) Basic and clinical studies of neuromuscular diseases by studying the biopsied peripheral nerves and muscles

4. Clinical Services

We see about 100 out-patients and 40 in-patients daily, and offer in and out-patient consultation services through the weekday and on weekends. We diagnose and treat stroke patients, as well as patients with epilepsy, headache, multiple sclerosis, Parkinson's disease, spinocerebellar ataxia, and hundreds of other neurological issues, some of which are acute, others may be chronic. We also have an out-patient clinic specialized to patients with dementia corresponding to needs of the rapidly aging society. 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.

5. Publications

Original Article

1. Hamaguchi T, Sakai K, Noguchi-Shinohara M, Nozaki I, Takumi I, Sanjo N, Sadakane A, Nakamura Y, Kitamoto T, Saito N, Mizusawa H, Yamada M. Insight into the frequent occurrence of dura mater graft-associated Creutzfeldt-Jakob disease in Japan. *J Neurol Neurosurg Psychiatry* 2013; 84: 1171-1175.
2. Higuma M, Sanjo N, Satoh K, Shiga Y, Sakai K, Nozaki I, Hamaguchi T, Nakamura Y, Kitamoto T, Shirabe S, Murayama S, Yamada M, Tateishi J, Mizusawa H. Relationships between Clinicopathological Features and Cerebrospinal Fluid Biomarkers in Japanese Patients with Genetic Prion Diseases. *PLoS One* 2013; 8: e60003.
3. Hori T, Sanjo N, Tomita M, Mizusawa H. Visual Reproduction on the Wechsler Memory Scale-Revised as a Predictor of Alzheimer's Disease in Japanese Patients with Mild Cognitive Impairments. *Dement Geriatr Cogn-Disord* 2013; 35: 165-176.
4. Ichijo M, Miki K, Ishibashi S, Tomita T, Kamata T, Fujigasaki H, Mizusawa H. Posterior cerebral artery laterality on MRA predicts long-term functional outcome in middle cerebral artery occlusion. *Stroke* 2013; 44: 512-515.
6. Iwasawa E, Ishibashi S, Miki K, Yoshino Y, Nemoto S, Mizusawa H. Reversible cognitive impairment with bithalamic lesions caused by a dural arteriovenous fistula. *Neurology*. 2013; 81(6): 38-39.
7. Kobayashi Z, Arai T, Yokota O, Tsuchiya K, Hosokawa M, Oshima K, Niizato K, Akiyama H, Mizusawa H. Atypical FTL-D-FUS associated with ALS-TDP: A case report. *Neuropathology* 2013; 33(1): 83-86.
8. Kobayashi Z, Akaza M, Numasawa Y, Ishihara S, Tomimitsu H, Nakamichi K, Saijo M, Morio T, Shimizu N, Sanjo N, Shintani S, Mizusawa H. Failure of mefloquine therapy in progressive multifocal leukoencephalopathy: Report of two Japanese patients without human immunodeficiency virus infection. *J Neurol Sci*. 2013; 324: 190-194.
9. Kobayashi Z, Akaza M, Ishihara S, Tomimitsu H, Inadome Y, Arai T, Shintani S. Thalamic hypoperfusion in early stage of progressive supranuclear palsy (Richardson's syndrome): report of an autopsy-confirmed case. *J Neurol Sci* 2013; 335: 224-227.
10. Kobayashi Z, Kawakami I, Arai T, Yokota O, Tsuchiya, Kondo H, Shimomura Y, Haga C, Aoki N, Hasegawa M, Hosokawa M, Oshima K, Niizato K, Ishizu H, Terada S, Onaya M, Ikeda M, Oyanagi K, Nakano I, Murayama S, Akiyama H, Mizusawa H. Pathological features of FTL-D-FUS in Japanese population: analyses of nine cases. *J Neurol Sci* 2013; 335: 89-95.
11. Kuwahara H, Matsumura K, Watanabe M, Fujigasaki H. Intravenous t-PA for the occlusion of an accessory MCA. *Intern Med* 2013; 52: 163.
12. Kuwahara H. Persistent hemichorea. *N Engl J Med* 2013 ; 368 : e26.
13. Kuwahara H, Suzuki S, Matsumura K, Watanabe M, Yakushiji F, Fujigasaki H. Ocular flutter, generalized myoclonus, and truncal ataxia in a patient with Graves' ophthalmopathy. *J Neurol* 2013; 260: 2906-2907.
14. Machida A, Kuwahara H, Mayra A, Kubodera T, Hirai T, Sunaga F, Tajiri M, Hirai Y, Shimada T, Mizusawa H, Yokota T. Intraperitoneal administration of AAV9-shRNA inhibits target gene expression in the dorsal root ganglia of neonatal mice. *Mol Pain* 2013; 9: 36.
15. Mitoma H, Nanri K, Mizusawa H. Is anti-gliadin antibody pathogenic in gluten ataxia? Analysis using rat cerebellar slices and patch-clamp recording. *Brain Disord Ther* 2013; 2: 105.
16. Mitsui J, Matsukawa T, Ishiura H, Fukuda Y, Ichikawa Y, Date H, Ahsan B, Nakahara Y, Momose Y, Takahashi Y, Iwata A, Goto J, Yamamoto Y, Komata M, Shirahige K, Hara K, Kakita A, Yamada M, Takahashi H, Onodera O, Nishizawa M, Takashima H, Kuwano R, Watanabe H, Ito M, Sobue G, Soma H, Yabe I, Sasaki H, Aoki M, Ishikawa K, Mizusawa H, Kanai K, Hattori T, Kuwabara S, Arai K, Koyano S, Kuroiwa Y, Hasegawa K, Yuasa T, Yasui K, Nakashima K, Ito H, Izumi Y, Kaji R, Kato T, Kusunoki S, Osaki Y, Horiuchi M, Kondo T, Murayama S, Hattori N, Yamamoto M, Murata M, Satake W, Toda T, Dürr A, Brice A, Filla A, Klockgether T, Wüllner U, Nicholson G, Gilman S, Shults CW, Tanner CM, Kukull WA, Lee VM, Masliah E, Low PA, Sandroni P, Trojanowski JQ, Ozelius L,

- Foroud T, Tsuji S. Multiple-System Atrophy Research Collaboration. Mutations in COQ2 in familial and sporadic multiple-system atrophy. *N Engl J Med* 2013; 369: 233-244.
17. Nakamichi K, Kishida S, Tanaka K, Suganuma A, Sano Y, Sano H, Kanda T, Maeda N, Kira J, Itoh A, Kato N, Tomimoto H, Kurane T, Chang-Kweng Lim, Mizusawa H, Saijo M. Sequential changes in the non-coding control region sequences of JC polyomaviruses from the cerebrospinal fluid of patients with progressive multifocal leukoencephalopathy. *Arch Virol*. 2013; 158: 639-650.
 18. Nanri K, Niwa H, Mitoma H, Takei A, Ikeda J, Harada T, Okita M, Takeguchi M, Taguchi T, Mizusawa H. Low-Titer Anti-GAD-Antibody-Positive Cerebellar Ataxia. *Cerebellum* 2013; 12(2): 171-175.
 19. Niimi Y, Takahashi M, Sugawara E, Umeda S, Obayashi M, Sato N, Ishiguro T, Higashi M, Eishi Y, Mizusawa H, Ishikawa K. Abnormal RNA structures (RNA foci) containing a penta-nucleotide repeat (UGGAA)_n in the Purkinje cell nucleus is associated with spinocerebellar ataxia type 31 pathogenesis. *Neuropathology* 2013; 33: 600-611.
 20. Nomoto N, Orimo S, Uchihara T, Takahashi K, Fujioka T. Lewy pathology in an autopsy case of FTL-D-MND with reduced cardiac MIBG uptake and depletion of cardiac sympathetic fibers. *Parkinsonism Relat Disord* 2013; 19: 472-473.
 21. Ohta A, Nagai M, Nishina M, Tomimitsu H, Kohsaka H. Age at onset and gender distribution of systemic lupus erythematosus, polymyositis/dermatomyositis, and systemic sclerosis in Japan. *Mod Rheumatol*. 2013; 23(4): 759-764.
 22. Ohyagi M, Ohkubo T, Yagi Y, Ishibashi S, Akiyama J, Nagahori M, Watanabe M, Yokota T, Mizusawa H. Chronic inflammatory demyelinating polyradiculoneuropathy in a patient with Crohn's disease. *Intern Med*. 2013; 52: 125-128.
 23. Ohyagi M, Tao O, Mizutani T, Takahashi M, Mizusawa H. Progression of bilateral internal carotid artery dissection during antiplatelet therapy. *Intern Med*. 2013; 52: 2821-2823.
 24. Sano K, Satoh K, Atarashi R, Takashima H, Iwasaki Y, Yoshida M, Sanjo N, Murai H, Mizusawa H, Schmitz M, Zerr I, Kim YS, Nishida N. Early Detection of Abnormal Prion Protein in Genetic Human Prion Diseases Now Possible Using Real-Time QUIC Assay. *PLoS One*. 2013; 8: e54915.
 25. Saito K, Shimizu F, Koga M, Sano Y, Tasaki A, Abe M, Haruki H, Maeda T, Suzuki S, Kusunoki S, Mizusawa H, Kanda T. Blood-brain barrier destruction determines Fisher/Bickerstaff clinical phenotypes: an in vitro study. *J NeurolNeurosurg Psychiatry*. 2013; 84: 756-765.
 26. Shintani S. Efficacy and ethics of artificial nutrition in patients with Neurologic impairments in home care. *J Clin Neurosci* 2013; 20: 220-223.
 27. Taira T, Ueta T, Katayama Y, Kimuzuka M, Nemoto A, Mizusawa H, Liu M, Koito M, Hiro Y, Tanabe H. Rate of Complications Among the Recipients of Intrathecal Baclofen Pump in Japan: A Multicenter Study. *Neuromodulation*. 2013; 16: 266-272.
 28. Takahashi M, Obayashi M, Ishiguro T, Sato N, Niimi Y, Ozaki K, Mogushi K, Mahmut Y, Tanaka H, Tsuruta F, Dolmetsch R, Yamada M, Takahashi H, Kato T, Mori O, Eishi Y, Mizusawa H, Ishikawa K. Cytoplasmic location of α 1A voltage-gated calcium channel C-terminal fragment (Cav2.1-CTF) aggregate is sufficient to cause cell death. *PLoS One* 2013; 8: e50121.
 29. Toru S, Murata T, Ohara M, Ishiguro T, Kobayashi T. Paradoxical cerebral embolism with patent foramen ovale and deep venous thrombosis caused by a massive myoma uteri. *Clin Neurol Neurosurg* 2013; 115: 760-761.
 30. Yagi Y, Sanjo N, Yokota T, Mizusawa H. Tacrolimus monotherapy: a promising option for ocular myasthenia gravis. *Europ Neurol* 2013; 69: 344-345.
 31. Yagi Y, Watanabe Y, Yokote H, Amino T, Kamata T. Lacunar thalamic infarction with isolated dysesthesia in contralateral fingers. *Acta Neurol Belg*. 2013; 113: 199-200.
 32. Yokote H, Yagi Y, Watanabe Y, Amino T, Kamata T, Mizusawa H. Serum amyloid A level is increased in neuromyelitis optica and atypical multiple sclerosis with smaller T2 lesion volume in brain MRI. *J Neuroimmunol* 2013; 259: 92-95.
 33. Yoshioka K, Ishibashi S, Shiraishi A, Yokota T, Mizusawa H. Distal hyperintense vessels on FLAIR images predict large-artery stenosis in patients with transient ischemic attack. *Neuroradiology* 2013; 55: 165-169.
 34. Sakai K, Hamaguchi T, Noguchi-Shinohara M, Nozaki I, Takumi I, Sanjo N, Nakamura Y, Kitamoto T, Saito N, Mizusawa H, Yamada M. Graft-related disease progression in dura mater graft-associated Creutzfeldt-Jakob disease: a cross-sectional study. *BMJ Open* 2013; 3(8): e0034000.
 35. Wenying Piao, Nishina K, Yoshida-Tanaka K, Kuwahara H, Nishina T, Sakata M, Mizusawa H and Yokota T. Efficient in vivo delivery of antisense oligonucleotide to choroid plexus. *J Med Dent Sci* 2013; 60: 9-16.

[Books]

1. Nanri K, Ihara M, Mitoma H, Tanaka N, Taguchi T, Mizusawa H. Gluten ataxia: anti-gliadin-antibody-positive cerebellar ataxia. In: Dane B. Walter. *Gluten*. Nova Science Publishers, 2013: 119-130.

- Akira Machida, Takuya Ohkubo, Takanori Yokota. Circulating MicroRNAs in the Cerebrospinal Fluid of Patients with Brain Diseases. *Methods in Molecular Biology*, Springer Japan, Tokyo. 2013; 1024: 203-209.

[Reviews]

- Nishina K, Mizusawa H, Yokota T. Short interfering RNA and the central nervous system: development of nonviral delivery systems. *Expert Opin Drug Deliv* 2013; 10: 282-292.
- Orimo S. Initial diagnosis of Parkinson's Disease - Neuroradiological diagnosis. *Rinsho Shinkeigaku* 2013; 53: 977-980.

[Presentations at academic meetings]

(Overseas / International)

- Hashimoto Y, Ishikawa K, Honda T, Nagao S, Mizusawa H. A novel system to evaluate the dynamic cerebellar motor learning capability and its application identifies a clinical marker in cerebellar ataxias. The 65th Annual Meeting, The American Academy of Neurology. San Diego. Mar 19, 2013.
- Ohyagi M, Ishikawa K, Ota K, Sato N, Ishibashi S, Mizusawa H. Efficacy of oral rifampicin in multiple system atrophy. The 65th Annual Meeting, The American Academy of Neurology. San Diego. Mar 20, 2013.
- Iwasawa E, Hashimoto Y, Honda T, Nagao S, Mizusawa H, Ishikawa K. Assessment of clinical status of patients with multiple system atrophy using a novel system to evaluate the dynamic cerebellar motor learning capability. The 65th Annual Meeting, The American Academy of Neurology. San Diego. Mar 21, 2013.
- Sato N, Ishikawa K, Niimi Y, Mizusawa H. A BAC transgenic mouse model of spinocerebellar ataxia type 31 (SCA31) exhibits RNA foci in Purkinje cells. The 65th Annual Meeting, The American Academy of Neurology. San Diego. Mar 21, 2013.
- Mizusawa H. Movement disorders in Asia-Oceania. The 17th International Congress of Parkinson's disease and Movement disorders. Sydney. Jun 17, 2013.
- Kuwahara H, Nishina K, Yoshida-Tanaka K, Nishina T, Wenying Piao, Mizusawa H, Yokota T. Efficient in vivo delivery of siRNA into brain capillary endothelial cells along with endogenous lipoprotein. The 10th International Conference on Cerebral Vascular Biology. Montreal. Jun 19-20, 2013.
- Nishina K, Wenying Piao, Yoshida-Tanaka K, Nishina T, Kuwahara H, Mizusawa H, Yokota T. Efficient in vivo delivery of antisense oligonucleotide to choroid plexus. The 10th International Conference on Cerebral Vascular Biology. Montreal. Jun 19-20, 2013.
- Higuma M, Sanjo N, Mitoma H, Ito Y, Hori T, Mizusawa H. Quantitative analysis of gait disorders in patients with Alzheimer's disease by using a portable gait rhythmograph. Alzheimer's Association International Conference. Boston. Jul 13-18, 2013.
- Furukawa F, Ishibashi S, Kurashige T, Matsumoto M, Mizusawa H. Serial magnetic resonance imaging changes in a patient in the early stages of sporadic Creutzfeldt-Jacob disease with valine homozygosity at codon 129 of PRNP. Asian Pacific Prion Symposium 2013. Nagasaki. 21 Jul, 2013.
- Hamaguchi T, Sakai K, Noguchi-Shinohara M, Nozaki I, Takumi I, Sanjo N, Nakamura Y, Kitamoto T, Saito N, Mizusawa H, Yamada M. Comparison of dura mater graft-associated Creutzfeldt-Jacob disease between Japan and other countries. Asian Pacific Prion Symposium 2013. Nagasaki. 21 Jul, 2013.
- Hizume M, Sanjo N, Nakamura Y, Kitamoto T, Yamada M, Hamaguchi T, Morikawa F, Aoki M, Kuroiwa Y, Nishizawa M, Takeda M, Inuzuka T, Abe K, Murai H, Murayama S, Satoh K, Harada M, Saito N, Takumi I, Mizusawa H. Human prion diseases in Japan: a prospective surveillance from 1999. Asian Pacific Prion Symposium 2013. Nagasaki. 21 Jul, 2013.
- Yokote H, Nose Y, Ishibashi S, Kamata T, Tanaka K, Takahashi T, Fujihara K, Yokota T, Mizusawa H. Spinal cord ring enhancement in patients with neuromyelitis optica. The 24th congress of the European committee for treatment and research in multiple sclerosis, Copenhagen, Oct 4, 2013.
- Yokote H, Yagi Y, Watanabe Y, Amino T, Kamata T, Mizusawa H. Serum amyloid A level is increased in neuromyelitis optica and atypical multiple sclerosis with smaller T2 lesion volume in brain MRI. The 6th congress of the Pan-Asian committee for treatment and research in multiple sclerosis, Kyoto, Nov 7, 2013.

Psychiatry and Behavioral Sciences

1. Staff members and Students

Professor	Toru NISHIKAWA	
Associate Professor	Akeo KURUMAJI	
Junior Associate Professor	Naoki YAMAMOTO	
Assistant Professor	Takashi TAKEUCHI, Mitsuhiro TAKEDA, Akihito UEZATO, Mizue HOBO	Hotsumi KYONO, Daisuke JITOKU, Hiroo MITSUSADA,
Technical Specialist	Asami UMINO	
Medical Staff	DaisukeIKEI(~2013.3), Kotaro KAWAMATA(~2013.9), Yuya TERASAWA, Yu TOMIOKA(2013.10~),	Shinichiro TAMAI(~2013.9), Kohei HINO, Atsuko HARADA(2013.10~)
Medical Fellow	Michio ITASAKA	
Technical Assistant	Yasuhiro OKA, Meri SASAKI, Ayano SOMEYA, Sayuri HASHIGUCHI, Ayako KITABATAKE(2013.10~)	Miyuki SAITO, Yoshihumi KANEKO(~2013.6), Ken MATSUNAGA , Sayuri ISHIWATA(2013.4~),
Graduate Students	Kenji SASAKI, Sayuri ISHIWATA(~2013.3), Kazuo TAKIGUCHI, Ayako KANIE, Emiko HARAMO(~2013.3), Tomoya SHIRAISHI, Misa NONAKA	Syunsuke TAKAGI, Masakazu UMINO, Takuya YOSHIKE, Megumi GOTO, Momoko KOBAYASHI, Keiko ONO,

2. Education

In the first term (two years) of postgraduate training, residents will learn basic laboratory procedures and diagnostic techniques, psychotherapy and drug treatment and laws and regulations related to clinical practice, and acquire other general knowledge, all being essential for biologic, la psychological, social, and ethical approaches to neuropsychiatric diseases. Following the two-year period of mandatory clinical training, basic professional training in psychiatry will be provided for 6-9 months mainly in the university. In the second term of training, they will acquire knowledge and clinical experience necessary for neuropsychiatrists, and undergo practical training at affiliated medical facilities to become qualified psychiatrists. Undergraduate education, which places emphasis on clinical clerkship training after a systematic series of lecture course and seminar-based classes, is designed to develop students' problem-solving skills, and increase their motivation to learn neuropsychiatry, with support from external facilities

3. Research

Our laboratory is committed to comprehensive research on endogenous psychosis, neurosis, and epilepsy through biological, psychological and social approaches. In collaboration with external research facilities, we are also involved in social psychiatry, child and adolescent psychiatry, and brain imaging studies:

1) Studies in neurochemistry

(i) Molecular genetic studies to clarify the causes and conditions of neuropsychiatric diseases:

Using animal models with psychotic symptom-causing agents, we are involved in a study to isolate new candidate gene clusters associated with the pathogenesis and pathophysiology of neuropsychiatric disorders from the viewpoint of developmental pharmacology. We are examining the effects of candidate gene clusters in patients with neuropsychiatric disorders.

(ii) Studies in biochemical pharmacology to develop new therapeutic methods for neuropsychiatric disorders.

We are working to examine the pharmacological/biochemical effects of candidate substances to develop new drugs for

neuropsychiatric disorders. Extensive research is being conducted to isolate agents associated with the metabolism of D-serine, an endogenous antipsychotic substance, and examine the effects of D-serine on neurotransmission in the brain.

2) Neurophysiological and psychophysiological studies

(i) A study of biological indicators in schizophrenia with eye cameras:

We are not only involved in studies of monozygotic twins, early-onset patients, and children at a high risk in Japan, but also in an international joint research project of the WHO as a center in charge of operations.

(ii) Studies of neurotransmitter receptor binding in neuropsychiatric disorders with PET:

We are working together with the National Institute of Radiological Sciences to investigate the binding activities of dopamine receptors in various brain areas of the patients with schizophrenia and mood disorders.

(iii) A study of sleep stages and behavior in neuropsychiatric diseases:

A study is being carried out to examine sleep stages and behavior using an originally developed automatic analysis device (polysomnography) in patients with various psychiatric disorders.

A study on brain functioning in psychiatric disorders by using the near-infrared spectroscopy (NIRS): To obtain an insight into biological markers of psychiatric disorders, changes in regional brain functions during psychological tasks are examined by measuring the relative concentrations of oxyhemoglobin using NIRS in combination with MRI in the brain areas of the patients with schizophrenia and mood disorders.

3) Psychopathological studies

We are conducting psychological studies of neuropsychiatric diseases from the aspects of phenomenology, anthropology, and linguistics, while employing a psychotherapeutic approach. Other research activities include a review of basic psychiatric concepts and a basic study for the classification and diagnosis of psychiatric disorders, which are important recent issues. In addition to endogenous psychosis including schizophrenia and manic depressive disorder, we are also involved in psychoanalytic studies of neurosis and borderline personality disorder, which are attracting increasing attention, and psychotherapies for them, as well as pathological research on pathography and art therapy in terms of creativity.

4. Clinical practice

Approximately eighty new outpatients visit our department every month, about 30% of which are classified as having "mood disorders" (F3) by ICD-10, followed by "neurotic, stress-related, and somatoform disorders" (F4) and "schizophrenia, schizophrenic and paranoid disorders" (F2). We are also actively involved in consultation and liaison psychiatry for inpatients in other departments. Patients with senile dementia, child and adolescent psychiatric disorders, substance dependence, and neurosis requiring intensive psychotherapy are often referred to related and advanced facilities for specialized treatment. Since this facility, the psychiatric department of a general hospital, is used for university education and training, most inpatients are classified as F2, followed by F4 and F3 (ICD-10). We also provide care and treatment for patients with sleep rhythm disorders and neurological disorders, including epilepsy and senile dementia. In addition to drug treatment, we have introduced and provided mECT (modified electroconvulsive therapy) for inpatients, and individual and group psychotherapy for the patients in our psychiatric ward and clinic and day care center in close collaboration with rehabilitation facilities in the community. The day care team consists of a doctor, two nurses, and a psycho-social-worker or a clinical psychologist. Day care (partial hospitalization) is the transitional element between inpatient and outpatient care and its indications have a wide range of psychiatric disorders as follows: schizophrenia, depression, bipolar disorder, adjustment disorder and personality disorders. Each member has the own aim and the team gives care with different types of framework. Our day care team regards the potentiality of group very important and the group process could contribute to therapeutic effect. With this kind of experience, patients could develop their ability to communicate with other people and readapt to social situations.

5. Publications (in English)

Original Articles

1. Umezaki Y, Katagiri A, Watanabe M, Takenoshita M, Sakuma T, Sako E, Sato Y, Toriihara A, Uezato A, Shibuya H, Nishikawa T, Motomura H, Toyofuku A. Brain perfusion asymmetry in patients with oral somatic delusions. *Eur Arch Psychiatry Clin Neurosci.* 263(4):315-23, 2013.
2. Ishiwata S, Ogata S, Umino A, Shiraku H, Ohashi Y, Kajii Y, Nishikawa T. Increasing effects of S-methyl-L-cysteine on the extracellular D-serine concentrations in the rat medial frontal cortex. *Amino Acids.* 44(5):1391-1395, 2013.

3. Ishiwata S, Umino A, Umino M, Yorita K, Fukui K, Nishikawa T. Modulation of extracellular d-serine content by calcium permeable AMPA receptors in rat medial prefrontal cortex as revealed by in vivo microdialysis. *Int J Neuropsychopharmacol.* 16(6):1395-1406,2013.
4. Hatta K, Kishi Y, Takeuchi T, Wada K, Odawara T, Usui C, Machida Y, Nakamura H; DELIRIA-J Group. The predictive value of a change in natural killer cell activity for delirium. *Prog Neuropsychopharmacol Biol Psychiatry.* 2014 Jan 3;48:26-31. doi: 10.1016/j.pnpbp.2013.09.08. Epub 2013 Sep 21.
5. Hatta K, Kishi Y, Wada K, Odawara T, Takeuchi T, Shiganami T, Tsuchida K, Oshima Y, Uchimura N, Akaho R, Watanabe A, Taira T, Nishimura K, Hashimoto N, Usui C, Nakamura H. Antipsychotics for delirium in the general hospital setting in consecutive 2453 inpatients: a prospective observational study. *Int J Geriatr Psychiatry.* 2013 Jun 25. doi: 10.1002/gps.3999. [Epub ahead of print]
6. Sasaki T, Kodaka F, Taniguchi G, Nishikawa T, Watanabe M. Experiential auditory hallucinations due to chronic epileptic discharges after radiotherapy for oligoastrocytoma. *Epileptic Disorder.* 15(2):188-192, 2013.
7. Darrick T Balu, Yan Li, Matthew D Puhl, Michael A Benneyworth, Alo C Basu, Shunsuke Takagi, Vadim Y Bolshakov, Joseph T Coyle. Multiple risk pathways for schizophrenia converge in serine racemase knockout mice, a mouse model of NMDA receptor hypofunction. *Proc Natl Acad Sci U S A.* 110(26), 2013.
8. Fuse-Nagase Y, Nishikawa T. Prolonged delusional state triggered by repeated ingestion of aromatic liquid in a past 5-methoxy-N, N-diisopropyltryptamine abuser *Addiction Science & Clinical Practice* 2013. 8:9.

Neurosurgery

1. Staffs and Students (April, 2013)

Professor:	Taketoshi Maehara	
Associate Professor:	Tadashi Nariai	
Assistant Professors:	Yoji Tanaka and Motoki Inaji	
Hospital stuffs:	Takashi Sugawara,	Yoshihisa Kawano,
	Kaoru Tamura,	Takumi Kudo,
	Kana Sawada,	Shihori Hayashi,
	Juri Kiyokawa,	Rena Kawanami,
	Natsumi Ito,	Satoka Hashimoto and Toshihiro Yamamura
Graduate Students:	Yohei Satoh,	Yoshihisa Kawano,
	Toshiya Momose,	Shin Hirota,
	Tomoyuki Kino,	Maki Mukawa,
	Masahumi Sasaki,	Yoshiteru Obata,
	Yousuke Ishii,	Sakyo Hirai,
	Yasuhiro Ueda,	Takahiro Ogishima,
	Juri Kiyokawa,	Shihori Hayashi and Dong Xlao Shu

2. Purpose of Education

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.

3. Research Subjects

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

4. Clinical services

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.

5. Publications

Original Articles

1. Aoyagi M, Kawano Y, Tamaki M, Tamura K, Ohno K: Combined extradural subtemporal and anterior transpetrosal approach to tumors located in the interpeduncular fossa and the upper clivus. *Acta Neurochir (Wien)* 155:1401-1407, 2013
2. Ayer RE, Ostrowski RP, Sugawara T, Ma Q, Jafarian N, Tang J, Zhang JH: Statin-induced T-lymphocyte modulation and neuroprotection following experimental subarachnoid hemorrhage. *Acta Neurochir Suppl* 115:259-66, 2013
3. Habib ERMS, Komuro R, Yan P, Hayashi S, Inaji M, Momose-Sato Y, et al: Evaluation of voltage-sensitive fluorescence dyes for monitoring neuronal activity in the embryonic central nervous system. *J Membr Biol* 246:679-688, 2013
4. Hara K, Maehara T, Miyajima M, Ohta K, Iino H, Inaji M, et al: Post-operative mismatch negativity recovery in a temporal lobe epilepsy patient with cavernous angioma. *Clin Neurol Neurosurg* 115:756-759, 2013
5. Hosoda C, Tanaka K, Nariai T, Honda M, Hanakawa T: Dynamic Neural Network Reorganization Associated with Second Language Vocabulary Acquisition: A Multimodal Imaging Study. *J Neurosci* 33:13663-13672, 2013
6. Hiura M, Nariai T, Ishii K, Sakata M, Oda K, Toyohara J, Ishiwata K: Changes in cerebral blood flow during steady-state cycling exercise: a study using oxygen-15-labeled water with PET. *J Cereb Blood Flow Metab*, Dec 4, 2013
7. Imai H, Tanaka Y, Nomura N, Tsutsumi Y, Doi H, Kanno Z, et al: Three-dimensional quantification of susceptibility artifacts from various metals in magnetic resonance images. *Acta Biomater* 9:8433-8439, 2013
8. Ishii Y, Nariai T, Tanaka Y, Mukawa M, Inaji M, Maehara T, Ohno K: Practical Clinical Use of Dynamic Susceptibility Contrast Magnetic Resonance Imaging (DSC-MRI) for the Surgical Treatment of Moyamoya Disease. *Neurosurgery*, Dec 12, 2013
9. Maehara T, Inaji M, Matsuura M: Surgical effects of focus resection for patients with intractable epilepsy. *Neurol Med Chir (Tokyo)* 53:281-286, 2013
10. Mukawa M, Nariai T, Matsushima Y, Ohno K: Clinical features of familial juvenile cases of moyamoya disease: analysis of patients treated in a single institute over a 28-year period. *J Neurosurg Pediatr* 12:175-180, 2013
11. Mullah SH, Inaji M, Nariai T, Ishibashi S, Ohno K: A selective adenosine A2A receptor antagonist ameliorated hyperlocomotion in an animal model of lateral fluid percussion brain injury. *Acta Neurochir Suppl* 118:89-92, 2013
12. Nariai T, Inaji M, Tanaka Y, Hiura M, Hosoda C, Ishii K, et al: PET molecular imaging to investigate higher brain dysfunction in patients with neurotrauma. *Acta Neurochir Suppl* 118:251-254, 2013
13. Sakata M, Oda K, Toyohara J, Ishii K, Nariai T, Ishiwata K: Direct comparison of radiation dosimetry of six PET tracers using human whole-body imaging and murine biodistribution studies. *Ann Nucl Med* 27:285-296, 2013
14. Sugawara T, Aoyagi M, Tanaka Y, Tamaki M, Kobayashi D, Ohno K: Chronic encapsulated expanding hematoma in nonfunctioning pituitary adenoma. *Neurosurg Rev* 36:395-402, 2013
15. Tamura K, Wakimoto H, Agarwal AS, Rabkin SD, Bhare D, Martuza RL, et al: Multimechanistic tumor targeted oncolytic virus overcomes resistance in brain tumors. *Mol Ther* 21:68-77, 2013
16. Tamura K, Aoyagi M, Ando N, Ogishima T, Wakimoto H, Yamamoto M, et al: Expansion of CD133-positive glioma cells in recurrent de novo glioblastomas after radiotherapy and chemotherapy. *J Neurosurg* 119:1145-1155, 2013
17. Tanaka Y, Ohno K: Chronic subdural hematoma - an up-to-date concept. *J Med Dent Sci* 60:55-61, 2013
18. Watanabe S, Hara K, Ohta K, Iino H, Miyajima M, Matsuda A, et al: Aroma helps to preserve information processing resources of the brain in healthy subjects but not in temporal lobe epilepsy. *Seizure* 22:59-63, 2013
19. Yamamoto M, Kawabe T, Sato Y, Higuchi Y, Nariai T, Barford BE, Kasuya H, Urakawa Y: A case-matched study of stereotactic radiosurgery for patients with multiple brain metastases: comparing treatment results for 1-4 vs ≥ 5 tumors: clinical article. *J Neurosurg* 118:1258-1268, 2013
20. Yamamoto M, Kawabe T, Higuchi Y, Sato Y, Nariai T, Barford BE, Kasuya H, Urakawa Y: Delayed complications in patients surviving at least 3 years after stereotactic radiosurgery for brain metastases. *Int J Radiat Oncol Biol Phys* 85:53-60, 2013

Endovascular Surgery

1. Staffs and Students (December 2013)

Professor	Shigeru Nemoto	
Associate Professor	Yoshikazu Yoshino	
Assistant Professor	Toshiki Tomori	
Assistant Professor	Kazunori Miki	
Clinical Fellow	Koichi Arimura	
Secretary	Yoko Yanagida,	Hitomi Kuwahara

2. Purpose of Education

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 students opportunity to acquire the proper technique as well as the broad knowledge, and to nurture the mind of exploration.

3. Research Subjects

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 lesions, 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.

4. Clinical services

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.

5. Publications

Original Articles

1. Namba K, Nemoto S: Swine hybrid aneurysm model for endovascular surgery training. *Interventional Neuroradiology* 2013 Jun 25;19(2):153-8. Epub 2013 May 21.
2. Namba K, Kawamura Y, Higaki A, Nemoto S: Percutaneous medial saphenous artery approach for swine central artery access. *Journal of Investigative Surgery* 2013 Dec;26(6):360-3.
3. K.Namba, S.Nemoto: Double Ophthalmic Artery Visualized with New Technology. *The Neuroradiology Journal* 26: 371-372, 2013
4. K.Namba, S.Nemoto: Parkes Weber Syndrome and Spinal Arteriovenous Malformations. letter to editor *AJNR* 34 : E110-E12, Sep 2013
5. Ichijo M, Miki K, Ishibashi S. Response to letter by Gomez-Choco and Valdueza regarding article, "Posterior cerebral artery laterality on magnetic resonance angiography predicts long-term functional outcome in middle cerebral artery occlusion". *Stroke*. 2013 Aug;44(8):e101.
6. Ichijo M, Miki K, Ishibashi S, Kamata T, Fujigasaki H, Mizusawa H. Posterior cerebral artery laterality sign on MRA predicts long-term functional outcome in patients with middle cerebral artery occlusion treated with intravenous rtPA. *Stroke* 2013 Feb;44(2):512-52012
7. Iwasawa E, Ishibashi S, Miki K, Yoshino Y, Nemoto S, Mizusawa H. Teaching NeuroImages: Reversible cognitive impairment with bithalamic lesions caused by a dural arteriovenous fistula. *Neurology*. 2013 Aug 6;81(6):e38-9.

NCNP Brain Physiology and Pathology

1. Staffs and Students

Collaborative Professor	Mikio HOSHINO
Collaborative Professor	Yu-ichi GOTO
Collaborative Professor	Hiroshi KUNUGI
Collaborative Professor	Manabu HONDA
Collaborative Professor	Noritaka ICHINOHE
Collaborative Associate Professor	Takashi OKADA
Collaborative Associate Professor	Yoshitaka NAGAI

2. Purpose of 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. Research Subjects

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 revealed that spatiotemporal control of neural stem cell identities plays a crucial role in producing various types of neurons (Seto et al., Nature Commun. 2014, Yamada et al., J. Neurosci. 2014).

2) Molecular genetic and genomic study for intellectual disability in Japan.

(Yu-ichi Goto, Department of Mental Retardation and Birth Defect Research, National Institute of Neuroscience, NCNP)

One of the major causes of intellectual disability (ID) is based on mutations in the related genes, which are timely and locally expressed in concert with one another in central nervous system. ID is a phenotype derived from the inappropriate expression of these genes. Recent advances in molecular genetics and genome medicine have pushed us on with systematic analysis of ID patients, especially on X-linked MR. In 2013, we investigated the genetic causes and pathophysiology of mitochondrial disease, Rett syndrome, and disease with cortical and white matter dysplasia.

3) Clinical research on mood disorders and schizophrenia

(Hiroshi Kunugi, Department of Mental Disorder Research, National Institute of Neuroscience, NCNP)

The pathogenesis and physiology of mood disorders and schizophrenia remain elusive, and their biomarkers have not yet been established. Our department, which is in collaboration with the National Center of Neurology and Psychiatry Hospital, is trying to develop objective diagnostic markers for these diseases, employing omics approach, brain imaging, and physiological studies. We also aim to develop new treatment on the basis of key molecules. We found characteristics of temperament and coping behavior depending on stress response in depressed patients (J Affect Disord, 2013; 2014). We developed a method to discriminate between depression and schizophrenia patients by using MRI imaging of the brain (J Psychiatr Res, 2013).

4) Noninvasive study on pathophysiology of human higher brain function.

(Manabu Honda, Department of Functional Brain Research, National Institute of Neuroscience, NCNP)

We try to reveal various human higher brain functions including sensory, motor, thought, emotion and *KANSEI* functions and pathophysiology underlying higher brain function disorders by integrating multiple noninvasive brain imaging techniques. We also pursue researches for developing a new technique of functional therapy by means of noninvasive brain stimulation.

5) Study of social primate brains: their development, anatomy, physiology and patho-physiology.

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

We are aiming to elucidate the neural circuit mechanisms of how social primate brain is working, using Common Marmoset, new Primate model animal. Emphases are on their development, anatomy, physiology and patho-physiology.

We studied the potential molecular mechanisms of pruning dendritic spines during developmental period in common marmosets. (Sasaki et al., *Biochem Biophys Res Commun.* 2014, Sasaki et al., *Biochem Biophys Res Commun.* 2014).

6) Basic research towards effective gene and cell therapy for neuromuscular diseases

(Takashi Okada, Department of Molecular Therapy, National Institute of Neuroscience, NCNP)

The characteristics of a recombinant adeno-associated virus (rAAV) with safety profile and long-term expression have made it an attractive transduction tool for clinical gene therapy. We developed a method of generating highly purified AAV vectors to meet labor-effective and large-scale production. We have adopted this intelligent system to investigate AAV vector-mediated transduction for the treatment of neuromuscular diseases. Our experience suggests that long-term transgene expression with therapeutic benefits would be achieved by the rAAV-mediated transduction strategy with an adequate regimen to regulate host immune response. In this respect, multipotent mesenchymal stromal cells (MSCs) are currently being tested in a number of clinical trials for various inflammatory diseases. To improve clinical benefits of gene and cell therapy, we have provided progress towards understanding MSCs phenotype, expansion features, differentiation ability and therapeutic benefits *in vivo*.

This year, unique transduction profile of the AAV vectors in the common marmoset was demonstrated (Okada H, *et al.*, *Molecular Therapy-Nucleic Acids*, 2013). Also, we certified the therapeutic benefits of the micro-dystrophin through the immune tolerance induction in the DMD dogs. Interestingly, genetic predisposition of the inflammatory response strongly affected DMD phenotype in the mice model (Kasahara Y, *et al.*, *Human Molecular Genetics*, in press).

7) Molecular pathogenesis and therapies of neurodegenerative diseases

(Yoshitaka Nagai, Department of Degenerative Neurological Diseases, National Institute of Neuroscience, NCNP)

As we face global aging of the population, a challenging theme has emerged, namely, to overcome late-onset incurable neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and polyglutamine diseases. Recent great progress of molecular genetics and biomedical research revealed that these diseases share a common molecular pathogenesis; protein misfolding and aggregation plays a central role in neurodegeneration. In our department, researchers with various backgrounds such as medicine, pharmacy, biology, and chemistry, are taking advantage of a variety of techniques including molecular genetics, molecular & structural biology, chemical biology, and various animal models (flies, mice, marmosets), to understand the molecular pathogenesis of and to develop therapies for these neurodegenerative diseases.

4. Publications

Original Articles

- 1) Esposito G, Yoshida S, Ohnishi R, Tsuneoka Y, Rostagno Mdel C, Yokota S, Okabe S, Kamiya K, Hoshino M, Shimizu M, Venuti P, Kikusui T, Kato T, Kuroda KO: Infant calming responses during maternal carrying in humans and mice. *Curr Biol*, 23 (9): 739-745, 2013.
- 2) Chonko KT, Jahan I, Stone J, Wright MC, Fujiyama T, Hoshino M, Fritsch B, Maricich SM: Atoh1 directs hair cell differentiation and survival in the late embryonic mouse inner ear. *Dev Biol*, 381 (2): 401-410, 2013.
- 3) Terakawa YW, Inoue YU, Asami J, Hoshino M, Inoue T: A sharp cadherin-6 gene expression boundary in the developing mouse cortical plate demarcates the future functional areal border. *Cereb Cortex*, 23 (10): 2293-2308, 2013.
- 4) Worzfeld T, Swiercz JM, Sentürk A, Genz B, Korostylev A, Deng S, Xia J, Hoshino M, Epstein JA, Chan AM, Vollmar B, Acker-Palmer A, Kuner R, Offermanns S: Genetic dissection of plexin signaling in vivo. *Proc Natl Acad Sci USA*, 111 (6): 2194-2199, 2014.
- 5) Seto Y, Nakatani T, Masuyama N, Taya S, Kumai M, Minaki Y, Hamaguchi A, Inoue YU, Inoue T, Miyashita S, Fujiyama T, Yamada M, Chapman H, Campbell K, Magnuson MA, Wright CV, Kawaguchi Y, Ikenaka K, Takebayashi H, Ishiwata S, Ono Y, Hoshino M: Temporal identity transition from Purkinje cell progenitors to GABAergic interneuron progenitors in the cerebellum. *Nat Commun*, 5 : 3337-3337, 2014.
- 6) Seto Y, Ishiwata S, Hoshino M: Characterization of Olig2 expression during cerebellar development. *Gene Expr Patterns*, 15 (1): 1-7, 2014.
- 7) Yamada M, Seto Y, Taya S, Owa T, Inoue YU, Inoue T, Kawaguchi Y, Nabeshima Y, Hoshino M: Specification of

- spatial identities of cerebellar neuron progenitors by *ptfla* and *atoh1* for proper production of GABAergic and glutamatergic neurons. *J Neurosci*, 34 (14): 4786-4800, 2014.
- 8) Waga C, Asano H, Tsuchiya A, Itoh M, Goto Y, Kohsaka S, Uchino S. Identification of novel SHANK3 transcript in the developing mouse neocortex. *J Neurochem* 2014;128(2):280-293.
 - 9) Miyake K, Yang C, Minakuchi Y, Ohori K, Soutome M, Endoh K, Hirasawa T, Kazuki Y, Adachi N, Suzuki S, Itoh M, Goto Y, Andoh T, Kurosawa H, Oshimura M, Sasaki M, Toyoda A, Kubota T. Comparison of genomic and epigenomic expression in monozygotic twins discordant for Rett syndrome. *PLoS ONE* 2013 Jun 21;8(6):e66729. Print 2013.
 - 10) Nagai S, Saito Y, Endo Y, Saito T, Kenji Sugai K, Ishiyama A, Komaki H, Nakagawa E, Sasaki M, Ito K, Saito Y, Sukigara S, Ito M, Goto Y, Ito S, Matsuoka K. Hypoalbuminemia in early-onset dentatorubral- pallidoluysonian atrophy due to leakage of albumin in multiple organs. *J Neurol* 2013;260:1263-1271.
 - 11) Jalsrai A, Numakawa T, Ooshima Y, Adachi N, Kunugi H: Phosphatase-mediated intracellular signaling contributes to neuroprotection by flavonoids of *Iris tenuifolia*. *Am J Chin Med*, 42(1):119-130, 2014.
 - 12) Richards M, Hori H, Sartorius N, Kunugi H: Cross-cultural comparisons of attitudes toward schizophrenia amongst the general population and physicians:a series of web-based surveys in Japan and the United States. *Psychiatry Res*, 215(2): 300-307, 2014.
 - 13) Sasayama D, Hori H, Yamamoto N, Nakamura S, Teraishi T, Tatsumi M, Hattori K, Ota M, Higuchi T, Kunugi H: ITIH3 polymorphism may confer susceptibility to psychiatric disorders by altering the expression levels of GLT8D1. *J Psychiatr Res*, 50:79-83, 2014.
 - 14) Ota M, Wakabayashi C, Matsuo J, Kinoshita Y, Hori H, Hattori K, Sasayama D, Teraishi T, Obu S, Ozawa H, Kunugi H: Effect of L-theanine on sensorimotor gating in healthy human subjects. *Psychiatry Clin Neurosci*, 2013.
 - 15) Suzuki N, Numakawa T, Chou J, de Vega S, Mizuniwa C, Sekimoto K, Adachi N, Kunugi H, Arikawa-Hirasawa E, Yamada Y, Akazawa C: Teneurin-4 promotes cellular protrusion formation and neurite outgrowth through focal adhesion kinase signaling. *FASEB J*, 28(3):1386-1397, 2014.
 - 16) Sasayama D, Hori H, Teraishi T, Hattori K, Ota M, Matsuo J, Kinoshita Y, Okazaki M, Arima K, Amano N, Higuchi T, Kunugi H: Benzodiazepines, benzodiazepine-like drugs, and typical antipsychotics impair manual dexterity in patients with schizophrenia. *J Psychiatr Res*, 49:37-42, 2014.
 - 17) Hori H, Teraishi T, Ota M, Hattori K, Matsuo J, Kinoshita Y, Ishida I, Nagashima A, Koga N, Higuchi T, Kunugi H: Psychological coping in depressed outpatients: association with cortisol response to the combined dexamethasone/CRH test. *J Affect Disord*, 152-154:441-447. 2014.
 - 18) Ota M, Hori H, Sato N, Sasayama D, Hattori K, Teraishi T, Obu S, Nakata Y, Kunugi H: Hypothalamic-pituitary-adrenal axis hyperactivity and brain differences in healthy women. *Neuropsychobiology*, 68(4):205-211, 2013.
 - 19) Hori H, Teraishi T, Sasayama D, Matsuo J, Kinoshita Y, Ota M, Hattori K, Kunugi H: A latent profile analysis of schizotypy, temperament and character in a nonclinical population: association with neurocognition. *J Psychiatr Res*, 48(1): 56-64, 2014.
 - 20) Richards M, Chiba S, Ninomiya M, Wakabayasi C, Kunugi H: Inhibition of olanzapine-induced weight gain by the retinoid analog AM-80. *Pharmacopsychiatry*, 46(7):267-73, 2013.
 - 21) Furuta M, Numakawa T, Chiba S, Ninomiya M, Kajiyama Y, Adachi N, Akema T, Kunugi H: Estrogen, predominantly via estrogen receptor α , attenuates postpartum-induced anxiety- and depression-like behaviors in female rats. *Endocrinology*, 154(10):3807-3816, 2013.
 - 22) Teraishi T, Sasayama D, Hori H, Yamamoto N, Fujii T, Matsuo J, Nagashima A, Kinoshita Y, Hattori K, Ota M, Fujii S, Kunugi H: Possible association between common variants of the phenylalanine hydroxylase (PAH) gene and memory performance in healthy adults. *Behav Brain Funct*, 9(1):30, 2013.
 - 23) Ota M, Ishikawa M, Sato N, Hori H, Sasayama D, Hattori K, Teraishi T, Noda T, Obu S, Nakata Y, Higuchi T, Kunugi H: Discrimination between schizophrenia and major depressive disorder by magnetic resonance imaging of the female brain. *J Psychiatr Res*, 47(10):1383-1388, 2013.
 - 24) Kunugi H, Koga N, Hashikura M, Noda T, Shimizu Y, Kobayashi T, Yamanaka J, Kanemoto N, Higuchi T: Validation of computer-administered clinical rating scale: Hamilton Depression Rating Scale assessment with Interactive Voice Response technology--Japanese version. *Psychiatry Clin Neurosci*, 67(4):253-258, 2013.
 - 25) Ota M, Sato N, Nakata Y, Ito K, Kamiya K, Maikusa N, Ogawa M, Okamoto T, Obu S, Noda T, Araki M, Yamamura T, Kunugi H: Abnormalities of cerebral blood flow in multiple sclerosis: a pseudocontinuous arterial spin labeling MRI study. *Magn Reson Imaging*, 31(6):990-995, 2013.
 - 26) Ota M, Nakata Y, Ito K, Kamiya K, Ogawa M, Murata M, Obu S, Kunugi H, Sato N: Differential diagnosis tool for

- parkinsonian syndrome using multiple structural brain measures. *Comput Math Methods Med*, 2013;571289, 2013.
- 27) Hori H, Matsuo J, Teraishi T, Sasayama D, Kawamoto Y, Kinoshita Y, Ota M, Hattori K, Kunugi H. Moderating effect of schizotypy on the relationship between smoking and neurocognition. *Eur Psychiatry*, 28(8):457-462, 2013.
 - 28) Hori H, Teraishi T, Sasayama D, Hattori K, Hashikura M, Higuchi T, Kunugi H: Relationship of temperament and character with cortisol reactivity to the combined dexamethasone/CRH test in depressed outpatients. *J Affect Disord*, 147(1-3):128-136, 2013.
 - 29) Maekawa T, Honda M, Nishina E, Kawai N, Oohashi T: Structural complexity of sounds necessary for the emergence of the hypersonic effect: Estimation of autocorrelation order, *Asiagraph Journal* Vol.8, No.2, 35- 40, 2013.
 - 30) Tanaka S, Ikeda H, Kasahara K, Kato R, Tsubomi H, Sugawara SK, Mori M, Hanakawa T, Sadato N, Honda M, Watanabe K: Larger right posterior parietal volume in action video game experts: a behavioral and voxel-based morphometry (VBM) study. *PLoS One*, 8 (6): e66998, 2013.
 - 31) Omata K, Hanakawa T, Morimoto M, Honda M: Spontaneous Slow Fluctuation of EEG Alpha Rhythm Reflects Activity in Deep-Brain Structures: A Simultaneous EEG-fMRI Study. *PLoS One*, 8 (6): e66869, 2013.
 - 32) Shitara H, Shinozaki T, Takagishi K, Honda M, Hanakawa T: Movement and afferent representations in human motor areas: a simultaneous neuroimaging and transcranial magnetic/peripheral nerve-stimulation study. *Front Hum Neurosci*, 7 (554): doi: 10.3389/fnhum.2013.00554, 2013.
 - 33) Kasahara K, Tanaka S, Hanakawa T, Senoo A, Honda M: Lateralization of activity in the parietal cortex predicts the effectiveness of bilateral transcranial direct current stimulation on performance of a mental calculation task. *Neurosci Lett*, 545: 86-90, 2013.
 - 34) Maekawa T, Honda M, Kawai N, Nishina E, Ueno O, Oohashi T: Heterogeneity and complexity of a simulated terrestrial environment account for superiority of the altruistic gene. *Proceedings of the twelfth European Conference on the Synthesis and Simulation of Living Systems ECAL2013*, 250-257, 2013.
 - 35) Oohashi T, Maekawa T, Ueno O, Kawai N, Nishina N, Honda M: Evolutionary Acquisition of a Mortal Genetic Program: The Origin of an Altruistic Gene. *Artif Life*, 20 (1): 95-110, 2013.
 - 36) Honda M, Kawai N, Yagi R, Fukushima A, Ueno O, Onodera E, Maekawa T, Oohashi T: Electroencephalographic index of the activity of functional neuronal network subserving the hypersonic effect. *Asiagraph Journal*, 8 (2): 41-46, 2013.
 - 37) Tanaka T, Takano Y, Tanaka S, Hironaka N, Kobayashi K, Hanakawa T, Watanabe K, Honda M: Transcranial direct-current stimulation increases the extracellular dopamine levels in the rat striatum. *Front Syst Neurosci*, 7 (6): 1-8, 2013.
 - 38) Hosoda C, Tanaka K, Nariai T Honda M, Hanakawa T: Dynamic neural network reorganization associated with second language vocabulary acquisition: a multimodal imaging study. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, 33 (34): 13663-72, 2013.
 - 39) Sasaki T, Oga T, Nakagaki K, Sakai K, Sumida K, Hoshino K, Miyawaki I, Saito K, Suto F, Ichinohe N: Developmental expression profiles of axon guidance signaling and the immune system in the marmoset cortex: Potential molecular mechanisms of pruning of dendritic spines during primate synapse formation in late infancy and prepuberty (I). *Biochem Biophys Res Commun*, 444 (3): 302-306, 2014
 - 40) Sasaki T, Oga T, Nakagaki K, Sakai K, Sumida K, Hoshino K, Miyawaki I, Saito K, Suto F, Ichinohe N: Developmental genetic profiles of glutamate receptor system, neuromodulator system, protector of normal tissue and mitochondria, and reelin in marmoset cortex: Potential molecular mechanisms of pruning phase of spines in primate synaptic formation process during the end of infancy and prepuberty (II). *Biochem Biophys Res Commun*, 444 (3): 307-310, 2014
 - 41) Nitahara-Kasahara Y, Hayashita-Kinoh H, Chiyo T, Nishiyama A, Okada H, Takeda S, Okada T: Dystrophic mdx mice develop severe cardiac and respiratory dysfunction following genetic ablation of the anti-inflammatory cytokine IL-10. *Human Molecular Genetics*, 2014 (in press)
 - 42) Kanagawa M, Yu CC, Ito C, Fukada S, Hozoji-Inada M, Chiyo T, Kuga A, Matsuo M, Sato K, Yamaguchi M, Ito T, Katanosaka Y, Miyagoe-Suzuki Y, Naruse K, Kobayashi K, Okada T, Takeda S, Toda T: Impaired viability of muscle precursor cells in muscular dystrophy with glycosylation defects and amelioration of its severe phenotype by limited gene expression. *Human Molecular Genetics*, 22(15):3003-15, 2013
 - 43) Okada H, Ishibashi H, Hayashita-Kinoh H, Chiyo T, Nitahara-Kasahara Y, Baba Y, Watanabe S, Takeda S, Okada T: Robust long-term transduction of common marmoset neuromuscular tissue with rAAV1 and rAAV9. *Molecular Therapy - Nucleic Acids*, 2:e95, 2013
 - 44) Ishibashi H, Motohashi HH, Kumon M, Yamamoto K, Okada H, Okada T, Seki K: Efficient embryo transfer in the

common marmoset monkey (*Callithrix jacchus*) with a reduced transfer volume: a non-surgical approach with cryo-preserved late-stage embryos. *Biol Reprod*, 88(5):115, 2013

- 45) Ishibashi H, Motohashi HH, Kumon M, Yamamoto K, Okada H, Okada T, Seki K: Ultrasound-guided non-surgical embryo collection in the common marmoset. *Reproductive Biology*, 13(2):139-44, 2013
- 46) Nakamura A, Kobayashi M, Kuraoka M, Yuasa K, Yugeta N, Okada T, Takeda S: Initial pulmonary respiration causes massive diaphragm damage and hyper-CKemia in Duchenne muscular dystrophy dog. *Sci Rep.*, 3:2183, 10.1038/srep02183, 2013
- 47) Higashi S, Kabuta T, Nagai Y, Tsuchiya Y, Akiyama H, Wada K: TDP-43 associates with stalled ribosomes and contributes to cell survival during cellular stress. *J Neurochem* 126 (2): 288-300, 2013.
- 48) Togashi K, Wakatsuki S, Furuno A, Tokunaga S, Nagai Y, Araki T: Na⁺/H⁺ exchangers induce autophagy in neurons and inhibit polyglutamine-induced aggregate formation. *PLoS One* 8 (11): e81313, 2013.
- 49) Azuma Y, Tokuda T, Shimamura M, Kyotani A, Sasayama H, Yoshida T, Mizuta I, Mizuno T, Nakagawa M, Fujikake N, Ueyama M, Nagai Y, Yamaguchi M: Identification of *ter94*, *Drosophila VCP*, as a strong modulator of motor neuron degeneration induced by knockdown of *Caz*, *Drosophila FUS*. *Hum Mol Genet* (in press)

Review Articles

- 1) Okada T: Efficient AAV vector production system: Towards gene therapy for Duchenne muscular dystrophy. In *Gene Therapy - Tools and Potential Applications* (ed. by Francisco Martin), InTech, pp429-440, 2013.

Books

- 1) Okada T, Takeda S: Current challenges and future directions in recombinant AAV-mediated gene therapy of Duchenne muscular dystrophy, *Pharmaceuticals* 6(7), 813-836, 2013
- 2) Popiel HA, Takeuchi T, Burke JR, Strittmatter WJ, Toda T, Wada K, Nagai Y: Inhibition of protein misfolding/aggregation using polyglutamine binding peptide QBP1 as a therapy for the polyglutamine diseases. *Neurotherapeutics* 10 (3): 440-446, 2013
- 3) Takeuchi T, Popiel HA, Futaki S, Wada K, Nagai Y: Peptide-based therapeutic approaches for treatment of the polyglutamine diseases. *Curr Med Chem* (in press)

Immune Regulation

1. Staffs and Students

Professor	Hajime KARASUYAMA	
Assistant Professor	Yohei KAWANO (until Sep.), Shingo SATO, Soichiro YOSHIKAWA	
Technical Official	Toshiyuki KOJIMA	
Project Researcher	Kazushige OBATA-NINOMIYA (until Dec.)	
Graduate Students	Yuichiro NEI (until Mar.), Mayumi EGAWA (until Mar.), LI Li Hua, Kayo HORIGUCHI, Misako IKI, Hidemitsu TSUTSUI, Sumika TOYAMA (Since Apr.), Tomoyuki BANDO (Since Apr.) Takuya OHTA, Hayato DEKI, Saori TAKAHASHI (Since Apr.)	
Physician Scientist	Mariko SUNAHARA,	Kensuke MIYAKE
Program Students		

2. Purpose of Education

Main objective of the immunology course for undergraduate students is to provide them the basic ideas how the immune system works and is regulated in various physiological and pathological settings including infections, cancer, autoimmune and allergic disorders, and organ transplantation. In the immunology course for graduate students, they study molecular mechanisms underlying the lymphocyte differentiation and the development of immune disorders including allergy, by employing advanced technology in molecular biology, biochemistry, cellular biology and developmental engineering.

3. Research Subjects

- 1) Role of basophils in immune disorders such as allergy
- 2) Role of basophils in protective immunity against infections
- 3) *in vivo* imaging of basophil-mediated immune responses

4. Publications

Original Articles

1. Obata-Ninomiya, K., Ishiwata, K., Tsutsui, H., Nei, Y., Yoshikawa, S., Kawano, Y., Minegishi, Y., Ohta, N., Watanabe, N., Kanuka H, and Karasuyama H.: The skin is an important bulwark of acquired immunity against intestinal helminths., *J Exp Med.*, 210:2583-2595, 2013
2. Noti, M., Wojno, ED., Kim, BS., Siracusa, MC., Giacomini, PR., Nair, MG., Benitez, AJ., Ruymann, KR., Muir, AB., Hill, DA., Chikwava, KR., Moghaddam, AE., Sattentau, QJ., Alex, A., Zhou, C., Yearley, JH., Menard-Katcher, P., Kubo, M., Obata-Ninomiya, K., Karasuyama, H., Comeau MR, Brown-Whitehorn, T., de Waal Malefyt, R., Sleiman, PM., Hakonarson, H., Cianferoni, A., Falk, GW., Wang, ML., Spergel, JM., and Artis, D.: Thymic stromal lymphopoietin-elicited basophil responses promote eosinophilic esophagitis., *Nat Med.*, 9:1005-1013, 2013
3. Anyan, WK., Seki, T., Kumagai, T., Obata-Ninomiya, K., Furushima-Shimogawara, R., Kwansa-Bentum, B., Akao, N., Bosompem, KM., Boakye, DA., Wilson, MD., Karasuyama, H., and Ohta, N.: Basophil depletion downregulates *Schistosoma mansoni* egg-induced granuloma formation., *Parasitol Int.*, 62:508-513, 2013
4. Kwansa-Bentum, B., Izumiyama, S., Kitamura, K., Obata-Ninomiya, K., Ohta, N., and Asahi, H.: Comparative studies of serum-free media and detection techniques for *in vitro* drug sensitivity assessment of *Plasmodium falciparum*, *Open Journal of Clinical Diagnostics.* 3, 2013
5. Nei, Y., Obata-Ninomiya, K., Tsutsui, H., Ishiwata, K., Miyasaka, M., Matsumoto, K., Nakae, S., Kanuka, H., Inase, N., and Karasuyama, H.: GATA-1 regulates the generation and function of basophils. *Proc Natl Acad Sci U S A.*, 110:18620-5, 2013
6. Egawa, M., Mukai, K., Yoshikawa, S, Iki, M., Mukaida, N., Kawano, Y., Minegishi, Y., and Karasuyama, H.: Inflammatory monocytes recruited to allergic skin acquire an anti-inflammatory M2 phenotype via basophil-derived interleukin-4. *Immunity.* 38: 570-580, 2013.

7. Shiraishi, Y., Jia, Y., Domenico, J., Joetham, A., Karasuyama, H., Takeda, K., and Gelfand, E.W.: Sequential engagement of Fc ϵ RI on mast cells and basophil histamine H4 receptor and Fc ϵ RI in allergic rhinitis. ***J. Immunol.*** 190: 539-548, 2013.
8. Ramadan, A., Pham, Van L., Machavoine, F., Dietrich, C., Alkan, M., Karasuyama, H., Schneider, E., Dy, M., and Thieblemont, N.: Activation of basophils by the double-stranded RNA poly(A:U) exacerbates allergic inflammation. ***Allergy*** 68: 732-738, 2013.
9. Torrero, M.N., Morris, C.P., Mitre, B.K., Hübner, M.P., Mueller, E., Karasuyama, H., and Mitre, E.: Basophils help establish protective immunity induced by irradiated larval vaccination for filariasis. ***Vaccine*** 31: 3675-3682, 2013.
10. Reber, L.L., Marichal, T., Mukai, K., Roers, A., Hartmann, K., Karasuyama, H., Nadeau, K.C., Tsai, M., and Galli, S.J.: Selective ablation of mast cells or basophils reduces peanut-induced anaphylaxis in mice. ***J. Allergy Clin. Immunol.*** 132: 881-888, 2013.
11. Leyva-Castillo, J.M., Hener, P., Michea, P., Karasuyama, H., Chan, S., Soumelis, V., and Li, M.: Skin TSLP initiates Th2 responses through an orchestrated immune cascade. ***Nat. Commun.*** 4:2847, 2013.
12. Kim, S., Karasuyama, H., Lopez, A.F., Ouyang, W., Li, X., Le Gros, G., and Min, B.: IL-4 Derived from Non-T Cells Induces Basophil- and IL-3-independent Th2 Immune Responses. ***Immune Netw.*** 13:249-56, 2013.

Molecular Virology

1. Staffs and Students (April 2013)

Professor	Shoji YAMAOKA	
Project Professor	Eiji IDO	
Assistant Professor	Yasunori SAITOH,	Ryuta SAKUMA,
	Hiroaki TAKEUCHI,	Takanori HORI
Medical Technologist	Yoshio INAGAKI	
Secretary	Kumiko THORPE-MATSUI	
Research Assitant	Akiko HAMANO,	Kanako MOCHIDA
-Students-		
Ph.D. course	Miho OHTSUKA,	Ensho CHO,
	Sayaka SUKEGAWA,	Hideki SAITO,
Master course	Akiko FUKUDA,	Eri TSURUYAMA,
	Haruka YAMAGUCHI,	Naoto SUZUKI,
	Masateru HOSODA,	Ryota OCHI

2. Purpose of Education

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.

3. Research Subjects

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.

4. Publications: Original articles

1. Nii-Trebi NI, Ibe S, Barnor JS, Ishikawa K, Brandful JA, Ofori SB, Yamaoka S, Ampofo WK, Sugiura W. HIV-1 drug-resistance surveillance among treatment-experienced and -naïve patients after the implementation of antiretroviral therapy in Ghana. *PLoS One*. 19;8(8):e71972. 2013.
2. Lee H, Komano J, Saitoh Y, Yamaoka S, Kozaki T, Misawa T, Takahama M, Satoh T, Takeuchi O, Yamamoto N, Matsuura Y, Saitoh T, Akira S. Zinc-finger antiviral protein mediates retinoic acid inducible gene I-like receptor-independent antiviral response to murine leukemia virus. *Natl Acad Sci U.S.A.* 23;110(30):12379-84. 2013.
3. Hori T, Takeuchi H, Saito H, Sakuma R, Inagaki Y, Yamaoka S. A carboxy-terminally truncated human CPSF6 lacking residues encoded by exon 6 inhibits HIV-1 cDNA synthesis and promotes capsid disassembly. *J Virol*. 87(13):7726-36. 2013.
4. Muramatsu S, Tanaka S, Mogushi K, Adikrisna R, Aihara A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Nakayama K, Tanaka H, Yamaoka S, Arii S. Visualization of stem cell features in human hepatocellular carcinoma reveals in vivo significance of tumor-host interaction and clinical course. *Hepatology* 58(1):218-28. 2013.
5. Sugiyama R., Abe M., Nishitsuji H., Murakami Y., Takeuchi H., and Takaku H. Induction of heat-shock protein 70 by prostaglandin A1 inhibits HIV-1 Vif-mediated degradation of APOBEC3G. *Antiviral Research* 99(3):307-11. 2013.

Immunotherapeutics

1. Staffs and Students (April, 2013)

Professor	Mari KANNAGI	
Associate Professor	Takao MASUDA	
Assistant Professor	Atsuhiko HASEGAWA (Lecturer)	
Assistant Professor	Yoshiko NAGANO	
Postdoctoral Fellow	Ayako TAKAMORI,	Shuichi KINPARA
Graduate Student	Yotaro TAMAI,	Yoko SATO,
	Satomi ANDO,	Tatsuro TAKAHATA,
	Yuji MURAKAMI,	Ayano AKIBA,
	Tomohiro IKUMA,	Touru KAKINUMA,
	Mami KIJIYAMA,	Kazuki MIURA

2. Purpose of Education

Our research area is in between clinical and basic science, involving immunology, microbiology, and molecular biology. We participate in education for undergraduate medical students in basic immunology and a part of clinical immunology. For graduate students, we provide opportunity to research for mechanisms of infectious disease and development of immunological therapeutics.

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.

3. 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.

4. Clinical Services

5. Publications

Original article

1. Kinpara S, Kijiyama M, Takamori A, Hasegawa A, Sasada A, Masuda T, Tanaka Y, Utsunomiya A, and Kannagi M. Interferon- α (IFN- α) suppresses HTLV-1 gene expression and cell cycling, while IFN- α combined with zidovudin induces p53 signaling and apoptosis in HTLV-1-infected cells. *Retrovirology*, 10:52, 2013
2. Tamai Y, Hasegawa A, Takamori A, Sasada A, Tanosaki R, Choi I, Utsunomiya A, Maeda Y, Yamano Y, Eto T, Koh KR, Nakamae H, Suehiro Y, Kato K, Takemoto S, Okamura J, Uike N, and Kannagi M. Potential contribution of a novel Tax epitope-specific CD4+ T cells to graft-versus-Tax effects in adult T-cell leukemia patients after allogeneic hematopoietic stem cell transplantation. *J. Immunol* 190: 4382-4392, 2013
3. Kannagi, M., A. Hasegawa, A. Takamori, S. Kinpara, and A. Utsunomiya. 2012. The roles of acquired and innate immunity in human T-cell leukemia virus type 1-mediated diseases. *Front Microbiol* 3:323. 2012
4. Mehra S, Golden NA, Stuckey K, Didier PJ, Doyle LA, Russell-Lodrigue KE, Sugimoto C, Hasegawa A, Sivasubramani SK, Roy CJ, Alvarez X, Kuroda MJ, Blanchard JL, Lackner AA, Kaushal D. The Mycobacterium tuberculosis stress response factor SigH is required for bacterial burden as well as immunopathology in primate lungs. *J Infect Dis*. 205(8):1203-13, 2012.
5. Yamaji O, Nagaishi T, Totsuka T, Onizawa M, Suzuki M, Tsuge N, Hasegawa A, Okamoto R, Tsuchiya K, Nakamura T, Arase H, Kanai T, Watanabe M. The development of colitogenic CD4(+) T cells is regulated by IL-7 in

collaboration with NK cell function in a murine model of colitis. *J. Immunol.* 188(6):2524-36, 2012.

International Scientific Meetings

1. Kannagi M, Kinpara S, Takamori Y, Sasada A, and Hasegawa A. Impact of innate and acquired immune responses in Adult T-cell Leukemia. AACR/JCA Joint Conference: Breakthroughs in Basic and Translational Cancer Research, taking place February 21-25, 2013, Maui. (Invited speaker)
2. Hasegawa A, Tamai Y, Takamori A, Sasada A, Tanosaki R, Choi I, Utsunomiya A, Maeda Y, Yamano Y, Etoh T, Koh KR, Nakamae H, Suehiro Y, Kato K, Takemoto S, Okamura J, Uike N, Kannagi M. Identification of a novel HLA-DR1-restricted dominant epitope recognized by HTLV-1 Tax-specific CD4⁺ T-cells augmenting HTLV-1-specific CTL expansion in ATL patients after allogeneic HSCT. The 9th AACR-Japanese cancer association joint conference, Feb. 2013, Maui.
3. Kannagi M. Allogeneic BM transplantation in ATL: Whom to transplant and which modality to use? Can we go beyond BM transplantation? 16th International Conference on Human Retrovirology HTLV and Related Viruses, Clinical trial workshop. June 26-30, 2013, Montréal. (Solicited speaker)
4. Hasegawa A, Tamai Y, Takamori A, Sasada A, Tanosaki R, Choi I, Utsunomiya A, Maeda Y, Yamano Y, Etoh T, Koh KR, Nakamae H, Suehiro Y, Kato K, Takemoto S, Okamura J, Uike N, Kannagi M. Augmentation of donor-derived Tax-specific CTL responses by a novel Tax epitope-specific CD4⁺ helper T-cells in ATL patients after allogeneic hematopoietic stem cell transplantation. 16th International Conference on Human Retrovirology HTLV and Related Viruses. June 26- 30, 2013, Montréal.
5. Kinpara S, Kijiyama M, Takamori A, Hasegawa A, Sasada A, Masuda T, Tanaka Y, Utsunomiya A, Kannagi M. IFN- α suppresses HTLV-1 expression via PKR in infected cells and renders them susceptible to AZT through p53 activation in AZT/IFN- α treatment. 16th International Conference on Human Retrovirology HTLV and Related Viruses June 26-30, 2013, Montréal. (Young Investigator Award)
6. Suehiro Y, Hasegawa A, Iino T, Sasada A, Watanabe N, Choi I, Fukuda T, Takaishi S, Tanosaki R, Utsunomiya A, Miura O, Matsuoka M, Teshima T, Akashi K, Okamura J, Kannagi M, Uike N. The phase-I study of a therapeutic vaccine to ATL patients with autologous dendritic cells pulsed with peptides corresponding to Tax-specific CTL epitopes. 16th International Conference on Human Retrovirology HTLV and Related Viruses. June 26-30, 2013, Montréal.
7. Kannagi M, Hasegawa A, Suehiro Y, Takamori A, Kinpara S, Ando S, Utsunomiya A, Choi I, Uike N. Immunological control of HTLV-1: Prospective therapy towards prophylaxis of disease. The 6th International Symposium on HTLV-1. August 23-25, 2013, Tokyo. (Invited speaker).
8. Atsuhiko Hasegawa. Unresponsiveness of Tax-specific CTLs in Rats Orally Infected with HTLV-1 and Reinduction of Functional Tax-specific CTLs by Peptide-pulsed BMDC Vaccine. The 4th JSH International Symposium. May 24-25, 2013, Ehime.

Cellular and Environmental Biology (General Isotope Research Division, Research Center for Medical and Dental Sciences)

1. Staffs and Students (April, 2013)

Associate Professor Masayuki HARA
Graduate Student Satoru MIYAKURA

2. Purpose of 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. 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.

Biodefense Research

1. Staffs and Students

Professor	Toshiaki Ohteki
Junior Associate Professor	Nobuyuki Onai
Assistant Professor	Hiroyuki Tezuka
Assistant Professor	Yusuke Nakanishi
Adjunct Lecturer (JST PRESTO)	Taku Sato
Project Junior Assistant Professor	Junpei Asano
Graduate Student	Shunsuke Kawamura
Research Technician	Shoko Kuroda
Research Technician	Kisho Shiseki
Research Technician	Rumiko Nakamura
Secretarial Assistant	Hisako Kamioka

2. Purpose of Education

Our research projects focus on maintenance and failure of immunological homeostasis. Our goal is to define the mechanism of immune cell and tissue stem cell behavior under conditions of health and disease. To accomplish this goal, we are trying to clarify the molecular basis of induction and failure of immunological tolerance by focusing on immune cells and tissue stem cells in the bone marrow, skin, and intestine including its associated lymphoid tissues. 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.

3. Research Subjects

- 1) Differentiation and function of dendritic cells.
- 2) Understanding of immunological diseases based on tissue stem cell disorder.
- 3) Mechanism of tolerance induction and its failure in the mucosa-associated lymphoid tissues.

4. Publications

[original papers]

1. Onai N, Kurabayashi K, Hosoi-Amaiike M, Toyama-Sorimachi N, Matsushima K, Inaba, K, and Ohteki T. A clonogenic progenitor with prominent plasmacytoid dendritic cell developmental potential. *Immunity* 38, 943-57 (2013).
2. Sato T, Ikeda M, Yotsumoto S, Shimada Y, Higuchi T, Kobayashi H, Fukuda T, Ohashi T, Suda T, and Ohteki T. Novel interferon-based pre-transplantation conditioning in the treatment of a congenital metabolic disorder. *Blood* 121, 3267-73 (2013).
3. Hayashi A, Sato T, Kamada N, Mikami Y, Matsuoka K, Hisamatsu T, Hibi T, Roers S, Yagita H, Ohteki T, Yshimura A, and Kanai T. A single strain of *Clostridium butyricum* induces intestinal IL-10-producing macrophages that suppress acute colitis. *Cell Host Microbe* 13, 711-22 (2013).
4. Sato T, Kitawaki T, Fujita H, Iwata M, Iyoda T, Inaba K, Ohteki T, Hasegawa S, Kawada K, Sakai Y, Ikeuchi H, Nakase H, Niwa A, Takaori-Kondo A, and Kadowaki N. Human CD1c⁺ myeloid dendritic cells acquire a high level of retinoic acid-producing capacity in response to vitamin D3. *J Immunol* 191, 3152-60 (2013).
5. Ohyagi H, Onai N, Sato T, Yotsumoto S, Liu J, Akiba H, Yagita H, Atarashi K, Honda K, Roers A, Muller W, Kurabayashi K, Hosoi-Amaiike M, Takahashi N, Hirokawa M, Matsushima K, Sawada K, and Ohteki T. Monocyte-derived dendritic cells perform hemophagocytosis to fine-tune excessive immune responses. *Immunity* 39, 584-98 (2013).
6. Yokota-Nakatsuma A, Takeuchi H, Ohoka Y, Kato C, Song SY, Hoshino T, Yagita H, Ohteki T, and Iwata M. Retinoic acid prevents mesenteric lymph node dendritic cells from inducing IL-13-producing inflammatory Th2 cells. *Mucosal Immunol* in press.

5. Presentation at international meetings

1. Ohteki T. New DC Progenitors with prominent pDC differentiation potential. KEYSTONE SYMPOSIA on Molecular and Cellular Biology 2013, Keystone, USA, 2013.3.6

2. Ohteki T. Discovery of a novel source of dendritic cells, the control tower of the immune system. Annual Meeting of the Japanese Society for Immunology, Technical Seminar, Chiba, 2013.12.11
3. Onai N, Toyama-Sorimachi N, Matsushima K, Inaba K, and Ohteki T. Identification of M-CSFR⁻ dendritic cell progenitors with prominent pDC developmental potential: Revised road map for dendritic cell development. Annual Meeting of the Japanese Society for Immunology, Chiba, 2013.12.12
4. Tezuka H, and Ohteki T. TNF/iNOS-producing dendritic cells are originated from inflammatory monocytes and regulate gut IgA production. Annual Meeting of the Japanese Society for Immunology, Chiba, 2013.12.12
5. Nakanishi Y, and Ohteki T. Commensal Gram-positive bacteria trigger the recruitment of monocyte/macrophage into the inflamed colon during development of colitis. Annual Meeting of the Japanese Society for Immunology, Chiba, 2013.12.13

Pathological Cell Biology

1. Staffs and Students

Professor	Shigeomi SHIMIZU	
Associate Professor	Norio SHIMIZU	
Junior Associate Professor	Tatsushi YOSHIDA	
Tokunin Junior Associate Professor	Masatsune TSUJIOKA	
Assistant Professor	Satoko ARAKAWA	
Tokunin Assistant Professor	Michiko MUROHASHI, YAMAGUCHI, Minkyon SHIN	Shinya HONDA, Hirofumi Tsutomu HASHIDUME,
Secretary	Ikuyo YOSHINO, Kyoko TSUJIMURA,	Mimi SAKAGUCHI, Sachiko OTSUKA
Graduate Student	Yuna SUGIMOTO, Meruna NAGATA, Megumi YAMASHITA, Ayumi NAKAJIMA, Miyuki NAKAI,	Dai MIYAZAKI, Mutsumi OHARA, Yuta GOTO, Hiromichi YAMAMOTO, Natsuki ODA

2. Purpose of 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.

3. Research Subjects

- 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

4. Publications

Original Article

1. Mizushima T, Arakawa S, Sanada Y, Yoshino I, Miyazaki D, Urushima H, Tsujimoto Y, Ito T, Shimizu S: Inhibition of epithelial cell death by Bcl-2 improved chronic colitis in IL10 KO mice. *Am J Pathol.* 183, 1936-44 (2013)
2. Kobayashi Z, Akaza M, Numasawa Y, Ishihara S, Tomimitsu H, Nakamichi K, Saijo M, Morio T, Shimizu N, Sanjo N, Shintani S, Mizusawa H: Failure of mefloquine therapy in progressive multifocal leukoencephalopathy: Report of two Japanese patients without human immunodeficiency virus infection. *Journal of the Neurological Sciences* 324, 190-194(2013)
3. Yan J, Ng SB, Tay JL, Lin B, Koh TL, Tan J, Selvarajan V, Liu SC, Bi C, Wang S, Choo SN, Shimizu N, Huang G, Yu Q, Chng WJ: EZH2 overexpression in natural killer/T-cell lymphoma confers growth advantage independently of histone methyltransferase activity. *blood* 121: 4512-4520(2013)
4. Tachikawa R, Tomii K, Seo R, Nagata K, Otsuka K, Nakagawa A, Otsuka K, Hashimoto H, Watanabe K, Shimizu N: Detection of Herpes Viruses by Multiplex and Real-Time Polymerase Chain Reaction in Bronchoalveolar Lavage Fluid of Patients with Acute Lung Injury or Acute Respiratory Distress Syndrome. *Respiration*, [Epub ahead of print] (2013)
5. Ito K, Shimizu N, Watanabe K, Saito T, Yoshioka Y, Sakane E, Tsunemine H, Akasaka H, Kodaka T, Takahashi T: Analysis of viral infection by multiplex polymerase chain reaction assays in patients with liver dysfunction. *Internal Medicine.* 52(2):201-11 (2013)

Immunology

1. Staffs and Students

Professor	Takeshi TSUBATA, M.D., Ph.D.	
Associate Professor	Takahiro ADACHI, Ph.D.	
Assistant Professor	Mitsuhiro SUZUKI, Ph.D.	
Assistant Professor	Naoko MATSUBARA,	Miduo XU,
	Chizuru AKATSU,	
Lecturer	Ji-Yang WANG	
Researcher	Soha Gomaa Ramadan Abdel SALAM	
Technician	Yukie KURUSU,	Shigeko NAKANO,
	Haruka MIYAKE,	Ai BEPPU
Secretary	Hiroko TAKAHASHI	
Graduate Student	Miao TANG,	Toshitaro TAKATA,
	Aslam MOHAMMAD,	Ayse Ucar KONUSKAN,
	Sumiyo EZAKI,	Xuyang JIAO
Research Student	Nazim MEDZHIDOV	
Undergraduate Student	Mayo YOSHIOKA	

2. Purpose of Education

Lecture course on immunology at the master course aims at giving the students the basic ideas how immune system recognize and respond to the antigens, and how immune system efficiently remove pathogens without responding to self-antigens and environmental antigens. In the lecture course in bioscience at the doctor course, lectures on immune responses are given so that the students are introduced with the current topics in the field of humoral immune responses. Research projects in both master and doctor courses aims at training the students to acquire basic research techniques on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

3. Research projects

The nature of immune responses depends on whether they respond to protein or non-protein antigens because T lymphocytes recognize only protein antigens. Normal immune system removes pathogens and cancer cells but does not respond to non-microbial foreign substances or self-antigens. Immune responses to non-microbial foreign substances and self-antigens cause allergy and autoimmune diseases, respectively. How the immune system distinguishes pathogens from non-microbial antigens and self-antigens is already clarified for protein antigens. However, little is known about such distinction for non-protein antigens. Immune responses to non-protein antigens play crucial roles in host defense against pathogens such as tuberculosis bacilli and meningococci, and autoimmune diseases such as lupus and immuno-neurological disorders. Thus, immune responses to non-protein antigens constitute a remaining frontier in immunology research. Followings are our research subjects.

- 1) Elucidation of the mechanisms for humoral immune responses to glycans, glyco-lipids and nucleic acids-related antigens.
- 2) Elucidation of the role of glycan signals in the regulation of humoral immune responses, and application of glycan signals to therapy.
- 3) Analysis of pathogenesis of lupus and immuno-neurological disorders.

4. Publications

[Original Article]

1. Shimoda, M., Bolduc, A., Takezaki, M., Amtani, Y., Huang, L., Nutt S. L., Kamanaka, M., Flavell, R. A., Mellor A. L., Tsubata, T. and Koni, P. (2013): Constitutively CD40-activated B cells regulate CD8 T cell inflammatory response by IL-10 induction. *J. Immunol.* 190: 3189-3196.
2. Xu, M., Hou, R., Sato-Hayashizaki, A., Man, R., Zhu, C., Wakabayashi, C., Hirose, S., Adachi, T. and Tsubata, T. (2013): *CD72* is a modifier gene that regulates *Fas*^{lpr}-induced autoimmune disease. *J. Immunol.* 190: 5436-5445.
3. Aslam, M., Kishi, Y. and Tsubata, T. (2013): Excess CD40L does not rescue anti-DNA B cells from clonal anergy. *F1000 Research* 2:218.

4. Naito-Matsui, Y., Takada, S., Kano, Y., Iyoda, T., Sugai, M, Shimizu, A., Inaba, K., Nitschke, L., Tsubata, T., Oka, S., Kozutsumi, Y. and Takematsu, H. (2014): Functional evaluation of activation-dependent alterations in the sialoglycan composition of T cells. *J. Biol. Chem.* 289: 1564-1579.

Pediatrics and Developmental Biology

1. Staffs and Students

Professor	Shuki MIZUTANI	
Associate Professor	Tomohiro MORIO	
Assistant Professor	Masatoshi TAKAGI,	Mitsunori NISHIYAMA (~June),
	Kenichi KASHIMADA (July~)	
Project Assistant Professor	Yaeko MOTOYOSHI,	Yuji SUGAWARA,
	Daisuke TOMIZAWA,	Kenichi KASHIMADA (~June)
	Manabu SUGIE,	Taku ISHII,
	Tomohiro UDAGAWA (~March)	
	(April~) Yuki AOKI,	Eriko TANAKA,
	Ai KATAOKA,	Mamiko HOTATE,
	Atsuko TAKI (December~)	
Graduate Students	Norimasa IHARA,	Susumu HOSOKAWA,
	Setuko KANEKO,	Kei TAKASAWA,
	Noriko MITSUIKI,	Takahiro KAMIYA,
	Tetsuro NAGASAWA,	Keisuke NAKAJIMA,
	Yohei MATSUBARA,	Akifumi ENDO,
	Keisuke TANAKA,	Chikako MORIOKA,
	Rina NISHII,	Toshiaki ONO,
	Tomohiro UDAGAWA,	Rie KUMAKI,
	Miko SHIGENO,	Yuri UCHIDA,
	Eri ENDO,	Lin LIN,
	(~March) Kaori NAKATANI,	Yuko MATSUURA,
	Eriko TANAKA,	Yuki AOKI,
	Fumihiko TAKIZAWA	
Special Study Student	Sayaka OSADA,	Kensuke KOJIMA
Collaborator	Minoru ASADA (Department of Pharmacology, Nippon Medical School)	
	Hatsume UNO (Sony Life Science Laboratories)	
Medical Fellow	Konka BOKU	

Department of Pediatrics, Neonatal and Maternal Medicine

Professor	Shozaburo DOI	
Associate Professor	Kohsuke IMAI	
Junior Associate Professor	(~Mar) Shigeru TAKISHIMA,	
	(Apr~) Yoshichika MAEDA	

Department of Research for Regional Pediatrics (~March)

Professor	Masayuki Nagasawa	
Assistant Professor	Kengo Moriyama,	Tomohiro Watanabe,
	Teppei Ookawa	

2. Educational activities

Field of Education: Education for the 3rd and the first half of the 4th graders of Medical students was proposed 34 lectures on the basis of two big standpoints, child developments and pediatric diseases, by the staffs of Department of Pediatrics and Developmental Biology, Department of Pediatrics, Perinatal and Maternal Medicine, Department of Research for Regional Pediatrics, and the part-time lecturers. The field of totally 34 lectures is widely covered, for example, Hematology, Oncology, Immunology, Cardiology, Neurology, Endocrinology, Neonatology, Nephrology, Allergy, Pulmonology, Infection, and Social Medicine and so on. Opportunities of training in scientific research were provided for the elective latter half of three 4th graders during so-called project semester. The 5th graders were divided into the small groups, and started and continued for three months to learn the introduction of Clinical Clerkship, so-called Pre-clerkship, classified by organs. We were engaged in the organs of Blood, Chest (Heart) and Neuron shared with the another Departments. Then one month practice in pediatric clinical trainings was provided for the 5th to 6th graders among 13

months, where every student belonged to one of the professional clinical teams (Hematology/Oncology/Immunology, Cardiology, Neurology, Endocrinology, Neonatology and Nephrology) in the University Hospital or some affiliated hospitals (Tsuchiura Kyodo General Hospital, Kawaguchi municipal Medical Center or North Tokyo Social Insurance Hospital), and studied clinical practice as one of the team members. Another mission of this Department was to provide lecture courses on general pediatrics for the students of Dental and School of Health Science.

Junior clinical fellows who are in the training course of pediatric practice under the supervision of senior staffs were also expected to supervise these medical students. The style of clinical training was maintained and the 1st year trainee as well as the 2nd year trainee could choose the training in the pediatric ward for two months. On the other hand, the 2nd year trainee was in general engaged in the basic training for one month in the pediatric ward in some affiliated hospitals (Musashino Red Cross Hospital, Soka Municipal Hospital or North Tokyo Social Insurance Hospital). Depending on the individuals, they could select the advanced training at the pediatric ward in The University Hospital for two to eight months.

Strategy of Education

It is a goal of education for the 3rd and 4th graders (first half) of medical students to learn the whole picture of general pediatric diseases, and for the 4th graders (latter half, so-called project semester) to touch the basic research, get the fundamental way of thinking and skills of experiments. On the other hand, it is a goal for the 5th and 6th graders (so-called pre-Clerkship and Clinical Clerkship), to be in charge of each patient with pediatric staffs and experience the general steps under the clinical medicine, for example, the following steps how to interview the medical history, get the physical findings, plan the laboratory examinations, differentially diagnose by analyzing the personal data, describe the clinical records, and discuss about the treatment planning. Junior clinical trainees, previously started to train the pediatrics from the 2nd year, became to be able to elect the pediatric training for two months from the 1st year, actually however, the fellows who desired to optionally choose the pediatric training did not necessarily perform it because of too many applicants. The 2nd year junior clinical trainees were divided two groups. Those only required pediatric training for one month were generally planned to experience the common pediatric diseases in the affiliated hospitals. On the other hand, those electively selected pediatrics were basically planned to train almost in university hospitals together with at the affiliated hospitals for one month. Senior clinical trainees were rotated among in the university hospitals and chief affiliated hospitals, planned to experience all kinds of pediatric diseases related to oncology, cardiology, neurology, infections and immunology, endocrinology and metabolic diseases, neonatology, nephrology, pulmonology, digestive diseases, and genomics. Moreover, we educate the students of dentistry and health care sciences, who learn not only general pediatric diseases but the importance of pediatrics as playing roles of total coordination and mutual cooperation beyond specialty for children's care.

3. Research Subjects

The final goal of our research is to elucidate the molecular mechanisms of intractable diseases in children and to develop novel measures to cure the diseases. We are interested in a broad spectrum of subjects in life science field as shown below.

1. Stem cells and hierarchy of infantile leukemic cells
2. Molecular mechanism of aberrant T-cell differentiation and lymphoma development in the absence of ATM
3. Molecular mechanism of Purkinje cell loss in Ataxia telangiectasia
4. Novel roles of ATM in cellular differentiation
5. Ras associated ALPS like syndrome
6. Systematic search for responsible gene for a subset of common variable immunodeficiency
7. Gene hunting for radiosensitive-hyperIgM syndrome
8. Negative regulation of granulocyte activation and apoptosis by Tec family protein
9. Development of innovative techniques for cell therapy and gene therapy
10. Skin barrier and development of atopic dermatitis and of GI allergy
11. Glycobiologic approach for molecular pathogenesis of IgA nephropathy developed in WASP deficiency
12. Involvement of Notch signaling pathway in the process of glomerular sclerosis
13. Molecular mechanisms of primary pulmonary hypertension
14. Lung injury induced by cytokines/monocytes/granulocytes
15. Pathogenesis of periventricular leukomalacia (PVL) and broncho-pulmonary dysplasia (BPD); Development of novel therapy using mesenchymal stem cells for PVL and BPD.
16. Sox family protein in sex differentiation
17. Intrauterine stem cell transplantation for congenital disorders

18. Coagulopathy in hematopoietic cell transplantation and alteration in membrane protein expression in red blood cells

We have been collaborating with Institute of Cancer Research in London (Prof Mel Greaves), Istituto Nazionale Tumori (Dr. D. Delia), University of Queensland (Prof. Peter Koopman), Erasmus University (Prof. Jacques van Dongen), Yonsei University (Profs. H. Kim, and SK Lee), Sony Life Science Laboratories, Medical Research Institute at TMDU, National Institute for Longevity Sciences, National Research Institute for Child Health and Development, RIKEN Research Center for Allergy and Immunology, Kazusa DNA Research Institute, National Institute of Advanced Industry and Technology, Metropolitan Institute for Neuroscience, Juntendo University, and many other laboratories.

The research projects of each subspecialty group in the department are as follows.

●Hematology/Oncology/Immunology Group(Basic Research)

Our research focuses on the dissection of molecular basis of cancer development, DNA damage repair response and immune regulation. The main projects include the following.

- # Development of *in vitro* and *in vivo* leukemogenesis model that stemmed from defective tumor surveillance system.
- # Molecular pathogenesis of tumor development in ATM deficiency
- # Identification of stem cells of infantile leukemia using leukemic-cell transplanted NOG-SCID mice.
- # Lymphoproliferation and immune dysregulation in Ras associated ALPS like disorder (RALD)
- # Responsible gene hunting for CVID and for radiosensitive hyper IgM syndrome using next generation sequencing system
- # Negative regulation of activation and apoptosis of granulocytes
- # Application of protein transduction strategy for congenital gene defect
- # Development of adoptive immunotherapy for immune reconstitution after SCT
- # Development of innovative technique for quality control and cell profiling for processed cells used in regenerative medicine/cell therapy
- # Dielectric spectrum cytometer for analysis of membrane protein expression in RBC in association with post-transplant coagulopathy

Our aim in research focusing on elucidation of molecular pathogenesis and development of therapeutic approach for pediatric catastrophic disease. Our research area is located in the field of tumor development, DNA damage response and primary immunodeficiencies. Some of these research is tightly linked each other. The directions; from bench to clinic and clinic to bench is favorably utilized for research style. Nationwide survey for common variable immunodeficiency (CVID) is executing under the leadership of Dr. Morio, Through the analysis of patient samples using next generation sequencing technology, we have identified several rare disease causing gene mutations from a CVID patients, and pursuing characterization. We have established iPS cells from Ataxia Telangiectasia (A-T) patients. Characterization of etiology in A-T, and development of therapeutic approach is pursuing using this iPS cells. Clinical features and outcome of RAS associated ALPS like disease (RALD) is not characterized well. Similarity and difference between Juvenile myelomonocytic leukemia (JMML) is discussing. RALD is the disease that located on the cross road of on leukemia and immunodeficiency. We have revealed some of JMML is regressed spontaneously. Interestingly, these patients still carries RAS mutated clone, and exhibit autoimmune phenotype.

In the oncology field, we have reported that loss of ATM allele accelerate blastic crisis of chronic myelogenous leukemia (CML). We also have been analyzing the hierarchy of leukemic stem cell using NOG SCID mice collaborated with RIKEN. This research will be lead to identification of novel therapeutic approach for pediatric leukemia. More basically, we have identified that Atrm1, endonuclease, generate DNA double strand breaks after DNA replication fork arrest, and ATM modulate topoisomerase II alpha, which involves, DNA catenation in cell cycle G2 phase, function.

To improve quality of life in PID patient, internet based database is established based on the view from clinical side and patient's side by Dr. Imai.

In the clinical setting, viral infection is one of a critical factor that affect the outcome of hematopoietic stem cell transplantation. To overcome this disadvantage, we have been starting the generation of multi virus specific cytotoxic T cell.

●Cardiology Group

The basic research consecutively focused on the analysis of mechanism by which pulmonary hypertension (PH) advances, and the development of treatment on PH. We have been recently interested in the inflammation, as well as lots of investigators all over the world, associated with vascular remodeling in PH. We studied the role of dipeptidyl

peptidase-4(DPP-4) in PH. DPP-4 inhibitors (Alogliptin), which are new drugs for type 2 diabetes mellitus, have an important role for cardiovascular protection by its anti-inflammation effect. In vivo study, Alogliptin markedly improved the survival and pulmonary artery pressure of monocrotaline (MCT)-induced PH rats by improving medial hypertrophy. In vitro experiments, Alogliptin dependently inhibited proliferation of PSMCs stimulated with TGF-beta and also suppressed p-Erk 1/2 protein levels induced by TGF-beta. Therefore, DPP-4 inhibitor has potential as a new therapeutic tool for PH because DPP-4 is associated with the progression of PH by causing TGF-beta-induced inflammation. On the other hand, omega-3 fatty acids (FA) such as eicosapentaenoic acid (EPA) were reported to exert potent anti-inflammatory effects through G protein-coupled receptor 120 (GPR120). We investigated the role of EPA in PH. In vivo study, EPA markedly improved survival, PH and medial hypertrophy of small pulmonary arteries. In vitro study, EPA inhibited dose-dependently pulmonary arterial smooth muscle cells (PASMCS) proliferation stimulated with TGF-beta or FGF2. EPA also suppressed nuclear factor-kappa B p65 translocation into the nucleus in PASMCS. We elucidated that EPA had anti-inflammatory effects through GPR120 in PH. EPA has also potential as a new therapeutic tool for PH. Both results were presented in The 78th Annual Scientific Meeting of Japanese Circulation Society and American Heart Association 2014.

As the clinical research, we were engaged in four multi-center-associated clinical studies. All of them were related to The Japanese Society of Pediatric Cardiology and Cardiac Surgery. These themes were "Clinical backgrounds of Eisenmenger syndrome", "Research of screening and management strategy for Long QT syndrome", "Efficacy of school-based heart examination in early detection of idiopathic pulmonary arterial hypertension" and "Research for protection of RSV infection in patients with congenital heart disease by palivizumab (Genetical Recombination) in Japan". We were also engaged in "Research for social background of heart transplantation in children" in Grants-in Aid for Scientific Research of Ministry of Health, Labour and Welfare.

●Neurology Group

- 1) Mechanism of neurodegeneration and therapeutic approach in xeroderma pigmentosum
- 2) Role of oxidative stress in childhood neurodegenerative disease
- 3) Analysis of multiple malformation disorders with or without intellectual disability using techniques of molecular genetics and cytogenetics (e.g. micro-array CGH) and clinical dysmorphology
- 4) Derivation of neural stem cell via iPS cell from ataxia telangiectasia
- 5) Efficacy and safety of very-low-dose betamethasone therapy in ataxia telangiectasia

●Endocrinology Group

Currently, our research is focused on elucidating the molecular mechanisms of congenital endocrine disorder, especially in adrenal glands and in gonads. As an ultimate goal, we are looking at developing the treatment systems for the congenital endocrine diseases by using regenerative medicine.

Our ongoing projects are bellows

#1: Elucidating molecular mechanisms of sexual determination.

- a: Disorder of sex development (DSDs) are among the most common forms of congenital diseases, and often highly traumatic for the patients and their parents. By collaborating with P. Koopman's lab (IMB. The university of Queensland, Brisbane, Australia), we are investigating the molecular mechanisms of sex determination and gonadal development in mammals. Recent our research is focused on the molecular mechanisms of early ovarian development in mammals, especially the function of an ovarian specific transcription factor, FOXL2. In recent three years, we have discovered novel functions of FOXL2 in ovarian development, resulting in three publications on *Endocrinology* (2011) and *FASEB J* (2011, 2014). Further we are planning couples of projects, such as elucidating transcriptional regulatory mechanisms of the sex determining gene, Sry; analyzing the role of SOX family transcription factor, i.e. Sry, Sox8, Sox9, Sox10 in the testicular development.
- b: We are also collaborating with Hiroshi Asahara (Department of Systems Bio Medicine), and analyzing the phenotype of the knock out mice generated by TALEN-mediated editing of the mouse Y chromosome.
- c: A senior physician of our group is now working at VR. Harley's lab in Melbourne (Prince Henry's Institute), and investigating the molecular mechanisms of human DSDs. His recent work, a review of human DSDs, has been published on *Nature Reviews Endocrinology* (2013).

#2: Clinical and genetic analysis of congenital adrenal hyperplasia (CAH)

- a: Our senior physician is a director of the newborn mass screening of CAH (21-hydroxylase deficiency) in Tokyo, and a half of CAH neonates discovered by newborn screening in Tokyo are referred to our hospital, following up more than

forty patients. We collected and analysed precise clinical data of the patients, and discovered some novel clinical features of 21OHD. Those findings resulted in three manuscripts (two were published on E Journal [2011, 2013], and one is submitting.)

b: Genetic analysis and elucidating the molecular mechanisms of CAH is another our important project. 3β HSD deficiency (3β HSDD) is a rare type of CAH caused by disruption of steroidogenic enzyme, 3β HSD. 3β HSDD is a rare type of CAH with the prevalence of one per a million. Recently we have discovered two novel 3β HSD missense mutations from one 3β HSDD patient. With functional analyses of the mutations in vitro, we reported the patient on Clinical Endocrinology (2013).

●Nephrology Group

We are conducting research to elucidate the mechanism of renal tubular injury progression of pediatric nephrotic patients. Oxidative stress is analysed utilizing urine from patients and cultured proximal tubular cells after protein overload. We presented the outcome of the research at Annual meeting of American Society of Nephrology.

We continued the analyses of glomerular epithelial cells (podocytes) unknown function in cooperation with Juntendo University, and Division of Nephrology and Hypertension, Miller School of Medicine, University of Miami. Outcome of this study was presented at World Congress of Nephrology and International Pediatric Nephrology Association Congress.

Glycosylation deficiency of IgA in Wiskott-Aldrich syndrome patients accompanied IgA nephropathy was analysed in cooperation with National Institute of Advanced Industrial Science and Technology.

●Neonatology group

1) We are analyzing the expression of angiogenesis-related factors both in placenta and in umbilical vessels in complicated pregnancies.

2) We are investigating a novel therapy with umbilical cord blood derived mesenchymal stem cells for treating periventricular leukomalacia and chronic lung disease using intrauterine infection model.

●Allergy Group

To elucidate molecular mechanisms for food allergy such as against milk and egg is one of the main projects of our group. In the light of recent progress of immunology, we analyze the function of regulatory T cells which inhibit Th2 type immune response. We also define the roles of innate immune responses in host defense against foreign antigens entering skin and mucosal tissues. We are one of the research members on the epidemiological study of allergic disorder supported by a grant-in-aid from Ministry of Health, Labor and Welfare, Japan. In collaboration with the Japanese Society of Pediatric Allergy and Clinical Immunology, we conduct several clinical studies to refine pharmacologic therapy listed in the Japanese pediatric guideline for the treatment and management of asthma. We collaborate with pharmaceutical companies on the study of clinical efficacy of leukotriene antagonist. Clinical and epidemiological study on food allergy is another major field in our study. We conduct clinical studies of specific oral tolerance induction in food allergy in which the offending food is administered orally in order to achieve tolerance.

4. Clinical Services

●Hematology/Oncology/Immunology Group

Hematology/Oncology/Immunology Group treats children with hematological malignancies, hematological disorders, malignant solid tumors, and primary immunodeficiency diseases. Our team consists of 8 staffs, including 6 senior with diplomate of board of pediatrics, hematology, and/or pediatric hematology/oncology and 2 junior staffs. We offer a team-based high-quality and evidence-based clinical care for both inpatients and outpatients. Additionally, we are on our way to establish cooperative system for medical liaison with other professional facilities including St. Luke's International Hospital and Juntendo University Hospital; joint clinical conference has started in 2013, and trainee exchange program will start in 2014.

1. Participation in multi-center cooperative clinical research group: In collaboration with national co-operative clinical research group, such as the Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG), we offer our patients opportunities to participate in the latest clinical trials and contribute to establish both standard and novel therapies for childhood cancers and other non-malignant diseases.

2. Participation in industry-based clinical trials for drug approval: In 2013, we participated in two industry-based trials; IgPro20, a subcutaneous immunoglobulin product, and OP-01, an Erwinia L-asparaginase.

3. Hematopoietic stem cell transplantation (HSCT): In 2013, we performed HSCT for 11 cases; related bone marrow transplantation (BMT) (n=3), unrelated BMT (n=2), unrelated cord blood transplantation (n=4), and related peripheral blood stem cell transplantation (n=2). Our experience of HSCT exceeds 150 cases including more than 50 cases with primary immunodeficiency diseases, so far. We are also working on novel HSCT methods, such as transplantation with haplo-identical donor and killer inhibitory receptor (KIR) ligand mismatched donor, and use of reduced-intensity conditioning aiming for reduction of late effects in HSCT recipients.
4. Analysis of pathogenesis and establishment of clinical service for rare diseases: Our group have identified a novel disease, "RALD (RAS-associated lymphoproliferative disease)," from an infant with somatic *RAS* mutation who exhibited both JMML (juvenile myelomonocytic leukemia)-like and ALPS (autoimmune lymphoproliferative syndrome)-like clinical features, and continuing research for this disorder. Not only for RALD, but for ataxia telangiectasia (A-T) and common variable immunodeficiency (CVID), group members are working as chief organizer of nation-wide clinical research projects financially supported by the Ministry of Health, Labour and Welfare of Japan.
5. long-term follow-up for childhood cancer survivors (CSS): In cooperation with pediatric endocrinologists, CLS (child life specialist) and psychotherapists, we are taking care of cancer survivors and supporting their quality of life.

●Cardiology Group

The University Hospital has been certified as a training institute to produce the expert in pediatric cardiology by Japanese Society of Pediatric Cardiology and Cardiac Surgery. There are three pediatric cardiology experts (Doi S, Nishiyama M, Ishii T), one general pediatric cardiologists (Maeda Y) and one senior resident in The University Hospital who were mainly engaged in the diagnosis and treatment for every kinds of heart disease patients both in the pediatric ward and the field for pediatric outpatients. On cardiac catheterization performed in every Friday, one postgraduate (Hosokawa S) was also joined to back up the procedures.

In-patients were 102 and chiefly introduced from the affiliated hospitals and out-patients field in The University Hospital. The diseases we dealt with were 42 congenital heart diseases, acquired heart diseases such as 17 Kawasaki diseases, 20 pulmonary hypertensions and 7 cardiomyopathies, and 12 cardiac arrhythmias. In 57 cardiac catheterizations per year were performed including catheter ablation for 3 cardiac arrhythmias. All the patients who needed surgical operation have been transferred to The Sakakibara Heart Institute until the last year. However, on January, surgical operation in children was restarted in The University Hospital after about 30 years blank. One ASD and one VSD patients were radically operated in this year.

The treatment strategy for Kawasaki Diseases (KD) was severity-dependent and active usage of glucocorticoids, urinastatin, infliximab and cyclosporine to protect the complications of coronary aneurysms. PH patients were admitted for diagnosis, evaluation of treatments or decision of treatment strategy. The most important thing is early diagnosis and early initiation of treatment for PH, which is nominated for difficult-cured and progressive disease. Therefore, we decide to positively treat by receiving up-front combination therapy (uCT) with three kinds of disease targeted drugs and inducing continuous venous infusion of epoprostenol. Four patients were treated with uCT and one patient was induced epoprostenol. As the result, we succeeded in decreasing pulmonary arterial pressure as well as increase in cardiac output and decrease in pulmonary vascular resistance. Among patients with cardiac arrhythmia, prolonged QT elongation (PQT) was examined to be diagnosed, on drug provocation test, exercise-tolerated ECG, face drop in cold water examination or gene mutation evaluation.

Out-patients for pediatric cardiology were up to 1,800 patients with the 1,500 examinations of echocardiogram. Moreover, Holter 24-hours ECG monitoring examination was performed on 102 patients, and Treadmill exercise tolerance examination were also performed on 89 patients. We have participated in the school heart screening program of Tokyo Metropolitan Institute for Preventive Medicine and Tokyo Medical Association, and checked 9,000 students ECG records in elementary, junior high and senior high schools. The students who were needed the third stage checkup visited The University Hospital, examined at out- or in-patients fields and finally decided the exercise restriction level in school life.

●Neurology Group

Child neurology group provides highly specialized diagnostic approach and medical care for neurological disorders such as epilepsy, neuromuscular disorders, infection of nervous system, neurodegenerative diseases and genetic syndromes. In particular, we provide therapeutic approach of xeroderma pigmentosum by using of clinicopathological analysis, and perform molecular genetic testing for multiple congenital malformation disorders with or without intellectual disability. In addition, in cooperation with the department of neurosurgery, we evaluate the indication for surgical treatment and then perform surgical operation such as focal brain resection to the patient of intractable epilepsy.

●Endocrinology Group

We provide highly specific diagnostic approach and therapy for pediatric endocrine disorders, such as growth retardation, hypogonadism, thyroid diseases, disorder of sex development, disorder of Ca-P-PTH metabolism, Type1 diabetes mellitus. In collaborating with the satellite hospitals, we are following more than a thousand patients in outpatients, and in our university hospital, the number of hospitalized children of endocrine disorders hit more than 100 yearly.

Senior physician of our group is an adviser of Tokyo Health Service Association, and directing the newborn screening of congenital adrenal hyperplasia in Tokyo.

Among many pediatric endocrine disorders, we are making great effort for the disorders of adrenal gland and sex development, and looking at establishing the clinical center for those patients by collaborating with pediatric-urologist and other co-medical staffs.

Type1 DM is another disease we put a great effort. We manage the Type 1 DM patients' association (Wakamatsu-kai) and organize the summer camp every year. The camp is consisted of more than a hundred participants and provides the valuable educational opportunities for the patients, the medical staffs and the medical students.

●Nephrology Group

Nephrology Group provides diagnosis and treatment for patients with acute and chronic glomerular diseases, nephrotic syndrome, and congenital abnormality of kidney and urinary tract. We performed kidney biopsy, renogram, MRU, ultrasonography etc. for above patients. We also participated actively in urinary analysis screening for school children.

In Medical Hospital of Tokyo Medical and Dental University, renal biopsy was performed to more than 40 patients. Congenital nephrotic syndrome, refractory nephrotic syndrome and treatment resistant IgA nephropathy was the main diseases we treated. We also performed acute hemodialysis treatment for two low body weight patients (7kg and 13kg) in cooperation with department of blood purification. We presented case reports of our patients at the meeting of Japanese society of nephrology, The Japanese society for pediatric nephrology, and Japanese society of pediatric renal failure.

We participate in multi-institutional joint research of refractory nephrotic syndrome operated by Japanese Study Group of Kidney Disease in Children. We take part in analysis of efficacy of methyl predonisolone pulse therapy in treatment of steroid resistant nephrotic syndrome patients. Clinical trial to examine the efficacy and safety of eculizumab for treatment of atypical hemolytic uremic syndrome patient was continued and completed this year. Eculizumab approved as a treatment for patients with atypical hemolytic uremic syndrome in Japan, which is a big improvement for treatment of this high mortality disease.

Group conference was held on 4th Thursday every month to discuss the rare cases and for presentation of research progress by graduate students. We also held conference with pediatric nephrologists in other institutions regularly and discussed about better treatment for serious kidney diseases. Some members of our group received training at National Research Institute for Child Health and Development to improve their skills.

●Neonatology group

- 1) Our NICU (Neonatal Intensive Care Unit) was established on April 2012 with 6 beds, and provide intensive care for preterm infants (> 30 weeks of gestation and/or >1000g of birth weights). We also take care of critically ill newborns, those with congenital heart disease, hematological disorder, etc., in cooperation with other pediatric subspecialty groups.
- 2) As a designated Perinatal Cooperation Hospital in Tokyo, we accept newborn patients from various areas in Tokyo.

●Allergy Group

Allergy Group provides diagnostic and medical care for patients with allergic diseases such as asthma, food allergy, atopic dermatitis mainly at outpatient clinic.

5. Publications

Original articles

1. Hosokawa S, Haraguchi G, Sasaki A, Arai H, Muto S, Itai A, Doi S, Isobe M, Pathophysiological roles of nuclear factor kappa B (NF-kB) in pulmonary arterial hypertension: effects of synthetic selective NF-kB inhibitor IMD-0354. *Cardiovasc Res.* 2013; 99(1): 35-43.
2. Kamae C, Nakagawa N, Sato H, Honma K, Mitsui N, Ohara O, Kanegane H, Pasic S, Pan-Hammarström Q, van Zelm MC, Morio T, Imai K, Nonoyama S. Common variable immunodeficiency classification by quantifying T-cell

- receptor and immunoglobulin κ -deleting recombination excision circles. *J Allergy Clin Immunol*. 2013; 131(5):1437-40.e5.
3. Nakajima K, Hayashi M. Immunohistochemical analysis of brainstem functions in autopsy cases of Fukuyama congenital muscular dystrophy. *No To Hattatu*. 2013;45:436-9.
 4. Matsubara Y, Ono M, Miyai K, Takizawa F, Takasawa K, Onishi T, Kashimada K, Mizutani S. Longitudinal analysis of growth and body composition of Japanese 21-OHD patients in childhood. *Endocr J*. 2013;60(2):149-54.
 5. Takasawa K, Ono M, Hijikata A, Matsubara Y, Katsumata N, Takagi M, Morio T, Ohara O, Kashimada K, Mizutani S. Two novel *HSD3B2* missense mutations with diverse residual enzymatic activities for $\Delta 5$ -steroids. *Clin Endocrinol (Oxf)*. 2013 Dec 27.
 6. Takizawa F, Mizutani S, Ogawa Y, Sawada N. Glucose-independent persistence of PAI-1 gene expression and H3K4 tri-methylation in type 1 diabetic mouse endothelium: implication in metabolic memory. *Biochem Biophys Res Commun*. 2013;433(1):66-72
 7. Iwasaki K, Komaki M, Yokoyama N, Tanaka Y, Taki A, Kimura Y, Takeda M, Oda S, Izumi Y, Morita I. Periodontal ligament stem cells possess the characteristics of pericytes. *J Periodontol*. 2013;84:1425-33.
 8. Udagawa T, Motoyoshi Y, Matsumura Y, Takei A, Ariji S, Ito E, Chiga M, Nagasawa M, Morio T, Mizutani S. Effect of eculizumab and recombinant human soluble thrombomodulin combination therapy in a 7-year-old girl with atypical hemolytic uremic syndrome due to anti-factor H autoantibodies. *CEN Case Reports* 2013 Sep
 9. Yamamoto A, Morio T, Kumaki E, Yamazaki H, Iwai H, Kubota T, Miyasaka N, Kohsaka H. A Case of Pyogenic Sterile Arthritis, Pyoderma Gangrenosum, and Acne (PAPA) Syndrome Accompanied by Nephrosclerosis, Splenomegaly and Intestinal Lesions. *J Genet Syndr Gene Ther*. 2013; 4:9.
 10. Nagasawa M, Ohkawa T, Endo A, Mitsui N, Ono T, Aoki Y, Isoda T, Tomizawa D, Takagi M, Kajiwarra M, Morio T, Mizutani S. Early coagulation disorder after allogeneic stem cell transplantation is a strong prognostic factor for transplantation-related mortality, and intervention with recombinant human thrombomodulin improves the outcome: a single-center experience. *Int J Hematol*. 2013; 98:533-42.
 11. Kumaki S, Sasahara Y, Kamachi Y, Muramatsu H, Morio T, Goi K, Sugita K, Urabe T, Takada H, Kojima S, Tsuchiya S, Hara T. B-cell function after unrelated umbilical cord blood transplantation using a minimal-intensity conditioning regimen in patients with X-SCID. *Int J Hematol*. 2013; 98:355-60.
 12. Machida S, Tomizawa D, Tamaichi H, Okawa T, Endo A, Imai K, Nagasawa M, Morio T, Mizutani S, Takagi M. Successful Treatment of Diffuse Large B-Cell Lymphoma in a Patient With Ataxia Telangiectasia Using Rituximab. *J Pediatr Hematol Oncol*. 2013; 35:482-5.
 13. Sugita S, Ogawa M, Shimizu N, Morio T, Ohguro N, Nakai K, Maruyama K, Nagata K, Takeda A, Usui Y, Sonoda K, Takeuchi M, Mochizuki M. Use of a comprehensive polymerase chain reaction system for diagnosis of ocular infectious diseases. *Ophthalmology*. 2013; 120:1761-8.
 14. Unno J, Takagi M, Piao J, Sugimoto M, Honda F, Maeda D, Masutani M, Kiyono T, Watanabe F, Morio T, Teraoka H, Mizutani S. Artemis-dependent DNA double-strand break formation at stalled replication forks. *Cancer Sci*. 2013; 104:703-10.
 15. Wada T, Muraoka M, Toma T, Imai T, Shigemura T, Agematsu K, Haraguchi K, Moriuchi H, Oh-Ishi T, Kitoh T, Ohara O, Morio T, Yachie A. Rapid Detection of Intracellular p47phox and p67phox by Flow Cytometry; Useful Screening Tests for Chronic Granulomatous Disease. *J Clin Immunol*. 2013; 33:857-64.
 16. Isoda T, Mitsui N, Ohkawa T, Kaneko S, Endo A, Ono T, Aoki Y, Tomizawa D, Kajiwarra M, Araki S, Nagasawa M, Morio T, Takagi M, Mizutani S. Irreversible Leukoencephalopathy After Reduced-intensity Stem Cell Transplantation in a Dyskeratosis Congenita Patient With *TINF2* Mutation. *J Pediatr Hematol Oncol*. 2013; 35:e178-82.
 17. Shimizu M, Kanegane H, Wada T, Motoyoshi Y, Morio T, Candotti F, Yachie A. Aberrant glycosylation of IgA in Wiskott-Aldrich syndrome and X-linked thrombocytopenia. *J Allergy Clin Immunol*. 2013; 131:587-90.
 18. Yoshimi A, Kamachi Y, Imai K, Watanabe N, Nakadate H, Kanazawa T, Ozono S, Kobayashi R, Yoshida M, Kobayashi C, Hama A, Muramatsu H, Sasahara Y, Jakob M, Morio T, Ehl S, Manabe A, Niemeyer C, Kojima S. Wiskott-Aldrich syndrome presenting with a clinical picture mimicking juvenile myelomonocytic leukaemia. *Pediatr Blood Cancer*. 2013; 60:836-41.
 19. Miyabe C, Miyabe Y, Miura NN, Takahashi K, Terashima Y, Morio T, Yamagata N, Ohno N, Shudo K, Suzuki J-I, Isobe M, Matsuhima K, Tsuboi R, Miyasaka N, and Nanki T. Am80, a retinoic acid receptor agonist, ameliorates murine vasculitis through the suppression of neutrophil migration and activation. *Arthritis Rheumatism*. 2013; 65:503-12.

20. Kamae C, Nakagawa N, Sato H, Honma K, Mitsui N, Ohara O, Kanegane H, Pasic S, Pan-Hammerstrom Q, van Zelm MC, Morio T, Imai K, Nonoyama S. Classification of common variable immunodeficiency by quantification of T cell receptor and Ig kappa-deleting recombination excision circles. *J Allerg Clin Immunol*. 2013; 131:1437-40.
21. Park TY, Kim SH, Shin YC, Lee NH, Lee RK, Shim JH, Glimcher LH, Mook-Jung I, Cheong E, Kim WK, Honda F, Morio T, Lim JS, Lee SK. Amelioration of neurodegenerative diseases by cell death-induced cytoplasmic delivery of humanin. *J Control Release*. 2013; 166:307-315.
22. Kawasaki Y, Toyoda H, Otsuki S, Iwasa T, Iwamoto S, Azuma E, Itoh-Habe N, Wada H, Fujimura Y, Morio T, Imai K, Mitsui N, Ohara O, Komada Y. A novel Wiskott-Aldrich syndrome protein mutation in an infant with thrombotic thrombocytopenic purpura. *Eur J Haematol*. 2013; 290:164-8.
23. Kobayashi Z, Akaza M, Numasawa Y, Ishihara S, Tomimitsu H, Nakamichi K, Saijo M, Morio T, Shimizu N, Sanjo N, Shintani S, Mizusawa H. Failure of mefloquine therapy in progressive multifocal leukoencephalopathy: report of two Japanese patients without human immunodeficiency virus infection. *J Neurol Sci*. 2013; 324:190-4.
24. Piao J, Sakurai N, Iwamoto S, Nishioka J, Nakatani K, Komada Y, Mizutani S, Takagi M. Functional studies of a novel germline p53 splicing mutation identified in a patient with Li-Fraumeni-like syndrome. *Mol Carcinog*. 2013; 52(10): 770-6.
25. Takagi M, Piao J, Lin L, Kawaguchi H, Imai C, Ogawa A, Watanabe A, Akiyama K, Kobayashi C, Mori M, Ko K, Sugimoto M, Mizutani S. Autoimmunity and persistent RAS-mutated clones long after the spontaneous regression of JMML. *Leukemia*. 2013; 27(9): 1926-8.
26. Takagi M, Sato M, Piao J, Miyamoto S, Isoda T, Kitagawa M, Honda H, Mizutani S. ATM-dependent DNA damage-response pathway as a determinant in chronic myelogenous leukemia. *DNA Repair (Amst)*. 2013; 12(7): 500-7.
27. Tamaichi H, Sato M, Porter AC, Shimizu T, Mizutani S, Takagi M. Ataxia telangiectasia mutated-dependent regulation of topoisomerase II alpha expression and sensitivity to topoisomerase II inhibitor. *Cancer Sci*. 2013; 104(2): 178-84.
28. Yasui N, Koh K, Kato M, Park MJ, Tomizawa D, Oshima K, Uchisaka N, Gocho Y, Arakawa A, Seki M, Oguma E, Kishimoto H, Watanabe S, Kikuchi A, Hanada R. Kasabach-Merritt Phenomenon: a Report of 11 Cases from a Single Institution. *J Pediatr Hematol Oncol*. 2013; 35(7): 554-8
29. Tomizawa D, Tawa A, Watanabe T, Moriya Saito A, Kudo K, Taga T, Iwamoto S, Shimada A, Terui K, Moritake H, Kinoshita A, Takahashi H, Nakayama H, Koh K, Kigasawa H, Kosaka Y, Miyachi H, Horibe K, Nakahata T, Adachi S. Excess treatment reduction including anthracyclines results in higher incidence of relapse in core binding factor acute myeloid leukemia in children. *Leukemia*. 2013; 27(12): 2413-6
30. Coenen EA, Zwaan CM, Reinhardt D, Harrison CJ, Haas OA, de Haas V, Mihál V, De Moerloose B, Jeison M, Rubnitz JE, Tomizawa D, Johnston D, Alonzo TA, Hasle H, Auvrignon A, Dworzak M, Pession A, van der Velden VH, Swansbury J, Wong KF, Terui K, Savasan S, Winstanley M, Vaitekeviciene G, Zimmermann M, Pieters R, van den Heuvel-Eibrink MM. Pediatric Acute Myeloid Leukemia with t(8;16)(p11;p13): a distinct clinical and biological entity, a collaborative study by the International-Berlin-Frankfurt-Münster AML-study group. *Blood*. 2013; 122(15): 2704-13
31. Tomizawa D, Tawa A, Watanabe T, Moriya Saito A, Kudo K, Taga T, Iwamoto S, Shimada A, Terui K, Moritake H, Kinoshita A, Takahashi H, Nakayama H, Kiyokawa N, Isoyama K, Mizutani S, Hara J, Horibe K, Nakahata T, Adachi S. Appropriate dose reduction in induction therapy is essential for the treatment of infants with acute myeloid leukemia: A report from the Japanese Pediatric Leukemia/Lymphoma Study Group. *Int J Hematol*. 2013; 98(5): 578-588
32. Kato M, Takahashi Y, Tomizawa D, Okamoto Y, Inagaki J, Koh K, Ogawa A, Okada K, Cho Y, Takita J, Goto H, Sakamaki H, Yabe H, Kawa K, Suzuki R, Kudo K, Kato K. Comparison of intravenous with oral busulfan in allogeneic hematopoietic stem cell transplantation with myeloablative conditioning regimens for pediatric acute leukemia. *Biol Blood Marrow Transplant* 2013; 19(12): 1690-4
33. Saito Y, Yuki H, Kuratani M, Hashizume Y, Takagi S, Honma T, Tanaka A, Shirouzu M, Mikuni J, Handa N, Ogahara I, Sone A, Najima Y, Tomabechi Y, Wakiyama M, Uchida N, Tomizawa-Murasawa M, Kaneko A, Tanaka S, Suzuki N, Kajita H, Aoki Y, Ohara O, Shultz LD., Fukami T, Goto T, Taniguchi S, Yokoyama S, Ishikawa F. A Pyrrolo-Pyrimidine Derivative Targets Human Primary AML Stem Cells in Vivo. *Sci Transl Med*. 2013;5(181);181ra52

Review Articles

1. Nakajima K, Masaharu H, Miyata R, Tanuma N, Mizutani S. Glial fibrillary acidic protein and S100 calcium-binding

protein B in the cerebrospinal fluid of children with acute neurological disorders. *Glial Cells* :chap5,107-116, Nova Science Publishers,Inc.2013

2. Ono M, Harley VR. Disorders of sex development: new genes, new concepts. *Nat Rev Endocrinol*. 2013 Feb;9(2):79-91
3. Mizutani S, Takagi M. XCIND as a genetic disease of X-irradiation hypersensitivity and cancer susceptibility. *Int J Hematol*. 2013; 97: 37-42

Medicine and Rheumatology

1. Staffs and Students (April, 2013)

Professor emeritus	Nobuyuki MIYASAKA	
Professor	Hitoshi KOHSAKA	
	Masayoshi HARIGAI(1)	
	Tetsuo KUBOTA(2)	
	Kazuki TAKADA(3)	
Associate Professor	Ryuji KOIKE(4)	
Junior Associate Professor	Hideyuki IWAI	
Assistant Professor	Makoto Soejima,	Akito TAKAMURA,
	Tetsuya SAITO	Ryoko SAKAI(1),
	Hayato YAMAZAKI(1),	Hisanori HASEGAWA,
	Waka YOKOYAMA	
Visiting Lecturer	Rieko TSUBATA,	Hiroyuki HAGIYAMA,
	Yoshiki NONOMURA,	Kenji NAGASAKA,
	Fumihito SUZUKI,	Kayoko KANEKO,
	Peter Y. Shane,	Toru KINO,
	Michi TANAKA	
Graduate Student	Tadashi HOSOYA,	Naoki KIMURA,
	Yusuke MATSUO,	Yoko Yoshihashi,
	Shin FUKUDA,	Kenchi TAKENAKA,
	Natsuka UMEZAWA,	Fumio HIRANO,
	Masako HONGO,	Sayoko HARADA
Resident Physician	Takeshi KUSUDA,	Takumi MATSUMOTO,
	Hirokazu SASAKI,	Fumiaki KONODO,
	Masako INAGAKI	
Office Administrator	Rie FUJIME,	Kaori KONNO,
	Tomoko TAKAHASHI(1),	Marie YAJIMA(1)
Technical Staff	Yuki ISHIGE,	Hidemi KASAHARA

(1) Department of Pharmacovigilance, (2) Health care sciences,
 (3) Clinical Clerkship Working Group, (4) Clinical Research Center

2. Purpose of 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. Research Subjects

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

- 1) Development of new therapeutics for the treatment of rheumatoid arthritis targeting cell cycle regulators, inflammatory molecules and synovial fibroblasts.
- 2) Investigation of mechanism and development of new therapeutics for the treatment of polymyositis.
- 3) Analysis of the roles of chemokine and bioactive lipid on the pathogenesis of rheumatic diseases.
- 4) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies.

4. Clinical Services

We have provided care to a large number of patients with diverse rheumatic diseases with 29,393 clinic visits and 301 hospital admissions in 2013. 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 rheumatoid arthritis patients through the conduct of various

pharmacovigilance studies.

5. Publications

Original Article

1. Tanaka Y, Yamamoto K, Takeuchi T, Yamanaka H, Ishiguro N, Eguchi K, et al. Long-term efficacy and safety of certolizumab pegol in Japanese rheumatoid arthritis patients who could not receive methotrexate: 52-week results from an open-label extension of the HIKARI study. *Mod Rheumatol*. 2013 Dec 29.
2. Cho SK, Sakai R, Nanki T, Koike R, Watanabe K, Yamazaki H, et al. A comparison of incidence and risk factors for serious adverse events in rheumatoid arthritis patients with etanercept or adalimumab in Korea and Japan. *Mod Rheumatol*. 2013 Dec 9.
3. Yamamoto K, Takeuchi T, Yamanaka H, Ishiguro N, Tanaka Y, Eguchi K, et al. Efficacy and safety of certolizumab pegol plus methotrexate in Japanese rheumatoid arthritis patients with an inadequate response to methotrexate: the J-RAPID randomized, placebo-controlled trial. *Mod Rheumatol*. 2013 Dec 9.
4. Koike T, Harigai M, Ishiguro N, Inokuma S, Takei S, Takeuchi T, et al. Safety and effectiveness of adalimumab in Japanese rheumatoid arthritis patients: Postmarketing surveillance report of 7740 patients. *Mod Rheumatol*. 2013 Nov 6.
5. Mizoguchi F, Takada K, Ishikawa K, Mizusawa H, Kohsaka H, Miyasaka N. A case of dermatomyositis with rhabdomyolysis, rescued by intravenous immunoglobulin. *Mod Rheumatol*. 2013 Nov 5.
6. Shimogaki S, Ito S, Komatsu S, Koike R, Miyasaka N, Umezawa K, et al. Inhibition of the NF-kappaB pathway as a candidate therapeutic strategy for cryopyrin-associated periodic syndrome. *Mod Rheumatol*. 2013 Nov 4.
7. Ohta A, Nagai M, Nishina M, Tomimitsu H, Kohsaka H. Prevalence and incidence of polymyositis and dermatomyositis in Japan. *Mod Rheumatol*. 2013 Oct 21.
8. Miyabe C, Okubo Y, Maeda T, Tsuboi R, Mitsunashi Y. Tiny disseminated angiomas from childhood. *Eur J Dermatol*. 2013 Sep-Oct;23(5):718-9.
9. Kihara M, Sugihara T, Hosoya T, Miyasaka N. Clinical significance of complement as a biomarker of disease activity in 4 cases of IgG4-related disease with retroperitoneal fibrosis. *Clin Exp Rheumatol*. 2013 Nov-Dec;31(6):947-9.
10. Mizoguchi F, Murakami Y, Saito T, Miyasaka N, Kohsaka H. miR-31 controls osteoclast formation and bone resorption by targeting RhoA. *Arthritis Res Ther*. 2013;15(5):R102.
11. Kawasaki A, Inoue N, Ajimi C, Sada KE, Kobayashi S, Yamada H, et al. Association of IRF5 polymorphism with MPO-ANCA-positive vasculitis in a Japanese population. *Genes Immun*. 2013 Dec;14(8):527-9.
12. Takayasu A, Miyabe Y, Yokoyama W, Kaneko K, Fukuda S, Miyasaka N, et al. CCL18 activates fibroblast-like synoviocytes in patients with rheumatoid arthritis. *J Rheumatol*. [Letter]. 2013 Jun;40(6):1026-8.
13. Miyabe Y, Miyabe C, Iwai Y, Takayasu A, Fukuda S, Yokoyama W, et al. Necessity of lysophosphatidic acid receptor 1 for development of arthritis. *Arthritis Rheum*. [Research Support, Non-U.S. Gov't]. 2013 Aug;65(8):2037-47.
14. Hasegawa H, Mizoguchi F, Kohsaka H, Miyasaka N. Systemic lupus erythematosus with cytophagic histiocytic panniculitis successfully treated with high-dose glucocorticoids and cyclosporine A. *Lupus*. 2013 Mar;22(3):316-9.
15. Murakami M, Harada M, Kamimura D, Ogura H, Okuyama Y, Kumai N, et al. Disease-association analysis of an inflammation-related feedback loop. *Cell Rep*. 2013 Mar 28;3(3):946-59.
16. Nanki T, Onoue I, Nagasaka K, Takayasu A, Ebisawa M, Hosoya T, et al. Suppression of elevations in serum C reactive protein levels by anti-IL-6 autoantibodies in two patients with severe bacterial infections. *Ann Rheum Dis*. 2013 Jun;72(6):1100-2.
17. Uto-Konomi A, McKibben B, Wirtz J, Sato Y, Takano A, Nanki T, et al. CXCR7 agonists inhibit the function of CXCL12 by down-regulation of CXCR4. *Biochem Biophys Res Commun*. 2013 Feb 22;431(4):772-6.
18. Matsuo Y, Mizoguchi F, Kohsaka H, Ito E, Eishi Y, Miyasaka N. Tocilizumab-induced immune complex glomerulonephritis in a patient with rheumatoid arthritis. *Rheumatology (Oxford)*. 2013 Jul;52(7):1341-3.
19. Tanaka Y, Kawai S, Takeuchi T, Yamamoto K, Miyasaka N. Prevention of joint destruction by tacrolimus in patients with early rheumatoid arthritis: a post hoc analysis of a double-blind, randomized, placebo-controlled study. *Mod Rheumatol*. 2013 Nov;23(6):1045-52.
20. Watanabe K, Sakai R, Koike R, Sakai F, Sugiyama H, Tanaka M, et al. Clinical characteristics and risk factors for *Pneumocystis jirovecii* pneumonia in patients with rheumatoid arthritis receiving adalimumab: a retrospective review and case-control study of 17 patients. *Mod Rheumatol*. 2013 Nov;23(6):1085-93.
21. Miyabe C, Miyabe Y, Miura NN, Takahashi K, Terashima Y, Toda E, et al. Am80, a retinoic acid receptor agonist, ameliorates murine vasculitis through the suppression of neutrophil migration and activation. *Arthritis Rheum*. 2013

Feb;65(2):503-12.

22. Takeuchi T, Miyasaka N, Zang C, Alvarez D, Fletcher T, Wajdula J, et al. A phase 3 randomized, double-blind, multicenter comparative study evaluating the effect of etanercept versus methotrexate on radiographic outcomes, disease activity, and safety in Japanese subjects with active rheumatoid arthritis. *Mod Rheumatol*. 2013 Jul;23(4):623-33.
23. Takeuchi T, Harigai M, Tanaka Y, Yamanaka H, Ishiguro N, Yamamoto K, et al. Golimumab monotherapy in Japanese patients with active rheumatoid arthritis despite prior treatment with disease-modifying antirheumatic drugs: results of the phase 2/3, multicentre, randomised, double-blind, placebo-controlled GO-MONO study through 24 weeks. *Ann Rheum Dis. Research Support, Non-U.S. Gov't*. 2013 Sep 1;72(9):1488-95.
24. Takenaka K, Komiya Y, Ota M, Yamazaki H, Nagasaka K. A dose-escalation regimen of trimethoprim-sulfamethoxazole is tolerable for prophylaxis against *Pneumocystis jiroveci* pneumonia in rheumatic diseases. *Mod Rheumatol*. 2013 Jul;23(4):752-8.
25. Ohta A, Nagai M, Nishina M, Tomimitsu H, Kohsaka H. Age at onset and gender distribution of systemic lupus erythematosus, polymyositis/dermatomyositis, and systemic sclerosis in Japan. *Mod Rheumatol*. 2013 Jul;23(4):759-64.
26. Nakasato M, Kohsaka H, Mizutani T, Watanabe G, Taya K, Nagaoka K. Pregnancy-associated plasma protein (PAPP)-A expressed in the mammary gland controls epithelial cell proliferation and differentiation. *Endocrine*. 2013 Apr;43(2):387-93.
27. Matsubara T, Yamana S, Tohma S, Takeuchi T, Kondo H, Kohsaka H, et al. Tolerability and efficacy of abatacept in Japanese patients with rheumatoid arthritis: a phase I study. *Mod Rheumatol*. 2013 Jul;23(4):634-45.
28. Takeuchi T, Matsubara T, Nitobe T, Suematsu E, Ohta S, Honjo S, et al. Phase II dose-response study of abatacept in Japanese patients with active rheumatoid arthritis with an inadequate response to methotrexate. *Mod Rheumatol*. 2013 Mar;23(2):226-35.
29. Harigai M, Takamura A, Atsumi T, Dohi M, Hirata S, Kameda H, et al. Elevation of KL-6 serum levels in clinical trials of tumor necrosis factor inhibitors in patients with rheumatoid arthritis: a report from the Japan College of Rheumatology Ad Hoc Committee for Safety of Biological DMARDs. *Mod Rheumatol*. 2013 Mar;23(2):284-96.
30. Takamura A, Hirata S, Nagasawa H, Kameda H, Seto Y, Atsumi T, et al. A retrospective study of serum KL-6 levels during treatment with biological disease-modifying antirheumatic drugs in rheumatoid arthritis patients: a report from the Ad Hoc Committee for Safety of Biological DMARDs of the Japan College of Rheumatology. *Mod Rheumatol*. 2013 Mar;23(2):297-303.
31. Miyabe C, Okubo Y, Maeda T, Tsuboi R, Mitsuhashi Y. Tiny disseminated angiomas from childhood. *Eur J Dermatol*. 2013; 23(5): 718-9.31.
32. Yamamoto A, Morio T, Kumaki E, Yamazaki H, Iwai H, Kubota T, Miyasaka N and Kohsaka H. A Case of Pyogenic Sterile Arthritis, Pyoderma Gangrenosum, and Acne(PAPA) Syndrome Accompanied by Nephrosclerosis, Splenomegaly and Intestinal Lesions. *J Genet Syndr Gene Ther* 4(9): 183.
33. Takeuchi T, Kawai S, Yamamoto K, Harigai M, Ishida K, Miyasaka N. Post-marketing surveillance of the safety and effectiveness of tacrolimus in 3,267 Japanese patients with rheumatoid arthritis. *Mod Rheumatol*. 2013 May 14.

Dermatology

1. Staffs and Students (April 2013)

Professor	Hiroo YOKOZEKI	
Junior Associate Professor	Kaoru TAKAYAMA, Ken IGAWA	Aya NISHIZAWA,
Assistant Professor	Takichi MUNETSUGU, Shoun TOKORO,	Hitomi SATOH, Tsukasa UGAJIN
Hospital Staff	Sayaka SHIBAMA, Risa WATANABE, Mayo KONDO, Michihisa TAKAHASHI,	Minako INAZAWA, Kohei KATOH, Naomi ZENRI,
Secretary	Yukako KIKUCHI, Kazumi SAEKI	Masae SAKATA,
Graduate students	Yuki TAKEHARA, Minako INAZAWA, Harutishi SUGUYAMA, Yasumasa KANAI, Makiko UENO, Aiko FURUYA, Sayaka SHIBAMA,	Rie YU, Chen YUE, Kazumi SAEKI, Tomoko FUJIMOTO, Takashi HASHIMOTO, Kohei KATOH, Takichi MUNETSUGU

2. Purpose of Education

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.

3. Research Subjects

- 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

4. Clinical Services

Dermatology clinic provides an advanced treatment for skin diseases; skin tumors, infectious diseases, skin allergy, collagen diseases and psoriasis. Recently, we established the gene therapies (STAT6 decoy ODN) for severe atopic dermatitis in the clinic.

5. Publications

Original Article

1. Fujimoto T, Kawahara K, Yokozeki H :Epidemiological study and considerations of primary focal hyperhidrosis in Japan: From questionnaire analysis. *J Dermatol.* 2013 40(11):886-890
2. Sakaguchi M, Bito T, Oda Y, Kikusawa A, Nishigori C, Munetsugu T, Yokozeki H, Itotani Y, Niguma T, Tsuruta D,

- Tateishi C, Ishii N, Koga H, Hashimoto T :Three cases of linear IgA/IgG bullous dermatosis showing IgA and IgG reactivity with multiple antigens, particularly laminin-332. *JAMA Dermatol.* 2013 Nov;149(11):1308-13.
3. Takehara Y, Satoh T, Nishizawa A, Saeki K, Nakamura M, Masuzawa M, Kaneda Y, Katayama I, Yokozeki H: Anti-tumor effects of inactivated Sendai virus particles with an IL-2 gene on angiosarcoma. *Clin Immunol.* 2013 Oct;149(1):1-10.
 4. Tanaka K, Mori H, Okazaki M, Nishizawa A, Yokozeki H: Long-term treatment outcome after only popliteal lymph node dissection for nodal metastasis in malignant melanoma of the heel: the only "interval node" dissection can be an adequate surgical treatment. *Case Rep Oncol Med.* 2013;2013:259326.
 5. Saeki K, Satoh T, Yokozeki H: α (1,3) Fucosyltransferases IV and VII are essential for the initial recruitment of basophils in chronic allergic inflammation. *J Invest Dermatol.* 2013 Sep;133(9):2161-9.
 6. Kato K, Satoh T, Tanaka-Fujimoto T, Ueda N, Yokozeki H.: IgG4-positive cells in skin lesions of cutaneous and systemic plasmacytosis. *Eur J Dermatol.* 2013 Apr 1;23(2):255-6.
 7. Kataoka N, Satoh T, Hirai A, Saeki K, Yokozeki H.:Indomethacin inhibits eosinophil migration to prostaglandin D2 : therapeutic potential of CRTH2 desensitization for eosinophilic pustular folliculitis. *Immunology.* 2013 Sep;140(1):78-86.
 8. Inoue R, Sohara E, Rai T, Satoh T, Yokozeki H, Sasaki S, Uchida S.:Immunolocalization and translocation of aquaporin-5 water channel in sweat glands. *J Dermatol Sci.* 2013 Apr;70(1):26-33.
 9. Takahashi E, Yokozeki H, Satoh T. Atrophic fibrous hamartoma of infancy with epidermal and adnexal changes. *J Dermatol.* 2013 Mar;40(3):212-4.
 10. Satoh T, Ikeda H, Yokozeki H.Acrosyringeal involvement of palmoplantar lesions of eosinophilic pustular folliculitis. *Acta Derm Venereol.* 2013 Jan;93(1):99.
 11. Inoue T, Yamaoka T, Murota H, Yokomi A, Tanemura A, Igawa K, Tani M, Katayama I. Effective Oral Psoralen Plus Ultraviolet A Therapy for Digital Ulcers with Revascularization in Systemic Sclerosis. *Acta Derm Venereol.* 2013 Aug 8.
 12. Hanafusa T, Matsui S, Murota H, Tani M, Igawa K, Katayama I. Increased frequency of skin-infiltrating FoxP3+ regulatory T cells as a diagnostic indicator of severe atopic dermatitis from cutaneous T cell lymphoma. *Clin Exp Immunol.* 2013 Jun;172(3):507-12.
 13. Hanafusa T, Igawa K, Kotobuki Y, Kitaba S, Tani M, Katayama I. Systemic lymphadenopathy with systemic sclerosis and Sjögren's syndrome: a case report. *J Dermatol.* 2013 Feb;40(2):124-5.
 14. Hashimoto T, Satoh T, Furuya A, Kataoka N, Yokozeki H: Kimura's disease with prurigo lesions treated with systemic indomethacin, *J Eur Acad Dermatol Venereol*, DOI: 10.1111/jdv.12339, 2013
 15. Shen L, Higuchi T, Tubbe I, Voltz N, Krummen M, Pektor S, Montermann E, Rausch K, Schmidt M, Schild H, Grabbe S, Bros M. A trifunctional dextran-based nanovaccine targets and activates murine dendritic cells, and induces potent cellular and humoral immune responses in vivo. *PLoS One.* 2013 Dec 5;8(12)
 16. Higuchi T, Satoh T, Yokozeki H. Using CD40 ligand expression to detect antigen-specific T cells in patients with drug eruptions. *Acta Derm Venereol.* 2014 Jan;94(1):86-7.
 17. Villarreal VA, Okiyama N, Tsuji G, Linton JT, Katz SI. CXCR3-Mediated Skin Homing of Autoreactive CD8 T Cells Is a Key Determinant in Murine Graft-Versus-Host Disease. *J Invest Dermatol.* 2014 Jan 3.
 18. Okiyama N, Furumoto Y, Villarreal VA, Linton JT, Tsai WL, Gutermuth J, Ghoreschi K, Gadina M, O'Shea JJ, Katz SI. Reversal of CD8 T-Cell-Mediated Mucocutaneous Graft-Versus-Host-Like Disease by the JAK Inhibitor Tofacitinib. *J Invest Dermatol.* 2013 Nov 8.
 19. Miyagawa F, Okiyama N, Villarreal V, Katz SI. Identification of CD3+CD4-CD8- T cells as potential regulatory cells in an experimental murine model of graft-versus-host skin disease (GVHD). *J Invest Dermatol.* 2013 Nov;133(11):2538-45.

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	Yamauchi, Junji

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 neurological disease mechanism and target molecules using molecular biology and tissue engineering
(Yamauchi, Junji; Dept. of Pharmacology, National Institute for Child Health and Development)

We focus on middle embryonic-to-neonatal neuronal developmental stages and specially study glial development. Many genetic neuropathies are known to be glial dystrophies, which involve demyelinating/demyelinating diseases. We believe

that knowing how glial cells develop is tightly related to clarifying how glial neuropathies occur. These studies will allow us to present novel drug-target-molecules for neuropathies, as well as to provide paradigm of neuronal regeneration.

4. Publications

Original Article

1. Tateno H, Matsushima A, Hiemori K, Onuma Y, Ito Y, Hasehira K, Nishimura K, Ohtaka M, Takayasu S, Nakanishi M, Ikehara Y, Nakanishi M, Ohnuma K, Chan T, Toyoda M, Akutsu H, Umezawa A, Asashima M, Hirabayashi J. Podocalyxin is a glycoprotein ligand of the human pluripotent stem cell-specific probe rBC2LCN. *Stem Cells Transl Med.* 2013; 2: 265-273.
2. Hiura H, Toyoda M, Okae H, Sakurai M, Miyauchi N, Sato A, Kiyokawa N, Okita H, Miyagawa Y, Akutsu H, Nishino K, Umezawa A, Arima T. Stability of genomic imprinting in human induced pluripotent stem cells. *BMC Genet.* 2013; 14: 32.
3. Kobayashi H, Yanagisawa E, Sakashita A, Sugawara N, Kumakura S, Ogawa H, Akutsu H, Hata K, Nakabayashi K, Kono T. Epigenetic and transcriptional features of the novel human imprinted lncRNA GPR1AS suggest it is a functional ortholog to mouse Zdbf2linc. *Epigenetics.* 2013; 8: 635-645.
4. Okumura N, Akutsu H, Sugawara T, Miura T, Takezawa Y, Hosoda A, Yoshida K, Ichida JK, Yamada M, Hamatani T, Kuji N, Miyado K, Yoshimura Y, Umezawa A. β -Catenin Functions Pleiotropically in Differentiation and Tumorigenesis in Mouse Embryo-Derived Stem Cells. *PLoS One* 2013; 8: e63265.
5. Iwao T, Toyota M, Miyagawa Y, Okita H, Kiyokawa N, Akutsu H, Umezawa A, Nagata K, Matsunaga T. Differentiation of Human Induced Pluripotent Stem Cells into Functional Enterocyte-Like Cells Using a Simple Method. *Drug Metab Pharmacokinet.* 2014; 29: 44-51.
6. Terai M, Izumiyama-Shimomura N, Aida J, Ishikawa N, Kuroiwa M, Poon SS, Arai T, Toyoda M, Akutsu H, Umezawa A, Nakamura KI, Takubo K. Investigation of telomere length dynamics in induced pluripotent stem cells using quantitative fluorescence in situ hybridization. *Tissue Cell.* 2013; 45: 407-413.
7. Yamada-Fukunaga T, Yamada M, Hamatani T, Chikazawa N, Ogawa S, Akutsu H, Miura T, Miyado K, Tarín JJ, Kuji N, Umezawa A, Yoshimura Y. Age-associated telomere shortening in mouse oocytes. *Reprod Biol Endocrinol.* 2013; 11(1): 108.
8. Kondo Y, Iwao T, Nakamura K, Sasaki T, Takahashi S, Kamada N, Matsubara T, Gonzalez FJ, Akutsu H, Miyagawa Y, Okita H, Kiyokawa N, Toyoda M, Umezawa A, Nagata K, Matsunaga T, Ohmori S. An Efficient Method for Differentiation of Human Induced Pluripotent Stem Cells into Hepatocyte-Like Cells Retaining Drug Metabolizing Activity. *Drug Metab Pharmacokinet.* 2013 Dec 10. [Epub ahead of print]
9. Yamazoe T, Shiraki N, Toyoda M, Kiyokawa N, Okita H, Miyagawa Y, Akutsu H, Umezawa A, Sasaki Y, Kume K, Kume S. A synthetic nanofibrillar matrix promotes in vitro hepatic differentiation of embryonic stem cells and induced pluripotent stem cells. *J Cell Sci.* 2013; 126(Pt 23): 5391-5399.
10. Nagasaki K, Tsuchiya S, Saitoh A, Ogata T, Fukami M. Neuromuscular Symptoms in a Patient with Familial Pseudohypoparathyroidism Type Ib Diagnosed by Methylation-Specific Multiplex Ligation-Dependent Probe Amplification. *Endocr J.* 60(2):231–236, 2013
11. Ayabe T, Matsubara K, Ogata T, Ayabe A, Murakami N, Nagai T, Fukami M. Birth Seasonality in Prader-Willi Syndrome Resulting from Chromosome 15 Microdeletion. *Am J Med Genet A.* 161(6):1495–1497, 2013
12. Yamaguchi R, Kato F, Hasegawa T, Katsumata N, Fukami M, Matsui T, Nagasaki K, Ogata T. A novel homozygous mutation of the nicotinamide nucleotide transhydrogenase gene in a Japanese patient with familial glucocorticoid deficiency. *Endocr J.* 60(7):855–859, 2013
13. Fukami M, Iso M, Sato N, Igarashi M, Seo M, Kazukawa I, Kinoshita E, Dateki S, Ogata T. Submicroscopic deletion involving the fibroblast growth factor receptor 1 gene in a patient with combined pituitary hormone deficiency. *Endocr J.* 60(8):1013–1020, 2013
14. Fukami M, Suzuki J, Nakabayashi K, Tsunasima R, Ogata T, Shozu M, Noguchi S. Lack of Genomic Rearrangements Involving the Aromatase Gene CYP19A1 in Breast Cancer. *Breast Cancer.* 2013 [Epub ahead of print]
15. Matsumura T, Imamichi Y, Mizutani T, Ju Y, Yazawa T, Kawabe S, Kanno M, Ayabe T, Katsumata N, Fukami M, Inatani M, Akagi Y, Umezawa A, Ogata T, Miyamoto K. Human glutathione S-transferase A (GSTA) family genes are regulated by steroidogenic factor 1 (SF-1) and are involved in steroidogenesis. *FASEB J.* 227(8):3198–3208, 2013
16. Hayashi M, Kataoka Y, Sugimura Y, Kato F, Fukami M, Ogata T, Homma K, Hasegawa T, Oiso Y, Sasano H, Tanaka H. A 68-year-old phenotypically male patient with 21-hydroxylase deficiency and concomitant adrenocortical neoplasm producing testosterone and cortisol. *Tohoku J Exp Med.* 231(2):75–84, 2013

17. Igarashi M, Dung VC, Suzuki E, Ida S, Nakacho M, Nakabayashi K, Mizuno K, Hayashi Y, Kohri K, Kojima Y, Ogata T, Fukami M. Cryptic Genomic Rearrangements in Three Patients with 46,XY Disorders of Sex Development. *Plos One*. 8(7):e68194, 2013
18. Fukami M, Tsuchiya T, Vollbach H, Brown KA, Abe S, Ohtsu S, Wabitsch M, Burger H, Simpson ER, Umezawa A, Shihara D, Nakabayashi K, Bulun SE, Shozu M, Ogata T. Genomic Basis of Aromatase Excess Syndrome: Recombination- and Replication-Mediated Rearrangements Leading to CYP19A1 Overexpression. *J Clin Endocrinol Metab*. 98(12):E2013-21, 2013
19. Nakashima S, Watanabe Y, Okada J, Ono H, Nagata E, Fukami M, Ogata T. Critical role of Yp inversion in PRKX/PRKY-mediated Xp:Yp translocation in a patient with 45,X testicular disorder of sex development. *Endocr J*. 60(12):1329-34, 2013
20. Shihara D, Miyado M, Nakabayashi K, Shozu M, Ogata T, Nagasaki K, Fukami M. Aromatase Excess Syndrome in a Family with Upstream Deletion of CYP19A1. *Clin Endocrinol* 2013 [Epub ahead of print]
21. Fukami M, Homma K, Hasegawa T, Ogata T. Backdoor pathway for Dihydrotestosterone Biosynthesis: Implications for normal and abnormal human sex development. *Dev Dyn* 242(4):320-329, 2013
22. Rakoczy J, Fernandez-Valverde SL, Glazov EA, Wainwright EN, Sato T, Takada S, Combes AN, Korbie DJ, Miller D, Grimmond SM, Little MH, Asahara H, Mattick JS, Taft RJ, Wilhelm D. MicroRNAs-140-5p/140-3p modulate Leydig cell numbers in the developing mouse testis. *Biology of Reproduction*, 88:143 (2013).
23. Shimizu H, Kubo A, Uchibe K, Hashimoto M, Yokoyama S, Takada S, Mitsuoka K, Asahara H. The AERO System: a 3D-like approach for recording gene expression patterns in the mouse whole embryo. *PLoS ONE*, 8:e75754 (2013)
24. Takada S, Sato T, Ito Y, Yamashita S, Kato T, Kawasumi M, Kanai-Azuma M, Igarashi A, Tamano M, Asahara H. Targeted gene deletion of miRNAs in mice by TALEN system. *PLoS ONE*, 8:e76004 (2013)
25. Kato T, Miyata K, Sonobe M, Yamashita S, Tamano M, Miyamoto S, Sakuma T, Yamamoto T, Inui M, Kikusui T, Asahara H, Takada S: Production of Sry knockout mouse using TALEN via oocyte injection. *Scientific Reports*, 3:3163 (2013)
26. Tomohiro Torii, Yuki Miyamoto, Naoko Onami, Hideki Tsumura, Noriko Nemoto, Katsumasa Kawahara, Minoru Kato, Jun Kotera, Kazuaki Nakamura, Akito Tanoue, and Junji Yamauchi* (2013) In vivo expression of the Arf6 guanine-nucleotide exchange factor cytohesin-1 in mice exhibits enhanced myelin thickness in nerves. *J. Mol. Neurosci*. 51, 522-531
27. Kazuaki Nakamura, Kazuko Aizawa, Junji Yamauchi, and Akito Tanoue (2013) Hyperforin inhibits cell proliferation and differentiation in mouse embryonic stem cells. *Cell Prolif*. 46, 529-537
28. Nobuo Terada, Yurika Saitoh, Nobuhiko Ohno, Masayuki Komada, Junji Yamauchi, and Shin-ichi Ohno (2013) Involvement of Src in the membrane skeletal complex, MPP6-4.1G, in Schmidt-Lanterman incisures of mouse myelinated nerve fibers in PNS. *Histochem. Cell Biol*. 140, 213-222
29. Yu Tezuka, Mizuki Okada, Yuka Tada, Junji Yamauchi, Hideo Nishigori, and Atsushi Sanbe (2013) Regulation of neurite growth by inorganic pyrophosphatase 1 via JNK dephosphorylation. *PLoS One* 8, e61649
30. Kazuaki Nakamura, Kazuko Aizawa, Kazuhiko Nakabayashi, Natsuko Kato, Junji Yamauchi, Kenichiro Hata, and Akito Tanoue (2013) DNA methyltransferase inhibitor zebularine inhibits human hepatic carcinoma cells proliferation and induces apoptosis. *PLoS One* 8, e54036
31. Yuki Miyamoto, Tomohiro Torii, Kazuaki Nakamura, Shou Takashima, Atsushi Sanbe, Akito Tanoue, and Junji Yamauchi* (2013) Signaling through Arf6 guanine-nucleotide exchange factor cytohesin-1 regulates migration in Schwann cells. *Cell. Signal*. 25, 1379-1387:
32. Atsushi Sanbe, Tetsuro Marunouchi, Tsutomu Abe, Yu Tezuka, Mizuki Okada, Sayuri Aoki, Hideki Tsumura, Junji Yamauchi, Kouichi Tanonaka, Hideo Nishigori, and Akito Tanoue (2013) Phenotype of cardiomyopathy in cardiac-specific heat shock protein B8 K141N transgenic mouse. *J. Biol. Chem*. 288, 8910-8921
33. Yuki Miyamoto, Tomohiro Torii, Natsuki Yamamori, Toru Ogata, Akito Tanoue, and Junji Yamauchi* (2013) Akt and PP2A reciprocally regulate the guanine nucleotide exchange factor Dock6 to control axon growth of sensory neurons. *Sci. Signal*. 6, ra15:

Human Pathology

1. Staff and Students

Professor	Yoshinobu EISHI	
Junior Associate Professor	Hiroshi KAWACHI	
Assistant Professor	Daisuke KOBAYASHI,	Takashi ITO,
	Maki KOBAYASHI,	Mariko NEGI
Laboratory Technician	Asuka FURUKAWA	
Technical Assistant	Yoshimi SUZUKI	
Secretary	Miho IWAMITSU	
Graduate Students	Naoki AKAZAWA,	Tadatsune IIDA,
	Akira TAKEMOTO,	Shohei TOMII,
	Atsuko KONTA,	Katsumi OISHI,
	Yoshimi SUZUKI,	Nilufar LOKMAN,
	Teruko NAKAMURA,	Kana MINEGISHI,
	Pariko YOROZU,	Kousuke TAKEMURA,
	Chisato ITO,	Sayoko CHIBA,
	Ayaka MATSUKAZE,	Tomohisa Ogawa,
	Yoko Tomoe,	Akiko Yoneyama
Reserch Student	Tomoya KAKEGAWA	

2. Purpose of education

Department of Human Pathology provides a graduate course for future pathologists to train the skills and knowledge of anatomical pathology and develop the abilities for medical researches. Graduate students are educated to associate their researches with problems in diagnosis and treatment of diseases and etiologies of the diseases of unknown causes. In the course, they usually spend the first two years for anatomical pathology training, searching for their own research theme and another two years for researches and thesis-writing.

3. Research Subjects

- 1) Endogenous infection (diseases caused by indigenous microorganisms in susceptible hosts)
- 2) Cancer research (histopathology, carcinogenesis, prognostic factors, and so on)

4. Clinical Services

Teaching staffs in Human Pathology support all functions of Surgical Pathology in our university hospital.

5. Publications

Original Article

1. Eishi Y. Etiologic link between sarcoidosis and *Propionibacterium acnes*. *Respir Investig.* 51(2):56-68,2013
2. Minegishi K, Aikawa C, Furukawa A, Watanabe T, Nakano T, Ogura Y, Ohtsubo Y, Kurokawa K, Hayashi T, Maruyama F, Nakagawa I, Eishi Y. Complete Genome Sequence of a *Propionibacterium acnes* Isolate from a Sarcoidosis Patient. *Genome Announc.* 1(1), 2013
3. Okamoto N, Kawachi H, Yoshida T, Kitagaki K, Sekine M, Kojima K, Kawano T, Eishi Y. "Crawling-type" adenocarcinoma of the stomach: a distinct entity preceding poorly differentiated adenocarcinoma. *Gastric Cancer.* 16(2):220-32,2013
4. Shiwaku H, Yagishita S, Eishi Y, Okazawa H. Bergmann glia are reduced in spinocerebellar ataxia type 1. *Neuroreport.* 24(11):620-5,2013
5. Matsuo Y, Mizoguchi F, Kohsaka H, Ito E, Eishi Y, Miyasaka N. Tocilizumab-induced immune complex glomerulonephritis in a patient with rheumatoid arthritis. *Rheumatology (Oxford).* 52(7):1341-3,2013
6. Asahina A, Miura K, Saito I, Oshikata C, Ishii N, Eishi Y. Cutaneous sarcoidosis with livedoid lesions: evidence of the involvement of *Propionibacterium acnes*. *J Dermatol.* 40(6):501-2,2013
7. Ueno H, Shirouzu K, Shimazaki H, Kawachi H, Eishi Y, Ajioka Y, Okuno K, Yamada K, Sato T, Kusumi T, Kushima R, Ikegami M, Kojima M, Ochiai A, Murata A, Akagi Y, Nakamura T, Sugihara K; Study Group for Perineural Invasion projected by the Japanese Society for Cancer of the Colon and Rectum (JSCCR). Histogenesis and

- prognostic value of myenteric spread in colorectal cancer: a Japanese multi-institutional study. *J Gastroenterol.* 2013 May 16. [Epub ahead of print]
8. Ueno H, Shirouzu K, Eishi Y, Yamada K, Kusumi T, Kushima R, Ikegami M, Murata A, Okuno K, Sato T, Ajioka Y, Ochiai A, Shimazaki H, Nakamura T, Kawachi H, Kojima M, Akagi Y, Sugihara K; Study Group for Perineural Invasion projected by the Japanese Society for Cancer of the Colon and Rectum (JSCCR). Characterization of perineural invasion as a component of colorectal cancer staging. *Am J Surg Pathol.* 37(10):1542-9,2013
 9. Niimi Y, Takahashi M, Sugawara E, Umeda S, Obayashi M, Sato N, Ishiguro T, Higashi M, Eishi Y, Mizusawa H, Ishikawa K. Abnormal RNA structures (RNA foci) containing a penta-nucleotide repeat (UGGAA)(n) in the Purkinje cell nucleus is associated with spinocerebellar ataxia type 31 pathogenesis. *Neuropathology.*33(6):600-11,2013
 10. Satoh F, Morita H, Tayama H, Inoue Y, Eishi Y, Yoshimura A. Renal Sarcoidosis With Limited Lung Manifestations Expressing *Propionibacterium acnes* Antigens in the Affected Tubulointerstitium. *Am J Med Sci.* 346(3):250-2,2013
 11. Fujita K, Nakamura Y, Oka T, Ito H, Tamura T, Tagawa K, Sasabe T, Katsuta A, Motoki K, Shiwaku H, Sone M, Yoshida C, Katsuno M, Eishi Y, Murata M, Taylor JP, Wanker EE, Kono K, Tashiro S, Sobue G, La Spada AR, Okazawa H. A functional deficiency of TERA/VCP/p97 contributes to impaired DNA repair in multiple polyglutamine diseases. *Nat Commun.* 4:1816,2013
 12. Takahashi M, Obayashi M, Ishiguro T, Sato N, Niimi Y, Ozaki K, Mogushi K, Mahmut Y, Tanaka H, Tsuruta F, Dolmetsch R, Yamada M, Takahashi H, Kato T, Mori O, Eishi Y, Mizusawa H, Ishikawa K. Cytoplasmic location of a 1A voltage-gated calcium channel C-terminal fragment (Cav2.1-CTF) aggregate is sufficient to cause cell death. *PLoS One.* 8(3):e50121,2013
 13. Okeda R, Ito K, Tsumura K, Eishi Y. Primary granulomatous angiitis of the CNS preferentially involving small veins with a granulomatous leukoencephalitis-like lesion in the cerebrum. *Neuropathology.* 33(5):547-52,2013
 14. Fukamachi H, Seol HS, Shimada S, Funasaka C, Baba K, Kim JH, Park YS, Kim MJ, Kato K, Inokuchi M, Kawachi H, Yook JH, Eishi Y, Kojima K, Kim WH, Jang SJ, Yuasa Y. CD49^f(high) cells retain sphere-forming and tumor-initiating activities in human gastric tumors. *PLoS One.* 8(8):e72438,2013
 15. Okada E, Araki A, Suzuki S, Watanabe H, Ikeda T, Watanabe T, Kurata M, Eishi Y, Watanabe M. Histological diagnosis of follicular lymphoma by biopsy of small intestinal normal mucosa. *Dig Endosc.* 25(5):544-6,2013
 16. Si MK, Mitaka C, Tulafu M, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M. Inhibition of poly (adenosine diphosphate-ribose) polymerase attenuates lung-kidney crosstalk induced by intratracheal lipopolysaccharide instillation in rats. *Respir Res.* 14:126,2013 [Epub ahead of print]
 17. Takeda T, Sato T, Ito T, Sumi Y, Kobayashi T, Kitagawa M, Hirokawa K, Uchihara T. Four-repeat tau-selective deposition in subthalamic nucleus and motor cortex in Alzheimer disease. *Clin Neurol Neurosurg.* 115:641-3, 2013
 18. Sugawara T, Aoyagi M, Tanaka Y, Tamaki M, Kobayashi D, Ohno K. Chronic encapsulated expanding hematoma in nonfunctioning pituitary adenoma. *Neurosurg Rev.* 36(3):395-402,2013

Physiology and Cell Biology

1. Staffs and Students

Professor Shu TAKEDA (July~)
Assistant Professor Toru FUKUDA

2. Purpose of Education

Our department is a branch of basic medical science. In the undergraduate course, our department deals with physiology and introductory cell biology. Our main object in the graduate course is to provide a wide range of views to understand human biology using various research techniques such as molecular biology, biochemistry, cell biology and mouse genetics.

3. Research Subjects

- 1) Molecular mechanism of bone-organ crosstalk.
- 2) Regulation of bone metabolism by sensory nerve system.
- 3) Regulation of bone metabolism by microRNA

4. Publications

Original Article

1. Fukuda T, Takeda S, Xu R, Ochi H, Sunamura S, Sato T, Shibata S, Yoshida Y, Gu Z, Kimura A, Ma C, Xu C, Bando W, Fujita K, Shinomiya K, Hirai T, Asou Y, Enomoto M, Okano H, Okawa A, Itoh H. *Sema3A regulates bone-mass accrual through sensory innervations.* *Nature* 2013; 497: 490-3.
2. Itoh S, Sekino Y, Shinomiya K, and Takeda S. The effects of risedronate administered in combination with a proton pump inhibitor for the treatment of osteoporosis. *J Bone Miner Metab* 2013; 31: 206-11.
3. Kinouchi K, Ichihara A, Sano M, Sun-Wada GH, Wada Y, Ochi H, Fukuda T, Bokuda K, Kurosawa H, Yoshida N, et al. The role of individual domains and the significance of shedding of ATP6AP2/(pro)renin receptor in vacuolar H(+)-ATPase biogenesis. *PLoS One* 2013; 8: e78603.
4. Kohata K, Itoh S, Takeda S, Kanai M, Yoshioka T, Suzuki H, and Yamashita K. Enhancement of fracture healing by electrical stimulation in the comminuted intraarticular fracture of distal radius. *Biomed Mater Eng* 2013; 23: 485-93.
5. Takarada T, Hinoi E, Nakazato R, Ochi H, Xu C, Tsuchikane A, Takeda S, Karsenty G, Abe T, Kiyonari H, Yoneda, Y. An analysis of skeletal development in osteoblast-specific and chondrocyte-specific runt-related transcription factor-2 (Runx2) knockout mice. *J Bone Miner Res* 2013; 28: 2064-9.
6. Piao J, Tsuji K, Ochi H, Iwata M, Koga D, Okawa A, Morita S, Takeda S, Asou Y. Sirt6 regulates postnatal growth plate differentiation and proliferation via Ihh signaling. *Sci Rep.* 2013 Oct 23;3:3022. doi: 10.1038/srep03022.

Molecular Cellular Cardiology

1. Staffs and Students

Professor	Tetsushi Furukawa, MD, PhD	
Assistant professor	Yusuke Ebana, MD, PhD	
Graduate Students	Yuya Karube, MD,	Akiko Koizumi, MD,
	Peng Zhang,	Lian Liu, MD,
	Yuto Orui,	Satomi Kojima,
	Sayuri Goryoda,	Miki Fujiduka,
	Kentaro Takahashi, MD (Cardiovascular Medicine), Koji Sugiyama, MD (Cardiovascular Medicine)	

2. Purpose of Education

This laboratory focuses on understanding pathogenesis of intractable and common cardiovascular diseases using multidisciplinary approach (patch-clamp, cell biology, optical recording, genetic analysis, and computational analysis). Our ultimate goal is to improve diagnosis and management of intractable and common cardiovascular diseases.

3. Research Subjects

- 1) Pathogenesis of atrial fibrillation (AF)
 - a. GWAS (genome-wide association study) in AF
(collaboration with Dr. Koichi Ozaki, Dr. Mitsuaki Kubo in RIKEN, Prof. Toshihiro Tanaka in Bio-resource Center)
 - b. Functional analysis of AF-associated genes for identification of novel pathogenic pathways and therapeutic strategies of AF
 - c. Risk stratification based on AF-associated SNPs for personalized medicine of AF
- 2) Pathogenesis of ventricular tachyarrhythmias and sudden cardiac death
 - a. The role of genetic disturbance of the His-Purkinje system-specific transcription factor, *Irx3*, in sudden cardiac death
 - b. Role of pannexins in ischemia-related sudden cardiac death
- 3) Use of iPS cells for arrhythmia research
 - a. Drug screening system using human iPS cells-derived cardiomyocytes
- 4) Use of state-of-art technology for cardiovascular research
 - a. Use of motion vector technology for in vitro analysis of cardiac contraction
(collaboration with Dr. Akio Yasuda, Dr. Eriko Matsui, Dr. Tomohiro Hayakawa, Dr. Hatsume Uno, and Dr. Kazuya Takahashi in Sony Co.)
 - b. Basic research for generation of 3-D simulator of cardiac electrical activity
(collaboration with Prof. Toshiaki Hisada, Prof. Seiryō Sugiura, and Dr. Junichi Okada in Graduate School of Frontier Sciences, The University of Tokyo)

4. Publications List

Original Article

1. Asayama M, Kurokawa J, Shirakawa K, Okuyama H, Kagawa T, Okada J, Sugiura S, Hisada T, Furukawa T. Effects of an hERG activator, ICA-105574, on electrophysiological properties of canine hearts. *J. Pharmacol. Sci.* 2013;121:1-8.
2. Kurokawa J, Furukawa T. Non-genomic action of sex steroid hormones and cardiac repolarization. *Biol. Pharm. Bull.* 2013;36:8-12.
3. Furukawa T, Ebana Y. Current overview of genetic background of atrial fibrillation: possible genetically therapeutic targets for the treatment of atrial fibrillation. *J. Arrhythm.* (in press)
4. Okata S, Yuasa S, Yamane T, Furukawa T, Fukuda K. The generation of induced pluripotent stem cells from a patient with *KCNH2* G603D, without LQT2 disease associated symptom. *J. Med. Dent. Sci.* 2013;60:17-22.
5. Terao C, Yoshifuji H, Kimura A, Matsumura T, Ohmura K, Takahashi M, Shimizu M, Kawaguchi T, Chen Z, Naruse TK, Sato-Otsubo A, Ebana Y, Maejima Y, Kinoshita H, Murakami K, Kawabata D, Wada Y, Narita I, Tazaki J, Kawaguchi Y, Yamanaka H, Yurugi K, Miura Y, Maekawa T, Ogawa S, Komuro I, Nagai R, Yamada R, Tabara Y,

Systemic Organ Regulation

Isobe M, Mimori T, Matsuda F. Two susceptibility loci to Takayasu arteritis reveal a synergistic role of the IL12B and HLA-B regions in a Japanese population. *Am. J. Hum. Genet.* 2013;93:289-97.

Review Articles

1. Kurokawa J, Furukawa T. Non-genomic action of sex steroid hormones and cardiac repolarization. *Biol. Pharmacol. Bull.* 2013;36:8-12.

Books

1. Tetsushi Furukawa. Ion Channel Expression and Function of iPSC-derived Cardiomyocytes. In:Cardiac Regeneration using Stem Cells. (eds.) Keiichi Fukuda, Shinsuke Yuasa. CRC Press, 2013.

Stem Cell Regulation

1. Staffs and Students

Professor	Tetsuya TAGA
Associate Professor	Tetsushi KAGAWA
Associate Professor	Ikuo NOBUHISA
Project Assistant Professor	Kouichi TABU
Administrative Assistant	Mako FUSHIMI
Technical Assistant	Kazuko INOUE
Graduate Student	Norihisa BIZEN
Graduate Student	Maha ANANI
Graduate Student	Genki SUDO
Graduate Student	Yasuhiro KOKUBU
Graduate Student	Wenqian WANG (April 2013-)
Graduate Student	Nozomi MURAMATSU (-March 2013)
Graduate Student	Kaho HARADA
Graduate Student	Mayumi AMANO
Graduate Student	Sachiko KANEKO
Graduate Student	Yoshitaka MUROTA
Graduate Student	Tomoyo IKENOUE (April 2013-)
Graduate Student	Ryosuke KIMURA (April 2013-)
Graduate Student	Kiyoka SAITO (April 2013-)
Graduate Student	Aoi MINOWA (April 2013-)
Research Student	Kazuo TERASHIMA

2. Purpose of 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.

3. Research Subjects

- 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

4. Publications

Original Article

1. Kusunoki S, Kato K, Tabu K, Inagaki T, Okabe H, Kaneda H, Suga S, Terao Y, Taga T and Takeda S: The inhibitory effect of salinomycin on the proliferation, migration and invasion of human endometrial cancer stem-like cells. *Gynecol. Oncol.*, 129: 598-605, 2013.
2. Uemura M, Ozawa A, Nagata T, Kurasawa K, Tsunekawa N, Nobuhisa I, Taga T, Hara K, Kudo A, Kawakami H, Saijoh Y, Kurohmaru M, Kanai-Azuma M and Kanai Y: Sox17 haploinsufficiency results in perinatal biliary atresia and hepatitis in C57BL6 background mice. *Development*, 140: 639-648, 2013.
3. Bizen N, Inoue T, Shimizu T, Tabu K, Kagawa T and Taga T: A growth-promoting signaling component cyclin D1 in neural stem cells has anti-astroglial function to execute self-renewal. *Stem Cells*, doi: 10.1002/stem.1613. 2013 [Epub ahead of print]

Review Article

1. Tabu K, Bizen N, Taga T, and Tanaka S. Gene regulation of Prominin-1 (CD133) in normal and cancerous Tissues. In *Prominin-1 (CD133): New Insights on Stem & Cancer Stem Cell Biology*. D. Corbeil Ed. (Springer) Adv. Exp. Med. Biol., Volume 777, 73-85, 2013.

Molecular Pharmacology

1. Staffs and Students

Professor:	Masaki Noda, M.D., Ph.D.	
Associate Professor:	Yoichi Ezura, M.D., Ph.D.	
Assistant Professor:	Tadayoshi Hayata, Ph.D.	
Research Instructor:	Takuya Notomi, Ph.D.	
Research Assistant Professor:	Smriti Aryal A.C, DDS, Ph.D.	
Secretary:	Naoko Ashizawa, Yoko Inoue.	Rei Fujiwara,
Graduate Students:	Makiri Kawasaki, Shuichi Moriya, Wanting Lin, Arina Hatta.	Jumpei Shirakawa, Takayuki Yamada, Chantida Pawaputanon na mahasarakham,

2. Purpose of Education

Osteoporosis is one of the serious diseases in aging societies in the world. Osteoporosis increases risk of fracture that results in loss of quality of life and threatens life of aged people. Therefore, it is crucial to understand how bone mass is regulated by specific factors to establish the therapy and prevention for osteoporosis. Graduate students will study bone metabolism through journal presentation and investigate bone metabolism using mice and tissue culture system by advanced molecular and cellular biological approaches.

3. Research Subjects

- 1) Molecular mechanisms of osteoblast and chondrocyte differentiation.
- 2) Mechanism of regulation of bone mass by nervous system.
- 3) Regulation of bone metabolism by mechanical stress.
- 4) Regulation of gene expression by hormones.
- 5) Molecular biology of function and formation of osteoclasts.

4. Publications

Original articles

1. Watanabe C, Morita M, Hayata T, Nakamoto T, Kikuguchi C, Li X, Kobayashi Y, Takahashi N, Notomi T, Moriyama K, Yamamoto T, Ezura Y, Noda M. Stability of mRNA influences osteoporotic bone mass via CNOT3. *Proc Natl Acad Sci U S A* 111:2692-7, 2014.
2. Komatsu K, Shimada A, Shibata T, Wada S, Ideno H, Nakashima K, Amizuka N, Noda M, Nifuji A. Alendronate promotes bone formation by inhibiting protein prenylation in osteoblasts in rat tooth replantation model. *J Endocrinol* 219:145-58, 2013.
3. Suzuki T, Notomi T, Miyajima D, Mizoguchi F, Hayata T, Nakamoto T, Hanyu R, Kamolratanakul P, Mizuno A, Suzuki M, Ezura Y, Izumi Y, Noda M. Osteoblastic differentiation enhances expression of TRPV4 that is required for calcium oscillation induced by mechanical force. *Bone* 54:172-8, 2013.
4. Aryal AC, Miyai K, Hayata T, Notomi T, Nakamoto T, Pawson T, Ezura Y, Noda M. Nck1 deficiency accelerates unloading-induced bone loss. *J Cell Physiol* 228:1397-403, 2013.

Epigenetics

1. Staffs and Students

Associate Professor	Takashi KOHDA	
Professor	Fumitoshi ISHINO	
Assistant Professor	Ryuichi ONO	
Tokunin Lecturer	Jiyoung LEE	
Tokunin Assistant Professor	Mie NARUSE	
Adjunct Lecturer	Shin KOBAYASHI,	
Secretary	Ikuko MAEDA	
Graduate students	Mami OIKAWA,	Saori TAKAHASHI,
	Miki SOMA,	Kiyotaka TAKAGI,
	Moe KITAZAWA,	Ayumi Matsuzawa

2. Purpose of Education

“Epigenetics” coupled with “Genetics” enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of organisms including our human beings. Genomic imprinting is one of the mammalian specific gene regulation mechanisms that gives rise to functional differences between paternally- and maternally-derived genomes in development, behavior and growth. Somatic cloned animals give us unique chances to examine ‘genetically identical but epigenetically diverged animals’. These studies show us how Epigenetics is important in mammalian biology. Our department focuses these mammalian specific genomic functions to elucidate how these genomic functions work and how new genomic functions have been evolved during evolution. Our final goal is to contribute to the 21st’s medicine and human biology by novel understanding of genomic functions.

3. Research Subjects

- 1) Genomic imprinting in human and mammalian development.
- 2) Placenta function and its evolution in mammals.
- 3) Somatic cloning: its epigenetic effects and application to regenerative medicine.
- 4) Assisted reproductive technology: its epigenetic effects and safer application.
- 5) Role of retrotransposon-derived genes in mammalian specific genomic functions.

4. Publications

Original Article

1. Wakayama S, Kohda T, Obokata H, Tokoro M, Li C, Terashita Y, Mizutani E, Nguyen VT, Kishigami S, Ishino F and Wakayama T. Successful serial recloning in the mouse over multiple generations. **Cell Stem Cell** 12(3), 293-297 (2013).
2. Oikawa M, Matoba S, Inoue K, Kamimura S, Hirose M, Ogonuki N, Shiura H, Sugimoto M, Abe K, Ishino F and Ogura A. RNAi-mediated Knockdown of Xist Does Not Rescue the Impaired Development of Female Cloned Mouse Embryos. **J Reprod Dev** 59(3), 231-237(2013).
3. Iwasaki S, Suzuki S, Clark H, Ono R, Shaw G, Renfree MB, Kaneko-Ishino T and Ishino F. Identification of novel *PNMA-MSI* in marsupials suggests LTR retrotransposon-derived *PNMA* genes differently expanded in marsupials and eutherians. **DNA Res** 20(5), 425-436 (2013).
4. Nishimoto M, Katano M, Yamagishi T, Hishida T, Kamon M, Nabeshima Y, Nabeshima Y, Katsura Y, Satta Y, Deakin JE, Graves JAM, Kuroki Y, Ono R, Ishino, F, Okazaki Y, Kato H and Okuda A.. *In vivo* function and evolution of the eutherian-specific pluripotency marker *UTF1*. **PLoS One** 8(7):e68119 (2013).
5. Kobayashi S, Totoki Y, Soma M, Matsumoto K, Fujihara Y, Toyoda A, Sakaki Y, Okabe M and Ishino F. Identification of an imprinted gene cluster in the X-inactivation center. **PLoS One** 8(8):e71222 (2013).
6. Kawasaki Y, Lee J, Matsuzawa A, Kohda T, Kaneko-Ishino T and Ishino F. Active DNA demethylation is required for complete imprint erasure in primordial germ cells. **Sci Rep** (in press).

Review Articles

1. Kohda T and Ishino F. Embryo manipulation via assisted reproductive technology and epigenetic asymmetry in mammalian early development. (Review) **Philos Trans R Soc Lond B Biol Sci**, 368(1609):20120353 (2013).
2. Kohda T. Effects of embryonic manipulation and epigenetics. **J Hum Genet** 58(7):416-420. (2013)

Chronobiology

1. Staffs (April. 2013)

Associate Professor Jun HIRAYAMA
E-mail address: hirayama.dbio@mri.tmd.ac.jp

2. Purpose of Education

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.

3. Research Subjects

- 1) Studies on the stress-activated protein kinase (SAPK/JNK) signaling pathway
- 2) Studies on the Hippo signaling pathway
- 3) Studies on the cell differentiation of mouse ES cells
- 4) Studies on liver formation using a small fish, Medaka, *Oryzias Latipes*
- 5) Studies on liver regeneration using mice
- 6) Studies on circadian clock using zebrafish and mice

4. Publications

Original Articles

1. Shimomura T, Miyamura N, Hata S, Miura R, Hirayama J* and Nishina H*. The PDZ-binding motif of Yes-associated protein is required for its co-activation of TEAD-mediated CTGF transcription and oncogenic cell transforming activity. *Biochem. Biophys. Res. Commun.* 2014; 443, 917-923 (*Corresponding authors).
2. Egg M, Köblitz L, Hirayama J, Schwerte T, Folterbauer C, Kurz A, Fiechtner B, Möst M, Salvenmoser W, Sassone-Corsi P, and Pelster B. Linking oxygen to time: The bidirectional interaction between the hypoxic signaling pathway and the circadian clock. *Chronobiol. Int.* 2013; 30, 510-529.

Stem cell Biology

1. Staffs and Students (April 2013)

Professor	Emi NISHIMURA	
Assistant Professor	Hiroyuki MATSUMURA	
Project Assistant Professor	Hironobu Morinaga	
JSPS Postdoctoral Fellow	Yasuaki Mohri	
Graduate Student	Makiko UENO,	Liu Nan,
	Sally Eshiba	
Technical Staff	Reiko Yajima,	Kazumasa Takenouchi
Secretary	Iku WATANABE	

2. Purpose of Education

Stem cell systems play fundamental roles in tissue turnover and homeostasis. Our goal is to understand the mechanisms of tissue homeostasis driven by stem cell systems and to apply the knowledge to better understand the mechanisms underlying the tissue decline, cancer development and other diseases associated with ageing. We further aim to apply those knowledges gained to regenerative medicine, treatment of cancer and other age-associated diseases.

3. Research Subjects

- 1) Identification of stem cells in the skin.
- 2) Mechanisms of stem cell maintenance
- 3) Mechanisms for MSC ageing and quality control of stem cell pools.
- 4) Mechanisms of tissue ageing
- 5) Mechanisms of cancer development in stem cell systems.

4. Publications

1. Ueno M, Aoto T, Mohri Y, Yokozeki H and Nishimura EK. Coupling of the radiosensitivity of melanocyte stem cells to their dormancy during the hair cycle. *Pigment Cell Melanoma Res. in press*
2. Morinaga H, Takenaka T, Hashiya F, Kizaki S, Hashiya K, Toshikazu B and Sugiyama H. Sequence-specific electron injection into DNA from an intermolecular electron donor. *Nucleic Acids Res. 41(8):4724-4728. 2013*

Respiratory Medicine

1. Staffs and Students (December, 2013)

Professor	Naohiko INASE	
Junior Associate Professor	Kimitake TSUCHIYA	
Assistant Professor	Toshihide FUJIE,	Tomoya TATEISHI,
	Haruhiko FURUSAWA,	Tsukasa OKAMOTO
Graduate Students	Sahoko CHIBA,	Yuichiro NEI,
	Yoshitoshi KOMAZAKI,	Mayuko TAO,
	Yumi SAKAKIBARA,	Masahiro ISHIZUKA,
	Kozo SUHARA,	Toshiharu TSUTSUI,
	Masahiro MASUO,	Tsuyoshi SHIRAI,
	Makiko SUGIURA	

2. Purpose of Education

Integrated pulmonology is a branch of internal medicine which deals with a variety of pulmonary diseases including tumors, infectious diseases, allergic diseases, non-allergic inflammatory diseases, and genetic disorders. Main objective of integrated pulmonology in the graduate course is to provide students to study specific diagnostic modalities as well as basic scientific findings regarding the pathogenesis of pulmonary diseases. Students are also taught on basic science and its related laboratory technology depending upon their research subject.

3. Research Subjects

- 1) Pathogenesis of hypersensitivity pneumonitis and detection of environmental causative antigen
- 2) Airway remodeling in bronchial asthma model
- 3) Acute exacerbation in pulmonary fibrosis
- 4) Proteomics of pulmonary fibrosis
- 5) Pathogenesis of pulmonary fibrosis and emphysema

4. Clinical Services

Integrated pulmonology 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.

5. Publications

Original Article

1. Miyazaki Y, Unoura K, Tateishi T, Akashi T, Takemura T, Inase N, Yoshizawa Y: Higher serum CCL17 maybe a promising predictor of acute exacerbation in chronic hypersensitivity pneumonitis. *Respir Res* 14: 57, 2013.
2. Komazaki Y, Sakashita H, Furuie M, Fujie T, Tamaoka M, Sumi Y, Miyazaki Y, Kojima K, Jin Y, Inase N: Feasibility study of adjuvant chemotherapy of S-1 and carboplatin for completely resected non-small cell lung cancer. *Chemotherapy* 59: 35-41, 2013.
3. Sakashita H, Inoue H, Akamine S, Ishida T, Inase N, Shirao K, Mori M, Minori K: Identification of the *NEDD4L* gene as a prognostic marker by integrated microarray analysis of copy number and gene expression in non-small cell lung cancer. *Ann Surg Oncol*.
4. Okamoto T, Miyazaki Y, Ogura T, Chida K, Kohno N, Kohno S, Taniguchi H, Akagawa S, Mochizuki Y, Yamauchi K, Takahashi H, Johkoh T, Homma S, Kishi K, Ikushima S, Konno S, Mishima M, Ohta K, Nishioka Y, Yoshimura N, Munakata M, Watanabe K, Miyashita Y, Inase N: A nationwide epidemiological survey of chronic hypersensitivity pneumonitis in Japan. *Respir Invest* 51: 191-199, 2013.
5. Nei Y, Obana-Ninomiya K, Tsutsui H, Ishiwata K, Miyasaka M, Matsumoto K, Nakae S, Kanuka H, Inase N, Karasuyama H: GATA-1 regulates the generation and function of basophils. *Proc Natl Acad Sci USA* 93: 18620-18625, 2013.
6. Chiba, Tsuchiya K, Sakashita H, Ito E, Inase N: Rifampicin-induced acute kidney injury during the initial treatment of pulmonary tuberculosis: A case report and literature review. *Intern Med* 52: 2457-2460, 2013.

7. Komazaki Y. Miyazaki Y. Fujie T. Sakashita H. Tsuchiya K. Tamaoka M. Sumi Y. Maruyama Y. Nanki T. Inase N: Serodiagnosis of *Mycobacterium avium* complex pulmonary disease in rheumatoid arthritis. Respiration DOI: 10.1159/000354791, 2013.

Gastroenterology and Hepatology

1. Staffs and Students (April, 2013)

Professor	Mamoru WATANABE	
Professor	Yasuhiro ASAHINA (Department for Hepatitis Control),	
Associate Professor	Kazuo OHTSUKA (Department of Endoscopic Diagnosis and Therapeutics)	
	Ryuichi OKAMOTO (Department of Advanced Therapeutics in Gastrointestinal Diseases)	
	Tetsuya NAKAMURA (Department of Advanced Therapeutics in Gastrointestinal Diseases)	
	Kiichiro TSUCHIYA (Department of Advanced Therapeutics in Gastrointestinal Diseases)	
	Shinya OOKA (Cancer Center)	
	Mina NAKAGAWA (Center for Interprofessional Education)	
Junior Associate Professor	Akihiro ARAKI,	
	Sei KAKINUMA (Department for Hepatitis Control),	
	Yasuhiro ITSUI (Department of General Medicine)	
Assistant Professor	Masakazu NAGAHORI,	Cheng-Hsin AZUMA,
	Shigeru OSHIMA,	Takashi NAGAISHI,
	Toshimitu FUJII,	Yasuhiro NEMOTO,
	Yoshiki WADA (Department of Endoscopic Diagnosis and Therapeutics)	
Tokunin Assistant Professor	Megumi FUJITA	
Hospital Staff	Yuki SAKURAI,	Eiko SAITO,
	Yoshihito KANO,	Yu ASANO (April~),
	Hanako SHISHIDO (April~),	Kento TAKENAKA (April~),
	Sayuri NITTA,	Kohei SUZUKI (April~),
	Masahiro SUZUKI (April~),	Taro WATABE (April~),
Medical Fellow	Tomohiro MIZUTANI	
Tokunin Fellow	Tatsuro MURANO	
Graduate Student	Michihiro SHIMIZU,	Miyako MURAKAWA,
	Masayoshi FUKUDA,	Kouhei YOSHINO,
	Go ITOH,	Nobukatsu HORITA,
	Yu MATSUZAWA,	Kengo NOZAKI,
	Masahiro TAKAHARA,	Hukiko KAWAI,
	Miki TANIGUCHI,	Hideto YAMANAKA,
	Kenji OOTANI,	Keita FUKUSHIMA
	Masanori KOBAYASHI,	Satoru FUJII,
	Hideji HIBIYA,	Yoichi NIBE,
	Fumio GOTO,	Toru NAKATA,
	Taichi MATSUMOTO,	Chiaki MAEYASHIKI
	Ryihei HAYASHI	

2. Education Principles

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.

3. Basic Research Projects

- Elucidating the pathophysiology of inflammatory bowel diseases and development of treatment by disease-specific immune-regulation.
- Development of novel therapeutics for inflammatory and allergic diseases based on gut-specific mucosal immune regulation.
- Basic research and clinical application of regenerative medicine in gastrointestinal diseases.
- Analysis of interferon-resistant hepatitis C virus.
- Comprehensive analysis of susceptibility genes for various gastrointestinal diseases.
- Crosstalk of the signaling pathways in intestinal epithelial cells.
- Functional analysis of the intestine using primary cell culture in vitro.

4. Expert Areas in Clinical Practice

- Immune-regulation based treatment of inflammatory bowel diseases.
- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.
- Clinical trial of innovative treatment for hepatocellular cancer.
- Diagnosis and treatment of small intestinal diseases by balloon enteroscopy and capsule enteroscopy.
- Advanced diagnosis and treatment of colonic diseases by colonoscopy.
- Development of minimally-invasive diagnostic modalities for gastrointestinal diseases (i.e. MR enteroclysis).
- Improved chemotherapy for gastric and pancreatic malignancies.

5. Publications

1. Asahina Y, Hayashi N, Hiramatsu N, Izumi N, Koike K, Kumada H, Oketani M, Suzuki F, Takikawa H, Tanaka A, Tsubouchi H, Yotsuyanagi H: Editors of the Drafting Committee for Hepatitis Management Guidelines: The Japan Society of Hepatology: Guidelines for the Management of Hepatitis C Virus Infection, **Hepato Res.** 43(1):1-34, 2013
2. Asahina Y, Nakagawa M, Kakinuma S, Watanabe M: Polymorphism Near the Interleukin-28B Gene and anti-Hepatitis C viral Response. **J Clin Transl Hepatol**, 1:39-44, 2013
3. Asahina Y, Tsuchiya K, Nishimura T, Muraoka M, Suzuki Y, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nakagawa M, Kakinuma S, Watanabe M, Izumi N: α -fetoprotein levels after interferon therapy and risk of hepatocarcinogenesis in chronic hepatitis C. **Hepatology**. 58(4):1253-1262, 2013
4. Asahina Y, Tsuchiya K, Nishimura T, Muraoka M, Suzuki Y, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nakagawa M, Kakinuma S, Watanabe M, Izumi N: Genetic variation near interleukin 28B and the risk of hepatocellular carcinoma in patients with chronic hepatitis C. **J Gastroentero** (Epub ahead of print), 2013
5. Fujii T, Naganuma M, Kitazume Y, Saito E, Nagahori M, Ohtsuka K, Watanabe M: Advancing MR imaging in Crohn's disease. **Digestion**. (in press), 2013
6. Ito G, Okamoto R, Murano T, Shimizu H, Fujii S, Nakata T, Mizutani T, Yui S, Akiyama-Morio J, Nemoto Y, Okada E, Araki A, Ohtsuka K, Tsuchiya K, Nakamura T, and Watanabe M: Lineage-specific expression of Bestrophin-2 and Bestrophin-4 in human intestinal epithelial cells. **PLoS One**. 8(11):e79693, 2013
7. Kano Y, Tsuchiya K, Zheng X, Horita N, Fukushima K, Hibiya S, Yamauchi Y, Nishimura T, Hinohara K, Gotoh N, Suzuki S, Okamoto R, Nakamura T, Watanabe M: The acquisition of malignant potential in colon cancer is regulated by the stabilization of Atonal homolog 1 protein. 1:432(1):175-181, **Biochem Biophys Res Commun**, 2013
8. Murano T, Okamoto R, Ito G, Nakata T, Hibiya S, Shimizu H, Fujii S, Kano Y, Mizutani T, Yui S, Akiyama-Morio J, Nemoto Y, Tsuchiya K, Nakamura T, Watanabe M: Hes1 promotes the IL-22-mediated antimicrobial response by enhancing STAT3-dependent transcription in human intestinal epithelial cells. **Biochem Biophys Res Commun** 2013; 443(3):840-846.
9. Nakagawa M, Sakamoto N, Watanabe T, Nishimura-Sakurai Y, Onozuka I, Azuma S, Kakinuma S, Nitta S, Kiyohashi K, Kusano-Kitazume A, Murakawa M, Yoshino K, Itsui Y, Tanaka Y, Mizokami M, Watanabe M, Ochanomizu Liver Conference Study Group: Association of ITPA gene variant and serum ribavirin concentration with blood cells

- decline in pegylated interferon-alfa plus ribavirin therapy for chronic hepatitis C. **Hepatol Int.** 7(1):153-161, 2013.
10. Nemoto Y, Kanai T, Takahara M, Oshima S, Nakamura T, Okamoto R, Kiichiro T, Watanabe M: Bone marrow-mesenchymal stem cells are a major source of interleukin-7 and sustain colitis by forming the niche for colitogenic CD4+ memory T cells. **Gut.** 62(8):1142-1152, 2013
 11. Nemoto Y, Kanai T, Takahara M, Oshima S, Okamoto R, Tsuchiya K, Matsumoto S, Watanabe M: Th1/Th17-Mediated Interstitial Pneumonia in Chronic Colitis Mice Independent of Intestinal Microbiota. **J Immunol.**190:6616-6625, 2013
 12. Nitta S, Sakamoto N, Nakagawa M, Kakinuma S, Mishima K, Kusano-Kitazume A, Kiyohashi K, Murakawa M, Nishimura-Sakurai Y, Azuma S, Tasaka-Fujita M, Asahina Y, Yoneyama M, Fujita T, Watanabe M: Hepatitis C virus NS4B protein targets STING and abrogates RIG-I-mediated type-I interferon-dependent innate immunity. **Hepatology.** 57(1):46-58, 2013
 13. Okada E, Araki A, Suzuki S, Watanabe H, Ikeda T, Watanabe T, Kurata M, Eishi M, Watanabe M: Histological diagnosis of follicular lymphoma by biopsy of small intestinal normal mucosa. **Digestive Endoscopy.** 39(5):544-546, 2013
 14. Okamoto R, Nagahori M, Watanabe M: Perspectives for IBD in Japan. **AGA Perspectives.** 9(2):18-19 2013
 15. Saito E, Nagahori M, Fujii T, Otsuka K, Watanabe M: Efficacy of salvage therapy and its effect on operative outcomes in patients with ulcerative colitis, **Digestion JGA Special Issue 2014.** (in press), 2013
 16. Takahara M, Nemoto Y, Oshima S, Matsuzawa Y, Kanai T, Okamoto R, Tsuchiya K, Nakamura T, Yamamoto K, Watanabe M: IL-7 promotes long-term in vitro survival of unique long-lived memory subset generated from mucosal effector memory CD4+ T cells in chronic colitis mice. **Immunol Lett.** 156:82-93, 2013
 17. Tsuchiya K, Asahina Y, Matsuda S, Muraok M, Nakata T, Suzuki Y, Tamaki N, Yasui Y, Suzuki S, Hosokawa T, Nishimura T, Ueda K, Kuzuya T, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Izumi N: These authors contributed equally to this study: Changes in plasma vascular endothelial growth factor at 8 weeks after sorafenib administration as predictors of survival for advanced hepatocellular carcinoma. **British Journal of Cancer.** (in press), 2013
 18. Watanabe M, Hanai H, Nishino H, Yokoyama T, Terada T, Suzuki Y: Comparison of QD and TID Oral Mesalazine for Maintenance of Remission in Quiescent Ulcerative Colitis: A Double - blind, Double - dummy, Randomized Multicenter Study. **Inflamm Bowel Dis.** 19(8):1681-1690, (Epub ahead of print), 2013
 19. Watanabe M, Nishino H, Sameshima Y, Ota A, Nakamura S, Hibi T: Randomised clinical trial: evaluation of the efficacy of mesalazine (mesalamine) suppositories in patients with ulcerative colitis and active rectal inflammation -a placebo- controlled study. **Aliment Pharmacol Ther.** 38(3):264-273, 2013
 20. Fordham RP, Yui S, Hannan NR, Soendergaard C, Madgwick A, Schweiger PJ, Nielsen OH, Vallier L, Pedersen RA, Nakamura T, Watanabe M, Jensen KB :Establishment of Fetal Enteric Progenitors as a Source for Transplantation . **Cell Stem Cell.** 13:734-744, 2013
 21. Fukata N, Okazaki K, Omiya M, Matsushita M, Watanabe M: Hematologic malignancies in the Japanese patients with inflammatory bowel disease. **J Gastroenterol.** (Epub ahead of print), 2013
 22. Hibi T, Sakuraba A, Watanabe M, Motoya S, Ito H, Sato N, Yoshinari T, Motegi K, Kinouchi Y, Takazoe M, Suzuki Y, Matsumoto T, Kawakami K, Matsumoto T, Hirata I, Tanaka S, Ashida T, Matsui T: C- reactive protein is an indicator of serum infliximab level in predicting loss of response in patients with Crohn's disease. **J Gastroenterol.** (Epub ahead of print), 2013
 23. Hisabe T, Hirai F, Matsui T, Watanabe M: Evaluation of diagnostic criteria for Crohn's disease in Japan. **J Gastroenterol.** (Epub ahead of print), 2013
 24. Kiyohashi K, Kakinuma S, Kamiya A, Sakamoto N, Nitta S, Yamanaka H, Yoshino K, Fujiki J, Murakawa M, Kusano-Kitazume A, Shimizu H, Okamoto R, Azuma S, Nakagawa M, Asahina Y, Tanimizu N, Kikuchi A, Nakauchi H, Watanabe M: Wnt5a signaling mediates biliary differentiation of fetal hepatic stem/progenitor cells. **Hepatology,** 57(6):2502-2513, 2013
 25. Kurosaki M, Tanaka Y, Nishida N, Sakamoto N, Enomoto N, Matsuura K, Asahina Y, Nakagawa M, Watanabe M, Sakamoto M, Maekawa S, Tokunaga K, Mizokami M, Izumi N: Model incorporating the ITPA genotype identifies patients at high risk of anemia and treatment failure with pegylated-interferon plus ribavirin therapy for chronic hepatitis C. **J Med Virol.** 85(3):449-458, 2013
 26. Kuwahara E, Asakura K, Nishiwaki Y, Inoue N, Watanabe M, Hibi T, Takebayashi T: Effects of family history on inflammatory bowel disease characteristics in Japanese patients. **J Gastroenterol.** 47(9):961-968, 2012
 27. Naganuma M, Fujii T, Kunisaki R, Yoshimura N, Takazoe M, Takeuchi Y, Saito E, Nagahori M, Asakura K,

- Takebayashi T, Watanabe M: Incidence and characteristics of the 2009 influenza (H1N1) infections in inflammatory bowel disease patients. **Journal of Crohn's & colitis**. 7(4):308-318, (Epub ahead of print), 2013
28. Naganuma M, Kunisaki R, Yoshimura N, Takeuchi Y, Watanabe M: A prospective analysis of the incidence and risk factors for opportunistic infections in patients with inflammatory bowel disease. **J Gastroenterol**. 48(5):595-560, 2013
 29. Naganuma M, Nagahori M, Fujii T, Morio J, Saito E, Watanabe M: Poor recall of prior exposure to varicella zoster, rubella, measles, or mumps in patients with IBD. *Inflamm Bowel Dis*. 19(2):418-422, (Epub ahead of print), 2013
 30. Ohyagi M, Ohkubo T, Yagi Y, Ishibashi S, Akiyama J, Nagahori M, Watanabe M, Yokota T, Mizusawa H: Chronic inflammatory demyelinating polyradiculoneuropathy in a patient with crohn's disease, **Intern Med**. 52(1)125-128, 2013
 31. Ueno F, Matsui T, Matsumoto T, Matsuoka K, Watanabe M, Hibi T, on behalf of the guideline project group of intractable Inflammatory Bowel Disease granted by the Ministry of Health, Labour and Welfare of Japan and the Guidelines Committee of the Japanese: Evidence-based clinical practice guidelines for Crohn's disease, integrated with formal consensus of experts in Japan. **J Gastroenterol**. 48(1)31-72, 2013
 32. Watanabe K, Sasaki I, Fukushima K, Futami K, Ikeushi H, Sugita A, Nezu R, Mizushima T, Kamoka S, Kusunoki M, Yoshioka K, Funayama Y, Watanabe T, Fujii H, Watanabe M: Long-term Incidence and Characteristics of Intestinal Failure in Crohn's disease:A Japanese Multicenter Study. **J Gastroenterol**.(in press), 2013
 33. Izumi N, Asahina Y, Kurosaki M, Yamada G, Kawai T, Kajiwara E, Okamura Y, Takeuchi T, Yokosuka O, Kariyama K, Toyoda J, Inao M, Tanaka E, Morikawa H, Adachi K, Katsushima S, Kudo M, Takaguchi K, Hiasa Y, Chayama K, Yatsushashi H, Oketani M, Kumada H: Inhibition of hepatocellular carcinoma by PegIFN α 2a in patients with chronic hepatitis C: a nationwide multi-center cooperative study. **J Gastroenterol**. 48(3):382-390, 2013
 34. Nakanishi H, Kurosaki M, Nakanishi K, Tsuchiya K, Noda T, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Itakura J, Anami K, Asahina Y, Enomoto N, Higuchi T, Izumi N: Impaired brain activity in cirrhotic patients with minimal hepatic encephalopathy. **Hepato Res**. (Epub ahead of print), 2013
 35. Tamaki N, Kurosaki M, Matsuda S, Nakata T, Muraoka M, Suzuki Y, Yasui Y, Suzuki S, Hosokawa T, Nishimura T, Ueda K, Tsuchiya K, Nakanishi H, Itakura J, Takahashi Y, Matsunaga K, Taki K, Asahina Y, Izumi N: Prospective comparison of real-time tissue elastography and serum fibrosis markers for the estimation of liver fibrosis in chronic hepatitis C patients. **Hepato Res**. (Epub ahead of print), 2013
 36. Tamaki N, Kurosaki M, Tanaka K, Suzuki Y, Hoshioka Y, Kato T, Yasui Y, Hosokawa T, Ueda K, Tsuchiya K, Nakanishi H, Itakura J, Asahina Y, Izumi N: Noninvasive estimation of fibrosis progression overtime using the FIB-4 index in chronic hepatitis C. **J Viral Hepat**. 20: 72-76, 2013.
 37. Toyoda J, Ozeki I, Asahina Y, Izumi N, Takahashi S, Kawakami Y, Chayama K, Kamiya N, Aoki K, Yamada I, Suzuki Y, Suzuki F, Kumada H: Virologic response and safety of 24-week telaprevir alone in Japanese patients infected with hepatitis C virus subtype 1b. **J Viral Hepat**. 20(3):167-173, 2013
 38. Yasui Y, Kudo A, Kurosaki M, Matsuda S, Muraoka M, Tamaki N, Suzuki S, Hosokawa T, Ueda K, Matsunaga K, Nakanishi H, Tsuchiya K, Itakura J, Takahashi Y, Tanaka S, Asahina Y, Enomoto N, Arie S, Izumi N: Reduced organic anion transporter expression is a risk factor for hepatocellular carcinoma in chronic hepatitis C patients: A propensity score matching study. **Oncology**. (in press), 2013
 39. Watanabe D, Kudo SE, Hayashi S, Mori Y, Kodama K, Wakamura K, Miyachi H, Yamamura F, Ohtsuka K, Mikogami T, Kimura S, Fukuchi K, Ikehara N : Endocytoscopy provides an in vivo virtual histopathological diagnosis of Whipple's disease. **Endoscopy**. 45(2)143-144,2013
 40. Callahan JA, Hammer GE, Agelides A, Duong BH, Oshima S, North J, Advincula R, Shifrin N, Truong HA, Paw J, Barrera J, DeFranco A, Rosenblum MD, Malynn BA, Ma A: Cutting edge: ABIN-1 protects against psoriasis by restricting MyD88 signals in dendritic cells. **J Immunol**. 191(2)535-539, 2013
 41. Shao L, Oshima S, Duong B, Advincula R, Barrera J, Malynn BA, Ma A: A20 restricts wnt signaling in intestinal epithelial cells and suppresses colon carcinogenesis. **PLoS One**. 8(5):e62223, 2013
 42. Kudo S, Mori Y, Wakamura K, Ikehara N, Ichimasa K, Wada Y, Kutsukawa M, Misawa M, Kudo T, Hayashi T, Miyachi H, Inoue H, Hamatani S: Endocytoscopy can provide additional diagnostic ability to magnifying chromoendoscopy for colorectal neoplasms. **J Gastroenterol Hepatol**. (Epub ahead of print) , 2013
 43. Kudo S, Sugihara Y, Kida H, Ishida F, Miyachi H, Mori Y, Misawa M, Hisayuki T, Kodama K, Wakamura K, Hayashi T, Wada Y, Hamatani S: Depressed-Type Colonic Lesions and "De Novo" Cancer in Familial Adenomatous Polyposis: A Colonoscopist's Viewpoint. *ISRN Gastroenterol*. (Epub ahead of print), 2013
 44. Kutsukawa M, Kudo S, Ikehara N, Ogawa Y, Wakamura K, Mori Y, Ichimasa K, Misawa M, Kudo T, Wada Y, Hayashi T, Miyachi H, Inoue H, Hamatani S: Efficiency of endocytoscopy in differentiating types of serrated polyps.

Gastrointestinal Endosc. (Epub ahead of print) , 2013

45. Misawa M, Kudo S, Wada Y, Nakamura H, Toyoshima N, Hayashi S, Mori Y, Kudo T, Hayashi T, Wakamura K, Miyachi H, Yamamura F, Hamatani S : Magnifying narrow-band imaging of surface patterns for diagnosing colorectal cancer. **Oncol Rep.** 30(1):350-356, 2013
46. Mori Y, Kudo S, Ikehara N, Wakamura K, Wada Y, Kutsukawa M, Misawa M, Kudo T, Kobayashi Y, Miyachi H, Yamamura F, Ohtsuka K, Inoue H, Hamatani S: Comprehensive diagnostic ability of endocytoscopy compared with biopsy for colorectal neoplasms: a prospective randomized noninferiority trial. **Endoscopy**, 45(2)98-105, 2013

Surgical Oncology

1. Staffs and Students

Professor:	Kenichi SUGIHARA	
Junior Associate Professor:	Satoru IIDA,	Mikito INOKUCHI
Assistant Professor:	Takanobu SATO,	Toshiaki ISHIKAWA,
	Tsuyoshi NAKAGAWA,	Keiji KATO,
	Makoto NAGAHARA,	Hirofumi SUGITA,
	Satoshi OKAZAKI,	Akifumi KIKUCHI
Professor:	Kazuyuki KOJIMA (Minimally invasive surgery center)	
Associate Professor:	Hiroto KOBAYASHI (Minimally invasive surgery center)	
Associate Professor:	Hiroyuki UETAKE (Translational oncology)	
Assistant Professor:	Megumi ISHIGURO (Translational oncology)	
Graduate Student:	Yasushi TAKATSUNO,	Sho OTSUKI,
	Goshi ODA,	Yoshitake FUJIMORI,
	Shinichi YAMAUCHI,	Kohji MIYAZAKI,
	Hideaki MURASE,	Hitoshi SUGIMOTO,
	Nobuko TAMURA,	Toshiyuki ISHIBA,
	Norihito OGAWA,	Taiki MASUDA,
	Mai KASAHARA,	Toshimitsu YANAKA,
	Ayako KAMIYA,	Yuya SATO,
	Masatoshi NAKAGAWA,	Hironobu BABA,
	Hidenori TAKAHASHI,	Noriko IWATA,
	Tokuko IWATA,	Yasunori SOMENO,
	Kyoko HIGUCHI,	Kenta KOBAYASHI

2. Purpose of Education

Main objective of surgical oncology in the graduate course is to provide students with opportunity to study oncology in order to become the well-rounded surgeon who has international and scientific feelings.

3. Research Subjects

- 1) Role of Cox-2 and VEGF in growth of solid tumor and angiogenesis
- 2) Identification of predictive factors for chemo-responsiveness and prognosis in cancer by molecular biological technique.

4. Clinical Services

Surgical oncology clinic performs less invasive operation for cancer of stomach, colon and rectum, and breast with new devices including laparoscope, thereby allowing physiological and neurological functions to be preserved. Moreover, treatment with chemotherapeutic agents for cancer is also conducted.

5. Publications

Original Articles

1. Gordon AC, Kojima K, Inokuchi M, Kato K, Sugihara K. Long-term comparison of laparoscopy-assisted distal gastrectomy and open distal gastrectomy in advanced gastric cancer. *Surg Endosc.*2013 ; 27(2):462-470
2. Inokuchi M, Kojima K, Yamada H, Kato K, Enjoji M, Hayashi M, Motoyama K, Sugihara K. Clinical Outcomes of Laparoscopy-assisted Gastrectomy for Patients With Heart Disease. *Surg Laparosc Endosc Percutan Tech.*2013 ; 23(1):69-73
3. Inokuchi M, Kojima K, Yamada H, Kato K, Hayashi M, Motoyama K, Sugihara K. Long-term outcomes of Roux-en-Y and Billroth-I reconstruction after laparoscopic distal gastrectomy. *Gastric Cancer.*2013 ; 16(1):67-73
4. Takatsuno Y, Mimori K, Yamamoto K, Sato T, Nishida A, Inoue H, Imoto S, Kawano S, Yamaguchi R, Toh H, Iimura H, Ishimaru S, Ishii H, Suzuki S, Tokudome S, Watanabe M, Tanaka J, Kudo S, Mochizuki H, Kusunoki M, Yamada K, Shimada Y, Moriya Y, Miyama S, Sugihara K, Mori M. The rs6983267 SNPs is associated with MYC transcription efficacy, which promotes progression and worsens prognosis of colorectal cancer. *Ann Surg*

Oncol.2013; 20(4):1395-1402

5. Miyazaki K, Inokuchi M, Takagi Y, Kato K, Kojima K, Sugihara K. EphA4 is a prognostic factor in gastric cancer. *BMC Clinical Pathology*.2013;13:19
6. Ishiguro M, Kotake K, Nishimura G, Tomita N, Ichikawa W, Takahashi K, Watanabe T, Furuhashi T, Kondo K, Mori M, Kakeji Y, Kanazawa A, Kobayashi M, Okajima M, Hyodo I, Miyakubo K, Sugihara K. Study protocol of the B-CAST study: a multicenter, prospective cohort study investigating the tumor biomarkers in adjuvant chemotherapy for stage III colon cancer. *BMC Cancer*.2013; 13:149
7. Inokuchi M, Kojima K, Kato K, Motoyama K, Sugita H, Sugihara K. Feasibility of laparoscopic-assisted gastrectomy for patients with chronic obstructive pulmonary disease. *Surg Endosc*. 2013; 27:2102-2109
8. Kobayashi H, Kotake K, Sugihara K. Prognostic significance of peritoneal lavage cytology in patients with colorectal cancer. *Int J Clin Oncol*.2013; 18:411-417
9. Ogawa N, Iseki H, Tsunozaki H, Hayashi M, Baba H, Matsuyama T, Uetake H, Sugihara K. An intra-abdominal desmoid tumor difficult to distinguish from a gastrointestinal stromal tumor : report of two cases. *Surg Today*. 2013;in print
10. Kobayashi H, Kotake K, Sugihara K. Prognostic scoring system for stage IV colorectal cancer: is the AJCC sub-classification of stage IV colorectal cancer appropriate? *Int J Clin Oncol*.2013; 18:696-703
11. Kobayashi H, Miyata H, Gotoh M, Baba H, Kimura W, Kitagawa Y, Nakagoe T, Shimada M, Tomita N, Sugihara K, Mori M. Risk model for right hemicolectomy based on 19,070 Japanese patients in the National Clinical Database. *J Gastroenterol*.2013;inprint
12. Watanabe T, Yoshino T, Uetake H, Yamazaki K, Ishiguro M, Kurokawa T, Saijo N, Ohashi Y, Sugihara K. KRAS Mutational Status in Japanese Patients with Colorectal Cancer:Results from a Nationwide, Multicenter, Cross-sectional Study. *Jpn J Clin Oncol*.2013; 43(7)706-712
13. Yamada Y, Takahashi D, Matsumoto H, Baba H, Nakamura M, Yoshida K, Yoshida M, Iwamoto S, Shimada K, Komatsu Y, Sasaki Y, Satoh T, Takahashi K, Mishima H, Muro K, Watanabe M, Sakata Y, Morita S, Shimada Y, Sugihara K. Leucovorin, fluorouracil, and oxaliplatin plus bevacizumab versus S-1 and oxaliplatin plus bevacizumab in patients with metastatic colorectal cancer(SOFT):an open-label, non-inferiority, randomised phase 3 trial. *Lancet Oncol*.2013; 14(13):1278-1286
14. Kinugasa Y, Arakawa T, Murakami G, Fujimiya M, Sugihara K. Nerve supply to the internal anal sphincter differs from that to the distal rectum:an immunohistochemical study of cadavers. *Int J Colorectal Dis*.2013;in print
15. Yamauchi S, Iida S, Ishiguro M, Ishikawa T, Uetake H, Sugihara K. Clinical significance of platelet-derived growth factor-C expression in colorectal cancer. *J Cancer therapy*.2013; in print
16. Kinugasa Y, Arakawa T, Abe H, Jose Francisco Rodriguez-Vazquez, Murakami G, Sugihara K. Female Longitudinal Anal Muscles or Conjoint Longitudinal Coats Extend into the Subcutaneous Tissue along the Vaginal Vestibule:A Histological Study Using Human Fetuses. *Yonsei Medical Journal*.2013; 54(3) : 778-784
17. Shiomi A, Kinugasa Y, Yamaguchi T, Tsukamoto S, Tomioka H, Kagawa H. Feasibility of Laparoscopic Intersphincteric Resection for Patients with cT1-T2 Low Rectal Cancer. *Digestive Surgery*.2013; 30 : 272-277

Review Articles

1. Ishiguro M, Watanabe T, Kotake K, Sugihara K. Japanese Society for Cancer of the Colon and Rectum Guidelines 2010 for the treatment of colorectal cancer:comparison with western guidelines.*Colorectal Cancer*.2013 ; 2(2)179-190.
2. Sato Y, Ojima H, Onaya H, Mori T, Hiraoka N, Kishi Y, Nara S, Esaki M, Shimada K, Kosuge T, Sugihara K, Kanai Y. Histopathological characteristics of hypervascular cholangiocellular carcinoma as an early stage of cholangiocellular carcinoma.*Hepatol Res* 2013;in print

Books

1. Sugihara K. Abdominoperineal resection, Chapter 4. Idezuki Y ed.In *Visual lectures on cancer operation in Japan*. Inter Medica 東京 2013年 179-186 Inter Medica

Cardiovascular Medicine

1. Staffs and Students (April, 2013)

Professor	Mitsuaki Isobe	
Clinical Professor	Kenzo Hirao	
Associate Professor	Takashi Ashikaga, Tetsuo Sasano (Graduate School of Health Care Sciences, Biofunctional Informatics)	
Junior Associate Professor	Yasuhiro Yokoyama,	Go Haraguchi (Department of Critical Care Medicine)
Assistant Professor	Mihoko Kawabata, Shunji Yoshikawa, Yasuaki Tanaka, Taro Sasaoka, Yusuke Ebana (Medical Research Institute, Bio-informational Pharmacology), Yasuhiro Maejima,	Ryoko Azuma, Ken Kurihara, Shingo Maeda,
Graduate Student	Chisato Takamura, Kentarō Takahashi, Masahiko Setoguchi, Tomoko Manno, Tomoyo Sugiyama, Koji Sugiyama, Ryota Iwatsuka, Yoko Kato, Yoichi Otaki, Atsuhiko Yagishita, Osamu Inaba, Naoyuki Miwa, Riri Watanabe, Norifumi Murai, Tetsuo Yamaguchi, Maki Ohno, Takashi Nakagawa, Ryo Watanabe,	Daisuke Tezuka Yu Hatano, Tetsuo Ohmi, Susumu Tao, Daisuke Ueshima, Kensuke Ihara, Kei Takayama, Toru Miyazaki, Yuji Konishi, Masaaki Takigawa, Tatsuya Fujinami, Masahito Suzuki, Rena Nakamura, Tomoyuki Umemoto, Shunsuke Hirose, Hironori Sato, Keiichi Hishikari, Hidetsugu Nomoto, Makiko Tsukahara

2. Education

The Department of Cardiovascular Medicine at Tokyo Medical and Dental University (TMDU) primarily aims at offering patient-centered care for every person who suffer from cardiovascular diseases, including ischemic heart diseases, arrhythmia, heart failure, valvular disorders and vasculitis. Our cardiologists are experts in electrophysiology, interventional cardiology, heart failure, and cardiac imaging who make full use of state-of-the-art diagnostic tests and therapeutic procedures to provide high-quality care for every patient. We also actively engage in basic and clinical research to elucidate the mechanism of heart & vessel disorders for providing novel therapeutic strategies to the patients of cardiovascular diseases. In addition to high-quality patient care and innovative research, our faculty members are vigorously involved in the education and training to the young physicians and researchers specializing in cardiovascular medicine. Thus, we are continuously making every effort to serve the highest quality of patient care, education and innovative research of cardiovascular medicine.

3. Research Subjects

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, thereby developing novel technologies for diagnosis and treatment. For that purpose we investigate clinical cases and experimental animal models. Our faculty members pursue a wide variety of basic research, ranging from investigations on the molecular mechanism of heart failure to the development of novel interventional devices for patients with angina pectoris. Current strengths of the program include innovation of the next-generation drug-eluting balloon for percutaneous coronary intervention by the Chief of this Department, Mitsuaki Isobe MD, and molecular cardiology under Yasuhiro Maejima MD, PhD. We also actively investigate immunocardiology, the molecular mechanism of pulmonary hypertension and

periodontitis-associated cardiovascular diseases.

- 1) Clinical study of gene therapy for coronary artery disease (Isobe)
- 2) Clinical study for treatment of acute coronary syndrome (Isobe, Ashikaga, Yoshikawa)
- 3) Molecular mechanism and treatment of myocardial ischemia and reperfusion injury (Isobe, Haraguchi)
- 4) Molecular mechanism and treatment of coronary restenosis and vascular disease (Isobe)
- 5) Gene therapy of myocarditis and cardiac chronic rejection (Isobe, Suzuki)
- 6) Cardiac rejection and immunological tolerance (development of safe immunosuppressive therapy) (Isobe, Suzuki)
- 7) Treatment of heart failure and cardiomyopathy by myocardial regeneration (Isobe, Maejima)
- 8) Regulation of arteriosclerosis by targeting transcription factors (Isobe, Maejima)
- 9) Gene therapy of vascular disease (Isobe)
- 10) Diagnostic imaging of aortitis (Isobe)
- 11) Molecular mechanism and treatment of aortitis (Isobe, Maejima)
- 12) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia (Isobe)
- 13) Application in gene therapy for heart failure and cardiomyopathy (Isobe, Maejima)
- 14) Molecular system of myocardial remodeling in heart failure and ventricular hypertrophy (Isobe)
- 15) Therapy of sleep apnea syndrome with heart failure (Isobe)
- 16) Assessment by imaging of coronary artery and cardiac function (Isobe, Tezuka)
- 17) System of origin with tachyarrhythmias (particularly supraventricular tachycardia) (Hirao)
- 18) Medical therapy and ablation for tachyarrhythmias (Hirao)
- 19) Research for the conduction of atrio-ventricular node (Hirao)
- 20) Research and Therapy for arrhythmia by using cardioendoscopy (Hirao)
- 21) Research of atrial fibrillation from origin of pulmonary vein (Hirao)
- 22) Research of genetic factor with atrial fibrillation (Hirao)
- 23) Research of ablation for atrial fibrillation (Hirao, Yokoyama)

There are many fruitful collaborative efforts between our department and other departments with the TMDU, such as the Department of Bio-informational Pharmacology, Medical Research Institute. Collaborations with other institutions are also common. Especially, we closely collaborate with the Department of Advanced Clinical Science and Therapeutics, University of Tokyo (Junichi Suzuki MD, PhD). Our cardiologists continuously contribute to establish evidence-based cardiovascular medicine through clinical researches. So far, we are engaged in over ten clinical studies. The targets of our clinical research include heart failure, ischemic heart disease, arrhythmia, cardiac imaging and Takayasu arteritis.

4. Clinical Services

Our clinical training program provides the trainee with outstanding skills in clinical cardiology. The trainees will develop their clinical knowledge, clinical judgment, procedural skills and interpersonal skills required as a specialist in cardiovascular diseases. The program provides clinical cardiology training not only at the University Hospital but also at our outstanding affiliate hospitals (N=22), including Kameda General Hospital, Musashino Red-Cross Hospital, Tsuchiura Kyodo Hospital and Yokosuka Kyosai Hospital. Our training program for research emphasizes developing academic cardiologists who will become leaders in cardiovascular research. The program offers training of basic, clinical and translational researches not only at the Graduate School of our department but also at other departments with the TMDU and at other institutions described above.

5. Publications

Review

1. Isobe M: Takayasu Arteritis: Advances in Diagnosis and Medical Treatment. *Clin Exp Nephrol* 17: 686-689, 2013
2. Isobe M: Takayasu Arteritis Revisited: Current Diagnosis and Treatment. *Int J Cardiol* 168(1): 3-10, 2013

Original Article

1. Aoyama N, Suzuki J, Ogawa M, Watanabe R, Kobayashi N, Hanatani T, Ashigaki N, Sekinishi A, Izumi Y, Isobe M: Toll-like receptor-2 plays a fundamental role in the periodontal bacteria-accelerated abdominal aortic aneurysms. *Circ J* 77(6): 1565-1573, 2013
2. Ashigaki N, Suzuki J, Ogawa M, Watanabe R, Aoyama N, Kobayashi N, Hanatani T, Sekinishi A, Zempo H, Tada Y,

- Takamura C, Wakayama K, Hirata Y, Nagai R, Izumi Y, Isobe M: Periodontal bacteria aggravate experimental autoimmune myocarditis in mice. *Am J Physiol Heart Circ Physiol* 304(5): H740-748, 2013
3. Ashigaki N, Suzuki J, Aoyama N, Ogawa M, Watanabe R, Kobayashi N, Komuro I, Izumi Y, Isobe M: The periodontal pathogen *Aggregatibacter actinomycetemcomitans* affects experimental autoimmune myocarditis in mice. *Int Heart J* 54: 412-416, 2013
 4. Hachiya H, Yamauchi Y, Iesaka Y, Yagishita A, Sasaki T, Higuchi K, Kawabata M, Sugiyama K, Tanaka Y, Kusa S, Nakamura H, Miyazaki S, Taniguchi H, Isobe M, Hirao K: Discrete prepotential as an indicator of successful ablation in patients with coronary cusp ventricular arrhythmia. *Circ Arrhythm Electrophysiol* 6(5): 898-904, 2013
 5. Hamaya R, Ogawa M, Suzuki J, Kobayashi N, Hirata Y, Nagai R, Komuro I, Isobe M: A selective peroxisome proliferator activated receptor- β/δ agonist attenuates neointimal hyperplasia after wire-mediated arterial injury. *Expert Opin Invest Drug* 22(9): 1095-106, 2013
 6. Hariharan N, Ikeda Y, Hong C, Alcendor RR, Usui S, Gao S, Maejima Y, Sadoshima J: Autophagy plays an essential role in mediating regression of hypertrophy during unloading of the heart. *PLoS One* 8: e51632, 2013
 7. Hayashi T, Naito S, Kumagai K, Ohshima S, Hachiya H, Hirao K, Isobe M: Ventricular tachycardia associated with a giant right atrial diverticulum. *J Am Coll Cardiol* 62: 2341, 2013
 8. Hayashi T, Kumagai K, Naito S, Goto K, Kaseno K, Ohshima S, Hachiya H, Hirao K, Isobe M: Preprocedural therapeutic international normalized ratio influence on bleeding complications in atrial fibrillation ablation with continued anticoagulation with warfarin. *Circ J* 77(2): 338-344, 2013
 9. Hikita H, Shigeta T, Kojima K, Oosaka Y, Hishikari K, Kawaguchi N, Nakashima E, Sugiyama T, Akiyama D, Kamiishi T, Kimura S, Takahashi Y, Kuwahara T, Sato A, Takahashi A, Isobe M: Lipoprotein(a) is an important factor to determine coronary artery plaque morphology in patients with acute myocardial infarction. *Coron Artery Dis* 24(5): 381-385, 2013
 10. Hikita H, Kuroda S, Oosaka Y, Kawaguchi N, Nakashima E, Sugiyama T, Akiyama D, Kamiishi T, Kimura S, Takahashi Y, Kuwahara T, Sato A, Takahashi A, Isobe M: Impact of statin use before the onset of acute myocardial infarction on coronary plaque morphology of the culprit lesion. *Angiology* 64(5): 375-378, 2013
 11. Hosokawa S, Haraguchi G, Sasaki A, Arai H, Muto S, Itai A, Doi S, Mizutani S, Isobe M: Pathophysiological roles of nuclear factor kappaB (NFkB) in pulmonary arterial hypertension: effects of synthetic selective NF-kB inhibitor IMD-0354. *Cardiovasc Res* 99(1): 35-43, 2013
 12. Ihara K, Nitta J, Hirao K, Isobe M: Atrial tachycardia originating from the hepatic segment of inferior vena cava in interruption of inferior vena cava with azygos continuation. *J Interv Card Electrophysiol* 36: 261-266, 2013
 13. Ishihara T, Haraguchi G, Tezuka D, Kamiishi T, Inagaki H, Isobe M: Diagnosis and assessment of Takayasu arteritis by multiple biomarkers. *Circ J* 77(2): 477-483, 2013
 14. Kanno Y, Suzuki J, Watanabe R, Ogawa M, Isobe M: Chlorogenic acid attenuates ventricular remodeling after myocardial infarction in mice. *Int Heart J* 54(3): 176-180, 2013
 15. Kawabata M, Yokoyama Y, Sasano T, Hachiya H, Tanaka Y, Yagishita A, Sugiyama K, Nakamura T, Suzuki M, Isobe M, Hirao K: Bleeding events and activated partial thromboplastin time with dabigatran in clinical practice. *J Cardiol* 62(2): 121-126, 2013
 16. Kawata H, Morita H, Yamada Y, Noda T, Satomi K, Aiba T, Isobe M, Nagase S, Nakamura K, Kusano KF, Ito H, Kamakura S, Shimizu W: Prognostic significance of early repolarization in inferolateral leads in Brugada patients with documented ventricular fibrillation: A novel risk factor for Brugada syndrome with ventricular fibrillation. *Heart Rhythm* 10(8): 1161-1168, 2013
 17. Kimura S, Inagaki H, Haraguchi G, Sugiyama T, Miyazaki T, Hatano Y, Yoshikawa S, Ashikaga T, Isobe M: Relationships of elevated systemic pentraxin-3 levels with high-risk coronary plaque components and impaired myocardial perfusion after percutaneous coronary intervention in patients with ST-elevation acute myocardial infarction. *Circ J* 78(1): 159-169, 2013
 18. Kurabayashi M, Okishige K, Asano M, Suzuki H, Shimura T, Iwai S, Kato N, Ihara K, Aoyagi H, Isobe M: Cardiopulmonary arrest caused by coronary spasm after coronary vasodilator withdrawal during peri-operative period of gastrectomy. *Intern Med* 52(1): 81-84, 2013
 19. Maeda S, Yamauchi Y, Tao S, Okada H, Obayashi T, Hirao K: Small reentrant atrial tachycardia adjacent to left aortic sinus of valsalva. *Circ J* 77(12): 3054-3055, 2013
 20. Maejima Y, Kyoj S, Zhai P, Liu T, Li H, Ivessa A, Sciarretta S, Del Re DP, Zablocki DK, Hsu CP, Lim DS, Isobe M, Sadoshima J: Mst1 inhibits autophagy by promoting the interaction between Beclin1 and Bcl-2. *Nat Med* 19(11): 1478-1488, 2013

21. Masumura M, Watanabe R, Nagashima A, Ogawa M, Suzuki J, Shichiri M, Komuro I, Isobe M: Anti-salusin- β antibody enhances angiogenesis after myocardial ischemia reperfusion injury. *Expert Opin Ther Tar* 17(9): 1003-1009, 2013
22. Miyabe C, Miyabe Y, Miura NN, Takahashi K, Terashima Y, Toda E, Honda F, Morio T, Yamagata N, Ohno N, Shudo K, Suzuki J, Isobe M, Matsushima K, Tsuboi R, Miyasaka N, Nanki T: Am80, a retinoic acid receptor agonist, ameliorates murine vasculitis through the suppression of neutrophil migration and activation. *Arthritis Rheum* 65(2): 503-512, 2013
23. Miyazaki S, Kobori A, Hocini M, Shar AJ, Taniguchi H, Kusa S, Uchiyama T, Nakamura H, Hachiya H, Isobe M, Hirao K, Haissaguerre M, Takahashi A, Iesaka Y: Clinical Utility of Adenosine-Infusion test at Repeat Atrial Fibrillation Ablation procedure. *Heart Rhythm* 10(5): 629-635, 2013
24. Miyazaki S, Uchiyama T, Komatsu Y, Taniguchi H, Kusa S, Nakamura H, Hachiya H, Isobe M, Hirao K, Iesaka Y: Long-term Complications of Implantable Defibrillator Therapy in Brugada Syndrome. *Am J Cardiol* 111(10): 1448-1451, 2013
25. Miyazaki S, Taniguchi H, Komatsu Y, Uchiyama T, Kusa S, Nakamura H, Hachiya H, Isobe M, Hirao K, Iesaka Y: Sequential biatrial linear defragmentation approach for persistent atrial fibrillation. *Heart Rhythm* 10(3): 338-346, 2013
26. Murai T, Lee T, Yonetsu T, Iwai T, Takagi T, Hishikari K, Masuda R, Iesaka Y, Isobe M, Kakuta T: Variability of Index of Microcirculatory Resistance and its Relationship with Fractional Flow Reserve in Patients with Intermediate Coronary Artery Lesions. *Circ J* 77(7): 1769-1777, 2013
27. Murakami M, Suzuki J, Yamazaki S, Ikezoe M, Matsushima R, Ashigaki N, Aoyama N, Kobayashi N, Wakayama K, Akazawa H, Komuro I, Izumi Y, Isobe M: High incidence of *Aggregatibacter actinomycetemcomitans* infection in patients with cerebral infarction and diabetic renal failure: A cross-sectional study. *BMC Infect Dis* 13: 557, 2013
28. Nakamura T, Hachiya H, Tanaka Y, Yagishita A, Sugiyama K, Suzuki M, Kawabata M, Sasano T, Hirao K, Isobe M: Distribution of the origin of adenosine triphosphate-sensitive atrial tachycardias with the earliest activation recorded in the His bundle catheter: Are they limited to the immediate vicinity of the His bundle? *Circ J* 77(3): 626-631, 2013
29. Setoguchi M, Iwasawa E, Hashimoto Y, Isobe M: A patient with infective endocarditis caused by community-acquired *Pseudomonas aeruginosa* infection. *Intern Med* 52(11): 1259-1262, 2013
30. Terao C, Yoshifuji H, Kimura A, Matsumura T, Ohmura K, Takahashi M, Shimizu M, Kawguchi T, Chen Z, Naruse TK, Sato-Otsubo A, Ebana Y, Maejima Y, Kinoshita H, Murakami K, Kawabana D, Wada Y, Narita I, Tazaki J, Kawaguchi Y, Yamanaka H, Yurugi K, Miura Y, Maekawa T, Ogawa S, Komuro I, Nagai R, Yamada R, Tabara Y, Isobe M, Mimori T, Matsuda F: Two susceptibility loci to Takayasu arteritis reveal a synergistic role of the IL12B and HLA-B regions in a Japanese population. *Am J Hum Genet* 93(2): 289-297, 2013
31. Takahashi K, Kakuta T, Yonetsu T, Lee T, Koura K, Hishikari K, Murai T, Iesaka Y, Isobe M: In vivo detection of lipid-rich plaque by using a 40-MHz intravascular ultrasound: a comparison with optical coherence tomography findings. *Cardiovasc Interv Ther* 28: 333-343, 2013
32. Tezuka D, Haraguchi G, Inagaki H, Isobe M: Progression of thrombogenesis in large coronary aneurysms during anticoagulant therapy in a Buerger's disease patient. *BMJ Case Reports* 2013; doi: 10. 2013-009945
33. Watanabe R, Azuma R, Suzuki J, Ogawa M, Itai A, Hirata Y, Komuro I, Isobe M: Inhibition of NF-kappaB activation by a novel IKK inhibitor reduces the severity of experimental autoimmune myocarditis via suppression of T-cell activation. *Am J Physiol Heart Circ Physiol* 305: H1761-H1771, 2013
34. Yagishita A, Hachiya H, Kawabata M, Nakamura T, Sugiyama K, Tanaka Y, Sasano T, Isobe M, Hirao K: Amiodarone-Induced Thyrotoxicosis Late after Amiodarone Withdrawal. *Circ J* 77(12): 2898-2903, 2013
35. Zempo H, Suzuki J, Ogawa M, Watanabe R, Tada Y, Takamura C, Isobe M: Chlorogenic acid suppresses a cell adhesion molecule in experimental autoimmune myocarditis in mice. *Immun Endocrinol Metab Agents Med Chem* 13: 232-236, 2013
36. Furukawa T, Hachiya H, Isobe M, Hirao K: Is head injury characteristic of arrhythmic syncope? *J of Arrhythmia* 29: 217-220, 2013
37. Higuchi K, Yamauchi Y, Hirao K, Marrouche NF: The importance of superior vena cava isolation in ablation of strategy for atrial fibrillation. *Curr Opin Cardiol* 28: 2-6, 2013
38. Miyazaki S, Taniguchi H, Kusa S, Uchiyama T, Hirao K, Iesaka Y: Conduction recovery after electrical isolation of superior vena cava: Prevalence and electrophysiological properties. *Circ J* 77: 352-358, 2013
39. Miyazaki S, Taniguchi H, Uchiyama T, Kusa S, Nakamura H, Hachiya H, Hirao K, Iesaka Y: Clinical Impact of

Adenosine Triphosphate Injection on Arrhythmogenic Superior Vena Cave in the Context of Atrial Fibrillation Ablation. *Circ Arrhythm Electrophysiol* 6: 898-904, 2013

40. Miyazaki S, Taniguchi H, Uchiyama T, Kusa S, Nakamura H, Hachiya H, Hirao K, Iesaka Y: Impact of low-dose dipyridamole injection on adenosine test after pulmonary vein isolation. *Pacing Clin Electrophysiol* 36: 1451-1459, 2013
41. Okumura K, Aizawa Y, Hirao K, et al. Guidelines for non-pharmacotherapy of cardiac arrhythmias (JCS2011). *Circ J* 77: 249-274, 2013
42. Takigawa M, Kuwahara T, Takahashi A, Kobori A, Takahashi Y, Okubo K, Watari Y, Kuroda S, Osaka Y, Kawaguchi N, Yamato K, Nakashima E, Sugiyama T, Akiyama D, Kamiishi T, Kimura S, Hikita H, Hirao K, Isobe M: Differences in catheter ablation of paroxysmal atrial fibrillation between male and female. *Int J Cardiol* 168: 1984-1991, 2013
43. Yokoyama Y, Hirao K: Atrial Fibrillation (AF) Termination by Ablation in Patients with Persistent AF. *Circ J* 77: 1399-400, 2013

Anesthesiology

1. Staffs and Students (April, 2013)

Professor	Koshi MAKITA	
Associate Professor	Koichi NAKAZAWA	
Junior Associate Professor	Tokujiro UCHIDA, Jiro KURATA	Seiji ISHIKAWA,
Assistant Professor	Akio MASUDA, Hiroyuki KOBINATA, Takashi HAKUSUI, Yoshie OTANI, Hiroto YAMAMOTO	Maiko SATOMOTO, Mamoru YAMAMOTO Eri IKEDA, Sonomi TANAKA,
Graduate Student	Wei FAN, Yutaka MIURA, Qi YU	Fukami NAKAJIMA, Hiroyuki ITO,

2. Purpose of Education

The Department of Anesthesiology is an integral part of the health care system providing valuable perioperative services as well as pain relief and critical care management. Our goals of education are understanding clinical pathophysiology and clinical pharmacology, which are essential for daily clinical activities to treat patients with critical illness undergoing major surgery and to relieve patients suffering from severe pain.

3. Research Subjects

- 1) Discovering most effective ventilation methods for injury lungs.
- 2) Therapeutic mechanism of mesenchymal stem cell for lung injury
- 3) Studies on the central nervous system effects of general anesthetics by human electrocorticogram and functional neuroimaging.
- 4) Studies on the mechanisms of cerebral pain processing and pain chronification by human functional magnetic resonance imaging and positron emission tomography.
- 5) Studies on ventilator mechanics and remote effects of protective one-lung ventilation during thoracic surgery.
- 6) Studies of epidemiology, early diagnosis, prevention and therapeutics of perioperative acute kidney injury.
- 7) Studies on the effect of anesthetics on the developing brain.

4. Clinical Services

Service of the department of anesthesiology covers perioperative management of surgical patients and pain relief services for patients suffering severe chronic pain.

5. Publications

1. Adachi YU, Satomoto M, Higuchi H, Watanabe K. The determinants of propofol induction time in anesthesia. *Korean J Anesthesiol.* 2013; 65: 121-6.
2. Fan W, Nakazawa K, Abe S, Inoue M, Kitagawa M, Nagahara N, Makita K. Inhaled aerosolized insulin ameliorates hyperglycemia-induced inflammatory responses in the lungs in an experimental model of acute lung injury. *Critical Care* 2013; 17: R83 (28 April 2013)
3. Griesdale D, Ishikawa S, Lohser J. About predictors of acute kidney injury after lung resection. Reply. *Anesth Analg* 2013; 116: 505-6.
4. Senda M, Uchida T, Kobinata H, Nakazawa K, Makita K: i-Gel Supraglottic Airway for Inexperienced Anesthesia Residents. *Open Journal of Anesthesiology*, 2013; 3: 64-66
5. Uchida T, Ohno N, Asahara M, Yamada Y, Yamaguchi O, Tomita M, Makita K. Soluble Isoform of the Receptor for Advanced Glycation End Products as a Biomarker for Postoperative Respiratory Failure after Cardiac Surgery *Plos One* 2013; 8: e70200

Cardiovascular Surgery

1. Staffs and Students (April, 2013)

Professor	Hirokuni ARAI	
Associate Professor	Tomohiro MIZUNO	
Junior Associate Professor	Keiji OI	
Assistant Professor	Masafumi YASHIMA, Susumu MANABE, Shogo SAKURAI,	Tsuyoshi HACHIMARU, Akane MIHARA, Kenji SAKAI
Graduate Student	Hidehito KUROKI, Tatsuki FUJIWARA	Taiju WATANABE,
Hospital Staff	5	

2. Purpose of 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. Research Subjects

- 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

4. Clinical Services

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.

5. Publications in English

Original Articles

1. Tamura K, Arai H, Kawaguchi S, Makita S, Miyagi N, Watanabe T, Fujiwara T. Long-Term Results of Modified Bentall Procedure Using Flanged Composite Aortic Prosthesis. *Ann Thorac Cardiovasc Surg* 2013 Apr; 19(2): 126-130
2. Hosokawa S, Haraguchi Go, Sasaki A, Arai H, Muto S, Itai A, Doi S, Mizutani S, Isobe M. Pathophysiological roles of nuclear factor kappaB (NF-kB) in pulmonary arterial hypertension: effects of synthetic selective NF-kB inhibitor IMD-0354. *Cardiovascular Research*. 2013 Apr; 99: 35-43
3. Fujiwara T, Nagaoka E, Watanabe T, Miyagi N, Kitao T, Sakota D, Mamiya T, Shinshi T, Arai H, Takatani S. New Generation Extracorporeal Membrane Oxygenation With MedTech Mag-Lev, a Single-Use, Magnetically Levitated, Centrifugal Blood Pump: Preclinical Evaluation in Calves. *Artif Organs*. 2013 May; 37(5): 447-56.
4. Fujita S, Tomita M, Moon S, Arai H. Proposal for Concise Method to Explore Reasonable Cutoffs from Clinical Databases by Exploiting Serial Testing. *Journal of the Korean Data Analysis Society* 2013 June; 15(3): 1139-1149
5. Hosokawa S, Haraguchi G, Sasaki A, Arai H, Muto S, Itai A, Doi S, Mizutani S, Isobe M. Pathophysiological roles of nuclear factor kappaB (NF-kB) in pulmonary arterial hypertension: effects of synthetic selective NF-kB inhibitor IMD-0354. *Cardiovascular Res*. 2013 Jul; 99(1):35-43
6. Oi K, Yoshida T, Takeshita M, Tsuruta G. False aneurysm on distal part of coarctation of the aorta in a parous Turner syndrome patient. *General Thoracic and Cardiovascular Surgery* 2013 Sep; 61(9): 531-3

7. Fujita S, Arai H, Tomita M, Mizuno T, Kawaguchi S, Manabe S, Hachimaru T, Miyagi N. Proposal of a Novel Index for Selection of Optimal Annuloplasty Ring Size for Tricuspid Annuloplication. *Circulation Journal* 2013 Oct; 77(10): 2505-2513

Presentation in international conference

1. Arai H. An Innovative Approach for FMR. 2nd Heart Care Heart International Symposium, Chiang Mai, Thailand, 16 Feb 2013
2. Arai H. Beating Heart MV Surgery. 2nd Heart Care Heart International Symposium, Chiang Mai, Thailand, 17 Feb 2013
3. Arai H. Imaging for CABG and Beyond - The Use and Clinical Implications of Intraoperative Imaging During Open Heart Surgery Using VeriQC; Impact of Intra - Operative Direct Coronary Scanning and Graft Validation Using VeriQC: Its Effectiveness and Application Beyond CABG. Luncheon Seminar The 21st Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery, Hyogo, Japan, 6 Apr 2013
4. Arai H. Management of subvalvular structure. Heart Valve Disease Forum 2013, Seoul, Korea, 31 Aug 2013
5. Arai H. OPCAB in Japan & Confirmation of Graft Patency. 2013 Winter Workshop of ISMICS, Seoul Korea, 9 Nov 2013
6. Arai H, Watanabe T, Hachimaru T, Manabe S, Mizuno T. New Concept of Valvular Surgery; Beating Mitral Valve Repair: Technique and Results The 21st Annual Meeting of the Asian Society for Cardiovascular and Thoracic Surgery, Hyogo, Japan, 6 Apr 2013
7. Arai H, Watanabe T, Manabe S, Nagaoka E, Fujiwara T, Hachimaru T, Kawaguchi S, Mizuno T. Influence of Procedural Difference on Mitral Valve Configuration in the Surgical Repair for Functional Mitral Regurgitation: In Which Direction Should Papillary Muscle be Relocated? 2013 AATS Mitral Conclave, New York, USA, 3 May 2013
8. Oi K, Miyata H, Motomura N, Sakata R, Yoshida T, Takamoto S. Carotid Artery Stenosis in CABG Patients with History of Neurologic Event. AATS Annual Meeting 2013, Minneapolis, USA, 7 May 2013
9. Watanabe T, Arai H, Mizuno T, Kawaguchi S, Manabe S, Hachimaru T, Kuroki H, Fujiwara T. Impact of intraoperative direct coronary scanning using 15MHz high frequency epicardial ultrasound 13 ISMICS Annual Scientific Meeting, Prague, Czech Republic, 13 Jun 2013
10. Manabe S, Sakai K, Chieko S, Sakurai S, Fujita S, Fujiwara T, Watanabe T, Kuroki H, Hachimaru T, Kawaguchi S, Mizuno T, Arai H. Short-term results of enclose II in off-pump CABG. Comparison with the conventional aortic clamping technique. 13 ISMICS Annual Scientific Meeting, Prague, Czech Republic, 13 Jun 2013
11. Manabe S, Kasegawa H, Sojung M, Okada T, Iwasaki K, Fujimoto T, Umezu M, Arai H. In-vitro hemodynamic assessment of newly developed stentless mitral valve (NORMO valve). 13 ISMICS Annual Scientific Meeting, Prague, Czech Republic, 13 Jun 2013
12. Fujiwara T, Mizuno T, Oi K, Yashima M, Manabe S, Hachimaru T, Kuroki H, Watanabe T, Mihara A, Sakurai S, Shibuya C, Sakai K, Kurashima N, Arai H. The Clinical Evaluation of MERA Monopivot Centrifugal Blood Pump as a Mechanical Circulatory Support Device. ISRBP 21th Congress of the International Society for Rotary Blood Pumps. Yokohama, Japan, 28 Sep 2013

Other

1. Arai H. (JCS Joint Working Group) Guidelines for the Clinical Application of Bypass Grafts and the Surgical Techniques (JCS 2011) Published in 2012. *Circulation Journal*. 2013 Jun; 77(6): 1608-1641

Nephrology

1. Staffs and Students (April, 2013)

Professor	Sei SASAKI	
Associate Professor	Shinichi UCHIDA, Tatemitsu RAI (Dept. of Blood Purification) Tomokazu OKADO (Dept. of Chronic Kidney Disease)	
Junior Associate Professor	Eisei SOHARA	
Assistant Professor	Akihito OHTA, Naofumi YUI (Dept. of Blood Purification), Hitoshi KUWANA (Dept. of Life Science and Bioethics Research Center), Hidenori NISHIDA (Dept. of Blood Purification)	
Teacher	Eriko OHTA (Dept. of Chronic Kidney Disease)	
Medical fellow	Mai WAKABAYASHI	
Project Assistant Professor	Soichiro IIMORI	
Hospital Staff	Hiroyuki TANAKA, Junichi ISHIGAMI Katsuhito IHARA, Wakaba YAMAGUCHI (Dept. of Blood Purification, 2013.4~), Haruna AZETSU (Dept. of Blood Purification, 2013.4~), Mayuko NOZAKI (2013.7~)	
Technician	Motoko CHIGA	
Secretary	Asa MURANO, Miki SAKIYAMA, Yukiko ITO	
Graduate Student	Koichiro SUSA, Kiyoshi ISOBE, Takayasu MORI, Yuichi INOUE, Daiei TAKAHASHI, Moko ZENIYA, Eriko KIKUCHI, Yuya ARAKI, Yutaro MORI, Fumiaki ANDO, Yuki YOSHIZAKI	

2. Purpose of Education

The policy of the *Department of Nephrology* is to accomplish trustworthy medicine and to educate excellent academic scientists and nephrologists.

Our department is one of the initial institutes that started the hemodialysis therapy in Japan, and thus, has a long experience of clinical practice of kidney diseases. Through the activities our department has brought up a number of leading nephrologists who contribute to establishing nephrology in Japan and in the world. Academic research is another important mission of our department. Research from bench experiments to clinical studies has been performed to understand the pathogenesis of the diseases and to develop new therapeutic strategies. Especially, our study on “water-electrolyte transport in the kidney and related diseases” is well known worldwide for its originality and high quality. We hope new young scientists and physicians join us for future science and nephrology.

3. Research Subjects

We have been studying renal membrane transporters and channels for more than 20 years. Most of the AQP water channels and CLC chloride channels were cloned in our laboratory in 1990s (*Nature*1993, *PNAS*1994, *JBC*1993&1994, *Neuron*1994, etc) and the physiological roles in vivo have been analyzed by generating the KO mice (*Nature Genet*1999, *PNAS*2006, etc). Recently, we are interested in regulators of transporters and channels (*JCB*2008), and discovered a novel kinase cascade (WNK-OSR1/SPAK-NCC) regulating NaCl balance in the body (*Cell Metab* 2007, *Hum Mol Genet* 2010, *JCS* 2011, *PLoS One* 2011, *Hypertension* 2012, 2013, *Cell Rep* 2013). Based on the molecular mechanisms we identified, we hope to find the way to regulate renal transporters and channels.

4. Clinical Services

We are taking care of a variety of kidney diseases including acute kidney injury, chronic kidney disease, blood purification, and renal transplantation. We routinely perform renal biopsy.

5. Publications

Original Articles

1. Ando F, Okado T, Sohara E, Rai T, Uchida S, Sasaki S. Development of minimal-change glomerular disease and Hashimoto's thyroiditis during the treatment of sarcoidosis. *CEN Case Rep.* 2: 248-51, 2013.
2. Ando F, Sohara E, Ito E, Okado T, Rai T, Uchida S, Sasaki S. Acute poststreptococcal glomerulonephritis with acute interstitial nephritis related to streptococcal pyrogenic exotoxin B. *Clin Kidney J.* 6 (3): 347-348, 2013.
3. Ando R, Kimura H, Sato H, Iwamoto S, Yoshizaki Y, Chida Y, Ishida Y, Takayama M, Yamada K, Tachibana K, Ohtsuka M, Kikuchi K, Inoue A. Multicenter study of long-term (two-year) efficacy of lanthanum carbonate. *Ther Apher Dial.* 17 Suppl 1: 2-8, 2013.
4. Arai Y, Tanaka H, Hirasawa S, Aki S, Inaba N, Aoyagi M, Tsuura Y, Tamura T. Sarcoidosis in a chronic dialysis patient diagnosed by sarcoidosis-related hypercalcemia with no common systemic clinical manifestations: a case report and review of the literature. *Intern Med.* 52(23): 2639-44, 2013.
5. Beaubrun AC, Kanda E, Bond TC, McClellan WM. Form CMS-2728 Data Versus Erythropoietin Claims Data: Implications for Quality of Care Studies. *Ren Fail.* 35: 320-6, 2013.
6. Chu PY, Cheng CJ, Wu YC, Fang YW, Chau T, Uchida S, Sasaki S, Yang SS, Lin SH. SPAK deficiency corrects pseudohypoaldosteronism II caused by WNK4 mutation. *PLoS One.* 8(9): e72969, 2013.
7. Feinstein TN, Yui N, Webber MJ, Wehbi VL, Stevenson HP, J King, D. Jr, Hallows KR, Brown D, Bouley R, Vilardaga JP. Noncanonical control of vasopressin receptor type 2 signaling by retromer and arrestin. *J Biol Chem.* 288: 27849-60, 2013.
8. Fukagawa M, Yokoyama K, Koiwa F, Taniguchi M, Shoji T, Kazama JJ, Komaba H, Ando R, Kakuta T, Fujii H, Nakayama M, Shibagaki Y, Fukumoto S, Fujii N, Hattori M, Ashida A, Iseki K, Shigematsu T, Tsukamoto Y, Tsubakihara Y, Tomo T, Hirakata H, Akizawa T. CKD-MBD Guideline Working Group; Clinical practice guideline for the management of chronic kidney disease-mineral and bone disorder. Japanese Society for Dialysis Therapy. *Ther Apher Dial.* 17: 247-288, 2013.
9. Hata T. Cannabis is an illegal drug in Japan by the enlightenment of United States. An opinion to "Medical Use of Marijuana" (correspondence). February 20, 2013 DOI: 10.1056/NEJMcld1300970.
10. Hata T, Ueda K, Suzuki H, Shimizu T, Maruyama H, Tomita H. Alternating Medical Dispatch Support Provided by the Japanese Red Cross Society after the Great East Japan Earthquake. *J Acad Emerg Med.* 12: 54-56, 2013.
11. Iimori S, Noda Y, Okado T, Naito S, Toda T, Chida Y, Kuwahara M, Ando R, Nishio Y, Maeda Y, Tanaka H, Tamura T, Kimoto S, Kanda E, Inoshita S, Yoshikawa M, Okutsu R, Tajima M, Kusaura T, Kobayashi K, Rai T, Uchida S, Sasaki S. Baseline characteristics and prevalence of cardiovascular disease in newly visiting or referred chronic kidney disease patients to nephrology centers in Japan: a prospective cohort study. *BMC Nephrol.* 14: 152, 2013.
12. Inoue R, Sohara E, Rai T, Satoh T, Yokozeiki H, Sasaki S, Uchida S. Immunolocalization and translocation of aquaporin-5 water channel in sweat glands. *J Dermatol Sci.* 70(1): 26-33, 2013.
13. Ishigami J, Onishi T, Shikuma S, Akita W, Mori Y, Asai T, Kuwahara M, Sasaki S, Tsukamoto Y. The impact of hyporesponsiveness to erythropoietin-stimulating agents on time-dependent mortality risk among CKD stage 5D patients: a single-center cohort study. *Clin Exp Nephrol.* 17: 106-14, 2013.
14. Ishimoto I, Sohara E, Ito E, Okado E, Rai T, Uchida S. Fibronectin glomerulopathy. *Clin Kidney J.* 6 (5): 513-515, 2013.
15. Isobe K, Mori T, Asano T, Kawaguchi H, Nonoyama S, Kumagai N, Kamada F, Morimoto T, Hayashi M, Sohara E, Rai T, Sasaki S, Uchida S. Development of enzyme-linked immunosorbent assays for urinary thiazide-sensitive Na-Cl cotransporter (NCC) measurement. *Am J Physiol Renal Physiol.* 305(9): F1374-81, 2013.
16. Kanda E, Ai M, Iwamoto A, Okazaki M, Maeda Y, Sasaki S, Yoshida M. Relationship between Icodextrin use and decreased level of small low-density lipoprotein cholesterol fractionated by high-performance gel permeation chromatography. *BMC Nephrol.* 14: 234, 2013.
17. Kanda E, Ai M, Okazaki M, Maeda Y, Sasaki S, Yoshida M. The association of very-low-density lipoprotein with ankle-brachial index in peritoneal dialysis patients with controlled serum low-density lipoprotein cholesterol level. *BMC Nephrol.* 14: 212, 2013.
18. Kanda E, Ai M, Yoshida M, Kuriyama R, Shiigai T. High serum bicarbonate level within the normal range prevents the progression of chronic kidney disease in elderly chronic kidney disease patients. *BMC Nephrol.* 14: 4, 2013.
19. Kikuchi H, Yoshimoto T, Tanaka H, Tsujimoto K, Yamamura C, Arai Y, Hirasawa S, Aki S, Inaba N, Aoyagi M, Ogawa Y, Tamura T. Periodic hypokalemia associated with cyclic Cushing's syndrome. *CEN Case Rep.* 2013.
20. Maeda Y, Hirose H, Inadome Y. Renin production site in the end-stage kidney. *Clin Exp Nephrol.* 17: 439-440, 2013.

21. Maeda Y, Yoshida S, Hirai T, Kawasaki T, Kuyama T: Estimated glomerular filtration rate – A more stable indicator than creatinine clearance in peritoneal dialysis practice. *J Rural Med.* 8: 171-175, 2013.
22. Mandai S, Aoyagi M, Nagahama K, Arai Y, Hirasawa S, Aki S, Inaba N, Tanaka H, Tsuura Y, Tamura T, Sasaki S. Post-Staphylococcal infection Henoch-Schönlein purpura nephritis: a case report and review of the literature. *Ren Fail.* 35: 869-74, 2013.
23. Mandai S, Kanda E, Arai Y, Hirasawa S, Hirai T, Aki S, Inaba N, Aoyagi M, Tanaka H, Ikeda T, Tamura T, Sasaki S. Anti-centromere antibody is an independent risk factor for chronic kidney disease in patients with primary biliary cirrhosis. *Clin Exp Nephrol.* 17: 405-10, 2013.
24. Mandai S, Kuwahara M, Kasagi Y, Kusaka K, Tanaka T, Shikuma S, Akita W, Sasaki S. Lower serum sodium level predicts higher risk of infection-related hospitalization in maintenance hemodialysis patients: an observational cohort study. *BMC Nephrol.* 14: 276-284, 2013.
25. Mori T, Kikuchi E, Watanabe Y, Fujii S, Ishigami-Yuasa M, Kagechika H, Sohara E, Rai T, Sasaki S, Uchida S. Chemical library screening for WNK signalling inhibitors using fluorescence correlation spectroscopy. *Biochem J.* 455: 339-45, 2013.
26. Mori Y, Wakabayashi M, Mori T, Araki Y, Sohara E, Rai T, Sasaki S, Uchida S. Decrease of WNK4 ubiquitination by disease-causing mutations of KLHL3 through different molecular mechanisms. *Biochem Biophys Res Commun.* 439: 30-4, 2013.
27. Morishita Y, Miki A, Okada M, Onishi A, Tsuboi S, Ishibashi K, Ando Y, Kusano E. Association of primary care physicians' exercise habits and their age, specialty, and workplace. *J Multidiscip Healthc.* 6: 409-414, 2013.
28. Nakaya I, Yahata M, Takahashi S, Sasajima T, Sakuma T, Shibagaki Y, Soma J. Long-term outcome and efficacy of cyclophosphamide therapy in Japanese patients with ANCA-associated microscopic polyangiitis: a retrospective study. *Intern Med.* 52(22): 2503-9, 2013.
29. Nomura N, Kamiya K, Ikeda K, Yui N, Chiga M, Sohara E, Rai T, Sasaki S, Uchida S. Treatment with 17-allylamino-17-demethoxygeldanamycin ameliorated symptoms of Bartter syndrome type caused by mutated *Bsnd* in mice. *Biochem Biophys Res Commun.* 441: 544-49, 2013.
30. Ohkubo A, Kurashima N, Nakamura A, Miyamoto S, Iimori S, Rai T. Solute Removal Capacity of High Cut-Off Membrane Plasma Separators. *Ther Apher Dial.* 17(5): 484-9, 2013.
31. Ohta A, Schumacher FR, Mehellou Y, Johnson C, Knebel A, Macartney TJ, Wood NT, Alessi DR, Kurz T. The CUL3-KLHL3 E3 ligase complex mutated in Gordon's hypertension syndrome interacts with and ubiquitylates WNK isoforms: disease-causing mutations in KLHL3 and WNK4 disrupt interaction. *Biochem J.* 1; 451(1): 111-22, 2013.
32. Osawa M, Ogura Y, Isobe K, Uchida S, Nonoyama S, Kawaguchi H. CUL3 gene analysis enables early intervention for pediatric pseudohypoaldosteronism type II in infancy. *Pediatr Nephrol.* 9: 1881-4, 2013.
33. Oshio M, Fujii T, Kusaura T, Nagahama K. Relapsing proliferative glomerulonephritis with monoclonal IgG deposits showing circumferential crescentic glomerulonephritis. *Clin Kidney J.* 6: 635-38, 2013.
34. Rieg T, Tang T, Uchida S, Hammond HK, Fenton RA, Vallon V. Adenylate cyclase 6 enhances NKCC2 expression and mediates vasopressin-induced phosphorylation of NKCC2 and NCC. *Am J Pathol.* 182: 96-106, 2013.
35. Sariras T, Borschewski A, McCormick JA, Paliege A, Dathe C, Uchida S, Terker A, Himmerkus N, Bleich M, Demarets S, Laghmani K, Delpire E, Ellison D, Bachmann S, Mutig K. SPAK differentially mediates vasopressin effects on sodium cotransporters. *J Am Soc Nephrol.* 24: 407-418, 2013.
36. Sasaki S, Chiga M, Kikuchi E, Rai T, Uchida S. Hereditary nephrogenic diabetes insipidus in Japanese patients: analysis of 78 families and report of 22 new mutations in AVPR2 and AQP2. *Clin Exp Nephrol.* 17: 338-344, 2013.
37. Satoh F, Morita H, Eishi Y, Yoshimura A. Renal sarcoidosis with limited lung manifestations expressing propionibacterium acnes antigens in the affected tubulointerstitium. *Am J Med Sci.* 346: 250-52, 2013.
38. Shida Y, Matsuoka H, Chiga M, Uchida S, Sasaki S, Sugihara S. Characterization of AQP-2 gene mutation (R254Q) in a family with dominant nephrogenic DI. *Pediatr Int.* 55(1): 105-7, 2013.
39. Shinoda T, Yamasaki M, Chida Y, Takagi M, Tanaka Y, Ando R, Suzuki T, Tagawa H. Improvement of MBD parameters in dialysis patients by a switch to, and combined use of lanthanum carbonate: Josai Dialysis Forum collaborative study. *Ther Apher Dial.* 17 Suppl 1: 29-34, 2013.
40. Takahashi D, Mori T, Wakabayashi M, Mori Y, Susa K, Zeniya M, Sohara E, Rai T, Sasaki S, Uchida S. KLHL2 interacts with and ubiquitinates WNK kinases. *Biochem Biophys Res Commun.* 437(3): 457-62, 2013.
41. Tsuji S, Yamashita M, Unishi G, Takewa R, Kimata T, Isobe K, Chiga M, Uchida S, Kaneko K. A young child with pseudohypoaldosteronism type II by a mutation of Cullin 3. *BMC Nephrol.* 14: 166, 2013.
42. Yahata M, Nakaya I, Sakuma T, Sato H, Aoki S, Soma J. Immunoglobulin A nephropathy with massive

- paramesangial deposits caused by anti-vascular endothelial growth factor therapy for metastatic rectal cancer: a case report and review of the literature. *BMC Res Notes*. 6: 450, 2013.
43. Yang SS, Fang YW, Tseng MH, Chu PY, Yu IS, Wu HC, Lin SW, Chau T, Uchida S, Sasaki S, Lin YF, Sytwu HK, Lin SH. Phosphorylation regulates NCC stability and transporter activity in vivo. *J Am Soc Nephrol*. 24(10): 1587-97, 2013.
 44. Yoshioka W, Mori T, Nagahama K, Tamura T. Biopsy-proven drug-induced tubulointerstitial nephritis in a patient with acute kidney injury and alcoholic severe acute pancreatitis. *BMJ Case Rep*. May 3, 2013.
 45. Yui N, Lu HJ, Chen Y, Nomura N, Bouley R, Brown D. Basolateral targeting and microtubule dependent transcytosis of the aquaporin-2 water channel. *Am J Physiol Cell Physiol*. 304: C38-48, 2013.
 46. Wakabayashi M, Mori T, Isobe K, Sohara E, Susa K, Araki Y, Chiga M, Kikuchi E, Nomura N, Mori Y, Matsuo H, Murata T, Nomura S, Asano T, Kawaguchi H, Nonoyama S, Rai T, Sasaki S, Uchida S. Impaired KLHL3-mediated ubiquitination of WNK4 causes human hypertension. *Cell Rep*. 3(3): 858-68, 2013.
 47. Wakui H, Tamura K, Masuda S, Tsurumi-Ikeya Y, Fujita M, Maeda A, Ohsawa M, Azushima K, Uneda K, Matsuda M, Kitamura K, Uchida S, Toya Y, Kobori H, Nagahama K, Yamashita A, Umemura S. Enhanced angiotensin receptor-associated protein in renal tubule suppresses angiotensin-dependent hypertension. *Hypertension*. 61(6): 1203-10, 2013.
 48. Zeniya M, Sohara E, Kita S, Iwamoto T, Susa K, Mori T, Oi K, Chiga M, Takahashi D, Yang SS, Lin SH, Rai T, Sasaki S, Uchida S. Dietary salt intake regulates WNK3-SPAK-NKCC1 phosphorylation cascade in mouse aorta through angiotensin II. *Hypertension*. 62(5): 872-878, 2013.

Review Articles

1. Kanda E. Dyslipidaemia in patients with chronic kidney disease and treatment. *OA Nephrology*. 1:10, 2013.

Comprehensive Reproductive Medicine (Maternal and Women's Clinic)

1. Staffs and Students (2013)

Professor :	Toshiro KUBOTA	
Associate Professor :	Satoshi OBAYASHI	
Professor(chairman) :	Naoyuki MIYASAKA	
Junior Associate Professor :	Naoyuki YOSHIKI,	Tatsuya HARADA,
Associate professor (chairman) :	Masakazu TERAUCHI	
Assistant professor :	Akira WAKABAYASHI,	Kimio WAKANA,
	Mikayo TOBA,	Rie OI,
	Makiko EGAWA,	Yuki IWAHARA,
	Noriko SUDO(OSHIMA),	Shiro HIRAMITSU,
	Masato YAMANAKA,	Asami HIRATA
Hospital Staff :	Takeru ICHIMURA,	Shunsuke ISHIYAMA,
	Rei HARUYAMA,	Masaomi WAKAMATSU
Graduate Student :	Masaya UNO,	Shiro HIRAMITSU,
	Yoshinori OKURA,	Reiko SHIRAI,
	Atsushi YAMAMOTO,	Makoto IIZUKA,
	Kiyotaka TAKAGI,	Izumi HONDA,
	Aiko MOTOSHITA,	Asuka KAJIYAMA,
	Takashi NAKASUJI,	Kazuki YAMADA,
	Yuki HIROSE,	Mikiko YAMADA

2. Purpose of 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. Research Subjects

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 IP_3
- 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

4. Clinical Services

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.

5. Publications

Original Article

1. Kubota T. Update in polycystic ovary syndrome:new criteria of diagnosis and treatment in Japan. *Reproductive Medicine and Biology* 12:71-77, 2013
2. Ye C, Katagiri S, Miyasaka N, Bharti P, Kobayashi H, Takeuchi Y, Momohara Y, Sekiguchi M, Takamine S, Nagasawa T, Izumi Y. The anti-phospholipid antibody-dependent and independent effects of periodontopathic bacteria on threatened preterm labor and preterm birth. *Archives of Gynecology and Obstetrics*. 288(1):65-72, 2013
3. Yamada I, Hikishima K, Miyasaka N, Tokairin Y, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H, Shibuya H. Diffusion-tensor MRI and tractography of the esophageal wall ex vivo. *Journal of Magnetic Resonance Imaging*, Published online 2013
4. Miyasaka N, Akiyoshi M, Kubota T. Relationship between autonomic nervous system activity and bone mineral density in non-medicated perimenopausal women. *Journal of Bone and Mineral Metabolism*, Published online 2013
5. Kishino M, Miyasaka N, Takeguchi Y, Ohashi I. Retrograde transvenous obliteration for uterine arteriovenous malformation. *Obstetrics and Gynecology* , Published online 2013
6. Yamada I, Hikishima K, Miyasaka N, Kawano T, Tokairin Y, Ito E, Kobayashi D, Eishi Y, Okano H. Esophageal carcinoma: ex vivo evaluation with diffusion-tensor MR Imaging and tractography at 7 T. *Radiology* (in press)
7. Terauchi M, Hiramitsu S, Obayashi S, Akiyoshi M, Owa Y, Kato K, Matsushima E, Kubota T. Associations among depression, anxiety, and somatic symptoms in peri- and postmenopausal women. *Journal of Obstetrics and Gynaecology Research* 39(5): 1007-1013, 2013
8. Terauchi M, Horiguchi N, Kajiyama A, Akiyoshi M, Owa Y, Kato K, Kubota T. Effects of grape seed proanthocyanidin extract on menopausal symptoms, body composition, and cardiovascular parameters in middle-aged women: a randomized, double-blind, placebo-controlled, pilot study. *Menopause* (in press)
9. Terauchi M, Hiramitsu S, Akiyoshi M, Owa Y, Kato K, Obayashi S, Matsushima E, Kubota T. Effects of the Kampo formula Tokishakuyakusan on headaches and concomitant depression in middle-aged women. *Evidence-Based Complementary and Alternative Medicine* (in press)
10. Egawa M, Hayashi S, Limin Yang, Sakamoto N, Sago H. Chorioamniotic membrane separation after fetoscopic laser surgery for twin-twin transfusion syndrome. *Prenatal Diagnosis* 33(1) :89-94, 2013
11. Hiramitsu S, Terauchi M, Kubota T. The effects of Dickkopf-4 on the proliferation, differentiation, and apoptosis of osteoblasts. *Endocrinology*154:4618-4626, 2013
12. Tsukamoto S, Yamamoto A. The role of autophagy in early mammalian embryonic development. *Japanese Society of Mammalian Ova Research* 30(3) :86-94, 2013
13. Tsukamoto S, Yamamoto A. et al. Functional analysis of lysosomes during mouse preimplantation embryo development. *Journal of Reproduction and Development* 59 :33-39, 2013

International Presentation

1. Terauchi M, Hiramitsu S, Akiyoshi M, Owa Y, Kato K, Obayashi S, Matsushima E, Kubota T. Effects of a Kampo formula Tokishakuyakusan on headaches and concomitant depression in middle-aged women. 17th International

- Congress of the International Society of Psychosomatic Obstetrics and Gynaecology (ISPOG), Berlin, May, 2013
2. Hiramitsu S, Terauchi M, Kubota T. The effects of Dickkopf-4 on the proliferation, differentiation, and apoptosis of osteoblasts. 2nd International Bone and Mineral Society and the Japanese Society for Bone and Mineral Research, Kobe, May, 2013
 3. Oi R. Consideration on the optimal time for effective fetal screening by ultrasonography in 2nd and 3rd trimester. 23rd World Congress on Ultrasound in Obstetrics and Gynecology, Sydney, Oct, 2013
 4. Obayashi S, Ohkura Y, Yamada Y, Yamada K, Ueno T, Uchiyama S, Kubota T. Enhanced vasorelaxation in ovariectomized rat tail arteries with S-equol supply. 16th North American Menopause Society annual meeting, Dallas, Oct, 2013
 5. Ohkura Y, Obayashi S, Yamada M, Yamada K, Ueno T, Uchiyama S, Kubota T. S-equol increases NO production of thoracic aorta in ovariectomized rats. 16th North American Menopause Society annual meeting, Dallas, Oct, 2013
 6. Obayashi S, Ohkura Y. Role of s-equol, an end product of isoflavone on endothelium and endometrium. Special research presentation, Department of Pediatrics, UT southwestern medical center, Dallas, Oct, 2013
 7. Obayashi S. Humonal regulation of endothelial function and atherosclerosis. Symposium 5 : Risk assessment of cardiovascular disease in postmenopausal women: Prevention and intervention. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 8. Terauchi M, Horiguchi N, Kajiyama A, Akiyoshi M, Owa Y, Kato K, Kubota T. The effects of grape seed extract proanthocyanidin on menopausal symptoms. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 9. Terauchi M, Akiyoshi M, Owa Y, Kato K, Kajiyama A, Hiramitsu S, Obayashi S, Matsushima E, Kubota T. Prevalence and Determinants of Lower Urinary Tract Symptoms in Peri- and Postmenopausal Women. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 10. Oshima-Sudo N, Honda I, Obayashi S, Terauchi M, Nakahama K, Kubota T, Morita I. Optimized method for culturing endothelial colony forming cells from human umbilical cord blood and tissue engineered capillary vessels using printing technology. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 11. Oshima-Sudo N, Terauchi M, Hirata A, Toba M, Wakana K, Wakabayashi A, Obayashi S, Kubota T. Effect of herbal medicine Daikenchuto for the prevention of postoperative ileus in gynecologic cancers. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 12. Hiramitsu S, Terauchi M, Kubota T. The effects of Dickkopf-4 on the proliferation, differentiation, and apoptosis of osteoblasts. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013
 13. Ohkura Y, Obayashi S, Yamada M, Yamada K, Ueno T, Uchiyama S, Kubota T. S-equol increases nitric oxide production of rat thoracic aorta endothelium. 5th Scientific Meeting of the Asia Pacific Menopause Federation, Tokyo, Oct, 2013

Urology

1. Staffs and Students (December, 2013)

Professor and Chairman	Kazunori Kihara	
Associate Professor	Yasuhisa Fujii	
Lecturer	Fumitaka Koga (~March), Noboru Numao (September~)	Kazutaka Saito,
Assistant Professor	Yoh Matsuoka, Minato Yokoyama (~February), Toshiki Kijima (April~),	Junichiro Ishioka (~August), Soichiro Yoshida, Yasukazu Nakanishi (September~)
Hospital Staff	Hideki Takeshita, Masaya Ito, Takayuki Nakayama, Hiroshi Fukushima, Masahiro Toide, Yusuke Uchida	Toshihiro Kanda, Masaharu Inoue, Saori Higuchi, Satoshi Yoshida, Yudai Ishikawa,
Graduate Student	Naoko Kawamura, Toshiki Kijima, Sachi Kitayama, Toshihiro Kanda, Masaya Ito, Hajime Tanaka, Saori Higuchi	Shuichiro Kobayashi, Naotaka Fukui, Yasukazu Nakanishi, Hideki Takeshita, Masaharu Inoue, Takayuki Nakayama,

2. Purpose of Education

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, which are listed below.

3. Research Subjects

Clinical Research

- 1) Innovation and establishment of minimally invasive, gasless single port access urological surgery
- 2) Development of optimal 3-dimensional prostate needle biopsy
- 3) Development of nomograms for optimal detection of prostate cancer
- 4) Sequential combination therapy to prolong survival of advanced prostate cancer patients
- 5) Development and establishment of curative and minimally invasive bladder preservation using low-dose chemoradiotherapy plus partial cystectomy
- 6) Development and establishment of minimally invasive, nonischemic nephron-sparing surgery against kidney cancer
- 7) Development and establishment of focal therapy using hemiablativ brachytherapy against prostate cancer
- 8) Sequential combination therapy to prolong survival of advanced kidney cancer patients, starting with immunotherapy combined with multiple molecular targeted agents
- 9) Application of diffusion-weighted MRI to diagnosis, assessment of therapeutic effects and monitoring of relapse in urological cancer
- 10) Application of serum C-reactive protein as a prognostic biomarker of urological malignancies and as a marker for surgical invasiveness

Translational Research

- 1) Development of differentiation-inducing therapy against hormone-resistant prostate carcinomas
- 2) Investigation on molecular mechanisms, in particular deregulation of the NO system, underlying voiding and erectile dysfunction to develop rational therapy
- 3) Overcoming therapeutic resistance to chemo- and/or radiotherapy against urological malignancies using novel

molecular targeted agents

- 4) Investigation on functional roles of p63 protein in urothelial carcinomas

4. Clinical Services

Our mission is to provide the best urological care to all patients. Besides offering urological practices of the international standard, we are making a continuous effort to improve daily practices. The gasless single port access urological surgery, which we have innovated its concept and developed surgical techniques specific to all urological organs, has been officially approved as medical services provided by the Japanese Governmental Health Insurance System in April 2008. These minimally invasive surgical techniques can be fundamentally applied to all patients having urological malignancies, even those having locally advanced disease and previous histories of abdominal surgery.

5. Publications (International)

Original Article

- Bae H, Yoshida S, Matsuoka Y, Nakajima H, Ito E, Tanaka H, Oya M, Nakayama T, Takeshita H, Kijima T, Ishioka J, Numao N, Koga F, Saito K, Akashi T, Fujii Y, Kihara K. Apparent diffusion coefficient value as a biomarker reflecting morphological and biological features of prostate cancer. *Int Urol Nephrol*. 2013 Sep 11. [Epub ahead of print]
- Fukui N, Kageyama Y, Higashi Y, Kihara K, Kizaka-Kondoh S, Hiraoka M, Shinojima T, Suzuki K, Oya M. Development of a novel interferon- α 2b gene construct with a repetitive hypoxia-inducible factor binding site and its suppressive effects on human renal cell carcinoma cell lines in vitro. *Int J Clin Oncol*. 2013 Jun 6. [Epub ahead of print]
- Fukushima H, Masuda H, Yokoyama M, Tatokoro M, Yoshida S, Ishioka J, Matsuoka Y, Numao N, Koga F, Saito K, Fujii Y, Kihara K. Diabetes mellitus with obesity is a predictor of recurrence in patients with non-metastatic renal cell carcinoma. *Jpn J Clin Oncol*. 43: 740-6, 2013.
- Hirono M, Kobayashi M, Tsushima T, Obara W, Shinohara N, Ito K, Eto M, Takayama T, Fujii Y, Nishikido M, Kimura G, Kishida T, Takahashi M, Miyao N, Naya Y, Abe T, Fujioka T, Ito K, Naito S; Members of the Japanese Society of Renal Cancer. *BMC Cancer*, in press
- Ito M, Masuda H, Kawakami S, Fujii Y, Koga F, Saito K, Yamamoto S, Yonese J, Fukui I, Kihara K. Impact of lower urinary tract symptoms on prostate cancer risk among Japanese men with prostate-specific antigen <10ng/mL and non-suspicious digital rectal examination. *Int J Urol*. 20:1163-8, 2013.
- Kijima T, Koga F, Fujii Y, Yoshida S, Tatokoro M, Kihara K. Zoledronic acid sensitizes renal cell carcinoma cells to radiation by downregulating STAT1. *PLoS One*. 8: e64615, 2013.
- Kobayashi S*, Fujii Y* (*equally contributed), Koga F, Yokoyama M, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kihara K. Impact of bladder neck involvement on progression in patients with primary non-muscle invasive bladder cancer: a prospective validation study. *Urol Oncol*, in press
- Kobayashi S, Koga F, Kajino K, Yoshida S, Ishii C, Tanaka H, Saito K, Masuda H, Fujii Y, Yamada T, Kihara K. Apparent diffusion coefficient value reflects invasive and proliferative potential of bladder cancer. *J Mag Reso Imaging*. 39:172-8, 2013.
- Koga F. Editorial comment from Dr Koga to Local control rate and prognosis after sequential chemoradiation for small cell carcinoma of the bladder. *Int J Urol*. 20: 785-6, 2013.
- Koga F, Numao N, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Sensitivity to chemoradiation predicts development of metastasis in muscle-invasive bladder cancer patients. *Urol Oncol*. 7: 1270-5, 2013.
- Komai Y, Sakai Y, Gotohda N, Kobayashi T, Kawakami S, Saito N. A novel 3-dimensional analysis system for case-specific kidney anatomy and surgical simulation to facilitate clampless partial nephrectomy. *Urology*. 2013. in press
- Komai Y, Numao N, Yoshida S, Matsuoka Y, Nakanishi Y, Ishii C, Koga F, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. High diagnostic ability of multiparametric magnetic resonance imaging to detect anterior prostate cancer missed by transrectal 12-core biopsy. *J Urol*. 190(3):867-73, 2013.
- Masuda H. Editorial comment to longitudinal leak point pressure measurements in rats using a modified port à cath system. *Int J Urol*. 20:1242, 2013.
- Masuda H, Fukushima H, Kawakami S, Numao N, Fujii Y, Saito K, Koga F, Ishioka J, Yokoyama M, Kihara K. Impact of advanced age on biochemical recurrence after radical prostatectomy in Japanese men according to pathological stage. *Jpn J Clin Oncol*. 43:410-6, 2013.
- Masuda H, Kagawa M, Kawakami S, Numao N, Matsuoka Y, Yokoyama M, Yamamoto S, Yonese J, Fukui I, Kihara

- K. Body mass index influences prostate cancer risk at biopsy in Japanese men. *Int J Urol.* 20:701-7, 2013.
16. Matsubara N, Mukai H, Naito Y, Itoh K, Komai Y, Sakai Y. First experience of active surveillance before systemic target therapy in patients with metastatic renal cell carcinoma. *Urology.* 82(1):118-23, 2013.
 17. Miyajima N, Tsutsumi S, Sourbier C, Beebe K, Mollapour M, Rivas C, Yoshida S, Trepel JB, Huang Y, Tatokoro M, Shinohara N, Nonomura K, Neckers L. The HSP90 inhibitor ganetespib synergizes with the MET kinase inhibitor crizotinib in both crizotinib-sensitive and -resistant MET-driven tumor models. *Cancer Res.* 73:7022-33, 2013.
 18. Moriyama S, Takeshita H, Adachi A, Arai Y, Higuchi S, Tokairin T, Chiba K, Nakagawa K, Noro A. Simultaneous bilateral testicular metastases from renal clear cell carcinoma: A case report and review of the literature. *Oncol Lett.* in press
 19. Naito S, Kinoshita H, Kondo T, Shinohara N, Kasahara T, Saito K, Takayama T, Masumori N, Takahashi W, Takahashi M, Terachi T, Ozono S, Naito S, Tomita Y. Prognostic factors of patients with metastatic renal cell carcinoma with removed metastases: a multicenter study of 556 patients. *Urology.* 82:846-51, 2013.
 20. Numao N, Yoshida S, Komai Y, Ishii C, Kagawa M, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Koga F, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Usefulness of pre-biopsy multiparametric magnetic resonance imaging and clinical variables to reduce initial prostate biopsy in men with suspected clinically localized prostate cancer. *J Urol.* 190:502-8, 2013.
 21. Takeshita H, Numao N, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Koga F, Saito K, Masuda H, Kawakami S, Yamamoto S, Yonese J, Fujii Y, Kihara K. Diagnostic performance of initial transperineal 14-core prostate biopsy to detect significant cancer. *Int Urol Nephrol.* 45:645-52, 2013.
 22. Takeshita H, Chiba K, Kitayama S, Moriyama S, Omura R, Noro A. Triplet chemotherapy with paclitaxel, gemcitabine, and cisplatin as second-line therapy for advanced urothelial carcinoma. *Modern chemotherapy.* 2:1-7, 2013.
 23. Tatokoro M, Kihara K, Masuda H, Ito M, Yoshida S, Kijima T, Yokoyama M, Saito K, Koga F, Kawakami S, Fujii Y. Successful reduction of hospital-acquired methicillin-resistant *Staphylococcus aureus* in a urology ward: a 10-year study. *BMC Urol.* 18(13):35, 2013.
 24. Tatokoro M. Editorial Comment to Acute bacterial prostatitis after transrectal ultrasound-guided prostate biopsy: Epidemiological, bacterial and treatment patterns from a 4-year prospective study. *Int J Urol.* 21:156, 2013.
 25. Yamamoto S, Fujii Y, Masuda H, Urakami S, Saito K, Kozuka T, Oguchi M, Fukui I, Yonese J. Longitudinal change in health-related quality of life after intensity-modulated radiation monotherapy for clinically localized prostate cancer. *Qual Life Res.* in press
 26. Yamamoto S, Kawakami S, Yonese J, Fujii Y, Urakami S, Kitsukawa S, Masuda H, Ishikawa Y, Kozuka T, Oguchi M, Kohno A, Fukui I. Long-term oncological outcome in men with T3 prostate cancer: radical prostatectomy versus external-beam radiation therapy at a single institution. *Int J Clin Oncol.* in press
 27. Yasuda Y, Fujii Y, Yuasa T, Kitsukawa S, Urakami S, Yamamoto S, Yonese J, Takahashi S, Fukui I. Possible improvement of survival with use of zoledronic acid in patients with bone metastases from renal cell carcinoma. *Int J Clin Oncol.* 18: 877-83, 2013.
 28. Yasuda Y, Saito K, Yuasa T, Kitsukawa S, Urakami S, Yamamoto S, Yonese J, Takahashi S, Fukui I. Prognostic impact of pretreatment C-reactive protein for patients with metastatic renal cell carcinoma treated with tyrosine kinase inhibitors. *Int J Clin Oncol.* 18:884-9, 2013.
 29. Yokoyama M, Masuda H, Kihara K. Letter to the Editor: Negative pressure wound therapy for surgical site infection associated with artificial urinary sphincter implantation. *Int J Urol.* 20: 1049-50, 2013.
 30. Yoshida S, Tsutsumi S, Muhlebach G, Sourbier C, Lee MJ, Lee S, Vartholomaiou E, Tatokoro M, Beebe K, Miyajima N, Mohny RP, Chen Y, Hasumi H, Xu W, Fukushima H, Nakamura K, Koga F, Kihara K, Trepel J, Picard D, Neckers L. Molecular chaperone TRAP1 regulates a metabolic switch between mitochondrial respiration and aerobic glycolysis. *Proc Natl Acad Sci U S A.* 110:E1604-12, 2013.
 31. Yoshida S, Kobayashi S, Koga F, Ishioka J, Ishii C, Tanaka H, Nakanishi Y, Matsuoka Y, Numao N, Saito K, Masuda H, Fujii Y, Kihara K. Apparent diffusion coefficient as a prognostic biomarker of upper urinary tract cancer: a preliminary report. *Eur Radiol.* 23:2206-14, 2013.
 32. Yuasa T, Kitsukawa S, Sukegawa G, Yamamoto S, Kudo K, Miyazawa K, Kozuka T, Harada S, Yonese J. Early onset recall pneumonitis during targeted therapy with sunitinib. *BMC Cancer.* 2013 Jan 2;13:3. doi: 10.1186/1471-2407-13-3.

Review Article

1. Koga F, Yokoyama M, Fukushima H. Small cell carcinoma of the urinary bladder: A contemporary review with a

special focus on bladder-sparing treatments. *Expert Rev Anticancer Ther.* 13:1269-79, 2013.

- Saito K, Kihara K. Role of C-reactive protein in urological cancers: a useful biomarker for predicting outcomes. *Int J Urol.* 20:161-71, 2013.

Award

- Koga F, Fujii Y, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kawakami S, Kihara K. Risk factors for intravesical tumor recurrence in muscle-invasive bladder cancer patients treated with selective bladder-sparing approaches. "Best Poster Presentation" The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
- Fukushima H, Saito K, Ishioka J, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Sakai Y, Arisawa C, Okuno T, Yonese J, Kamata S, Nagahama K, Akira Noro, Morimoto S, Tsujii T, Kitahara S, Gotoh S, Higasi Y, Kihara K. Equivalent survival after distal ureterectomy compared to nephroureterectomy in patients with urothelial carcinoma of the distal ureter: A propensity score-matched multi-center study. "Best Poster Presentation" The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/16.

Presentations at International Meetings

- Fukushima H, Saito K, Ishioka J, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii F, Sakai S, Arisawa C, Okuno T, Yonese J, Kamata S, Nagahama K, Noro A, Morimoto S, Tsujii T, Kitahara S, Gotoh S, Higashi Y, Kihara K. Equivalent survival after distal ureterectomy compared to nephroureterectomy in patients with urothelial carcinoma of the distal ureter: A propensity score-matched multi-center study. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/16.
- Fujii Y, Yamamoto S, Yonese J, Masuda H, Urakami S, Kitsukawa S, Kihara K, Fukui I. Long-term results of the processus vaginalis transection method to prevent postradical prostatectomy inguinal hernia. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/5.
- Ishioka J, Saito K, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Sakai Y, Okuno T, Arisawa C, Kamata S, Nagahama K, Yonese J, Noro A, Tsujii T, Morimoto S, Kitahara S, Goto S, Higashi Y, Kihara K. Risk stratification model for predicting bladder recurrence after radical nephroureterectomy for upper urinary tract urothelial carcinoma. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/18.
- Ishioka J, Saito K, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Sakai Y, Okuno T, Arisawa C, Kamata S, Nagahama K, Yonese J, Noro A, Tsujii T, Morimoto S, Kitahara S, Goto S, Higashi Y, Kihara K. Risk stratification for bladder recurrence after radical nephroureterectomy for upper urinary tract urothelial carcinoma. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/5.
- Ishioka J, Saito K, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Sakai Y, Okuno T, Arisawa C, Kamata S, Nagahama K, Yonese J, Noro A, Tsujii T, Morimoto S, Kitahara S, Goto S, Higashi Y, Kihara K. Bimodal pattern in the association between body mass index and cancer specific survival of upper urinary tract urothelial carcinoma. Analysis of a Japanese multicenter cohort of the Tokyo Metropolitan Database of Urologic Disease (TMDU). The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/5.
- Kihara K, Fujii Y, Masuda H, Saito K, Koga F, Numao N, Matsuoka Y. New 3-dimensional head-mounted display system (RoboSurgeon system) applied to gasless, single-port access adrenalectomy. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
- Kihara K, Fujii Y, Masuda H, Saito K, Koga F, Numao N, Matsuoka Y. New 3-dimensional head-mounted display system (RoboSurgeon system) applied to gasless, single-port access, clampless partial nephrectomy. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
- Kijima T, Kihara K, Yokoyama M, Ishioka J, Matsuoka Y, Numao N, Saito K, Koga F, Fujii Y. Gasless laparoendoscopic single-port radical prostatectomy The 30th Congress of the Pan-Pacific Surgical Association Japan Chapter, Honolulu, USA, 2013/2/8.
- Kijima T, Koga F, Fujii Y, Yoshida S, Tatokoro M, Kihara K. Zoledronic acid sensitizes renal cell carcinoma cells to radiation by downregulating STAT1 The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
- Kijima T, Koga F, Fujii Y, Yoshida S, Tatokoro M, Kihara K. Radiosensitizing effect of zoledronic acid on renal cell carcinoma cells by downregulating STAT1. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
- Kobayashi S, Asano T, Yano M, Nakayama T, Ohtsuka Y, Kitahara S. Safety of transperineal prostate biopsy in

- patients receiving antiplatelet/anticoagulant therapy: a propensity score matching analysis. The 33rd Congress of Société Internationale d'Urologie, Vancouver, Canada, 2013/9/9.
12. Koga F, Fujii Y, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kawakami S, Kihara K. Risk factors for intravesical tumor recurrence in muscle-invasive bladder cancer patients treated with selective bladder-sparing approaches. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/16.
 13. Koga F, Kobayashi S, Fujii Y, Yokoyama M, Nakanishi Y, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kihara K. Prognostic significance of positive urine cytology in non-muscle invasive bladder cancer patients (Podium session). AUA 2013 annual meeting, San Diego, USA, 2013/5/7.
 14. Koga F, Fujii Y, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kawakami S, Kihara K. Predictors of intravesical tumor recurrence following selective bladder preservation in muscle-invasive bladder cancer patients. AUA 2013 annual meeting, San Diego, USA, 2013/5/7.
 15. Komai Y, Sakai Y, Gotohda N, Koabayashi T, Saito N. Initial experience of an application of a novel high-speed 3D image/volume analyzer to clampless partial nephrectomy. The 28th Annual Congress of the European Association of Urology (Poster), Milan, Italy, 2013/3/16.
 16. Matsuoka Y, Ishioka J, Numao N, Tanaka H, Yoshida S, Yokoyama M, Koga F, Saito K, Masuda H, Fujii Y, Kihara K. Simple prediction model of side-specific extracapsular extension based on percent positive biopsy cores and tumor contact length with the capsule on MRI. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
 17. Matsuoka Y, Numao N, Saito K, Tanaka H, Yoshida S, Yokoyama M, Ishioka J, Koga F, Masuda H, Fujii Y, Kihara K. Candidate selection for quadrant-ablation focal therapy of prostate cancer through a combination of extended 14-core biopsy and MRI. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
 18. Matsuoka Y, Ishioka J, Numao N, Tanaka H, Yoshida S, Yokoyama M, Koga F, Saito K, Masuda H, Fujii Y, Kihara K. Impact of MRI on the prediction of side-specific extracapsular extension: Nomogram based on tumor contact length and percent positive biopsy cores. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/5.
 19. Matsuoka Y, Numao N, Saito K, Tanaka H, Yoshida S, Yokoyama M, Ishioka J, Koga F, Masuda H, Fujii Y, Kihara K. Combination of extended biopsy and MRI identifies candidates for quadrant-ablation focal therapy of prostate cancer. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
 20. Matsuoka Y, Numao N, Saito K, Tanaka H, Yoshida S, Yokoyama M, Ishioka J, Koga F, Masuda H, Fujii Y, Kihara K. Quadrant-ablation focal therapy of prostate cancer: candidate selection through a combination of extended biopsy and MRI. 6th International Symposium on Focal Therapy and Imaging 2013, Amsterdam, The Netherlands, 2013/5/29.
 21. Nakanishi Y, Komai Y, Masuda H, Matsuoka Y, Numao N, Yoshimoto T, Saito K, Koga F, Fujii Y, Ogawa Y, Kihara K. The abnormality of glucose tolerance test in pheochromocytoma: one of the significant findings of postoperative hypoglycemia. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
 22. Numao N, Ito M, Fukushima H, Takeshita H, Yoshida S, Matsuoka Y, Koga F, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Magnetic resonance imaging guided prostate biopsy versus systematic 14-core prostate biopsy including anterior samplings in detecting significant cancer and assessing cancer aggressiveness. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
 23. Numao N, Yoshida S, Ishii C, Komai Y, Kijima T, Yokoyama M, Ishioka J, Matsuoka Y, Koga F, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Potential of prebiopsy multiparametric magnetic resonance imaging to reduce initial biopsies in men with suspected clinically localized prostate cancer. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
 24. Numao N, Ito M, Takeshita H, Yoshida S, Matsuoka Y, Koga F, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Comparison of diagnostic performance between magnetic resonance imaging guided prostate biopsy and systematic 14-core biopsy including anterior samplings. 6th International Symposium on Focal Therapy and Imaging in Prostate and Kidney Cancer, Noordwijk, Netherlands, 2013/5/30.
 25. Saito K, Kijima T, Ishioka J, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Hayashi K, Shibuya H, Kihara K. Focal therapy for prostate cancer using I125 seed implantation: Hemiblastic brachytherapy for patients selected by extended biopsy and MRI. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/17.
 26. Saito K, Matsuoka Y, Numao N, Kijima T, Yoshida Y, Yokoyama M, Ishioka J, Koga F, Masuda H, Fujii F, Hayashi K, Shibuya H, Kihara K. Hemi-gland brachytherapy for unilateral prostate cancer. 6th International Symposium on

Focal Therapy and Imaging in Prostate & Kidney Cancer, Amsterdam, The Netherlands, 2013/5/29.

27. Takeshita H, Masuda H, Saito K, Tanaka H, Komai Y, Sakai Y, Koga F, Yonese J, Noro A, Kawakami S, Yamada T, Fujii Y, Kihara K. Serum C-reactive protein as an indicator of survival after surgery for adrenal metastasis from multiple primary sites. The 107th annual meeting of the American Urological Association, San Diego, CA, USA, 2013/5/4.
28. Tanaka H, Yuasa T, Ito M, Saito K, Sakura M, Kitsukawa S, Urakami S, Yamamoto S, Masuda H, Fukui I, Yonese J. Clinical efficacy, feasibility, and prognostic factors for sequential docetaxel therapy in the patients with castration-resistant prostate cancer. The 107th annual meeting of the American Urological Association, San Diego, USA, 2013/5/6.
29. Yoshida S, Kobayashi S, Koga F, et al. The ADC value is a prognostic biomarker of upper urinary tract cancer: Potential application to preoperative risk stratification. The 28th Annual Congress of the European Association of Urology, Milan, Italy, 2013/3/16.
30. Waseda Y, Saito K, Ishioka J, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Sakai Y, Okuno T, Arisawa C, Kamata S, Nagahama K, Yonese J, Noro A, Tsujii T, Morimoto S, Higashi Y, Fukui I, Kihara K. Presence of ureteral tumor was associated with poor prognosis in upper urinary tract urothelial carcinoma patients treated by nephroureterectomy: a multicenter database study of 1063 patients. The 107th annual meeting of the American Urological Association, San Diego, CA, USA, 2013/5/5.

Invited Lecture and International Symposium

1. Fujii Y. Case-Based Discussion: Pitfalls of Radical Nephrectomy in the Management of Locally Advanced Cases of Renal Cancer. *Advancements in Urology 2013: An AUA/JUA Symposium*. Las Vegas, USA, 2013/2/13.
2. Fujii Y. Video case discussion 1: Minimally invasive surgery - partial nephrectomy. The 107th annual meeting of the American Urological Association, The 8th AUA/JUA International Affiliate Society Meeting, San Diego, USA, 2013/5/5.
3. Kihara K. New three-dimensional head-mounted display (RoboSurgeon system) applied to gasless, single-port access urologic surgeries. The 101th annual meeting of the Japanese Urological Association, AUA/EAU/UAA/JUA joint session, Sapporo, 2013/4/24.
4. Masuda H, Yokoyama M. 70 cases of artificial urinary sphincter implantation for male prostatectomy incontinence. Nagoya Shinshu Forum. 2013/9/22.
5. Masuda H. Speaker of LUTS section. The Best of AUA Japan. Tokyo, 2013/10/6.

Esophageal and General Surgery

1. Staffs and Students

Professor	Tatsuyuki KAWANO	
Associate Professor	Yoichi KUMAGAI,	Yasuaki NAKAJIMA
Junior Associate Professor	Yoshinori INOUE	
Assistant Professor	Kagami NAGAI,	Toshifumi KUDO,
	Kenro KAWADA,	Yutaka TOKAIRIN,
	Koji TANAKA,	Takuya OKADA,
	Masatoshi JIBIKI,	Takahiro TOYOFUKU
Project Assistant Professor	Yutaka MIYAWAKI	
Graduate Student	Hidetoshi UCHIYAMA,	Shinya KOIZUMI,
	Kimihiro IGARI,	Shunsuke OHTA,
	Tairo RYOTOKUJI,	Naoto FUJIWARA,
	Masato NISHIZAWA,	Katsumasa SAITO,
	Hisashi FUJIWARA,	Sotaro KATSUI,
	Masafumi OKUDA,	Taichi OGO,
	Masahiro NAKAMURA,	Tuerxun REXIATI,
	Jirawat SWANGSRI,	Ablimitie ZYNUR

2. Purpose of Education

The history of the department started as the First Department of Surgery 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. Research Subjects

- 1) Development of esophageal surgery.
- 2) Development of vascular surgery.

4. Clinical Services

Main clinical services are diagnosis and treatment for esophageal and vascular diseases. Post-graduate students learn and study general surgery and sub-specialty, e.g. esophageal surgery, vascular 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.

5. Publications

1. Kumagai Y, Nagata K, Ishiguro T, Haga N, Kuwabara K, Sobajima J, Kumamoto K, Ishibashi K, Baba H, Shimizu M, Tamura J, Kawano T, Takubo K, Ishida H. Clinicopathological characteristics and clinical outcomes of esophageal basaloid squamous carcinoma: Experience at a single institution. *Int Surg* 2013; 98: 450-454.
2. Kumagai Y, Ishiguro T, Haga N, Kuwabara K, Kawano T, Ishida H. Hemodynamics of the reconstructed gastric tube during esophagectomy: assessment of outcomes using indocyanine green fluorescence. *World J Surg* 2014; 38: 138-143.
3. Kumagai Y, Kawada K, Takubo K. Endocytoscopic observation of the esophageal mucosa: A trial to examine the feasibility of omitting biopsy histology. *Annals of the New York Academy of Sciences* in press.
4. Kumagai Y, Kawada K, Higashi M, Ishiguro T, Sobajima J, Fukuchi M, Ishibashi K, Baba H, Mochiki E, Aida J, Kawano T, Ishida H, Takubo K. Endocytoscopic observation of various esophageal lesions at x600: can nuclear abnormality be recognized? *Dis Eso* accept in press.
5. Kumagai Y, Ishiguro T, Kuwabara K, Sobajima J, Fukuchi M, Ishibashi K, Baba H, Mochiki E, Aida J, Takemoto A, Kawano T, Takubo K, Ishida H. Primary mucoepidermoid carcinoma of the esophagus: Review of the literature. *Esophagus* accept in press.

6. Kawada K, Kawano T, Sugimoto T. Key points and Techniques for Trans-nasal Endoscopic Screening for superficial Hypopharyngeal cancer. *Treatment Strategies* 2013; 2: 42.
7. Miyawaki Y, Imoto I, Tokairin Y, Kawada K, Nakajima Y, Nishikage T, Nagai K, Kajiwara M, Inazawa J, Kawano T. Esophageal squamous cell carcinoma developed 11 years after allogeneic bone marrow transplantation for acute lymphatic leukemia. *Jpn J Clin Oncol* 2013; 43(1): 69-73.
8. Okada T, Kawada K, Nakajima Y, Tokairin Y, Nagai K, Kawano T. Internal pressure of the conduit during endoscopy on the day after esophagectomy. *Dig Surg*. 2013; 30(3): 183-189.
9. Ito H, Kumagai Y, Iida M, Yamazaki S, Odajima H, Kawano T. A patient with esophageal cancer showing remission of nephritic syndrome after esophagectomy: report of a case. *Surg Today*, 2013; 43: 1452-1456.
10. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y, Kawano T. Quantitative evaluation of the outcomes of revascularization procedures for peripheral arterial disease using indocyanine green angiography. *Eur J Vasc Endovasc Surg* 2013; 46: 460-465.
11. Okamoto N, Kawachi H, Yoshida T, Kitagaki K, Sekine M, Kojima K, Kawano T, Eishi Y. "Crawling-type" adenocarcinoma of the stomach: a distinct entity preceding poorly differentiated adenocarcinoma *Gastric Cancer*, 2013; 16: 220-232.
12. Yamada I, Hikishima K, Miyasaka N, Tokairin Y, Kawano T, Ito E, Kobayashi D, Eishi Y, Okano H, Shibuya H. Diffusion-Tensor MR Imaging and Tractography of the Esophageal Wall Ex Vivo. *J Magn Reson Imaging* (in press).
13. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. A case of disseminated intravascular coagulation caused by a ruptured abdominal aortic aneurysm for which recombinant human soluble thrombomodulin was effective. *J Vasc Med Surg*; 1: 109, 2013.
14. Igari K, Hirokawa M, Uchiyama H, Toyofuku T, Kudo T, Jibiki M, Kurihara N, Inoue Y. Anatomical variation at the sapheno-femoral junction. *AVD*: 6, 702-705, 2013.
15. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y, Tanaka K, Okazaki M. Combined arterial reconstruction and free tissue transfer for patients with critical limb ischemia. *AVD*: 6, 706-710, 2013
16. Terasaki H, Inoue Y, Sugano N, Jibiki M, Kudo T, Lepántalo M, Venermo M. A quantitative method for evaluating local perfusion using indocyanine green fluorescence imaging. *Ann Vasc Surg*. 27: 1154-1161, 2013.
17. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. Successful endovascular repair of ruptured isolated bilateral internal iliac artery aneurysms. *Eur J Vasc Endovasc Surg* 2013;45:218-9.
18. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. Surgical Treatment with or without Embolotherapy for Arteriovenous Malformations. *Ann Vasc Dis* 2013;6:46-51.
19. Igari K, Toyofuku T, Uchiyama H, Koizumi S, Yonekura K, Kudo T, Jibiki M, Sugano N, Inoue Y. Maggot debridement therapy for peripheral arterial disease. *Ann Vasc Dis* 2013;6:145-9.
20. Igari K, Ochiai T, Yamazaki S. POSSUM and P-POSSUM for risk assessment in general surgery in the elderly. *Hepatogastroenterology* 2013;60:1320-7.
21. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. Surgical treatment of aneurysms in the upper limbs. *Ann Vasc Dis* 2013;6:637-41.
22. Igari K, Kudo T, Mori K, Onuki M, Hirooka K, Inoue Y. Two cases of successful inferior mesenteric artery preservation with bare metal stent in endovascular iliac artery aneurysm repair. *Ann Vasc Dis* 2013;6:674-7.
23. Igari K, Hirokawa M, Uchiyama H, Toyofuku T, Kudo T, Jibiki M, Kurihara N, Inoue Y. Anatomical variation at the sapheno-femoral junction. *Ann Vasc Dis* 2013;6:702-5.
24. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y, Tanaka K, Okazaki M. Combined arterial reconstruction and free tissue transfer for patients with critical limb ischemia. *Ann Vasc Dis* 2013;6:706-10.
25. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. An operative case of abdominal aortic pseudo-aneurysm in delayed development due to blunt trauma. *EJVES Extra* 2013;25:e48-e49.
26. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. A case of disseminated intravascular coagulation caused by a ruptured abdominal aortic aneurysm for which recombinant human soluble thrombomodulin was effective. *J Vasc Med Surg* 2013;1:109.

Thoracic Surgery

1. Staffs and Students

Professor:	Kenichi OKUBO	
Junior Associate Professor:	Hironori ISHIBASHI	
Assistant Professor:	Masashi KOBAYASHI	
Hospital Staff:	Akiko UI,	Katsutoshi SETO,
	Ryo WAKESHIMA,	Ayaka ASAKAWA

2. Purpose of Education

Main objective of Thoracic Surgery in the graduate course is to provide students with opportunity to study surgical anatomy, pathophysiology, and combined modality treatment in order to become the specialized surgeons who have international and scientific feelings.

3. Research Subjects

- 1) Establishing surgical skills and multimodality treatments for thoracic oncology
- 2) Developing minimal invasive technique/surgery for thoracic diseases
- 3) Molecular biological approaches for thoracic malignancies

4. Clinical Services

Thoracic Surgery clinic performs surgical treatments for the diseases of lung, chest wall, and mediastinum. Lung cancer, pleural diseases, and mediastinal tumor are mainly treated with surgery using minimal invasive techniques or function-preserved techniques. Advanced diseases are also treated with extended resection and/or multimodality approach.

5. Publications

1. Sonobe M, Date H, Wada H, Okubo K, Hamakawa H, Teramukai S, Matsumura A, Nakagawa T, Sumitomo S, Miyamoto Y, Okumura N, Takeo S, Kawakami K, Aoki M, Kosaka S; The Japan-Multinational Trial Organization. Prognostic factors after complete resection of pN2 non-small cell lung cancer. *J Thorac Cardiovasc Surg.* 2013;146:788-95.
2. Hironori Ishibashi, Chihiro Takasaki, Kenichi Okubo: Phrenic nerve paralysis from recurrence of stage I thymoma with myasthenia gravis 10 years after complete resection. *Gen Thorac Cardiovasc Surg.* 2013 Aug 15. [Epub ahead of print]
3. Hironori Ishibashi, Chihiro Takasaki, Kenichi Okubo: Port-site recurrence after complete resection of stage I thymoma by video-assisted thoracoscopic surgery: Report of a case. *Surgery Today* 2013 Nov 17. [Epub ahead of print]
4. Kobayashi Masashi, Cheng-long Huang, Makoto Sonobe, Ryutaro Kikuchi, Masashi Ishikawa, Naoto Imamura, Jiro Kitamura, Shotaro Iwakiri, Kazumi Ito, Ryoji Yasumizu, Hiroshi Date: Snail expression is associated with a poor prognosis in malignant pleural mesotheliomas. *Ann Thorac Surg.* 2013 Apr;95(4):1181-8
5. Akihiro Ohsumi, Fengshi Chen, Jin Sakamoto, Daisuke Nakajima, Masashi Kobayashi, Toru Bando, Hiroshi Date: Protective Effect of Surfactant Inhalation against Warm Ischemic Injury in an Isolated Rat Lung Ventilation Model. *PLoS One.* Aug 29;8(8), 2013
6. Shinji Sumiyoshi, Akihiko Yoshizawa, Makoto Sonobe, Masashi Kobayashi, Masakazu Fujimoto, Tatsuaki Tsuruyama, Hiroshi Date, Hironori Haga: Pulmonary adenocarcinomas with micropapillary component significantly correlate with recurrence, but can be well controlled with EGFR tyrosine kinase in the early stages. *Lung Cancer.* 2013 Jul;81(1):53-9
7. Masakazu Fujimoto, Akihiko Yoshizawa MD, Shinji Sumiyoshi MD, Makoto Sonobe, Masashi Kobayashi, Itsuko Koyanagi, Wulamujiang Aini, Tatsuaki Tsuruyama, Hiroshi Date, Hironori Haga: Stromal plasma cells expressing immunoglobulin G4 subclass in non-small cell lung cancer. *Hum Pathol.* 2013 Aug;44(8):1569-76

6. International conference

1. Okubo K. Induction chemoradiotherapy and pulmonary resection for N2-stage IIIA Lung cancer. Thoracic Conference, Clinica Las Condes 8/19/2013, Santiago, Chile

2. Okubo K. Surgical treatment of pulmonary metastasis for colorectal cancer. 2nd International Symposium of Digestive Tumors. 8/26/2013 Quito, Ecuador
3. Hironori Ishibashi, Ken Takahashi, Sachiko Kumazawa, Ryo Maeda, Kenichi Okubo Coughing at extubation of endotracheal tube causes extra air leakage: Laryngeal mask for extubation without coughing 21th European Conference on General Thoracic Surgery, Birmingham, UK 25- 29 May 2013(poster)

Igakuken Disease-oriented Molecular Biology

1. Staffs and Students

Visiting Professor	Takahiko Hara	
Visiting Professor	Masanari Itokawa	
Visiting Professor	Masato Hasegawa	
Visiting Professor	Haruo Okado	
Graduate School Students	Kazuya Miyashita,	Ayami Takahashi

2. Purpose of 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. Research Subjects

[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.

[Masanari Itokawa] 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.

4. Publications

Original Articles

1. K. Tanegashima, K. Suzuki, Y. Nakayama, K. Tsuji, A. Shigenaga, A. Otaka, and T. Hara. CXCL14 is a natural inhibitor of the CXCL12-CXCR4 signaling axis. *FEBS Letters*, 587: 1731-1735, 2013.
2. K. Tanaka, K. Kondo, K. Kitajima, M. Muraoka, A. Nozawa, and T. Hara. Tumor-suppressive function of protein-tyrosine phosphatase non-receptor type 23 in testicular germ cell tumors is lost upon overexpression of miR142-3p microRNA. *J. Biol. Chem.*, 288: 23990-23999, 2013.
3. K. Kitajima, M. Kawaguchi, M. Iacovino, M. Kyba, and T. Hara. Molecular functions of the LIM-homeobox transcription factor *Lhx2* in hematopoietic progenitor cells derived from mouse embryonic stem cells. *Stem Cells*, 31: 2680-2689, 2013.
4. K. Tanegashima, K. Tsuji, K. Suzuki, A. Shigenaga, A. Otaka, and T. Hara. Dimeric peptides of the C-terminal region of CXCL14 function as CXCL12 inhibitors. *FEBS Letters*, 587: 3770-3775, 2013.
5. K. Tsuji, K. Tanegashima, A. Shigenaga, K. Aihara, M. Denda, H. Ding, T. Hara, and A. Otaka. Synthesis of antagonistic peptide for putative CXCL14 receptor protein and their identification. *Peptide Science* 2012, p31-32, 2013.
6. M. Miyashita, M. Arai, A. Kobori, T. Ichikawa, K. Toriumi, K. Niizato, K. Oshima, Y. Okazaki, T. Yoshikawa, N. Amano, T. Miyata, and M. Itokawa. Clinical Features of Schizophrenia With Enhanced Carbonyl Stress. *Schizophr. Bull.*, 2013 Sep 23. [Epub ahead of print]

7. M. Miyashita, M. Arai, H. Yuzawa, K. Niizato, K. Oshima, I. Kushima, R. Hashimoto, M. Fukumoto, S. Koike, T. Toyota, H. Ujike, T. Arinami, K. Kasai, M. Takeda, N. Ozaki, Y. Okazaki, T. Yoshikawa, N. Amano, T. Miyata, and M. Itokawa. Replication of enhanced carbonyl stress in a subpopulation of schizophrenia. *Psychiatry Clin. Neurosci.*, 68: 83-84, 2014.
8. Y. Suto, M. Hirai, M. Akiyama, G. Kobashi, M. Itokawa, M. Akashi, and N. Sugiura. Biodosimetry of restoration workers for the Tokyo electric power company (TEPCO) Fukushima daiichi nuclear power station accident. *Health Phys.*, 105: 366-373, 2013.
9. M. Furukawa, M. Tochigi, T. Otowa, T. Arinami, T. Inada, H. Ujike, Y. Watanabe, N. Iwata, M. Itokawa, H. Kunugi, R. Hashimoto, N. Ozaki, C. Kakiuchi, K. Kasai, and T. Sasaki. An association analysis of the cardiomyopathy-associated 5 (CMYA5) gene with schizophrenia in a Japanese population. *Psychiatr. Genet.*, 23: 179-180, 2013.
10. Y. Aoki, L. Orikabe, Y. Takayanagi, N. Yahata, Y. Mozue, Y. Sudo, T. Ishii, M. Itokawa, M. Suzuki, M. Kurachi, Y. Okazaki, K. Kasai, and H. Yamasue. Volume reductions in frontopolar and left perisylvian cortices in methamphetamine induced psychosis. *Schizophr. Res.*, 147: 355-361, 2013.
11. H. Shibata, K. Yamamoto, Z. Sun, A. Oka, H. Inoko, T. Arinami, T. Inada, H. Ujike, M. Itokawa, M. Tochigi, Y. Watanabe, T. Someya, H. Kunugi, T. Suzuki, N. Iwata, N. Ozaki, and Y. Fukumaki. Genome-wide association study of schizophrenia using microsatellite markers in the Japanese population. *Psychiatr. Genet.*, 23: 117-123, 2013.
12. T. Nonaka, M. Masuda-Suzukake, T. Arai, Y. Hasegawa, H. Akatsu, T. Obi, M. Yoshida, S. Murayama, D. M. Mann, H. Akiyama, and M. Hasegawa. Prion-like Properties of Pathological TDP-43 Aggregates from Diseased Brains. *Cell Rep.*, 4: 124-34, 2013.
13. M. Masuda-Suzukake, T. Nonaka, M. Hosokawa, T. Oikawa, T. Arai, H. Akiyama, D. Mann, and M. Hasegawa. Prion-like spreading of pathological alpha-synuclein in brain. *Brain*, 136: 1128-38, 2013.
14. A. Dan, M. Takahashi, M. Masuda-Suzukake, F. Kametani, T. Nonaka, H. Kondo, H. Akiyama, T. Arai, D. M. A. Mann, Y. Saito, H. Hatsuta, S. Murayama, and M. Hasegawa. Extensive deamidation at asparagine residue 279 accounts for weak immunoreactivity of tau with RD4 antibody in Alzheimer's disease brain. *Acta. Neuropathol. Comm.*, 1: 54, 2013.
15. D. M. A. Mann, S. Rollinson, A. C. Robinson, J. Callister, J. S. Snowden, T. Gendron, L. Petrucelli, M. Masuda-Suzukake, M. Hasegawa, Y. S. Davidson, and S. Pickering-Brown. Dipeptide repeat proteins are present in the p62 positive inclusions in patients with Frontotemporal Lobar Degeneration and Motor Neuron Disease associated with expansions in C9ORF72. *Acta. Neuropathol. Comm.*, 1: 68, 2013.
16. Z. Kobayashi, I. Kawakami, T. Arai, O. Yokota, K. Tsuchiya, H. Kondo, Y. Shimomura, C. Haga, N. Aoki, M. Hasegawa, M. Hosokawa, K. Oshima, K. Niizato, H. Ishizu, S. Terada, M. Onaya, M. Ikeda, K. Oyanagi, I. Nakano, S. Murayama, H. Akiyama, and H. Mizusawa. Pathological features of FTL-D-FUS in a Japanese population: Analyses of nine cases. *J Neurol. Sci.*, 335: 89-95, 2013.
17. P. G. Foulds, P. Diggle, D. Mitchell, A. Parker, M. Hasegawa, M. Masuda-Suzukake, D. M. A. Mann, and D. Allsop. A longitudinal study on alpha-synuclein in blood plasma as a biomarker for Parkinson's disease. *Sci. Rep.*, 3: 2540, 2013.
18. D. Moujalled, J. L. James, S. J. Parker, G. E. Lidgerwood, C. Duncan, J. Meyerowitz, T. Nonaka, M. Hasegawa, K. M. Kanninen, A. Grubman, J. R. Liddell, P. J. Crouch, and A. R. White. Kinase Inhibitor Screening Identifies Cyclin-Dependent Kinases and Glycogen Synthase Kinase 3 as Potential Modulators of TDP-43 Cytosolic Accumulation during Cell Stress. *PLoS ONE*, 8: e67433, 2013.
19. T. Kimura, K. Tsutsumi, M. Taoka, T. Saito, M. Masuda-Suzukake, K. Ishiguro, F. Plattner, T. Uchida, T. Ishobe, M. Hasegawa, and S.-I. Hisanaga. Pin1 Stimulates Dephosphorylation of Tau at Cdk5-Dependent Alzheimer Phosphorylation Sites. *J. Biol. Chem.*, 288: 7968-77, 2013.
20. J. I. Heng, Z. Qu, C. Ohtaka-Maruyama, H. Okado, M. Kasai, D. Castro, F. Guillemot, and S. S. Tan. The Zinc Finger Transcription Factor RP58 Negatively Regulates Rnd2 for the Control of Neuronal Migration During Cerebral Cortical Development. *Cereb. Cortex.*, (in press)
21. S. Hayashizaki, S. Hirai, Y. Ito, Y. Honda, Y. Arime, I. Sora, H. Okado, T. Kodama, and M. Takada. Methamphetamine increases locomotion and dopamine transporter activity in dopamine D5 receptor-deficient mice. *PLoS ONE*, 8: e75975, 2013.
22. C. Ohtaka-Maruyama, S. Hirai, A. Miwa, J. I. Heng, H. Shitara, R. Ishii, C. Taya, H. Kawano, M. Kasai, K. Nakajima, and H. Okado. RP58 regulates the multipolar-bipolar transition of newborn neurons in the developing cerebral cortex. *Cell Rep.*, 3: 458-471, 2013.

Clinical Anatomy

1. Staffs and Students

Professor	Keiichi AKITA	
Junior Associate Professor	Akimoto NIMURA, Kumiko YAMAGUCHI (Department of Professional Development in Health Science)	
Assistant Professor	Masayo HARADA	
Research Technician	Hisayo NASU, Sadaaki HEIMA	Kiyomi SAIKAWA,
Graduate Student	Hisayo NASU(~March), Kazuhiro SAKAMOTO, Kazuhiro SEKIZAWA, Hitomi FUJISHIRO, Tatsuya TAMAKI, Ryuhei OKADA(April~), Motoki TANAKA(April~)	Yasuo NAKAJIMA, Atsushi TASAKI, Masataka NAKAZAWA, Keiko OKUMURA , Sachiyuki TUKADA, Eiichirou KAGAWA(April~),

2. Purpose of 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.

3. Research Subjects

- 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.

4. Publications

Original Article

1. Hatsushika D, Nimura A, Mochizuki T, Yamaguchi K, Muneta T, Akita K: Attachments of separate small bundles of human posterior cruciate ligament: an anatomic study. *Knee Surg Sports Traumatol Arthrosc.* 2013 21(5): 998-1004.
2. Suzuki M, Tsunoda A, Kudo T, Okada R, Toyoda M : Successful management of hypoparathyroidism following total thyroidectomy with vitamin D3 alone. *Auris Nasus Larynx*, 41: 53-55, 2013.
3. Nimura A, Akita K. Reply to: "The superior capsule of the shoulder joint complements the insertion of the rotator cuff". *J Shoulder Elbow Surg.* 2013 22(2): e20-1.
4. Araki J, Nishizawa Y, Sato T, Naito M, Akita, K, et al. (2013) Anorectal Transplantation in Human Cadavers: Mock Anorectal Allotransplantation. *PLoS ONE* 8(7): e68977.

Systems BioMedicine

1. Staffs and Students

Professor	Hiroshi ASAHARA	
Junior Associate Professor	Masahiro SHINOHARA	
Assistant Professor	Yoshiaki ITO,	Astushi KUBO
Project Assistant Professor	Yoko TANAKA,	Takahide MATSUSHIMA
Research Associate	Tomoki CHIBA	
Graduate Students	Takeshi SAITO,	Akira TAKAHASHI,
	Kentaro ABE,	Kensuke KATAOKA,
	Yohei MATSUBARA ,	Naoki KODA,
	Hidetsugu SUZUKI,	Takashi NAKASUJI,
	Ryo NAKAMICHI,	Tomohiro KAYAMA,
	Masashi NAITO,	Yusuke MOCHIZUKI

2. Purpose of Education

Undergraduate:

Conducting “Molecular Genetics”, which is a series of lectures to understand the gene expression machinery and human genetics and their application to current medicine and biology. Under graduate students can join the lab works to learn the skills for molecular biology and pathology.

Graduate School:

Organizing “Development and Regeneration” lecture series to understand the basis for regenerative medicine and reproduction at the level of molecular genetics.

Students can join the Lab to perform researches using various experimental techniques, such as microarray, cell-based high throughput screening etc. Using these techniques, core molecular network for tissue development and inflammatory diseases will be examined, which forms the basis of systems biomedicine.

3. Research Subjects

- The function of non-coding RNA in development and diseases will be examined.
- Development and regeneration using genome editing technologies, such as TALEN and CRISPR/Cas9 will be analyzed.
- Genome dynamics during embryogenesis will be monitored by new techniques.
- Novel systems approaches will be established and applied for developmental biology and medicine.

4. Publications

Original Articles

1. Kato T, Miyata K, Sonobe M, Yamashita S, Tamano M, Miura K, Kanai Y, Miyamoto S, Sakuma T, Yamamoto T, Inui M, Kikusui T, Asahara H*, and Takada S*. Production of Sry knockout mouse using TALEN via oocyte injection. *Scientific Rep.* 3,
2. Takada S, Sato T, Ito Y, Yamashita S, Kato T, Kawasumi M, Kanai-Azuma M, Igarashi A, Kato T, Tamano M, Asahara H. Targeted gene deletion of miRNAs in mice by TALEN system, *PLoS ONE* 8(10): e76004.
3. Shimizu H, Kubo A, Uchibe K, Hashimoto M, Yokoyama S, Takada S, Mitsuoka K, Asahara H, The AERO System: a 3D-like Approach for Recording Gene Expression Patterns in the Whole Mouse Embryo, *PLOS One.* 8(10):e75754.
4. Yoshitaka T, Kawai A, Miyaki S, Numoto K, Kikuta K, Ozaki T, Lotz M, Asahara H. Analysis of microRNAs expressions in chondrosarcoma. *J Orthop Res.* Volume 31(12):1861-2039,2013
5. Nakahara H, Hasegawa A, Otabe K, Ayabe F, Matsukawa T, Onizuka N, Ito Y, Ozaki T, Lotz MK, Asahara H. Transcription factor mohawk and the pathogenesis of human anterior cruciate ligament degradation. *Arthritis Rheum.* 65(8):2081-9
6. Watanabe T, Oyama T, Asada M, Harada D, Ito Y, Inagawa M, Suzuki Y, Sugano S, Katsube K, Karsenty G, Komori T, Kitagawa M, Asahara H. MAML1 enhances the transcriptional activity of Runx2 and plays a role in bone development. *PLOS Genetics.* 9(1):e1003132.
7. Takata A, Otsuka M, Yoshikawa T, Kishikawa T, Hikiba Y, Obi S, Goto T, Kang YJ, Maeda S, Yoshida H, Omata M, Asahara H, Koike K. MiRNA-140 acts as a liver tumor suppressor by controlling NF-kB activity via directly

targeting Dnmt1 expression. *Hepatology* 57(1):162-70, PMID: 22898998

Review Articles

1. Furumatsu T, Asahara H. Chromatin assembly and in vitro transcription analyses for evaluation of individual protein activities in multicomponent transcriptional complexes. *Methods Mol Biol.* 977:193-202.

Invited Lecture

1. Asahara H. A systems approach reveals molecular network regulating musculoskeletal tissues development and homeostasis. The 86th Annual Meeting of the Japanese Biochemical Society, PACIFICO Yokohama, Sep.12
2. Asahara H. MicroRNA and Arthritis. American College of Rheumatology, San Diego, USA Oct.26

Comprehensive Pathology

1. Staffs and Students

Professor	Masanobu KITAGAWA Morito KURATA (on administrative leave)
Assistant Professor	Kouhei YAMAMOTO, Shinya ABE, Shiho ABE
Laboratory Technician	Miori INOUE
Technical Assistant	Sachiko ISHIBASHI
Graduate Students	Iichiro ONISHI, Ruri DAGET, Na LI, Kenichi MIYAMOTO, Kazuhito SUZUKI, Masafumi INOUE, Kenichiro KATO, Xiao Hai JIN

2. Purpose of Education

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).

3. Research Subjects

- 1) Clinico-pathological study by morphological findings, immunohistochemistry, and electron microscope, etc.
- 2) Molecular analysis of leukomogenesis induced by Friend leukemia virus (FLV)
- 3) Enhancement of apoptosis by virus-derived protein and development of apoptosis-induction cancer therapy
- 4) Molecular pathology of the myelodysplastic syndromes (MDS)
- 5) Clarification of drug resistance mechanism for hematopoietic malignancies
- 6) Comprehensive research for aging focus on the decreased immune competence
- 7) Molecular biology of the cancer progression and metastasis

4. Publications

Original Article

1. Tulafu M, Mitaka C, Hnin Si MK, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M: Atrial natriuretic peptide attenuates kidney-lung crosstalk in kidney injury. *J Surg Res* 2014; 186: 217-225.
2. Si MK, Mitaka C, Tulafu M, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M. Inhibition of poly (adenosine diphosphate-ribose) polymerase attenuates lung-kidney crosstalk induced by intratracheal lipopolysaccharide instillation in rats. *Respir Res.* 2013; 14(1): 126.
3. Li N, Abe S, Kurata M, Abe-Suzuki S, Onishi I, Kirimura S, Murayama T, Hidaka M, Kawano F, Kitagawa M. Over-Expression of Cancerous Inhibitor of PP2A (CIP2A) in Bone Marrow Cells from Patients with a Group of High-Risk Myelodysplastic Syndromes. *Pathol Oncol Res.* 2013 Oct 26.
4. Fan W, Nakazawa K, Abe S, Inoue M, Kitagawa M, Nagahara N, Makita K: Inhaled aerosolized insulin ameliorates hyperglycemia-induced inflammatory responses in the lungs in experimental model of acute lung injury. *Critical Care* 2013; 17: R83.
5. Miwa Y, Tomohito H, Suzuki S, Abe S, Onishi I, Kirimura S, Kitagawa M, Kurata M: Up-regulated expression of CXCL12 in spleens with extramedullary hematopoiesis. *Pathology* 2013; 45(4): 408-416.
6. Kurata M, Suzuki S, Abe S, Onishi I, Kitagawa M: Bone marrow cell death and proliferation: Controlling mechanisms in normal and leukemic state (review). *World Journal of Hematology* 2013; 2(1):1-5.
7. Hirokawa K, Utsuyama M, Hayashi Y, Kitagawa M, Makinodan T, Fulop T: Slower immune system aging in women versus men in the Japanese population. *Immun Ageing.* 2013 May 15;10(1):19.
8. Takeda T, Sato T, Ito T, Sumi Y, Kobayashi T, Kitagawa M, Hirokawa K, Uchihara T. Four-repeat tau-selective deposition in subthalamic nucleus and motor cortex in Alzheimer disease. *Clinical Neurology and Neurosurgery* 2013; 115:641-643.
9. Yagi K, Yamamoto K, Umeda S, Abe S, Suzuki S, Ohnishi I, Kirimura S, Fukayama M, Arai A, Murayama T, Hideki M, Kitagawa M, Kurata M. Expression of *multidrug resistance 1* gene in B-cell lymphomas: association with follicular dendritic cells. *Histopathology* 2013 62:414-420.

10. Takagi M, Sato M, Piao J, Miyamoto S, Isoda T, Kitagawa M, Honda H, Mizutani S. ATM-dependent DNA-damage-response pathway as a determinant in chronic myelogenous leukemia. *DNA Repair* 2013; 12:500-507.

【National meeting】

Kohei Yamamoto, Yukiko Tone, Rimpei Niwa, Shuko Harada, Xuan Hao T. Doan, Jonathan Said, Phillip Koeffler and Masahide Tone *Regulation of CD20 expression through alternative splicing*. 2013 Immunology LA meeting, California, USA.

Molecular Oncology

1. Staffs and Students

Professor	Yasuhito YUASA	
Associate Professor	Yoshimitsu AKIYAMA	Hiroshi FUKAMACHI
Assistant Professor	Shu SHIMADA	
Medical Technologist	Hiromi NAGASAKI	
JSPS Research Fellow	Yutaka HASHIMOTO	Rika TSUCHIDA
Graduate Students	Shogo KOJIMA	Ayuna SAKAMOTO
	Taketo NISHIKAWAJI	Kanako BABA

2. Purpose of Education

Undergraduate course:

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, and food poisoning.

Graduate course:

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 biweekly 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.

3. Research Subjects

- 1) Cellular and molecular analyses of cancer-related genes, such as oncogenes and tumor suppressor genes, in gastroenterological cancers
- 2) Molecular mechanism of cell growth, differentiation and apoptosis
- 3) Involvement of differentiation-related genes in gastroenterological diseases
- 4) Cancer stem cells
- 5) DNA methylation and cancer
- 6) Transcription factors and cancer
- 7) Mouse model of gastric cancer
- 8) Effect of environmental factors on gene expression and DNA methylation
- 9) Involvement of microRNA in gastric carcinogenesis

4. Publications

Original Article

- 1) Rotkrua P*, Shimada S*, Mogushi K, Akiyama Y, Tanaka H, Yuasa Y. Circulating microRNAs as biomarkers for early detection of diffuse-type gastric cancer using a mouse model. *Brit J. Cancer.* 108(4), 932-940, 2013. (*contributed equally)
- 2) Wang D, Zhou J, Liu X, Lu D, Shen C, Du Y, Wei FZ, Song B, Lu X, Yu Y, Wang L, Zhao Y, Wang H, Yang Y, Akiyama Y, Zhang H, Zhu WG. Methylation of SUV39H1 by SET7/9 results in heterochromatin relaxation and genome instability. *Proc. Natl Acad. Sci. U S A.* 110(14), 5516-5521, 2013.
- 3) Hashimoto Y, Akiyama Y, Yuasa Y. Multiple-to-multiple relationships between microRNAs and target genes in gastric cancer. *PLoS One.* 8(5), e62589, 2013.
- 4) Fukamachi H, Seol HS, Shimada S, Funasaka C, Baba K, Kim JH, Park YS, Kim MJ, Kato K, Inokuchi M, Kawachi H, Yook JH, Eishi Y, Kojima K, Kim WH, Jang SJ, Yuasa Y. CD49^{high} cells retain sphere-forming and tumor-initiating activities in human gastric tumors. *PLoS One.* 8(8), e72438, 2013.
- 5) Seol HS, Suh YA, Ryu YJ, Kim HJ, Chun SM, Na DC, Fukamachi H, Jeong SY, Choi EK, Jang SJ. A patient-derived xenograft mouse model generated from primary cultured cells recapitulates patient tumors phenotypically and genetically. *J. Cancer Res. Clin. Oncol.* 139(9), 1471-1480, 2013.
- 6) Fukamachi H, Kato S, Asashima M, Ichinose M, Yuasa Y. Activin A regulates growth of gastro-intestinal epithelial

cells by mediating epithelial-mesenchymal interaction. *Dev. Growth Differ.* 55(9), 786-791, 2013.

- 7) Osawa T, Tsuchida R, Muramatsu M, Shimamura T, Wang F, Suehiro J, Kanki Y, Wada Y, Yuasa Y, Aburatani H, Miyano S, Minami T, Kodama T, Shibuya M. Inhibition of histone demethylase JMJD1A improves anti-angiogenic therapy and reduces tumor associated macrophages. *Cancer Res.* 73; 3019-3028, 2013.

Review Article

- 1) Akiyama Y. Gastric cancer. *Epigenetics and Diseases (Gene Medicine Mook Vol. 25)*, 64-69. 2013 (In Japanese).

Surgical Pathology

1. Staff and Students

Professor	Yoshinobu EISHI	
Associate Professor	Takumi AKASHI	
Assistant Professor	Eisaku ITO,	Yuan Bae,
	Emiko SUGAWARA	
Hospital Staff Doctor	Keiko MIURA	
Secretary	Ayako KOBAYASHI	

2. Purpose of education

Main object of surgical pathology in the course of graduate school is to provide medical students opportunity to study 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.

3. Research Subjects

- 1) Improvement of diagnostic methods of gastrointestinal, liver, renal and respiratory diseases by anatomical, immunohistochemical, microbiological and molecular technologies.
- 2) Analysis of the pathophysiology of the disease, especially invasion mechanism of lung and gastrointestinal cancers by molecular biological technology.

4. Clinical Services

In cooperation with departments of human pathology and comprehensive pathology, department of surgical pathology provides autopsy services (100 case in a year), cytopathology services (12,000 cases in a year) and surgical pathology (10,000 cases in a year) for the clinicians of the affiliated hospital. Diagnosis is mostly done by the organ-subspecialized staffs. Clinico-pathological conferences are held more than one hundred times in a year.

5. Publications

Original Article

1. Eishi Y. Etiologic link between sarcoidosis and *Propionibacterium acnes*. *Respir Investig.* 51(2):56-68,2013
2. Minegishi K, Aikawa C, Furukawa A, Watanabe T, Nakano T, Ogura Y, Ohtsubo Y, Kurokawa K, Hayashi T, Maruyama F, Nakagawa I, Eishi Y. Complete Genome Sequence of a *Propionibacterium acnes* Isolate from a Sarcoidosis Patient. *Genome Announc.* 1(1), 2013
3. Okamoto N, Kawachi H, Yoshida T, Kitagaki K, Sekine M, Kojima K, Kawano T, Eishi Y. "Crawling-type" adenocarcinoma of the stomach: a distinct entity preceding poorly differentiated adenocarcinoma. *Gastric Cancer.* 16(2):220-32,2013
4. Kurata M, Suzuki S, Abe S, Onishi I, Kitagawa M. Bone marrow cell death and proliferation: Controlling mechanisms in normal and leukemic state (review). *World Journal of Hematology.* 2(1):1-5,2013
5. Miyazaki Y, Unoura K, Tateishi T, Akashi T, Takemura T, Tomita M, Inase N, Yoshizawa Y: Higher serum CCL17 may be a promising predictor of acute exacerbations in chronic hypersensitivity pneumonitis, *Respiratory research,* 14:57,2013
6. Pal SK, Sakamoto K, Aragaki T, Akashi T, Yamaguchi A: The expression profiles of acidic epithelial keratins in ameloblastoma, *Oral surgery, oral medicine, oral pathology and oral radiology,* 115:523-531,2013
7. Shiwaku H, Yagishita S, Eishi Y, Okazawa H. Bergmann glia are reduced in spinocerebellar ataxia type 1. *Neuroreport.* 24(11):620-5,2013
8. Matsuo Y, Mizoguchi F, Kohsaka H, Ito E, Eishi Y, Miyasaka N. Tocilizumab-induced immune complex glomerulonephritis in a patient with rheumatoid arthritis. *Rheumatology (Oxford).* 52(7):1341-3,2013
9. Asahina A, Miura K, Saito I, Oshikata C, Ishii N, Eishi Y. Cutaneous sarcoidosis with livedoid lesions: evidence of the involvement of *Propionibacterium acnes*. *J Dermatol.* 40(6):501-2,2013
10. Ueno H, Shirouzu K, Shimazaki H, Kawachi H, Eishi Y, Ajioka Y, Okuno K, Yamada K, Sato T, Kusumi T, Kushima R, Ikegami M, Kojima M, Ochiai A, Murata A, Akagi Y, Nakamura T, Sugihara K; Study Group for Perineural Invasion projected by the Japanese Society for Cancer of the Colon and Rectum (JSCCR). Histogenesis and

- prognostic value of myenteric spread in colorectal cancer: a Japanese multi-institutional study. *J Gastroenterol.* 2013 May 16. [Epub ahead of print]
11. Ueno H, Shirouzu K, Eishi Y, Yamada K, Kusumi T, Kushima R, Ikegami M, Murata A, Okuno K, Sato T, Ajioka Y, Ochiai A, Shimazaki H, Nakamura T, Kawachi H, Kojima M, Akagi Y, Sugihara K; Study Group for Perineural Invasion projected by the Japanese Society for Cancer of the Colon and Rectum (JSCCR). Characterization of perineural invasion as a component of colorectal cancer staging. *Am J Surg Pathol.* 37(10):1542-9,2013
 12. Niimi Y, Takahashi M, Sugawara E, Umeda S, Obayashi M, Sato N, Ishiguro T, Higashi M, Eishi Y, Mizusawa H, Ishikawa K. Abnormal RNA structures (RNA foci) containing a penta-nucleotide repeat (UGGAA)(n) in the Purkinje cell nucleus is associated with spinocerebellar ataxia type 31 pathogenesis. *Neuropathology.*33(6):600-11,2013
 13. Satoh F, Morita H, Tayama H, Inoue Y, Eishi Y, Yoshimura A. Renal Sarcoidosis With Limited Lung Manifestations Expressing Propionibacterium acnes Antigens in the Affected Tubulointerstitium. *Am J Med Sci.* 346(3):250-2,2013
 14. Fujita K, Nakamura Y, Oka T, Ito H, Tamura T, Tagawa K, Sasabe T, Katsuta A, Motoki K, Shiwaku H, Sone M, Yoshida C, Katsuno M, Eishi Y, Murata M, Taylor JP, Wanker EE, Kono K, Tashiro S, Sobue G, La Spada AR, Okazawa H. A functional deficiency of TERA/VCP/p97 contributes to impaired DNA repair in multiple polyglutamine diseases. *Nat Commun.* 4:1816,2013
 15. Takahashi M, Obayashi M, Ishiguro T, Sato N, Niimi Y, Ozaki K, Mogushi K, Mahmut Y, Tanaka H, Tsuruta F, Dolmetsch R, Yamada M, Takahashi H, Kato T, Mori O, Eishi Y, Mizusawa H, Ishikawa K. Cytoplasmic location of a 1A voltage-gated calcium channel C-terminal fragment (Cav2.1-CTF) aggregate is sufficient to cause cell death. *PLoS One.* 8(3):e50121,2013
 16. Okeda R, Ito K, Tsumura K, Eishi Y. Primary granulomatous angiitis of the CNS preferentially involving small veins with a granulomatous leukoencephalitis-like lesion in the cerebrum. *Neuropathology.* 33(5):547-52,2013
 17. Fukamachi H, Seol HS, Shimada S, Funasaka C, Baba K, Kim JH, Park YS, Kim MJ, Kato K, Inokuchi M, Kawachi H, Yook JH, Eishi Y, Kojima K, Kim WH, Jang SJ, Yuasa Y. CD49f(high) cells retain sphere-forming and tumor-initiating activities in human gastric tumors. *PLoS One.* 8(8):e72438,2013
 18. Okada E, Araki A, Suzuki S, Watanabe H, Ikeda T, Watanabe T, Kurata M, Eishi Y, Watanabe M. Histological diagnosis of follicular lymphoma by biopsy of small intestinal normal mucosa. *Dig Endosc.* 25(5):544-6,2013
 19. Si MK, Mitaka C, Tulafu M, Abe S, Kitagawa M, Ikeda S, Eishi Y, Kurata S, Tomita M. Inhibition of poly (adenosine diphosphate-ribose) polymerase attenuates lung-kidney crosstalk induced by intratracheal lipopolysaccharide instillation in rats. *Respir Res.* 14(1):126,2013
 20. Takeda T, Sato T, Ito T, Sumi Y, Kobayashi T, Kitagawa M, Hirokawa K, Uchihara T. Four-repeat tau-selective deposition in subthalamic nucleus and motor cortex in Alzheimer disease. *Clin Neurol Neurosurg.* 115:641-3, 2013
 21. Sugawara T, Aoyagi M, Tanaka Y, Tamaki M, Kobayashi D, Ohno K. Chronic encapsulated expanding hematoma in nonfunctioning pituitary adenoma. *Neurosurg Rev.* 36(3):395-402,2013
 22. Li N, Abe S, Kurata M, Abe-Suzuki S, Onishi I, Kirimura S, Murayama T, Hidaka M, Kawano F, Kitagawa M. Over-Expression of Cancerous Inhibitor of PP2A (CIP2A) in Bone Marrow Cells from Patients with a Group of High-Risk Myelodysplastic Syndromes. *Pathol Oncol Res.* 2013 Oct 26.
 23. Fan W, Nakazawa K, Abe S, Inoue M, Kitagawa M, Nagahara N, Makita K: Inhaled aerosolized insulin ameliorates hyperglycemia-induced inflammatory responses in the lungs in experimental model of acute lung injury. *Critical Care.* 17: R83,2013
 24. Miwa Y, Tomohito H, Suzuki S, Abe S, Onishi I, Kirimura S, Kitagawa M, Kurata M: Up-regulated expression of CXCL12 in spleens with extramedullary hematopoiesis. *Pathology.* 45(4): 408-416,2013
 25. Hirokawa K, Utsuyama M, Hayashi Y, Kitagawa M, Makinodan T, Fulop T: Slower immune system aging in women versus men in the Japanese population. *Immun Ageing.* 15:10(1):19,2013

Book

1. Yoshinobu Eishi. Sarcoidosis. 290 pages , In Tech. Croatia, March 13, 2013

Lecture meeting

1. Eishi Y (invited lecture) Pathologic safety criteria in the endoscopic resection of colon cancer. Second Latin0American Symposium ENDOSUR, Santiagom Chile, August 20, 2013
2. Eishi Y (invited lecture) Why do we need colorectal cancer screening with appropriate procedures? Second International Symposium of Digestive Tumors. Quito, Ecuador, August 26, 2013
3. Eishi Y (invited lecture) Limits of endoscopic resection and oncology safety concept. Second International

Symposium of Digestive Tumors. Quito, Ecuador, August 26, 2013

Experimental Animal Model for Human Disease

1. Staffs

Professor	Masami Kanai-Azuma	
Assistant Professor	Shu Endo,	Miyuri Kawasumi,
	Hitomi Suzuki	

2. Research Subject

- 1) **Sox17** function for the foregut endoderm development.
(Etiology – Mouse Hepatitis)
- 2) The functional analysis of **SoxF** group
- 3) Mechanisms of bile duct development
- 4) Functional analysis of transcription factor Sox17 for implantation.
- 5) Mechanism of primordial follicle activation in mammalian ovary

3. Publications

Original Articles

1. Targeted Gene Deletion of miRNAs in Mice by TALEN System. Takada S, Sato T, Ito Y, Yamashita S, Kato T, Kawasumi M, Kanai-Azuma M, Igarashi A, Kato T, Tamano M, Asahara H., PLoS One. 8 (10) : e76004. 2013
2. Heterogeneity in sexual bipotentiality and plasticity of granulosa cells in developing mouse ovaries. Harikae K, Miura K, Shinomura M, Matoba S, Hiramatsu R, Tsunekawa N, Kanai-Azuma M, Kurohmaru M, Morohashi KI, Kanai Y., J Cell Sci. 126:2834-2844. 2013
3. Targeted gene silencing in mouse germ cells by insertion of a homologous DNA into a piRNA generating locus. Yamamoto Y, Watanabe T, Hoki Y, Shirane K, Li Y, Ichiiyanagi K, Kuramochi-Miyagawa S, Toyoda A, Fujiyama A, Oginuma M, Suzuki H, Sado T, Nakano T, *Sasaki H., Genome Res. 23(2):292-299. 2013
4. Sox17 haploinsufficiency results in perinatal biliary atresia and hepatitis in C57BL/6 background mice. Uemura M, Ozawa A, Nagata T, Kurasawa K, Tsunekawa N, Nobuhisa I, Taga T, Hara K, Kudo A, Kawakami H, Saijoh Y, Kurohmaru M, Kanai-Azuma M*, Kanai Y*.(equally contribution) Development. 140:639-648. 2013
5. Generation of a germ cell-specific mouse transgenic CHERRY reporter, *Sohlh1-mCherry-Flag* Suzuki H. and *Rajkovic A., Genesis. 51(1):50-58. 2013

Conference Paper Index

Japan

1. Mai Shinomura¹, Hiromi Kanezashi¹, Yoshimi Aiyama¹, Kasane Kishi¹, Yoshiko Kuroda¹, Miyuri Kawasumi², Naoki Tsunekawa¹, Masamichi Kuromaru¹, Masami Kanai-Azuma², Yoshiakira Kanai¹ (¹Tokyo Univ. Veterinary Anatomy, ²TMDU Center for Experimental Animal). “*Establishment and Application of AMH-TREK mouse that can kill Sertoli cells*”. The Society for Reproduction and Development, 106th meeting at TUAT. Sep 12th to 14th, 2013.
2. Kento Miura¹, Kyoko Harikae¹, Mai Shinomura¹, Mayu Nakaguchi¹, Ayako Tomita¹, Naoki Tsunekawa¹, Hitomi Suzuki², Masami Kanai-Azuma², Masamichi Kuromaru¹, Yoshiakira Kanai¹ (¹Tokyo Univ. Veterinary Anatomy, ²TMDU Center for Experimental Animal). “*Identification of Target Gene for SRY, the testis determination factor, with Hsp-Sry Tg mouse*”. The Society for Reproduction and Development, 106th meeting at TUAT. Sep 12th to 14th, 2013.
3. Hitomi Suzuki and Masami Kanai-Azuma. “*The Regulation Mechanism for Maintenance and Activation of Primordial Follicle in Mouse Ovary*”. The Moroccan Workshop at RIKEN BRC. Jun 28th to 29th, 2013. Poster P-1 (2013/06/29)
4. Miyuri Kawasumi¹, Ryuto Hiramatsu², Yoshiakira Kanai², Masami Kanai-Azuma¹ (¹TMDU, Center for Experimental Animal, ²Tokyo Univ. Veterinary Anatomy). “*Analysis of the implantation mechanism with Sox17-GFP Tg mice*”. The Moroccan Workshop at RIKEN BRC. Jun 28th to 29th, 2013. Poster P-1 (2013/06/29)
5. Ikuo Nobuhisa¹, Mitsujiro Osawa³, Mami Uemura^{4,5}, Yoko Kishikawa², Maha Anani¹, Kaho Harada¹, Haruna Takagi³, Masami Kanai-Azuma⁴, Yoshiakira Kanai¹, Atsushi Iwama³, Tetsuya Taga¹, (¹Dept. of Stem Cell Regulation, Tokyo Med. and Dent. Univ., ²Dept. of Cell Fate Modulation, Institute of Molecular Embryology and Genetics, Kumamoto Univ., ³Dept of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba Univ., ⁴Cent. For Exp. Anim., Tokyo Med. and Dent. Univ., ⁵Dept. of Vet. Anat., Univ. of Tokyo). *Sox17 protein –mediated maintenance of cells*

with stem cell phenotype in the hematopoietic cell clusters in the fetal AGM region. The 11th Stem Cell Research Symposium, May 17-18, 2013, Tokyo Univ.

6. Miyuri Kawasumi¹, Ryuto Hiramatsu², Hitomi Suzuki¹, Yoshiakira Kanai², Masami Kanai-Azuma¹ (¹TMDU, Center for Experimental Animal, ²Tokyo Univ. Veterinary Anatomy). "Analysis of the implantation mechanism with Sox17-GFP Tg mice.". The 60th annual meeting, JALAS at Tsukuba May 15th to 17th, 2013.
7. Hitomi Suzuki, Masami Kanai-Azuma (¹TMDU, Center for Experimental Animal). "*The Regulation Mechanism for Maintenance and Activation of Primordial Follicle in Mouse Ovary*". The 60th annual meeting, JALAS at Tsukuba May 15th to 17th, 2013.

Abroad

1. Masami Kanai-Azuma¹, Yoshimi Aiyama², Miyuri Kawasumi¹, Yoshiakira Kanai², (¹Cent. For Exp. Anim., Tokyo Med. and Dent. Univ., ²Dept. of Vet. Anat., Univ. of Tokyo), LUMINAL FLUID FLOW SUPPORTS CONTINUOUS SPERMATOGENESIS THROUGH THE BALANCED GDNF REGULATION, Gordon Research conference on germinal Stem Cell Biology(14-19July 2013) Hongkong
2. Kenta Yashiro¹, Ioannis kokkinopoulos¹, Rie Saba¹, Hidekazu Ishida¹, Yumiko Saga², Masami Kanai-Azuma^{3,4}, Keiko Kitajima⁵, Chikara Meno⁵, Yoshiakira Kanai³, Peter Koopman⁶, Hiroshi Hamada⁷ & Ken Suzuki¹, Tetsuya Taga¹, (¹Translation Medicine and Therapeutics, Willian Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary Univ. of London, ²Dep. of Genetics, Sokendai, ³Dept. of Vet. Anat., Univ. of Tokyo ⁴Cent. For Exp. Anim., Tokyo Med. and Dent. Univ., ⁵Dept. of Developmental Biology, Graduate School of Med. Science, Kyushu Univ., ⁶Div. of Molecular Genetics and Development, Institute for Molecular Bioscience, The Univ. of Queensland, ⁷Development Genetics, Graduate School of Frontier Bioscience, Osaka Univ.), Single-Cell cDNA Analyses of embryonic cardiac progenitor cells, 17th International Congress of Developmental Biology, 16-20Jun2013 Cancun Mexico

[Funding]

Grant-in-Aid for Scientific Research (C)

Masami Kanai-Azuma

Title: Application of Sox 17 halpoin sufficiency in perinatal biliary atresia for a human disease model.

Grant-in-Aid for Young Scientists (B)

Miyuri Kawasumi

Title: Analysis of the implantation mechanism with Sox17-GFP Tg mice.

Grant-in-Aid for Young Scientists (B)

Hitomi Suzuki

Title: The analysis of molecular mechanisms for the primordial follicle activation that supports a female reproductive life

Tenure-track Project (JSPS)

Hitomi Suzuki

Human Gene Sciences Center (Signal Gene Regulation)

1. Staff and Student

Professor	Masataka NAKAMURA (Director)
Junior Associate Professor	Noriko FUNATO
Assistant Professor	Mariko MIZUGUCHI
Foreign Researcher	Patrick Daniel Varga-Weisz (July~September)
Postdoctoral Fellow	Mamami YOSHITA (~March), Hideaki MATSUKI (April~)
Graduate Student	Tomoaki KUMAGAI, Lindsay PRESTON (~September)

2. Purpose of Education

The aim of Human Gene Sciences Center is to provide laboratory equipment, room and information for researches in advanced molecular and cellular biology. In educational objectives in the graduate school, our Center gives lecture, seminar, training course and individual assistance in research fields of molecular genetics, immunology and virology.

3. Research Subject

- 1) Molecular mechanism of tumorigenesis by human T-cell leukemia virus type I (HTLV-I).
- 2) Roles of transcription factors in cell differentiation.
- 3) Implication of prostaglandin D2 receptor (CRTH2) in allergy reactions.

5. Publications

Original Article

1. Murata T, Aritake K, Tsubosaka Y, Maruyama T, Nakagawa T, Hori M, Hirai H, Nakamura M, Narumiya S, Urade Y, Ozaki H: Anti-inflammatory role of PGD₂ in acute lung inflammation and therapeutic application of its signal enhancement. *Pro. Natl. Acad. Sci. USA.* 110: 5205-5210, 2013.
2. Taketomi Y, Ueno N, Kojima T, Sato H, Murse R, Yamamoto K, Tanaka S, Sakanaka M, Nakamura M, Hishito Y, Kawana M, Kambe N, Ikeda K, Taguchi R, Nakamizo S, Kabashima K, Gelb M H, Arita M, Yokomizo T, Nakamura M, Watanabe K, Hirai H, Nakamura M, Okayama Y, Ra C, Aritake K, Urade Y, Morimoto K, Sugimoto Y, Shimizu T, Narumiya S, Hara S, Murakami M: Mast cell maturation is driven via a group III phospholipase A₂-prostaglandin D₂-DP1 receptor paracrine axis. *Nature Immunol.* 14: 554-563, 2013.
3. Mizukoshi T, Komori H, Mizuguchi M, Abdelaziz H, Hara T, Higuchi M, Tanaka Y, Ohara Y, Funato N, Fujii M, Nakamura M: Failure in activation of the canonical NF- κ B pathway by human T-cell leukemia virus type 1 Tax in non-hematopoietic cell lines. *Virology.* 443: 226-235, 2013.
4. Tsukahara T, Ohmine K, Yamamoto C, Uchibori R, Ido H, Teruya T, Urabe M, Mizukami H, Kume A, Nakamura M, Mineno J, Takesako K, Riviere I, Sadelain M, Brentjens R, Ozawa K: CD19 target-engineered T-cells accumulate at tumor lesions in human B-cell lymphoma xenograft mouse models. *Biophys. Biochem. Res. Commun.* 438: 84-89, 2013.
5. Takehara Y, Satoh T, Nishizawa A, Saeki K, Nakamura M, Matsuzawa M, Kaneda Y, Katayama I, Yokozeki H: Anti-tumor effects of inactivated Sendai virus particles with an IL-2 gene on angiosarcoma. *Clin. Immunol.* 149: 1-10, 2013.
6. Takahashi M, Higuchi M, Makokha GN, Matsuki H, Yoshita M, Tanaka Y, Fujii M: HTLV-1 Tax oncoprotein stimulates ROS production and apoptosis in T-cells by interacting with USP10. *Blood.* 122: 715-725, 2013.
7. Matsuki H, Takahashi M, Higuchi M, Makokha GN, Oie M, Fujii M: Both G3BP1 and G3BP2 contribute to stress granule formation. *Genes Cells.* 18: 135-146, 2013.
8. Takahashi M, Higuchi M, Matsuki H, Yoshita M, Ohsawa T, Oie M, Fujii M: Stress granules inhibit apoptosis by reducing reactive oxygen species production. *Mol. Cell. Biol.* 33: 815-829, 2013.

Biofunctional Molecular Science

1. Staffs and Students

Associate Professor	Tomoya Hirano	
Assistant Professor	Shigeru Ito,	Ayumi Osaki
Technician	Hiroyuki Masuno	
Graduate Student	Shotaro Iihama,	Akihito Naka,
	Yuta Endo,	Teppey Komiyama

2. Purpose of Education

Biofunctional Molecular Science covers several aspects of organic chemistry, analytical chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand and train the experimental techniques related to these scientific fields.

Our laboratory is working on the developments of functional molecules, which can “modulate” or “sense” the physiological functions, such as enzyme inhibitors and fluorescent sensors for elucidating intracellular or extracellular signal transduction pathway. In addition, we also focus on the development of novel drug and diagnostic tools for various diseases.

3. Research Subject

1) Construction of a facile method to develop various fluorescent sensors for elucidating physiological functions

We construct a facile method to develop various fluorescent sensors, which can sense the change of the concentration or activity of each biologically important analyte.

2) Development of histone methyltransferase inhibitors

Post-translational modification of histone proteins plays an important role in the regulation of gene expression, and can be controlled by histone modifying enzymes, such as histone methyltransferase (HMT). We are developing some inhibitors against these HMTs.

3) Development of fluorescent sensors by modulating the complex formation of fluorophores

The control of intermolecular or intramolecular complex formation between two fluorophores or between a fluorophore and another molecular species has been utilized for the development of fluorescent sensors for some post-translational modifications of tyrosine residues or the visualization of some receptor proteins.

4. Publications

Original articles

1. Niwa H, Handa N, Tomabechi Y, Honda K, Toyama M, Ohsawa N, Shirouzu M, Kagechika H, Hirano T, Umehara T, Yokoyama S: Structures of histone methyltransferase SET7/9 in complexes with adenosylmethionine derivatives. *Acta Crystallogr Sect D* 69: 595 – 602, 2013.

Review articles

1. Hirano T: Development of Functional Molecules for Elucidation of the Physiological Roles of Several Nuclear Receptors and Their Endogenous Ligands. *Chem Pharm Bull* 61: 111 – 120, 2013.

Medicinal Chemistry

1. Staffs and Students (April, 2013)

Professor	Hirokazu TAMAMURA	
Associate Professor	Wataru NOMURA	
Assistant Professor	Tetsuo NARUMI,	Haruo AIKAWA
Research Staff	Nami OHASHI,	Chie HASHIMOTO
Technical Staff	Miho TANABE	
Secretary	Rika NARUMI	
Graduate Student	Yosuke NONAKA,	Shohei TAKETOMI,
	Atsushi ITO,	Taisuke KOSEKI,
	Takuya KOBAYAKAWA,	Hikaru TAKANO,
	Yuki HIROTA,	Daichi MATSUMOTO,
	Yu IRAHARA,	Tsugunori OKABE,
	Ryosuke KOBAYASHI,	Sho SAKAMOTO,
	YUZUNA HONDA	

2. Purpose of Education

Our department teaches chemical biology targeted to elucidation and regulation of biological phenomena based on organic chemistry and advanced synthetic chemistry, medicinal chemistry and advanced drug discovery of a post-genomena era. Our department performs periodically journal clubs and research progress meetings.

3. Research Subjects

- 1) Development of conformational-constrained templates for drug discovery.
- 2) Development of bio-probes, bio-sensing, medicinal chemistry towards chemical biology.
- 3) Structural analysis of the interactions between receptors/enzymes and their ligands.
- 4) Development of applications of zinc finger protein for gene therapy and nano technology.

4. Publications

Original Article

- 1) Hashimoto C, Narumi T, Otsuki H, Hirota Y, Arai H, Yoshimura K, Harada S, Ohashi N, Nomura W, Miura T, Igarashi T, Matsushita S, Tamamura H. A CD4 Mimic as an HIV Entry Inhibitor: Pharmacokinetics. *Bioorg Med Chem* 21(24): 7884–7889, 2013.
- 2) Hashimoto C, Nomura W, Narumi T, Fujino M, Nakahara T, Yamamoto N, Murakami T, Tamamura H. CXCR4-derived Synthetic Peptides Inducing Anti-HIV-1 Antibodies. *Bioorg Med Chem* 21(22): 6878–6885, 2013.
- 3) Otsuki H, Hishiki T, Miura T, Hashimoto C, Narumi T, Tamamura H, Yoshimura K, Matsushita S, Igarashi T. Generation of a Replication-competent Simian–human Immunodeficiency Virus, the Neutralisation Sensitivity of Which can be Enhanced in the Presence of a Small Molecule CD4 Mimic. *J Gen Virol* 94(12): 2710–2716, 2013.
- 4) Nomura W, Aikawa H, Ohashi N, Urano E, Metfiofi M, Fujino M, Maddali K, Ozaki T, Nozue A, Narumi T, Hashimoto C, Tanaka T, Pommier Y, Yamamoto N, Komano J, Murakami T, Tamamura H. Cell-Permeable Stapled Peptides Based on HIV-1 Integrase Inhibitors Derived from HIV-1 Gene Product. *ACS Chem Biol* 8(10): 2235–2244, 2013.
- 5) Hashimoto C, Nomura W, Narumi T, Fujino M, Tsutsumi H, Haseyama M, Yamamoto N, Murakami T, Tamamura H. Anti-HIV-1 Peptide Derivatives Based on the HIV-1 Co-receptor CXCR4. *ChemMedChem* 8(10): 1668–1672, 2013.
- 6) Nomura W, Hashimoto C, Suzuki T, Ohashi N, Fujino M, Murakami T, Yamamoto N, Tamamura H. Multimerized CHR-derived Peptides as HIV-1 Fusion Inhibitors. *Bioorg Med Chem* 21(15): 4452–4458, 2013.
- 7) Narumi T, Arai H, Yoshimura K, Harada S, Hirota Y, Ohashi N, Hashimoto C, Nomura W, Matsushita S, Tamamura H. CD4 Mimics as HIV Entry Inhibitors: Lead Optimization Studies of the Aromatic Substituents. *Bioorg Med Chem* 21(9): 2518–2526, 2013.
- 8) Narumi T, Aikawa H, Tanaka T, Hashimoto C, Ohashi N, Nomura W, Kobayakawa T, Takano H, Hirota Y, Murakami T, Yamamoto N, Tamamura H. Low Molecular Weight CXCR4 Ligands with Variable Spacers. *ChemMedChem* 8(1): 118–124, 2013.

Books

- 1) Nomura W, Tanaka T, Aikawa H, Narumi T, Tamamura H. Development of Cell-Penetrating ZIP Tag-Probe Systems for Fluorescent Imaging of Protein Dynamics in Cells. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 113-114, 2013
- 2) Masuda A, Nomura W, Tamamura H. Quantitative Analysis of Sequence-Specific Reactions by Artificial DNA Recombinases. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 21-22, 2013
- 3) Hashimoto C, Nomura W, Komano JA, Tamamura H. Synthesis of an Artificial gp41-C34 Trimer as an HIV-1 Fusion Inhibitor. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 45-46, 2013
- 4) Nomura W, Ohashi N, Narumi T, Tamamura H. Tag-Probe System for Imaging of Intracellular Proteins. Proceedings of the 23rd American Peptide Symposium, Michal Lebl (Ed.), American Peptide Society, Hawaii, pp. 174-175, 2013.
- 5) Nomura W, Tanaka T, Aoki T, Narumi T, Tamamura H. Biological Effects of Bivalent-Type CXCR4 Ligands with Rigid Linkers. Proceedings of the 23rd American Peptide Symposium, Michal Lebl (Ed.), American Peptide Society, Hawaii, pp. 176-177, 2013.

Review

- 1) Ohashi N, Nomura W, Narumi T, Tamamura H. Peptide-based Ligand Screening and Functional Analysis of Protein Kinase C. *Biopolymers: Peptide Science* 100(6): 613-620, 2013.

Medical Instrument (Biomedical Information)

1. Staffs and Students

Professor	Kenji YASUDA
Associate Professor	Fumimasa NOMURA
Assistant Professor	Hideyuki TERAZONO
Project Assistant Professor	
Graduate Student	

2. Purpose of Education

Medical instrument (Biomedical information) is a branch of institute of biomaterials and bioengineering which deals with the measurement of epigenetic information and memorization stored in living system such as brain (neural network system), immune system, and cardio systems caused by environmental hysteresis. Main objective of medical instrument in the graduate course is to provide students opportunity to study fusion of latest technologies of nano- and bio-tech, and to develop artificial organ model on chip for drug discovery and toxicology use.

3. Research Subjects

- 1) Studies on Epigenetic Information Stored Living System.
- 2) Constructing "On-chip Organ Model" using Nano-Bio Technology.
- 3) Bio-computing using "Real Neural Network on Chip".
- 4) New Drug Discovery Technology applying Single Molecule Measurement.

4. Publications

Original Articles

1. Yasuda K, Hattori A, Hyonchol K, Terazono H, Hayashi M, Takei H, Kaneko T, Nomura F: Non-destructive on-chip imaging flow cell-sorting system for on-chip cellomics. *Microfluid Nanofluid* 14(6): 907-931, 2013.
2. Yasuda K: On-Chip Cellomics: Single-Cell-Based Constructive Cell-Network Assay for Quasi-In Vivo Screening of Cardiotoxicity. *Proceedings of 35th Annual International Conference of IEEE EMBS* 2825, 2013.
3. Kaneko T, Takizawa E, Nomura F, Hamada T, Hattori A, Yasuda K: On-Chip Single-Cell-Shape Control Technology for Understanding Contractile Motion of Cardiomyocytes Measured Using Optical Image Analysis System. *Jpn J Appl Phys* 52: 06GK06, 2013.
4. Hamada H, Kaneko T, Nomura H, Yasuda K: Physiological Sample Uniformity and Time-Course Stability in Lined-Up Structure of Human Cardiomyocyte Network for In vitro Predictive Drug-Induced Cardiotoxicity. *Jpn J Appl Phys* 52: 06GK05, 2013.
5. Terazono H, Hattori A, Kim H, Takei H, Nomura F, Kaneko T, Yasuda K: Temperature-Shift Speed Dependence of Nonspecific Amplification of Polymerase Chain Reaction Examined by 1480nm Photothermal Transition Speed Controllable High-Speed Polymerase Chain Reaction System. *Jpn J Appl Phys* 52: 06GK02, 2013.
6. Nomura F, Kaneko T, Hamada T, Hattori A, Yasuda K: Advanced Ring-Shaped Microelectrode Assay Combined with Small Rectangular Electrode for Quasi-In vivo Measurement of Cell-to-Cell Conductance in Cardiomyocyte Network. *Jpn J Appl Phys* 52: 06GK07, 2013.
7. Brunell C.A, Jokinen V, Sakha P, Terazono H, Nomura F, Kaneko T, Lauri S.E, Franssila S, Rivera C, Yasuda K, Huttunen H.J: Microtechnologies to fuel neurobiological research with nanometer precision. *J Nanobiotech* 11: 11, 2013.
8. Hamada H, Nomura F, Kaneko T, Yasuda K, Okamoto M: Exploring the implicit interlayer regulatory mechanism between cells and tissue: Stochastic mathematical analyses of the spontaneous ordering in beating synchronization. *BioSystems* 111: 208-215, 2013.

Invited Talks

1. Kenji Yasuda. On-chip cardiomyocyte network screening assay for predictive cardiotoxicity. HESI Cardiac Safety Committee Workshop: Stem Cell-Derived Cardiomyocytes as Models of Cardiac Pathobiology and Toxicity, Cambridge, USA, March 2013
2. Kenji Yasuda. On-chip quasi-in vivo cardiomyocyte network screening assay for predictive cardiotoxicity beyond hERG and QT assays. *Stem Cells & Cell Signaling -2013 Meeting*, Waltham, USA, May 2013

3. Kenji Yasuda. On-chip quasi-in vivo pre-clinical cardiac toxicity: Testing compounds beyond hERG and QT assay using spatiotemporal human cardiomyocytes measurement. Collectis Science seminar "Stem cells in Drug Discovery", Tokyo, May 2013
4. Kenji Yasuda. On-Chip Cellomics: Single-Cell-Based Constructive Cell-Network Assay for Quasi-In Vivo Screening of Cardiotoxicity. 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC'13), Osaka, Japan, July 2013
5. Kenji Yasuda. On-Chip Quasi-In Vivo iPS Cardiomyocyte Network Screening Assay for Predictive Cardiotoxicity beyond hERG and QT Assays. 5th TMDU International Summer Program Symposium 2013, Tokyo, Japan, August 2013
6. Kenji Yasuda. Development of Screening Technology of Circulating Tumor Cells Using Multi-imaging Cell Sorter. Bio Japan 2013, Tokyo, Japan, October 2013
7. Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Akihiro Hattori. On-chip cellomics technology for studying dynamics of cellular networks. 5th Hiroshima Conference on Education and Science in Dentistry, Hiroshima, Japan, October 2013

Meetings

1. Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Quasi-in Vivo Electrocardiogram Measurement Using Convolution of Field Potential Propagation in the On-Chip Cardiomyocytes Network Circuit. Biophysical Society 56th Annual Meeting, San Diego, USA, Feb. 2012.
2. Tomoyo Hamada, Fumimasa Nomura, Hideyuki Terazono, Akihiro Hattori, Peter Sartipy, Mitsuhiro Edagawa, Thomas Meyer, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (I). Development of spatial conductance fluctuation measurement assay using a human cardiomyocyte line-network cell chip with multielectrode array system for in vitro predictive proarrhythmic cardiotoxicity. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
3. Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (II). Importance of spatial arrangement of cardiomyocyte network for precise and stable in vitro drug screening measurement. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
4. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Tomoyo Hamada, Fumimasa Nomura, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (III): Noninvasive Identification and Purification Method of Target Cardiomyocyte Cells Using Nuclease Digestive Magnet-Beads-Attached ssDNA Aptamers. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
5. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Fumimasa Nomura, Tomoyo Hamada, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (IV): Fabrication of Direction-Controlled Artificial Neuronal Networks Using Agarose-Microetching Method and Single-Cell-Electrodes for Quantitative Evaluation of Neuropsychiatric Disorders. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
6. Yumiko Asahi, Yasuyuki Abe, Kiyoshi Takasuna, Atsushi Sanbuissho, Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada. Evaluation of Fluctuation of Temporal Field Potential Duration and Spatial Conduction Time in Linear Network of Human-iPS Cell Derived Cardiomyocytes for Predictive Cardiotoxicity Measurement. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
7. Hyonchol Kim, Hideyuki Terazono, Hiroyuki Takei, Kenji Yasuda. Fabrication of Cup-Shaped Superparamagnetic Metal Hemispheres for Size-Selective Target Cell Collection. MNC2013, Sapporo, Japan, Nov. 2013.
8. Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Matsu-ura, Hideyuki Terazono, Kenji Yasuda. Importance of Spatial Arrangement of Cell Network Patterns for Precise and Stable Measurement of in Vitro Properties of Cells. MNC2013, Sapporo, Japan, Nov. 7. 2013.
9. Akihiro Hattori, Hyonchol Kim, Kenji Yasuda. Development of On-chip Flow Cytometry System based on Bright Field/Fluorescent Dual-image Analysis. MNC2013, Sapporo, Japan, Nov. 2013.
10. Kenji Matsuura, Akihiro Hattori, Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Kenji Yasuda. Quantitative Evaluation of Origin of Changes in Electrophysiological Properties of Cells on Micro Electrodes using Impedances Analysis Measurement Setup. MNC2013, Sapporo, Japan, Nov. 2013.
11. Hideyuki Terazono, Hyonchol Kim, Hiroyuki Takei, Akihiro Hattori, Kenji Yasuda. Development of Ultra-high-speed Microfluidic Submicron-droplet PCR Device using Circulating Water System and a photo detector. MNC2013, Sapporo, Japan, Nov. 2013.

Biomechanics

1. Staffs and Students

Professor	Kenji KAWASHIMA
Associate Professor	Gen ENDO
Assistant Professor	Takahiro KANNO
Project Researcher	In KIM
Graduate Students	Ryoken MIYAZAKI

2. Purpose of Education

Enhance the ability to design and develop medical devices based on biomechanics.

3. Research Subjects

- 1) Development of Forceps Manipulator for Surgical Robot
- 2) Assist Device using Pneumatic Artificial Rubber Muscle
- 3) Teleoperation Control using Biological Signals
- 4) Evaluation of Surgical Robot System

4. Publications

Original Article

1. Li H., Kawashima K., Tadano K., Shameek G., Nakano S. (2013). Achieving Haptic Perception in Forceps Manipulator using Pneumatic Artificial Muscle, IEEE/ASME Transactions on Mechatronics (TMECH) , 18(1):74-85
2. Li J., Kawashima K., Fujita T., Kagawa T. (2013). Control Design of a Pneumatic Cylinder with Distributed Model of Pipelines, Precision Engineering, 37(4): 880–887

International Conference

1. Haraguchi D., Tadano K., Kawashima K. Development of a Pneumatically-Driven Robotic Forceps with a Flexible Wrist, Procedia CIRP, Vol. 5, 61-65 (2013)
2. Kanno T., Haraguchi D., Tadano K., Kawashima K. Design of a 4-DOF Forceps Manipulator for Robotic Surgery, IEEE/SICE SII2013, Kobe, Dec.(2013)
3. Kanno T., Yokokohji Y. Avoiding Conflicts of Operators in Multi-user Teleoperation Systems. IEEE World Haptics Conference, 401-406 (2013) etc. total 8 articles

Material Biofunctions

1. Staffs and Students

Associate Professor	Akiko Nagai
Assistant Professor	Kosuke Nozaki
Project Associate Professor	Hiroshi Masuda
Technical Assistant	Minako Segawa
Technical Assistant	Kasumi Yamanaka

2. Purpose of Education

There is a growing demand on the researchers to know huge knowledge of biomaterials development. For these purposes, the first lecture is aimed to teach the scientific aspects of biomaterials features. The second lecture deals with interfacial biological and chemical reactions between materials and living tissue. The students learn the principle of biomaterials through laboratory practice. Following these learnings, they must acquire an adequate background to develop new generation of biomaterials.

3. Research Subjects

- (1) Reaction mechanism between materials and living tissues

Development of standard evaluation process for the safety, biocompatibility, and biofunction of biomedical materials and devices, based on interfacial reactions between the materials and living tissue.

- (2) Effects of medical materials and devices on human health

Systematization of influences of biofunctional materials and artificial organs on the human body from the viewpoint of medicine.

- (3) Development of functional materials accelerating bone formation

Development of new surface modification processes of bioimplants to accelerate bone formation.

- (4) Development of evaluation methods for studying interaction of materials with biological function

Development of new intravital observation methods for evaluating biological effects of physical and chemical factors.

4. Publications

Original Article

- (1) Nagai A, Hattori T, Hirose M, Ogura A, Nozaki K, Aizawa M, Yamashita K. Mouse embryonic stem cells cultured under serum- and feeder-free conditions maintain their self-renewal capacity on hydroxyapatite. *Mater Sci Engineer C*, 34, 214-220, 2014.
- (2) Nakamura M, Toyama T, Morita A, Horiuchi N, Nozaki K, Nagai A, Yamashita K, Electric Poling of Cement Composites of Hydroxyapatite Whiskers with Chitosan and their Chemical Properties in Simulated Body Fluid, *J. Ceram. Soc. Jpn.*, 121 (10), 895-900, 2013.
- (3) Horiuchi N, Endo J, Nozaki K, Nakamura M, Nagai A, Katayama K, Yamashita K, Dielectric Evaluation of Fluorine Substituted Hydroxyapatite, *J. Ceram. Soc. Jpn.*, 121 (9), 770-774, 2013.
- (4) Nemoto R, Nozaki K, Fukui Y, Yamashita K, Miura H. Effect of framework design on the surface strain of zirconia fixed partial dentures. *Dent Mater J*. 32(2):289-95(2013).

Genetic Regulation

1. Staffs and Students (in 2013)

Professor	Akinori KIMURA	
Associate Professor	Takeharu HAYASHI	
Assistant Professor	Daisuke SAKURAI	
Research Associate	Taeko NARUSE	
Graduate Student	Junji IIZULA	
Graduate Student (Biomedical Science PhD program)	Jianbo AN,	Kei KATSURAGI
Visiting Graduate Student	Shinya KOIZUMI	

2. Purpose of Education

Structural and functional diversity of human genome, are involved in the etiology and pathogenesis of human diseases. Main objective of Genetic Regulation is to identify the gene mutations or polymorphisms and to decipher the molecular mechanisms involved in the etiology and pathogenesis of intractable diseases, in order to develop new strategies for diagnosis, treatment and/or prevention of the diseases. Current research is focused on the intractable cardiovascular diseases (e.g. idiopathic cardiomyopathy, idiopathic arrhythmia, and coronary heart disease), autoimmune diseases (e.g. Burger disease, Graves disease, and rheumatoid arthritis) and infectious diseases (e.g. HIV/AIDS). In addition, genome diversity in immune-related genes is investigated from the view-point of primate evolution.

3. Research Subjects

- 1) Identification and functional analysis of disease-related genes for cardiovascular diseases
- 2) Identification and functional analysis of disease-related genes for autoimmune diseases
- 3) Identification and functional analysis of disease-related genes for infectious diseases
- 4) Structural, functional and evolutionary analyses of MHC and immune-related genes in vaccination

4. Publications

Original Article

1. Sharma G, Ohtani H, Kaur G, Naruse TK, Sharma SK, Vajpayee M, Kimura A, Mehra NK. Status of TIM-1 exon 4 haplotypes and CD4+T cell counts in HIV-1 seroprevalent North Indians. *Hum Immunol.* 2013; 74(2): 163-165.
2. Ishikawa T, Takahashi N, Ohno S, Sakurada H, Nakamura K, On YK, Park JE, Makiyama T, Horie M, Arimura T, Makita N, Kimura A. Novel SCN3B mutation associated with Brugada syndrome affects intracellular trafficking and function of Nav1.5. *Circ J.* 2013; 77(4): 959-967.
3. Takahashi N, Nomura T, Takahara Y, Yamamoto H, Shiino T, Takeda A, Inoue M, Iida A, Hara H, Shu T, Hasegawa M, Sakawaki H, Miura T, Igarashi T, Koyanagi Y, Naruse TK, Kimura A, *Matano T. A novel protective MHC-I haplotype not associated with dominant Gag-specific CD8+ T-cell responses in SIVmac239 infection of Burmese rhesus macaques. *PLoS ONE.* 2013; 8(1): e54300.
4. Deng Y, Zhao J, Sakurai D, Kaufman KM, Edberg JC, Kimberly RP, Kamen DL, Gilkeson GS, Jacob CO, Scofield RH, Langefeld CD, Kelly JA, Ramsey-Goldman R, Petri MA, Reveille JD, Vilá LM, Alarcón GS, Vyse TJ, Pons-Estel BA, Freedman BI, Gaffney PM, Sivits KM, James JA, Gregersen PK, Anaya JM, Niewold TB, Merrill JT, Criswell LA, Stevens AM, Boackle SA, Cantor RM, Chen W, Grossman JM, Hahn BH, Harley JB, Alarcón Riquelme ME, Brown EE, Tsao BP. MicroRNA-3148 modulates allelic expression of Toll-like receptor 7 variant associated with systemic lupus erythematosus. *PLoS Genetics* 9(2): e1003336, 2013.
5. Kashiwakura Y, Sakurai D, Kanno Y, Hashiguchi M, Kobayashi A, Kurosu A, Tokudome S, Kobata T, Kojima H. CD2-mediated regulation of peripheral CD4(+) CD25(+) regulatory T cell apoptosis accompanied by downregulation of Bim. *Immunology* 2013; 139(1): 48-60.
6. Chan K, Patel RS, Newcombe P, Nelsone CP, Qasim A, Epstein SE, Burnett S, Vaccarino V, Zafari AM, Shah SH, Anderson JL, Carlquist JF, Hartiala J, Allayee H, Hinohara K, Lee BS, Erl A, Ellis KL, Goel A, Schaefer AS, Eddine N, Mokhtari NEE, Goldstein BA, Hlatky MA, Go AS, Shen GQ, Gong Y, Pepine C, Laxton RC, Wittaker JC, Tang WHW, Johnson JA, Wang QK, Assimes TL, Nöthlings U, Farrall M, Watkins H, Richards MA, Cameron VA, Muendlein A, Drexel H, Koch W, Park JE, Kimura A, Shen WF, Simpson IA, Hazen SL, Horne BD, Hauser ER, Quyyumi AA, Reilly MP, Samani NJ, Ye S. Association between the chromosome 9p21 locus and angiographic

- coronary artery disease burden - a collaborative meta-analysis. *J Am Col Cardiol.* 2013; 61(9): 957-970.
7. Nakayama EE, Nakajima T, Kaur G, Miyama J, Terunuma H, Mehra NK, Kimura A, Shioda T. A naturally occurring single amino acid substitution in human TRIM5a linker region affects its anti-HIV-1 activity and susceptibility to HIV-1 infection. *AIDS Res Hum Retroviruses.* 2013; 29(6): 919-924.
 8. Crocini C, Arimura T, Reischmann S, Eder A, Braren I, Hansen A, Eschenhagen T, Kimura A, Carrier L. Impact of ANKRD1 mutations associated with hypertrophic cardiomyopathy on contraction parameters of engineered heart tissue. *Basic Res Cardiol.* 2013; 108(3): 349.
 9. Arimura T, Onoue K, Takahashi-Tanaka Y, Ishikawa T, Kuwahara M, Setou M, Shigenbu S, Yamaguchi K, Bertrand AT, Machida N, Takayama K, Fukusato M, Tanaka R, Somekawa T, Nakano T, Yamane Y, Kuba K, Imai Y, Saito N, Bonne G, Kimura A. Nuclear accumulation of androgen receptor in gender difference of dilated cardiomyopathy due to lamin A/C mutations. *Cardiovasc Res.* 2013; 99(3): 382-394.
 10. Terao C, Yoshifuji H, Ohmura K, Murakami K, Kawabata D, Yurugi K, Tazaki J, Kinoshita H, Kimura A, Akizuki M, Kawaguchi Y, Yamanaka H, Miura Y, Maekawa T, Saji H, Mimori T, Matsuda F. Association of Takayasu arteritis with HLA-B*67:01 and two amino acids in HLA-B protein. *Rheumatol.* 2013; 52(10): 1769-1774.
 11. Terao C, Yoshifuji H, Kimura A, Matsumura T, Ohmura K, Takahashi M, Shimizu M, Kawaguchi T, Chen Z, Naruse TK, Sato-Otubo A, Ebana Y, Maejima Y, Kinoshita H, Murakami K, Kawabata D, Wada Y, Narita I, Tazaki J, Kawaguchi Y, Yamanaka H, Yurugi K, Miura Y, Maekawa T, Ogawa S, Komuro I, Nagai R, Yamada R, Tabara Y, Isobe M, Mimori T, Matsuda F. Two susceptibility loci to Takayasu arteritis reveal a synergistic role of the IL12B and HLA-B regions in a Japanese population. *Am J Hum Genet.* 2013; 93(2): 289-297.
 12. Sakurai D, Zhao J, Deng Y, Kelly JA, Brown EE, Harley JB, Bae SC, Alarcón GS, Kaufman KM, Vyse TJ, Jacob CO, Gaffney PM, Sivills KM, James JA, Kamen DL, Gilkeson GS, Niewold TB, Merrill JT, Scofield RH, Criswell LA, Stevens AM21, Boackle SA, Kim JH, Choi J, Pons-Estel BA, Freedman BI, Anaya JM, Martin J, Yu CY, Chang DM, Song YW, Langefeld CD, Chen W, Grossman JM, Cantor RM, Hahn BH, Tsao BP. Preferential Binding to Elk-1 by SLE-Associated IL10 risk allele up-regulates IL10 expression. *PLoS Genetics* 2013; 10, e1003870.
 13. Nakane T, Nomura T, Shi S, Nakamura M, Naruse TK, Kimura A, Matano T, *Yamamoto H. Limited impact of passive non-neutralizing antibody immunization in acute SIV infection on viremia control in rhesus macaques. *PLoS ONE* 2013; 8(9): e73453.
 14. An J, Nakajima T, Shibata H, Arimura T, Yasunami M, Kimura A. A novel link of HLA locus to the regulation of immunity and infection: NFKBIL1 regulates alternative splicing of human immune-related genes and influenza virus M gene. *J Autoimmun.* 2013; 47: 25-33.
 15. Arimura T, Takeya R, Ishikawa T, Yamano T, Matsuo A, Tatsumi T, Nomura T, Sumimoto H, Kimura A. Dilated cardiomyopathy-associated FHOD3 variant impairs the ability to induce activation of transcription factor SRF. *Circ J.* 2013; 77(12): 2990-2996.
 16. Sato T, Suzuki T, Watanabe H, Kadowaki A, Fukamizu A, Liu PP, Kimura A, Ito H, Penninger JM, Imai Y, Kuba K. Apelin is a positive regulator of ACE2 in failing hearts. *J Clin Invest.* 2013; 123(12): 5203-5211.
 17. Ichihara S, Yamamoto K, Asano H, Nakatochi M, Sukegawa M, Ichihara G, Izawa H, Hirashiki A, Takatsu MF, Umeda H, Iwase M, Inagaki H, Hirayama H, Sone T, Nishigaki K, Minatoguchi S, Cho MC, Jang Y, Kim HS, Park JE, Tada-Oikawa S, Kitajima H, Matsubara T, Sunagawa K, Shimokawa H, Kimura A, Lee JY, Murohara T, Inoue I, Yokota M. Identification of a glutamic acid repeat polymorphism of ALMS1 as a novel genetic risk marker for early-onset myocardial infarction by genome-wide linkage analysis. *Circ Cardiovasc Genet.* 2013; 6(6): 569-578.
 18. An J, Kimura A. IκBL mapped within the HLA region is a novel regulator of alternative splicing involved in the pathogenesis of immune-related diseases. *MHC.* 2013; 20(3):191-197.

[Book Chapter]

1. Kimura A, Ohtani H, Naruse TK, Nakajima T, Akari H, Mori K, Matano T. Evolutional medicine: an approach to identify the human genome diversity associated with HIV-1/AIDS. In *Proceeding of the International Conference on Emerging Frontiers and Challenges in HIV/AIDS Research* (Bandivdekar A, Puri CP, eds), pp11-23, Varum Enderprises, Mumbai, 2013 (ISBN No. 978-81-910540-5-7)

Applied Gene Medicine (Molecular Genetics)

1. Staffs and Students (April, 2013)

Professor	Yoshio MIKI	
Associate Professor	Akira NAKANISHI	
Project Lecturer	Koichi NAGASAKI	
Assistant professor	Katsuya TAKENAKA	
Project Assistant Professor	Ken MIYAGUCHI	
Graduate Student	Nadila WALI,	Nurmaa DASHZEVEG,
	Yuya KAGAMI,	Shota TESHIROGI,
	Taichi KURASHINA,	Mai KONNO,
	Yuka SHIMIZU	

2. Purpose of 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.

3. Research Subject

- 1) Functional analysis of the BRCA2 gene.
 - ① Synthetic lethality effect for chemotherapy using BRCA2-deficient breast cancers
 - ② Enhancement of the ATPase activity of nonmuscle myosin (NM)-IIC by BRCA2
 - ③ Analysis of intramolecular BRCA2 region concerning the numerical integrity of centrosomes by an automated centrosome counting system
- 2) Regulatory mechanisms of tumor cells in the apoptotic response to DNA damage
 - ① PKCdelta regulates Mdm2 independently negative regulator of p53 in the apoptotic response to DNA damage.
 - ② Identification of Evi-1 as a novel effector of PKCdelta in the apoptotic response to DNA damage.

4. Publication

Original Article

1. Wali N, Hosokawa K, Malik S, Saito H, Miyaguchi K, Imajoh-Ohmi S, Miki Y, Nakanishi A. Centrosomal BRCA2 is a target protein of membrane type-1 matrix metalloproteinase (MT1-MMP). *Biochem Biophys Res Commun* 2014, 443:1148-1154.
2. Wada Y, Matsuura M, Sugawara M, Ushijima M, Miyata S, Nagasaki K, Noda T, Miki Y. Development of detection method for novel fusion gene using GeneChip exon array. *J Clin Bioinforma* 2014, 4:3.
3. Takaoka M, Saito H, Takenaka K, Miki Y, Nakanishi A. BRCA2 Phosphorylated by PLK1 Moves to the Midbody to Regulate Cytokinesis Mediated by Nonmuscle Myosin IIC. *Cancer Res* 2014.
4. Nakamura S, Takahashi M, Tozaki M, Nakayama T, Nomizu T, Miki Y, Murakami Y, Aoki D, Iwase T, Nishimura S, et al. Prevalence and differentiation of hereditary breast and ovarian cancers in Japan. *Breast Cancer* 2013.
5. Mimoto R, Taira N, Takahashi H, Yamaguchi T, Okabe M, Uchida K, Miki Y, Yoshida K. DYRK2 controls the epithelial-mesenchymal transition in breast cancer by degrading Snail. *Cancer Lett* 2013, 339:214-225.
6. Low SK, Takahashi A, Ashikawa K, Inazawa J, Miki Y, Kubo M, Nakamura Y, Katagiri T. Genome-wide association study of breast cancer in the Japanese population. *PLoS One* 2013, 8:e76463.
7. Kawazu M, Ueno T, Kontani K, Ogita Y, Ando M, Fukumura K, Yamato A, Soda M, Takeuchi K, Miki Y, et al. Transforming mutations of RAC guanosine triphosphatases in human cancers. *Proc Natl Acad Sci U S A* 2013, 110:3029-3034.

Molecular Cytogenetics

1. Staffs and Students

Professor	Johji Inazawa M.D., Ph.D.	
Associate Professor	Ken-ichi Kozaki D.D.S., Ph.D.	
Assistant Professor	Jun Inoue Ph.D.	
Assistant Professor (Genome Laboratory)	Kosuke Tanimoto Ph.D.	
Tokunin Lecturer	Shin Hayashi M.D., Ph.D.	
Doctoral course students (PD2)	Tomoki Muramatsu	
Global COE program Advanced I super student (AISS)		
Graduate Student	Nuylan Michelle Loyola,	Daniela Tiaki Uehara
	Sujata Sakha,	Naoki Imaoka,
	Rie Mifuji,	Kaede Miyata,
	Sho Morisawa	
Research Student	Hiroaki Nagata,	Reiko Iwadate,
	Hiroyoshi Takahashi	

2. Purpose of Education

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. Research Subjects

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.

4. Clinical Services

5. Publications

Original Article

1. Dobashi Y, Sato E, Oda Y, Inazawa J, Ooi A: Significance of Akt activation and AKT gene increases in soft tissue tumors. *Hum Pathol* 45:127-36, 2014
2. Takemura K, Kawachi H, Eishi Y, Kitagaki K, Negi M, Kobayashi M, Uchida K, Inoue J, Inazawa J, Kawano T, Board PG: γ -Glutamylcyclotransferase as a novel immunohistochemical biomarker for the malignancy of esophageal squamous tumors. *Hum Pathol* 45:331-41, 2014
3. Yamamoto S, Inoue J, Kawano T, Kozaki K, Omura K, Inazawa J: The impact of miRNA-based molecular diagnostics and treatment of NRF2-stabilized tumors. *Mol Cancer Res* 12:58-68, 2014
4. Low SK, Takahashi A, Ashikawa K, Inazawa J, Miki Y, Kubo M, Nakamura Y, Katagiri T: Genome-wide association study of breast cancer in the Japanese population. *PLoS One* 8:e76463, 2013

5. Yamamoto Y, Konishi H, Ichikawa D, Arita T, Shoda K, Komatsu S, Shiozaki A, Ikoma H, Fujiwara H, Okamoto K, Ochiai T, Inoue J, Inazawa J, Otsuji E: Significance of GSTP1 for predicting the prognosis and chemotherapeutic efficacy in esophageal squamous cell carcinoma. *Oncol Rep* 30:1687-94, 2013
6. Harazono Y, Muramatsu T, Endo H, Uzawa N, Kawano T, Harada K, Inazawa J, Kozaki K: miR-655 is an EMT-suppressive microRNA targeting ZEB1 and TGFBR2. *PLoS One* 8:e62757, 2013
7. Furuta M, Kozaki K, Tanimoto K, Tanaka S, Arie S, Shimamura T, Niida A, Miyano S, Inazawa J: The tumor-suppressive miR-497-195 cluster targets multiple cell-cycle regulators in hepatocellular carcinoma. *PLoS One* 8:e60155, 2013

Biochemical Genetics

1. Staffs and Students

Professor	Shigetaka Kitajima MD, PhD	
Associate Professor	Yujiro Tanaka MD, PhD	
Assistant Professor	Junya Kawauchi MD, PhD	
Graduate Student	Makoto Inoue,	Hiroto Goshima,
	Makoto Edagawa,	Satoshi Fukumoto,
	Syunsuke Takaya	
Research Student	Takuya Takahashi,	Natsuki Arai,
	Akihisa Fujisawa,	Takuya Suzuki
Foreign Scholar	Liu Jia, MD	
Technical Assistant	Yohei Uchida	

2. Purpose of Education

Transcriptional regulation is one of the most important processes by which genome information is expressed from DNA to mRNA to protein. The faithful synthesis of mRNA is achieved by transcriptional machinery comprised of RNA polymerase II, basal factors and many other protein factors, whose dysfunction is implicated in various human diseases. Our research interest is focused on the basic mechanism of transcription cycle and implication of early response transcription factors in determining cell fate in stress response.

Key words

- To provide novel paradigm of transcriptional regulation
- To understand role of transcription factor in cell fate determination

3. Research Subjects

- 1) Transcription
 - Elongin A plays dual roles in stress response
 - A novel function of FCP1
- 2) Cell fate determination by activating transcription factor (ATF) 3
 - Pro-apoptotic role of ATF3 and its implication in anti-cancer therapy
 - Genome-wide screen of the role of ATF3 in stress response and human cancer
 - ATF3 complex; transcriptional repressor or activator
 - ATF3 transcriptionally regulates microRNA
- 3) H3K36-specific histone methyltransferase ASH1.

4. Clinical Services

none

5. Publications

Original Article

1. Liu J, Edagawa M, Goshima H, Inoue M, Yagita H, Liu Z, Kitajima S. Role of ATF3 in synergistic cancer cell killing by a combination of HDAC inhibitors and agonistic anti-DR5 antibody through ER stress in human colon cancer cells. *BBRC* in press.
2. Kawauchi J, Inoue M, Fukuda M, Uchida Y, Yasukawa T, Conaway RC, Conaway JW, Aso T, Kitajima S. Transcriptional properties of mammalian Elongin A and its role in stress response. *J Biol Chem*. 2013 Aug 23;288(34):24302-15. doi: 10.1074/jbc.M113.496703. Epub 2013 Jul 3.
3. Lee YS, Sasaki T, Kobayashi M, Kikuchi O, Kim HJ, Yokota-Hashimoto H, Shimpuku M, Susanti VY, Ido-Kitamura Y, Kimura K, Inoue H, Tanaka-Okamoto M, Ishizaki H, Miyoshi J, Ohya S, Tanaka Y, Kitajima S, Kitamura T. Hypothalamic ATF3 is involved in regulating glucose and energy metabolism in mice. *Diabetologia*. 2013 Jun;56(6):1383-93. doi: 10.1007/s00125-013-2879-z. Epub 2013 Mar 6.

Hematology

1. Staffs and Students

Professor	Osamu MIURA	
Junior Associate Professor	Ayako ARAI	
Assistant Professor	Tetsuya FUKUDA, Masahide YAMAMOTO,	Tetsuya KUROSU, Toshikage NAGAO
Specially Appointed Professor	Chizuko SAKASHITA,	Ken WATANABE
Hospital Staff	Hiroki AKIYAMA, Emi UCHIDA,	Keiichiro HATTORI Yusuke OTANI
Graduate Student	Minako JINTA, Ayako ICHIKAWA, Lu Dan Wang	Shihoko SUWA Ayako NOGAMI

2. Purpose of Education

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. We offer the lectures of basic knowledge of hematological diseases for the 4th grade medical students, and we provide the opportunity to study process of diagnosis and management of hematological disorder for the 5th and 6th grade medical students as clinical clerkship, CC1 and CC3.

In our clinical residency, the junior resident have the opportunity to obtain knowledge and skills for dissolving hematological, oncological and infectious problems.

The senior residents are making profound efforts in their clinical experiences to be hematological experts.

3. Research Subjects

- 1) Cell signaling for the hematopoiesis and hematological oncogenesis
- 2) Molecular mechanism of lymphomagenesis
- 3) Regulation of hematopoietic cell death after chemotherapeutic reagents
- 4) Mechanism of resistance against tyrosine kinase inhibitors
- 5) Mechanism of EB virus associated disease

4. Clinical Services

We provide the highest quality of patient care for a wide spectrum of blood diseases and cancers.

5. Publications

1. Kurosu T, Nagao T, Wu N, Oshikawa G, Miura O.: Inhibition of the PI3K/Akt/GSK3 pathway downstream of BCR/ABL, Jak2-V617F, or FLT3-ITD downregulates DNA damage-induced Chk1 activation as well as G2/M arrest and prominently enhances induction of apoptosis. *PLoS One* 8(11):e79478, 2013.
2. Nakaima Y, Watanabe K, Koyama T, Miura O, Fukuda T.: CD137 is induced by the CD40 signal on chronic lymphocytic leukemia B cells and transduces the survival signal via NF- κ B activation. *PLoS One* 8(5):e64425, 2013.
3. Wu N, Kurosu T, Oshikawa G, Nagao T, Miura O.: PECAM-1 is involved in BCR/ABL signaling and may downregulate imatinib-induced apoptosis of Philadelphia chromosome-positive leukemia cells. *Int J Oncol* 42(2):419-28, 2013
4. Ichikawa A, Arakawa F, Kiyasu J, Sato K, Miyoshi H, Niino D, Kimura Y, Takeuchi M, Yoshida M, Ishibashi Y, Nakashima S, Sugita Y, Miura O, Ohshima K.: Methotrexate/iatrogenic lymphoproliferative disorders in rheumatoid arthritis: histology, Epstein-Barr virus, and clonality are important predictors of disease progression and regression. *European J of Haematol* 91(1):20-8, 2013
5. Yagi K, Yamamoto K, Umeda S, Abe S, Suzuki S, Onishi I, Kirimura S, Fukayama M, Arai A, Kitagawa M, Kurata M.: Expression of multidrug resistance 1 gene in B-cell lymphomas association with follicular dendritic cells. *Histopathology* 62:414-20, 2013.

Molecular Endocrinology and Metabolism

1. Staffs and Students (2013)

Professor	Yoshihiro Ogawa	
Junior Associate Professor	Takanobu Yoshimoto,	Hajime Izumiyama
Assistant Professor	Masatomo Mihara,	Isao Minami,
	Kyoichiro Tsuchiya	
Resident	Michiya Kida,	Noriaki Okiba,
	Kumiko Shiba,	Masanori Murakami,
	Takuya Ohashi,	Nana Komatsu
Medical Fellow	Miyako Tanaka	
JSPS RPD Fellow	Rumi Hachiya	
Project Assistant Professor	Misa Saijo	
Graduate Students (Doctor's course)	Takako Watanabe,	Kenji Ikeda,
	Naoto Tsuda,	Yorihiro Iwasaki,
	Chikako Aoyama,	Toshiyuki Sakurai,
	Chikara Komiya,	Yasutaka Chiba,
	Kazutaka Tsujimoto,	Yasutaka Miyachi,
	Hideaki Kato	
Graduate Students (Master's course)	Tomomi Kasahara,	Erina Tamura,
	Yukino Hatazawa	
Joint Research Fellow	Masanobu Kanou	
Research Student	Takuya Shiihashi	
Part-time Lecturer	Isao Uchimura,	Mitsunobu Kawamura,
	Toshiyuki Horiuchi,	Motoyoshi Tsujino,
	Masaharu Morohoshi,	Masaru Doi
Project Professor*	Takayoshi Suganami	
Project Associate Professor**	Koshi Hashimoto	
Project Assistant Professor*	Michiko Ito,	Xunmei Yuan,
	Ibuki Shirakawa	

*Department of Organ Network and Metabolism,

**Department of Preemptive Medicine and Metabolism

2. Purpose of Education

Our training program enables postdoctoral trainees to prepare for the future academic careers and the clinical practice in the broad discipline of endocrinology and metabolism. The research program provides mentor-based training in experimental design, laboratory and clinical research techniques and methodology, and interpretation and analysis of the results obtained from cellular and molecular biology, physiology, clinical physiology, clinical therapeutics, and health sciences. This training program is designed to educate and establish 'physician-scientist' in the field of endocrinology and metabolism.

3. Research Subjects

- 1) Role of adipose tissue inflammation in the metabolic syndrome
- 2) Molecular mechanisms of saturated fatty acid-induced chronic inflammation
- 3) Molecular mechanism of vascular injury in diabetes, endocrine and metabolic diseases
- 4) Role of epigenetic regulation in metabolism
- 5) Mechanism of pathogenesis in endocrine tumors
- 6) Development of novel diagnostic and therapeutic tools in endocrine and metabolic diseases

4. Clinical Services

Comprehensive inpatient and outpatient services in the area of endocrine and metabolic disorders, including:

- diseases of the thyroid, pituitary and adrenal glands.

- diabetes mellitus, diabetic complications, metabolic syndrome, and obesity
- primary and secondary hypertension
- disorders of calcium metabolism

5. Publications

1) Peer-reviewed Journal

1. Itoh M, Kato H, Suganami T, Konuma K, Marumoto Y, Terai S, Sakugawa H, Kanai S, Hamaguchi M, Fukaishi T, Aoe S, Akiyoshi K, Komohara Y, Takeya M, Sakaida I, Ogawa Y. Hepatic crown-like structure: a unique histological feature in non-alcoholic steatohepatitis in mice and humans. **PLoS One**. 2013;8(12):e82163.
2. Mori T, Maeda N, Inoue K, Sekimoto R, Tsushima Y, Matsuda K, Yamaoka M, Suganami T, Nishizawa H, Ogawa Y, Funahashi T, Shimomura I. A novel role for adipose ephrin-B1 in inflammatory response. **PLoS One**. 2013;8(10):e76199.
3. Takahashi M, Kamei Y, Ehara T, Yuan X, Suganami T, Takai-Igarashi T, Hatada I, Ogawa Y. Analysis of DNA methylation change induced by Dnmt3b in mouse hepatocytes. **Biochem Biophys Res Commun**. 2013;434(4):873-8.
4. Takizawa F, Mizutani S, Ogawa Y, Sawada N. Glucose-independent persistence of PAI-1 gene expression and H3K4 tri-methylation in type 1 diabetic mouse endothelium: implication in metabolic memory. **Biochem Biophys Res Commun**. 2013;433(1):66-72.
5. Kohmura YK, Kanayama N, Muramatsu K, Tamura N, Yaguchi C, Uchida T, Suzuki K, Sugihara K, Aoe S, Sasaki T, Suganami T, Ogawa Y, Itoh H. Association between body weight at weaning and remodeling in the subcutaneous adipose tissue of obese adult mice with undernourishment in utero. **Reprod Sci**. 2013;20(7):813-27.
6. Kida M, Sugiyama T, Yoshimoto T, Ogawa Y. Hydrogen sulfide increases nitric oxide production with calcium-dependent activation of endothelial nitric oxide synthase in endothelial cells. **Eur J Pharm Sci**. 2013;48(1-2):211-5.
7. Kikuchi H, Yoshimoto T, Tanaka H, Tsujimoto K, Yamamura C, Arai Y, Hirasawa S, Aki S, Inaba N, Aoyagi M, Ogawa Y, Tamura T. Periodic hypokalemia associated with cyclic Cushing's syndrome. **CEN Case Rep**. DOI 10.1007/s13730-013-0090-1, 2013
8. Yamakawa N, Ohto U, Akashi-Takamura S, Takahashi K, Saitoh S, Tanimura N, Suganami T, Ogawa Y, Shibata T, Shimizu T, Miyake K. Human TLR4 polymorphism D299G/T399I alters TLR4/MD-2 conformation and response to a weak ligand monophosphoryl lipid A. **Int Immunol**. 2013;25(1):45-52.
9. Yogosawa S, Mizutani S, Ogawa Y, Izumi T. Activin receptor-like kinase 7 suppresses lipolysis to accumulate fat in obesity through downregulation of peroxisome proliferator-activated receptor γ and C/EBP α . **Diabetes**. 2013;62(1):115-23.

2) International Meeting/Symposium

1. Ogawa Y : Chronic Inflammation and Ectopic Fat Accumulation: **The 2013 Asian Diabetes Forum in Tokushima**, Tokushima (2013.1)
2. Ogawa Y : Adipose tissue inflammation and ectopic fat accumulation : **International Symposium on Development of Medical Technologies for Treating Intractable Cancers and Cardiovascular Diseases**, Tokyo (2013.3)
3. Hashimoto K : Serum triglyceride regulation by thyroid hormone via stearoyl-CoA desaturase (SCD)-1 : Meet the Professor Workshop **83rd Annual Meeting of the American Thyroid Association**, San Juan, Puerto Rico (2013.3)
4. Iwasaki Y, Suganami T, Hachiya R, Shirakawa I, Hamaguchi M, and Ogawa Y : ATF4 Plays Critical Roles in Saturated Fatty Acid induced Il-6 Expression in Macrophages **The Endocrine Society's 95 th. Annual Meeting & Expo**, San Francisco, US (2013. 6)
5. Murakami M, Une N, Nishizawa M, Suzuki S, Takekawa S, Iwashima F, Ito H, Ogawa Y and Horiuchi T : Incretin secretion stimulated by ursodeoxycholic acid in healthy subjects and diabetics. **The Endocrine Society's 95 th. Annual Meeting & Expo**, San Francisco, US (2013. 6)
6. Ogawa Y : Regulation of Metabolic Genes by DNA Methylation: **8th World Congress on Developmental Origins of Health and Disease**, Singapore (2013.11)
7. Ikeda K, Tanaka M, Suganami T, Komiya C, Ochi K, Shirakawa I, Hamaguchi M, Ogawa Y: Role of Mincle, a novel pathogen sensor in macrophages, in obesity-induced adipose tissue inflammation and fibrosis. **2014 Keystone Symposia Conference, Obesity: A Multisystems Perspective**. Vancouver, Canada (2014.1)

Hepatobiliary and Pancreatic Surgery

1. Staffs and Students

Professor	Minoru Tanabe (April , 2013~)
Associate Professor	Shinji Tanaka
Assistant Professor	Noriaki Nakamura (~December, 2013), Atsushi Kudo, Takumi Irie, Takanori Ochiai, Daisuke Ban, Satoshi Matsumura
Graduate Student	Yuichiro Watanabe (~January, 2013), Kouta Sato(~January, 2013), Chisato Okajima (~March, 2013), Kousuke Ogawa (~March, 2013), Tomoya Miura, Hiroko Matsunaga, Eriko Katsuta, Takaki Furuyama, Hiromitsu Ito, Keisuke Nakao, Keiichi Akahoshi, Hiroki Ueda (April, 2013~), Yoshiteru Ohata (April, 2013~), Taku Sato (April, 2013~October, 2013), Xirali Mamat (~March, 2013), Maynur Abdurahman (~March, 2013)

2. Educational Vision

Medical School Education: Our mission is to educate students and transform them into high quality surgeons. Leading edge training, from basic to advanced, is provided through one-on-one interaction with advisers. Furthermore, students, as medical professionals, learn how to interact with patients, and establish strong ethics and morals. Especially, in regard to breaking bad news, students learn by dealing with real cases. While students mainly acquire surgical techniques during post-graduate clinical internships, they need to participate in many high difficulty hepato-biliary-pancreatic operations as assistant. About an educational side students are expected to educate to lower grade students.

Post-graduate Education: Our mission is to cultivate the capability of students as surgeons and physicians, in order to provide the highest quality patient care. Each student is expected to obtain a specialization in surgery within 5 or 6 years after graduation from medical school. During post-graduate education, we provide incentives for students to become excellent surgeons, conduct original medical research, and allow them to demonstrate their capability in the real world.

3. Research

We are making researches in the important issues which are remained to be resolved in the hepato-biliary-pancreatic surgery and diseases. The research subjects are as follows;

- 1) Research in the molecular mechanisms on the progression of hepato-biliary -pancreatic malignancies
- 2) Research in development of the molecular-targeting therapy for hepato-biliary -pancreatic malignancies.
- 3) Research in the mechanisms of cancer stem cells
- 4) Research in the extended indication of the hepatic resection for hepato-biliary malignancies.
- 5) Research in the microcirculation of the liver
- 6) Research in technical improvement of laparoscopic surgery
- 7) Research in the improvement of preservation of the liver for transplantation.
- 8) Research in development of therapy for neuroendocrine tumor
- 9) Research in development of diagnostic imaging for hepato-biliary malignancies.

4. Clinical practice

The major diseases we treat are those of liver, biliary tract including gallbladder, pancreas, and spleen, particularly malignant diseases of those organs. Especially, our mission is to treat advanced cancers with multidisciplinary strategy although our mainstay is surgical method. Living liver transplantation is also undertaken for end -stage liver diseases.

Laparoscopic surgery is applied to neoplastic diseases as well as benign diseases from the viewpoint of less invasive surgery. The malignant cases we resected was 158 in 2013, which was ranked among high volume centers of our country.

5. Publications

Original Article

1. Sato K, Tanaka S, Mitsunori Y, Mogushi K, Yasen M, Aihara A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanaka H, Arii S. Contrast-enhanced intraoperative ultrasonography for vascular imaging of hepatocellular carcinoma; clinical and biological significance. *Hepatology*, 2013;57(4):1436-1447
2. Muramatsu S, Tanaka S, Mogushi K, Adikrisna R, Aihara A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanaka H, Nakayama K, Tanaka H, Yamaoka S, Arii S. Visualization of stem cell features in human hepatocellular carcinoma enlightened in vivo significance of tumor-host interaction and clinical implication. *Hepatology*, 2013;58(1):218-228.
3. Mitsunori Y, Tanaka S, Nakamura N, Ban D, Irie T, Noguchi N, Kudo A, Iijima H, Arii S. Contrast-enhanced intraoperative ultrasound for hepatocellular carcinoma: high sensitivity of diagnosis and therapeutic impact. *J Hepatobiliary Pancreat Sci.* 2013;20(2):234-242.
4. Ogawa K, Tanaka S, Matsumura S, Murakata A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanabe M, Arii S. EpCAM-Targeted therapy for human hepatocellular carcinoma. *Annals of Surgical Oncology*, in press
5. Katsuta E, Tanaka S, Mogushi K, Matsumura S, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Tanaka H, Tanabe M, Arii S. Age-related clinicopathological and molecular features of patients received curative hepatectomy for hepatocellular carcinoma. *American Journal of Surgery*, in press
6. Furuta M, Kozaki KI, Tanimoto K, Tanaka S, Arii S, Shimamura T, Niida A, Miyano S, Inazawa J. The Tumor-suppressive mir-497-195 cluster targets multiple cell-cycle regulators in hepatocellular carcinoma. *PLoS One.* 2013;8(3):e60155.
7. Mayinuer A, Yasen M, Mogushi K, Obulhasim G, Xieraili M, Aihara A, Tanaka S, Mizushima H, Tanaka H, Arii S. Upregulation of protein tyrosine phosphatase type IVA member 3 (PTP4A3/PRL-3) associated with tumor differentiation and a poor prognosis in human hepatocellular carcinoma. *Annals of Surgical Oncology*, 2013;20(1):305-317.
8. Katayama Y, Maeda M, Miyaguchi K, Nemoto S, Yasen M, Tanaka S, Mizushima H, Fukuoka Y, Arii S, Tanaka H. Identification of pathogenesis-related microRNAs in hepatocellular carcinoma by expression profiling. *Oncol Lett.* 2012;4(4):817-823.
9. Dohi O, Yasui K, Gen Y, Takada H, Endo M, Tsuji K, Konishi C, Yamada N, Mitsuyoshi H, Naito Y, Tanaka S, Arii S, Yoshikawa T. Epigenetic silencing of miR-335 and its host gene MEST in hepatocellular carcinoma. *Int J Oncol.* 2013;42(2):411-418.
10. Endo M, Yasui K, Zen Y, Gen Y, Zen K, Tsuji K, Dohi O, Mitsuyoshi H, Tanaka S, Taniwaki M, Nakanuma Y, Arii S, Yoshikawa T. Alterations of the SWI/SNF chromatin remodeling subunit-BRG1 and BRM in hepatocellular carcinoma. *Liver Int.* 2013;33(1):105-117.
11. Obulhasim G, Yasen M, Kajino K, Mogushi K, Tanaka S, Mizushima H, Tanaka H, Arii S, Hino O. Up-regulation of dbpA mRNA in hepatocellular carcinoma associated with metabolic syndrome. *Hepatology International*, in press
12. Kudo A, Tanaka S, Ban D, Matsumura S, Irie T, Ochiai T, Nakamura N, Arii S, Tanabe M. Alcohol consumption and recurrence of non-B or non-C hepatocellular carcinoma after hepatectomy: a propensity score analysis. *J Gastroenterol.* 2013 Oct 18. [Epub ahead of print]
13. Kudo A, Tanaka S, Ban D, Matsumura S, Irie T, Nakamura N, Arii S. Anatomic resection reduces the recurrence of solitary hepatocellular carcinoma <5 cm without macrovascular invasion. *Am J Surg.* 2013 Oct 8. pii: S0002-9610(13)00510-2. doi: 10.1016/j.amjsurg.2013.06.009. [Epub ahead of print]
14. Kudo A, Igari T, Kumagai J, Ban D, Tanaka S, Arii S. A simple index to predict liver functional reserve after hepatectomy. *Hepato-Gastroenterology*, in press
15. Kudo A, Mogushi K, Takayama T, Matsumura S, Ban D, Irie T, Ochiai T, Tanaka H, Anzai N, Sakamoto M, Tanaka S, Arii S. Mitochondrial metabolism in the Noncancerous Liver Determine the Occurrence of Hepatocellular Carcinoma: A Prospective Study. *Journal of Gastroenterology*, in press
16. Ochiai T, Igari K, Furuyama T, Ito H, Mitsunori Y, Aihara A, Kumagai Y, Iida M, Odajima H, Tanaka S, Arii S, Yamazaki S. Favorable response after gemcitabine-radiotherapy for invasive pancreatic intraductal papillary mucinous neoplasm: a case report. *International Surgery*, 2013;98(4):340-345.
17. Ochiai T, Ohta K, Iida M, Kumagai Y, Mitsunori Y, Aihara A, Noguchi N, Arii S, Yamazaki S. High resectability of

- colorectal liver metastases with aggressive chemotherapy in the era of molecular target-based agents. *Hepato-Gastroenterology*, 2013;60(125)955-960.
18. Yasui Y, Kudo A, Kurosaki M, Matsuda S, Muraoka M, Tamaki N, Suzuki S, Hosokawa T, Ueda K, Matsunaga K, Nakanishi H, Tshuchiya K, Itakura J, Takahashi Y, Tanaka S, Asahina Y, Enomoto N, Arie S, Izumi N. Reduced organic anion transporter expression is a risk factor for hepatocellular carcinoma in chronic hepatitis C patients. *Oncology*, 2013;86(1)53-62.
 19. Tateno C, Miya F, Wake K, Kataoka M, Ishida Y, Yamasaki C, Yanagi A, Kakuni M, Wisse E, Verheyen F, Inoue K, Sato K, Kudo A, Arie S, Itamoto T, Asahara T, Tsunoda T, Yoshizato K. Morphological and microarray analyses of human hepatocytes from xenogeneic host livers. *Laboratory Investigation*, 2013;93(1)54-71.
 20. Igari K, Ochiai T, Yamazaki S. POSSUM and P-POSSUM for risk assessment in general surgery in the elderly. *Hepato-Gastroenterology*, 2013;60(126):1320-1327.
 21. Machida Y, Takemoto A, Ban D, Yoshumoto T, Mihara M, Shibuya H. Adrenal cortical adenoma arising from an adrenohepatic union. *Japanese Journal of Radiology*, 2013;31(9)623-626.
 22. Fujimura N, Obara H, Suda K, Takeuchi H, Miyasho T, Kawasako K, Du W, Yamada S, Ono S, Matsumoto K, Matsuda S, Yagi H, Kitago M, Shinoda M, Itano O, Tanabe M, Sakamoto M, Maruyama I, Kitagawa Y. Neutrophil elastase inhibitor improves survival rate after ischemia reperfusion injury caused by supravisceral aortic clamping in rats. *Journal of Surgical Research*, 2013;180(1):e31-36.
 23. Yagi H, Fukumitsu K, Fukuda K, Kitago M, Shinoda M, Obara H, Itano O, Kawachi S, Tanabe M, Coudriet GM, Piquanelli JD, Gilbert TW, Aoto-Gutierrez A, Kitagawa Y. Human-scale whole-organ bioengineering for liver transplantation: a regenerative medicine approach. *Cell Transplantation*, 2013;22(2)231-242.

Review Article, Case Report, etc.

1. Sakai S, Tanaka S, Kawakami K, Arie S. Cell-enclosing microparticles and microcapsules production using a water-immiscible fluid under laminar flow and application to cell therapy. in *Bioencapsulation of Living Cells for Diverse Medical Applications*, ed. Brandtner EM, Dangerfield JA. Pp153-177, (Bentham Science Publishers), 2013
2. Ochiai T, Igari K, Furuyama T, Ito H, Mitsunori Y, Aihara A, Kumagai Y, Iida M, Odajima H, Tanaka S, Arie S, Yamazaki S. Favorable response after gemcitabine-radiotherapy for invasive pancreatic intraductal papillary mucinous neoplasm: a case report. *International Surgery*, 2013;98(4)340-345.
3. Ito H, Kudo A, Matsumura S, Ban D, Irie T, Ochiai T, Nakamura N, Tanaka S, Tanabe M. Mixed adenoneuroendocrine carcinoma of the colon progressed rapidly after hepatic rupture: Report of a case. *Int Surg*, 2014 Jan-Feb;99(1):40-4.
4. Miura T, Ban D, Koyama T, Kudo A, Ochiai T, Irie T, Nakamura N, Tanaka S, Arie S. Severe postoperative hemorrhage caused by antibody-mediated coagulation factor deficiencies: report of two cases. *Surgery Today*, in press
5. Jibiki M, Inoue Y, Kudo T, Toyofuku T, Saito K, Kihara K, Kudo A, Ban D, Arie S. Combined resection of a tumor and the inferior vena cava: report of two cases. *Surgery Today*, 2013;44(1)166-170.
6. Shinoda M, Kadota Y, Tsujikawa H, Masugi Y, Itano O, Ueno A, Mihara K, Hibi T, Abe Y, Yagi H, Kitago M, Kawachi S, Tanimoto A, Sakamoto M, Tanabe M, Kitagawa Y. Lymphoepithelioma-like hepatocellular carcinoma: a case report and a review of the literature. *World J Surg Oncol*, in press
7. Kadota Y, Shinoda M, Tanabe M, Tsujikawa H, Ueno A, Masugi Y, Oshima G, Nishiyama R, Tanaka M, Mihara K, Abe Y, Yagi H, Kitago M, Itano O, Kawachi S, Aiura K, Tanimoto A, Sakamaoto M, Kitagawa Y. Concomitant pancreatic endocrine neoplasm and intraductal papillary mucinous neoplasm: a case report and literature review. *World J Surg Oncol*, in press

International Presentation

1. Shinoda M, Tanabe M, Tanaka M, Nishiyama R, Oshima G, Takano K, Maruyama I, Kitagawa Y. Hemoadsorption of high-mobility group box 1 in a swine acute liver failure model. *International Surgical Week ISW 2013, Helsinki*, 2013.
2. Tanaka M, Shinoda M, Tanabe M, Takayanagi A, Nishiyama R, Yagi H, Maruyama I, Kitagawa Y. Gene transfer of a box domain of high mobility group box 1 in rat acute liver failure model. *International Surgical Week ISW 2013, Helsinki*, 2013.
3. Hibi T, Kitago M, Aiura K, Tanabe M, Itano O, Shinoda M, Abe Y, Yagi H, Kitagawa Y. Phase I/II trial of neoadjuvant chemoradiotherapy with 5-FU, cisplatin, mitomycin C, and heparin for borderline resectable pancreatic cancer. *American Society of Clinical Oncology 2013 Gastrointestinal Cancers Symposium (ASCO-GI), San Francisco*, 2013.

2013.01

4. Ei S, Tanabe M, Hibi T, Itano O, Shinoda M, Kitago M, Abe Y, Yagi H, Okabayashi K, Odaira M, Kadota Y, Fujimura T, Katsuki Y, Tanaka M, Tsutsui R, Wakabayashi G, Kitagawa Y. Cryoablation compared with radiofrequency ablation and microwave coagulation therapy for the local control of primary hepatocellular carcinoma. American Society of Clinical Oncology 2013 Gastrointestinal Cancers Symposium (ASCO-GI), San Francisco, 2013.01
5. Itano O, Tanaka M, Nishiyama R, Tanabe M, Shinoda M, Kitago M, Abe Y, Hibi T, Yagi H, Kitagawa Y. Optimal surgical strategy for advanced gallbladder carcinoma: Single-center analysis of long-term survivors. American Hepato-Pancreato-Biliary Association (AHPBA) Annual Meeting 2013, Miami, 2013.02
6. Hibi T, Itano O, Fujimura T, Shinoda M, Kitago M, Yagi H, Abe Y, Tanabe M, Kitagawa Y. Prognostic factors after hepatectomy for intrahepatic cholangiocarcinoma: Relevance of lymph node dissection. American Hepato-Pancreato-Biliary Association (AHPBA) Annual Meeting 2013, Miami, 2013.02
7. Abe Y, Tanabe M, Hibi T, Itano O, Shinoda M, Kitago M, Yagi H, Wada N, Kitagawa Y. New paradigm in laparoscopic liver resection: the "pouch-in-a-pouch" technique. SAGES 2013 Scientific Session & Postgraduate Courses, Baltimore, 2013.04
8. Yagi H, Soto-Gutierrez A, Kadota Y, Hibi T, Abe Y, Kitago M, Shinoda M, Itano O, Tanabe M, Kitagawa Y. Human-scale transplantable liver graft using decellularized whole-organ scaffold. The 48th Annual Meeting of the European Association for the Study of the Liver (EASL), Amsterdam, 2013.04
9. Shinoda M, Tanabe M, Tanaka M, Nishiyama R, Takano K, Maruyama I, Kitagawa Y. Reducing plasma high-mobility group box 1 levels using a hemoabsorption column in swine acute liver failure. 48th Congress of the European Society for Surgical Research (ESSR), Istanbul, 2013.05
10. Tanaka M, Shinoda M, Tanabe M, Takayanagi A, Nishiyama R, Yagi H, Maruyama I, Kitagawa Y. Gene transfer of high mobility group box 1 inhibitor, a box, rat acute liver failure model. 48th Congress of the European Society for Surgical Research (ESSR), Istanbul, 2013.05
11. Ban D, Kudo A, Matsumura S, Ochiai T, Irie T, Nakamura N, Tanaka S, Tanabe M. Efficacy of wrapping the pancreatic stump with a bioabsorbable sheet and fibrin glue after distal pancreatectomy. The Society for Surgery of the Alimentary (SSAT), DDW 2013, Orlando, USA, 2013.5.20.
12. Ei S, Shinoda M, Tanabe M, Itano O, Kitago M, Yagi H, Abe Y, Hibi T, Kitagawa Y. Reduced dose of sorafenib for the treatment of advanced hepatocellular carcinoma. Asian Pacific Association for the Study of the Liver (APASL), Singapore, 2013.06
13. Shinoda M, Tanabe M, Ei S, Itano O, Kitago M, Yagi H, Abe Y, Hibi T, Aiura K, Kitagawa Y. Long term complete response of advanced hepatocellular carcinoma treated with reduced dose of sorafenib. A case report. Asian Pacific Association for the Study of the Liver (APASL), Singapore, 2013.06
14. Yagi H, Alejandro Soto-Gutierrez, Hibi T, Abe Y, Tanaka K, Kitago M, Shinoda M, Obara H, Itano O, Tanabe M, Kitagawa Y. Transplantable decellularized whole-organ scaffold for liver regenerative therapy in large animal model. International Society for Stem Cell Research (ISSCR) 11th Annual Meeting, Boston, 2013.06
15. Hibi T, Tanabe M, Itano O, Obara H, Shinoda M, Kitago M, Tanaka K, Yagi H, Abe Y, Kitagawa Y. Outcomes of adult living donor liver transplantation for acute liver failure: The impact of ABO-incompatibility and validation of a novel Japanese scoring system. The International Liver Transplantation Society 19th Annual International Congress, Sydney, 2013.06
16. Hibi T, Tanabe M, Hoshino K, Shimojima N, Fujino A, Itano O, Shinoda M, Kitago M, Yagi H, Abe Y, Kuroda T, Kitagawa Y. Long-term follow-up of adult living donors for small bowel transplant in pediatric recipients. XIII International Small Bowel Transplant Symposium, Oxford, 2013.06
17. Ban D, Akita K, Miyoshi T, Matsumura S, Ochiai T, Irie T, Kudo A, Nakamura N, Tanaka S, Tanabe M. Where is the optimal cut line of the jejunum for pancreatoduodenectomy? ~ from a viewpoint of surgical anatomy. IAP&KPBA2013. Seoul, Korea, 2013.9.20.
18. Ban D, Akita K, Miyoshi T, Matsumura S, Ochiai T, Irie T, Kudo A, Nakamura N, Tanaka S, Tanabe M. Treiz ligament as a good landmark for the left side approach to mobilize the duodenum in pancreatoduodenectomy: A Thiel soft fix cadaver study. IAP&KPBA2013. Seoul, Korea, 2013.9.20.
19. Tanaka S, Muramatsu S, Adikrisna R, Mogushi K, Matsumura S, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Nakayama K, Tanaka H, Yamaoka S, Tanabe M, Aii S. Visualization of stem cell features in human hepatocellular carcinoma; tumor-host Interaction and clinical impact. 64th Annual Meeting of the American Association for the Study of Liver diseases, Washington DC, USA, 2013.11.5.

20. Tanaka M, Sinoda M, Tanabe M, Takayanagi R, Nishiyama H, Yagi H, Maruyama I, Kitagawa Y. Gene transfer of a box domain of high mobility group box 1 in rat acute liver failure model. ISW2013, Helsinki, 2013.08
21. Sinoda M, Tanabe M, Tanaka M, Nishiyama R, Oshima G, Takano K, Maruyama I, Kitagawa Y. Hemoadsorption of high-mobility group box 1 in a swine acute liver failure model. ISW2013, Helsinki, 2013.08
22. Nakamura N, Irie T, Matsumura S, Ban D, Ochiai T, Kudo A, Tanaka S, Arie S. Result of surgical treatment for peritoneal dissemination of hepatocellular carcinoma(HCC). ISW2013, Helsinki, Finland, 2013.8.26-28.
23. Ochiai T, Matsumura S, Ban D, Irie T, Kudo A, Nakamura N, Tanaka S. Survival analysis of patients with spontaneous rupture of hepatoma. ISW2013, Helsinki, Finland, 2013.8.26-28.
24. Ochiai T, Kudo A, Nakamura N, Kumagai Y, Iida M, Arie S, Yamazaki S, Tanaka S. Prognostic factors of ampullary carcinoma: analysis of 53 cases resected by pancreatoduodenectomy, pylorus preserving pancreatoduodenectomy or subtotal stomach preserving pancreatoduodenectomy. ISW2013, Helsinki, Finland, 2013.8.26-28.
25. Ochiai T, Matsumura S, Ban D, Irie T, Kudo A, Nakamura N, Inoue Y and Tanaka S. The impact of maintaining intraoperative hemodynamics for inferior vena cava resection in a porcine model of aortic and superior mesenteric arterial cross-clamping. ISW2013, Helsinki, Finland, 2013.8.26-28.
26. Akahoshi K, Kudo A, Tanaka S, Ban D, Matsumura S, Irie T, Nakamura N, Arie S, Tanabe M. Anatomic resection reduces the recurrence of solitary hepatocellular carcinoma ≤ 5 cm without macro-vascular invasion. 1st International Conference of Federation of Asian Clinical Oncology(FACO), Xiamen, China, 2013.9.26.
27. Shinoda M, Tanabe M, Itano O, Obara H, Kitago M, Hibi T, Abe Y, Yagi H, Shimojima N, Fujino A, Hoshino K, Kuroda T, Kitagawa Y. Living donor liver transplantation for fulminant hepatic failure from ABO-incompatible donors. The 13th Congress of the Asian Society of Transplantation (CAST), Kyoto, 2013.09
28. Ei S, Shinoda M, Ono Y, Itano O, Obara H, Kitago M, Tanaka K, Yagi H, Abe Y, Hibi T, Hoshino K, Kuroda T, Tanabe M, Kitagawa Y. Effects of early enteral feeding support after living donor liver transplantation. The 13th Congress of the Asian Society of Transplantation (CAST), Kyoto, 2013.09
29. Hibi T, Shinoda M, Inomata K, Yamagishi Y, Itano O, Obara H, Kitago M, Yagi H, Abe Y, Hoshino K, Fujino A, Tomita H, Ebinuma H, Kuroda T, Tanabe M, Kitagawa Y. Treatment strategy for acute liver failure: indication and timing of liver transplantation. The 13th Congress of the Asian Society of Transplantation (CAST), Kyoto, 2013.09

Invited lecture

1. Tanabe M. Theoretical Session. State of the art in ablation therapy (radiofrequency, micro wave and cryoablation). IRCAD France Advanced Course "New Perspectives in Hepatobiliary Surgery", Strasbourg, France, 2013.4.4.
2. Tanabe M. Experimental laboratory-Personalised training on live tissue. Laparoscopic partial hepatectomy. IRCAD France Advanced Course "New Perspectives in Hepatobiliary Surgery", Strasbourg, France, 2013.4.4.
3. Tanabe M. Theoretical Session. Single port liver resection: modification for extended indication. IRCAD France Advanced Course "New Perspectives in Hepatobiliary Surgery", Strasbourg, France, 2013.4.5.
4. Tanabe M. Experimental laboratory-Personalised training on live tissue. Laparoscopic partial hepatectomy. IRCAD France Advanced Course "New Perspectives in Hepatobiliary Surgery", Strasbourg, France, 2013.4.5.
5. Tanabe M. State of Art in radiofrequency, micro-wave, and cryoablation. I IRCAD Taiwan Advanced Course in hepatic and pancreatic surgery, Changhua, Taiwan, 2013.5.25.
6. Tanabe M. SILS hepatectomy. IRCAD Taiwan Advanced Course in hepatic and pancreatic surgery, Changhua, Taiwan, 2013.5.25.

Orthopaedic and Spinal Surgery

1. Staffs and Students (April, 2013)

Professor	Atsushi OKAWA	
Junior Associate Professor	Tetsuya JINNO,	Yoshiaki WAKABAYASHI,
	Shigenori KAWABATA	
Assistant Professor	Tsuyoshi KATO,	Daisuke KOGA,
	Toshitaka YOSHII,	Chigusa SAWAMURA,
	Hiroyuki INOSE	
Graduate Student	Masato YUASA,	Dai UKEGAWA,
	Takashi TANIYAMA,	Yoto OH,
	Madoka UKEGAWA,	Yuki FUNAUCHI,
	Sei JO,	Ren XU,
	Chengshan MA,	Gaku KOYANO,
	Hidetoshi KABURAGI,	Satoshi SUMIYA,
	Hidetsugu SUZUKI,	Masanori SAITO,
	Hiroaki Yasuda,	Takuya Oyaizu

Department of Orthopaedics Research and Development

Associate Professor	Shinichi Sotome,	Yoshinori Asou
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2. Activities

As the department of orthopaedic surgery, we execute medical treatment, research, and education in cooperation with the section of Orthopaedic Joint Surgery. Orthopaedics deals with musculoskeletal systems such as bone, cartilage, joint, tendon and muscle in addition to nervous systems such as spinal cord and peripheral nerves. Orthopaedics treats various disorders such as trauma, degeneration, neoplasm, and systemic disease. Thus, our research should be extended to a broad area of basic and clinical fields. Currently, our research projects include reconstruction of motor function, clinical application of regenerative medicine, development of biomaterials and artificial joints, and pain control.

(1) Research Subjects

- 1) Development and evaluation of a novel artificial bone – porous hydroxyapatite / collagen composite
- 2) Reconstruction of bone defects using bone marrow stromal cells and artificial bone substitutes
- 3) Reconstruction of bone defects using bone morphogenetic proteins and artificial bone substitutes
- 4) Analysis of the mechanisms of musculoskeletal aging and its prevention
- 5) Genome-wide analysis for bone and soft tissue tumor
- 6) Clinical applications of spinal cord evoked potentials
- 7) Development of novel diagnostic method for spinal cord function using magnetic field
- 8) Development of cell therapy to repair injured spinal cord
- 9) Development of multidisciplinary therapy for musculoskeletal malignant neoplasm

(2) Clinical Services

With the popularity of sports and aging society, the need for orthopaedic medicine is growing rapidly. We carry out not only treatment of the associated diseases but also the repair of functional disability for the improvement of QOL by advancing therapeutic strategies.

In spinal operation unit, microscopic or endoscopic surgery and spinal cord monitoring yield safety and secure decompression, resulting in early postoperative ambulation and satisfactory outcome.

Hand and upper limb surgery unit has applied microsurgical technique for atraumatic operation and micro-vascular anastomosis. Today, microsurgery is indispensable for re-implantation, nerve repair and transfer, and vascularized tissue transfer. Arthroscopic surgery for the upper limb is also available, and provides less-invasive operation alternative.

In musculoskeletal tumor surgery, limb-salvaging surgery is the first choice based on the concept of safety surgical margin from the systematic evaluation of surgical specimens. Also, functional reconstruction of the affected limb after tumor surgery is exerted by plastic and microsurgery technique and through the application of regenerative medicine.

Examples of advanced treatments for adult hip diseases are one-stage bilateral total hip arthroplasty, less-invasive

technique for adult hip reconstruction, and accelerated rehabilitation after hip arthroplasty.

(3) Education

The faculty in the department is responsible for assisting graduate students in developing professional research, and teaching the skills of both clinical and basic science in the field of orthopaedic surgery. Morning conferences are held three times a week, and special guest lectures are sometimes provided to give up-to-date information. We are participating in the center of excellence program, frontier research on molecular destruction and reconstruction of tooth and bone in the Tokyo medical and dental university and providing a learning environment for the students.

For first year orthopaedic residents, an annual meeting is held to discuss clinical and basic research with the faculty outside of Tokyo. Furthermore, we provide several open meetings and many orthopaedic surgeons join our educational lectures to study recent clinical applications via special guest speakers or oral presentation of case reports by the residents.

3. Publications

Original Article

1. Yoshii T, Yamada T, Hirai T, Taniyama T, Kato T, Enomoto M, Inose H, Sumiya S, Kawabata S, Shinomiya K, Okawa A. Dynamic Changes in Spinal Cord Compression by Cervical Ossification of the Posterior Longitudinal Ligament Evaluated by Kinematic Computed Tomography Myelography. *Spine (Phila Pa 1976)*. 2013 Oct 22. [Epub ahead of print]
2. Arai Y, Hirai T, Yoshii T, Sakai K, Kato T, Enomoto M, Matsumoto R, Yamada T, Kawabata S, Shinomiya K, Okawa A. A Prospective Comparative Study of Two Minimally Invasive Decompression Procedures for Lumbar Spinal Canal Stenosis - Unilateral Laminotomy for Bilateral Decompression (ULBD) versus Muscle-preserving Interlaminar Decompression (MILD). *Spine (Phila Pa 1976)*. 2013 Nov 13. [Epub ahead of print]
3. Yoshii T, Yuasa M, Sotome S, Yamada T, Sakaki K, Hirai T, Taniyama T, Inose H, Kato T, Arai Y, Kawabata S, Tomizawa S, Enomoto M, Shinomiya K, Okawa A. Porous/Dense Composite Hydroxyapatite for Anterior Cervical Discectomy and Fusion. *Spine (Phila Pa 1976)*. 2013 May 1;38(10):833-40.
4. Egawa S, Yoshii T, Sakaki K, Inose H, Kato T, Kawabata S, Tomizawa S, Okawa A. Dural closure for the treatment of superficial siderosis. *Journal of Neurosurgery Spine. J Neurosurg Spine*. 2013 Apr;18(4):388-93.
5. Yamada T, Yuasa M, Masaoka T, Taniyama T, Maehara H, Torigoe I, Yoshii T, Shinomiya K, Okawa A, Sotome S.: After repeated division, bone marrow stromal cells express inhibitory factors with osteogenic capabilities, and EphA5 is a primary candidate. *Bone*. Dec;57(2):343-54, 2013
6. Sasaki K, Inose H, Kawabata S, Yoshii T, Kato T, Saito M, Okawa A. Combined surgical and radiosurgical treatment for a symptomatic cervical metastasis in a case of malignant paraganglioma: a case report. *BMC Res Notes*. 2013 Dec 1;6:494.
7. Ukegawa D, Kawabata S, Sakaki K, Ishii S, Tomizawa S, Inose H, Yoshii T, Kato T, Enomoto M, Okawa A. Efficacy of biphasic transcranial electric stimulation in intraoperative motor evoked potential monitoring for cervical compression myelopathy. *Spine (Phila Pa 1976)*. (In press)
8. Araya N, Inose H, Kato T, Saito M, Sumiya S, Yamada T, Yoshii T, Kawabata S, Okawa A. A spinal deformity caused by hyper IgE syndrome: A case report. *J Neurosurg Spine*. (In press)
9. Wakasugi T, Shirasaka R, Kimura H, Wakabayashi Y : Flexor tendon rupture of the little finger caused by calcium pyrophosphate dehydrate crystal deposition disease of the pisotriquetrum joint. *Hand Surgery*, 18(3):413-415, 2013.
10. Sawamura C, Matsumoto S, Shimoji T, Ae K, Okawa: Lymphadenectomy and histologic subtype affect overall survival of soft tissue sarcoma patients with nodal metastases. *Clin Orthop Relat Res*. Mar;471(3):926-31, 2013
11. Koyanagi H, Ae K, Maehara H, Yuasa M, Masaoka T, Yamada T, Taniyama T, Saito M, Funauchi Y, Yoshii T, Okawa A, Sotome S: Massive Bone Reconstruction with Heat-Treated Bone Graft Loaded Autologous Bone Marrow-Derived Stromal Cells and b-Tricalcium Phosphate Composites in Canine Models. *Journal of orthopaedic research*. Aug;31(8):1308-16, 2013
12. Yamada T, Yuasa M, Masaoka T, Taniyama T, Maehara H, Torigoe I, Yoshii T, Shinomiya K, Okawa A, Sotome S: After repeated division, bone marrow stromal cells express inhibitory factors with osteogenic capabilities, and EphA5 is a primary candidate. *Bone* Dec;57(2):343-54, 2013

Disease Genomics

1. Staffs and Students

Professor	Shumpei Ishikawa	
Assistant Professor	Takayuki Isagawa,	Hiroto Kato
Collaborative Researcher	Hiroyuki Nishida	
Technical Assistant	Reiko Sato,	Satoko Aihara,
	Kazuki Kishi,	Ryouhei Suzuki
Secretary	Miharu Tamukai	

2. Purpose of Education

Tumor tissue is a complex system composed of tumor cells and multiple types of stromal cells. Our purpose is to understand the dynamic multicellular interactions in such a complexed biological system by measuring a large amount of data at the genomic level, which leads the identifications of therapeutic targets and biomarkers. Another objective in the graduate course is to learn the applications, methods and interpretations of the disease genomics and to understand how to apply disease genomics to clinical fields through analyzing clinical human samples.

3. Research Subjects

- ① Genomic approach for cancer - stromal interaction
- ② Functional genomic screening in cancer
- ③ Functional analysis of cancer associated molecules
- ④ Genomic analysis of clinical cancer samples

4. Clinical Services

none

5. Publications

1. Li W, Katoh H, Wang L, Yu X, Du Z, Yan X, Zheng P, Liu Y. FOXP3 regulates sensitivity of cancer cells to irradiation by transcriptional repression of BRCA1. *Cancer Res.* 2013 Apr 1;73(7):2170-80.
2. Sato T, Kaneda A, Tsuji S, Isagawa T, Yamamoto S, Fujita T, Yamanaka R, Tanaka Y, Nukiwa T, Marquez VE, Ishikawa Y, Ichinose M, Aburatani H. PRC2 overexpression and PRC2-target gene repression relating to poorer prognosis in small cell lung cancer. *Sci Rep.* 2013;3:1911.
3. Tanaka M, Suzuki HI, Shibahara J, Kunita A, Isagawa T, Yoshimi A, Kurokawa M, Miyazono K, Aburatani H, Ishikawa S, Fukayama M. EVI1 oncogene promotes KRAS pathway through suppression of microRNA-96 in pancreatic carcinogenesis. *Oncogene.* 2013 Jun 10. [Epub ahead of print]
4. Nakaya T, Kikuchi Y, Kunita A, Ishikawa S, Matsusaka K, Hino R, Aburatani H, Fukayama M. Enrichment of stem-like cell population comprises transformation ability of Epstein-Barr virus latent membrane protein 2A for non-transformed cells. *Virus Res.* 2013 Jun;174(1-2):108-15.
5. Yamamoto S, Tateishi K, Kudo Y, Yamamoto K, Isagawa T, Nagae G, Nakatsuka T, Asaoka Y, Ijichi H, Hirata Y, Otsuka M, Ikenoue T, Aburatani H, Omata M, Koike K. Histone demethylase KDM4C regulates sphere formation by mediating the cross talk between Wnt and Notch pathways in colonic cancer cells. *Carcinogenesis.* 2013 Oct;34(10):2380-8.
6. Saito T, Takeda N, Amiya E, Nakao T, Abe H, Semba H, Soma K, Koyama K, Hosoya Y, Imai Y, Isagawa T, Watanabe M, Manabe I, Komuro I, Nagai R, Maemura K. VEGF-A induces its negative regulator, soluble form of VEGFR-1, by modulating its alternative splicing. *FEBS Lett.* 2013 Jul 11;587(14):2179-85.
7. Kon A, Shih LY, Minamino M, Sanada M, Shiraishi Y, Nagata Y, Yoshida K, Okuno Y, Bando M, Nakato R, Ishikawa S, Sato-Otsubo A, Nagae G, Nishimoto A, Haferlach C, Nowak D, Sato Y, Alpermann T, Nagasaki M, Shimamura T, Tanaka H, Chiba K, Yamamoto R, Yamaguchi T, Otsu M, Obara N, Sakata-Yanagimoto M, Nakamaki T, Ishiyama K, Nolte F, Hofmann WK, Miyawaki S, Chiba S, Mori H, Nakauchi H, Koeffler HP, Aburatani H, Haferlach T, Shirahige K, Miyano S, Ogawa S. Recurrent mutations in multiple components of the cohesin complex in myeloid neoplasms. *Nat Genet.* 2013 Oct;45(10):1232-7.
8. Fustin JM, Doi M, Yamaguchi Y, Hayashi H, Nishimura S, Yoshida M, Isagawa T, Suimye-Morioka M, Kakeya H, Manabe I, *Okamura H. RNA-methylation-dependent RNA processing controls the speed of the circadian clock. *Cell.* 2013 Nov 7;155(4):793-806.

9. Goda S, Isagawa T, Chikaoka Y, Kawamura T, Aburatani H. Control of Histone H3 Lysine 9 (H3K9) Methylation State via Cooperative Two-step Demethylation by Jumonji Domain Containing 1A (JMJD1A) Homodimer. *J Biol Chem*. 2013 Dec 27;288(52):36948-56
10. Hayashi A, Morikawa T, Kawai T, Kume H, Ishikawa S, Homma Y, Fukayama M. Clinicopathological and prognostic significance of EZH2 expression in upper urinary tract carcinoma. *Virchows Arch*. 2014 Jan 21. [Epub ahead of print]
11. Ichimura T, Morikawa T, Kawai T, Nakagawa T, Matsushita H, Kakimi K, Kume H, Ishikawa S, Homma Y, Fukayama M. Prognostic Significance of CD204-Positive Macrophages in Upper Urinary Tract Cancer. *Ann Surg Oncol*. 2014 Feb 4. [Epub ahead of print]
12. Ui T, Morishima K, Saito S, Sakuma Y, Fujii H, Hosoya Y, Ishikawa S, Aburatani H, Fukayama M, Niki T, Yasuda Y. The HSP90 inhibitor 17-N-allylamino-17-demethoxy geldanamycin (17-AAG) synergizes with cisplatin and induces apoptosis in cisplatin-resistant esophageal squamous cell carcinoma cell lines via the Akt/XIAP pathway. *Oncol Rep*. 2014 Feb;31(2):619-24.

Human Genetics and Disease Diversity

1. Staffs and Students

Professor Toshihiro Tanaka
 Tenure Track Junior Associate Professor
 Yukinori Okada

2. Purpose of Education

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. Research Subjects

- 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

4. Publications

1. Okada Y, Wu D, Trynka G, Raj T, Terao C, Ikari K, Kochi Y, Ohmura K, Suzuki A, Yoshida S, Graham RR, Manoharan A, Ortmann W, Bhangale B, Denny JC, Carroll RJ, Eyler AE, Greenberg JD, Kremer JM, Pappas DA, Jiang L, Yin J, Ye L, Su D, Yang J, Xie G, Keystone E, Westra H, Esko T, Metspalu A, Zhou X, Gupta N, Mirel D, Stahl EA, Diogo D, Cui J, Liao K, Guo MH, Myouzen K, Kawaguchi T, Coenen MJH, van Riel PL, van de Laar MA, Guchelaar H, Huizinga TW, Dieudé P, Mariette X, Bridges Jr. SL, Zhernakova A, Toes RE, Tak PP, Miceli-Richard C, Bang S, Lee H, Martin J, Gonzalez-Gay MA, Rodriguez-Rodriguez L, Rantapää-Dahlqvist S, Ärlestig L, Choi HK, Kamatani Y, Galan P, Lathrop M, the RACI consortium, the GARNET consortium, Eyre S, Bowes J, Barton A, de Vries N, Moreland LW, Criswell LA, Karlson EW, Taniguchi A, Yamada R, Kubo M, Liu JS, Bae S, Worthington J, Padyukov L, Klareskog L, Gregersen PK, Raychaudhuri S, Stranger BE, De Jager PL, Franke L, Visscher PM, Brown MA, Yamanaka H, Mimori T, Takahashi A, Xu H, Behrens TW, Siminovitch KA, Momohara S, Matsuda F, Yamamoto K, Plenge RM. Genetics of rheumatoid arthritis contributes to biology and drug discovery. *Nature* 506:376-381 (2014).
2. Lubitz SA, Lunetta KL, Lin H, Arking DE, Trompet S, Li G, Krijthe BP, Chasman DI, Barnard J, Kleber ME, Dörr M, Ozaki K, Smith AV, Müller M, Walter S, Agarwal SK, Bis JC, Brody JA, Chen LY, Everett BM, Ford I, Franco OH, Harris TB, Hofman A, Kääb S, Mahida S, Kathiresan S, Kubo M, Launer LJ, MacFarlane PW, Magnani JW, McKnight B, McManus DD, Peters A, Psaty BM, Rose LM, Rotter JI, Silbernagel G, Smith JD, Sotoodehnia N, Stott DJ, Taylor K, Tomaschitz A, Tsunoda T, Uitterlinden AG, VanWagoner DR, Völker U, Völzke H, Murabito JM, Sinner MF, Gudnason V, Felix SB, März W, Chung M, Albert CM, Stricker BH, Tanaka T, Heckbert SR, Jukema JW, Alonso A, Benjamin EJ, Ellinor PT. Novel genetic markers associate with atrial fibrillation risk in Europeans and Japanese. *Journal of the American College of Cardiology*, 63:1200-1210 (2014).
3. Behr ER, Ritchie MD, Tanaka T, Kääb S, Crawford DC, Nicoletti P, Floratos A, Sinner MF, Kannankeril PJ, AA. M. Wilde, Bezzina CR, Schulze-Bahr E, Zumhagen S, Guicheney P, Bishopric NH, Marshall V, Shakir S, Dalageorgou C, Bevan S, Jamshidi Y, Bastiaenen R, Myerberg RJ, Schott J-J, Camm AJ, Steinbeck G, Norris K, Altman RB, Tatonetti N, Jeffery S, Kubo M, Nakamura Y, Shen Y, George, Jr. AL. Genome wide analysis of drug-induced *Torsades de Pointes*: lack of common variants with large effect sizes. *PLoS One* 8:e78511 (2013).
4. Suna S, Sakata Y, Nakatani D, Okuda K, Shimizu M, Usami M, Matsumoto S, Hara M, Ozaki K, Mizuno H, Minamino T, Takashima S, Nishino M, Matsumura Y, Takeda H, Tanaka T, Sato H, Hori M, Komuro I. Decreased mortality associated with statin treatment in patients with acute myocardial infarction and lymphotoxin-alpha C804A polymorphism. *Atherosclerosis* 227:373-379 (2013).
5. Liao KP, Diogo D, Cui J, Cai T, Okada Y, Gainer VS, Murphy SN, Gupta N, Mirel D, Ananthakrishnan AN, Szolovits P, Shaw SY, Raychaudhuri S, Churchill S, Kohane I, Karlson EW, Plenge RM. The association between low density lipoprotein (LDL) and RA genetic factors with LDL levels in rheumatoid arthritis and non-RA controls. *Ann Rheum Dis* doi:10.1136/annrheumdis-2012-203202.

6. Tanikawa C, [Okada Y](#), Takahashi A, Oda K, Kamatani N, Kubo M, Nakamura Y, Matsuda K. Genome Wide Association Study of Age at Menarche in the Japanese Population. *PLoS One* 8:e63821 (2013).
7. Cui J, Stahl EA, Saevarsdottir S, Miceli C, Diogo D, Trynka G, Raj T, Mirkov MU, Canhao H, Ikari K, Terao C, [Okada Y](#), Wedrén S, Askling J, Yamanaka H, Momohara S, Taniguchi A, Ohmura K, Matsuda F, Mimori T, Gupta N, Kuchroo M, Morgan AW, Isaacs JD, Wilson AG, Hyrich KL, Herenius M, Doorenspleet ME, Tak PP, Crusius JB, van der Horst-Bruinsma IE, Wolbink GJ, van Riel PL, van de Laar M, Guchelaar HJ, Shadick NA, Allaart CF, Huizinga TW, Toes RE, Kimberly RP, Bridges SL Jr, Criswell LA, Moreland LW, Fonseca JE, de Vries N, Stranger BE, De Jager PL, Raychaudhuri S, Weinblatt ME, Gregersen PK, Mariette X, Barton A, Padyukov L, Coenen MJ, Karlson EW, Plenge RM. Genome-Wide Association Study and Gene Expression Analysis Identifies CD84 as a Predictor of Response to Etanercept Therapy in Rheumatoid Arthritis. *PLoS Genet* 9:e1003394 (2013).
8. Fritsche LG, Chen W, Schu M, Yaspan BL, Yu Y, Thorleifsson G, Zack DJ, Arakawa S, Cipriani V, Ripke S, Igo RP Jr, Buitendijk GH, Sim X, Weeks DE, Guymer RH, Merriam JE, Francis PJ, Hannum G, Agarwal A, Armbrecht AM, Audo I, Aung T, Barile GR, Benchaboune M, Bird AC, Bishop PN, Branham KE, Brooks M, Brucker AJ, Cade WH, Cain MS, Campochiaro PA, Chan CC, Cheng CY, Chew EY, Chin KA, Chowers I, Clayton DG, Cojocaru R, Conley YP, Cornes BK, Daly MJ, Dhillon B, Edwards AO, Evangelou E, Fagerness J, Ferreyra HA, Friedman JS, Geirsdottir A, George RJ, Gieger C, Gupta N, Hagstrom SA, Harding SP, Haritoglou C, Heckenlively JR, Holz FG, Hughes G, Ioannidis JP, Ishibashi T, Joseph P, Jun G, Kamatani Y, Katsanis N, Keilhauer C, Khan JC, Kim IK, Kiyohara Y, Klein BE, Klein R, Kovach JL, Kozak I, Lee CJ, Lee KE, Lichtner P, Lotery AJ, Meitinger T, Mitchell P, Mohand-Said S, Moore AT, Morgan DJ, Morrison MA, Myers CE, Naj AC, Nakamura Y, [Okada Y](#), Orlin A, Ortube MC, Othman MI, Pappas C, Park KH, Pauer GJ, Peachey NS, Poch O, Priya RR, Reynolds R, Richardson AJ, Ripp R, Rudolph G, Ryu E, Sahel JA, Schaumberg DA, Scholl HP, Schwartz SG, Scott WK, Shahid H, Sigurdsson H, Silvestri G, Sivakumaran TA, Smith RT, Sobrin L, Souied EH, Stambolian DE, Stefansson H, Sturgill-Short GM, Takahashi A, Tosakulwong N, Truitt BJ, Tsironi EE, Uitterlinden AG, van Duijn CM, Vijaya L, Vingerling JR, Vithana EN, Webster AR, Wichmann HE, Winkler TW, Wong TY, Wright AF, Zelenika D, Zhang M, Zhao L, Zhang K, Klein ML, Hageman GS, Lathrop GM, Stefansson K, Allikmets R, Baird PN, Gorin MB, Wang JJ, Klaver CC, Seddon JM, Pericak-Vance MA, Iyengar SK, Yates JR, Swaroop A, Weber BH, Kubo M, Deangelis MM, Léveillard T, Thorsteinsdottir U, Haines JL, Farrer LA, Heid IM, Abecasis GR, AMD Gene Consortium. Seven new loci associated with age-related macular degeneration. *Nat Genet* 45:433-439 (2013).
9. Chen Z, Tang H, Qayyum R, Schick UM, Nalls MA, Handsaker R, Li J, Lu Y, Yanek LR, Keating B, Meng Y, van Rooij FJ, [Okada Y](#), Kubo M, Rasmussen-Torvik L, Keller MF, Lange L, Evans M, Bottinger EP, Linderman MD, Ruderfer DM, Hakonarson H, Papanicolaou G, Zonderman AB, Gottesman O, BioBank Japan Project, CHARGE Consortium, Thomson C, Ziv E, Singleton AB, Loos RJ, Sleiman PM, Ganesh S, McCarroll S, Becker DM, Wilson JG, Lettre G, Reiner AP. Genome-wide association analysis of red blood cell traits in African Americans: the COGENT Network. *Hum Mol Genet* 22:2529-2538 (2013).
10. Shimane K, Kochi Y, Suzuki A, [Okada Y](#), Ishii T, Horita T, Saito K, Okamoto A, Nishimoto N, Myouzen K, Kubo M, Hirakata M, Sumida T, Takasaki Y, Yamada R, Nakamura Y, Kamatani N, Yamamoto K. An association analysis of HLA-DRB1 with systemic lupus erythematosus and rheumatoid arthritis in a Japanese population: effects of *09:01 allele on disease phenotypes. *Rheumatology* 52:1172-1182 (2013).
11. Köttgen A, Albrecht E, Teumer A, Vitart V, Krumsiek J, Hundertmark C, Pistis G, Ruggiero D, O'Seaghdha CM, Haller T, Yang Q, Tanaka T, Johnson AD, Kutalik Z, Smith AV, Shi J, Struchalin M, Middelberg RP, Brown MJ, Gaffo AL, Pirastu N, Li G, Hayward C, Zemunik T, Huffman J, Yengo L, Zhao JH, Demirkan A, Feitosa MF, Liu X, Malerba G, Lopez LM, van der Harst P, Li X, Kleber ME, Hicks AA, Nolte IM, Johansson A, Murgia F, Wild SH, Bakker SJ, Peden JF, Dehghan A, Steri M, Tenesa A, Lagou V, Salo P, Mangino M, Rose LM, Lehtimäki T, Woodward OM, [Okada Y](#), Tin A, Müller C, Oldmeadow C, Putku M, Czamara D, Kraft P, Frogger L, Thun GA, Grotevendt A, Gislason GK, Harris TB, Launer LJ, McArdle P, Shuldiner AR, Boerwinkle E, Coresh J, Schmidt H, Schallert M, Martin NG, Montgomery GW, Kubo M, Nakamura Y, [Tanaka T](#), Munroe PB, Samani NJ, Jacobs DR Jr, Liu K, D'Adamo P, Ulivi S, Rotter JI, Psaty BM, Vollenweider P, Waeber G, Campbell S, Devuyst O, Navarro P, Kolcic I, Hastie N, Balkau B, Froguel P, Esko T, Salumets A, Khaw KT, Langenberg C, Wareham NJ, Isaacs A, Kraja A, Zhang Q, Wild PS, Scott RJ, Holliday EG, Org E, Viigimaa M, Bandinelli S, Metter JE, Lupo A, Trabetti E, Sorice R, Döring A, Lattka E, Strauch K, Theis F, Waldenberger M, Wichmann HE, Davies G, Gow AJ, Bruinenberg M, LifeLines Cohort Study, Stolk RP, Kooner JS, Zhang W, Winkelmann BR, Boehm BO, Lucae S, Penninx BW, Smit JH, Curhan G, Mudgal P, Plenge RM, Portas L, Persico I, Kirin M, Wilson JF, Mateo Leach I, van Gilst WH, Goel A, Ongen H, Hofman A, Rivadeneira F, Uitterlinden AG, Imboden M, von Eckardstein A, Cucca F, Nagaraja R, Piras MG, Nauck M, Schurmann C, Budde K, Ernst F, Farrington SM, Theodoratou E, Prokopenko I, Stumvoll M, Julia A, Perola M, Salomaa V, Shin SY, Spector TD, Sala C, Ridker PM, Kähönen M, Viikari J,

Hengstenberg C, Nelson CP, CARDIoGRAM Consortium, DIAGRAM Consortium, ICBP Consortium, MAGIC Consortium, Meschia JF, Nalls MA, Sharma P, Singleton AB, Kamatani N, Zeller T, Burnier M, Attia J, Laan M, Klopp N, Hillege HL, Kloiber S, Choi H, Pirastu M, Tore S, Probst-Hensch NM, Völzke H, Gudnason V, Parsa A, Schmidt R, Whitfield JB, Fornage M, Gasparini P, Siscovick DS, Polašek O, Campbell H, Rudan I, Bouatia-Naji N, Metspalu A, Loos RJ, van Duijn CM, Borecki IB, Ferrucci L, Gambaro G, Deary IJ, Wolffenbuttel BH, Chambers JC, März W, Pramstaller PP, Snieder H, Gyllenstein U, Wright AF, Navis G, Watkins H, Witteman JC, Sanna S, Schipf S, Dunlop MG, Tönjes A, Ripatti S, Soranzo N, Toniolo D, Chasman DI, Raitakari O, Kao WH, Ciullo M, Fox CS, Caulfield M, Bochud M, Gieger C. Genome-wide association analyses identify 18 new loci associated with serum urate concentrations. *Nat Genet* 45:145-154 (2013).

12. Aarnink A, Garchon HJ, Okada Y, Takahashi A, Matsuda K, Kubo M, Nakamura Y, Blancher A. Comparative analysis in cynomolgus macaque identifies a novel human MHC locus controlling platelet blood counts independently of BAK1. *J Thromb Haemost* 11:384-386 (2013).

4. Review Articles

1. Okada Y, Plenge RM. Entering the age of whole-exome sequencing in rheumatic diseases: novel Insights into disease pathogenicity. *Arthritis Rheum* 65:1975-1979 (2013).

5. Plenary Lectures and Symposiums

1. Tanaka T. Genetic Epidemiology ~understanding human diversity~. Seminar at Health Sciences University of Mongolia (Ulaanbaatar, Mongolia) Sep, 2013.

6. International Meeting Presentations

(Oral Presentations)

1. Okada Y, Diogo D, Liao KP, Fulton RS, Graham RR, Cui J, Greenberg JD, Eyre S, Bowes J, Lee AT, Pappas DA, Kremer JM, Barton A, Coenen MJH, Mariette X, Richard-Miceli C, Canhao H, Fonseca JE, de Vries N, Kurreeman F, Mikuls TR, Kohane I, Denny JC, Worthington J, Raychaudhuri S, Behrens TW, Seldin MF, Gregersen PK, Mardis ER, Plenge RM. Potential of Integrating Human Genetics and Electronic Medical Records for Drug Discovery: The Example of TYK2 and Rheumatoid Arthritis. *American College of Rheumatology Annual Meeting* Oct 30, 2013.
2. Okada Y, Wu D, Terao C, Ikari K, Kochi Y, Ikari K, Kochi Y, Ohmura K, Suzuki A, Yamanaka H, Denny JC, Greenberg JD, Graham RR, Brown MA, the RACI consortium, the GARNET consortium, Bae SC, Worthington J, Padyukov L, Klareskog L, Gregersen PK, Visscher PM, Siminovitch KA, Plenge RM. Biological Insights From Genetics of Rheumatoid Arthritis Contribute to Drug Discovery. *American College of Rheumatology Annual Meeting* Oct, 28, 2013.
3. Okada Y, Wu D, Terao C, Ikari K, Kochi Y, Ikari K, Kochi Y, Ohmura K, Suzuki A, Yamanaka H, Denny JC, Greenberg JD, Graham RR, Brown MA, the RACI consortium, the GARNET consortium, Bae SC, Worthington J, Padyukov L, Klareskog L, Gregersen PK, Visscher PM, Siminovitch KA, Plenge RM. Biological Insights from Genetics and biology of rheumatoid arthritis contribute to drug discovery. *American Society of Human Genetics Annual Meeting* Oct, 26, 2013.

(Poster Presentations)

1. Ozaki K, Morizono T, Onouchi Y, Takahashi A, Tsunoda T, Kubo M, Nakamura Y, Tanaka T. Genome wide association study for Arteriosclerosis Obliterans in a Japanese population. *American Society of Human Genetics Annual Meeting* Oct, 2013.
2. Onouchi Y, Fukazawa R, Ozaki K, Terai M, Hamada H, Honda T, Suzuki H, Suenaga T, Takeuchi T, Yasukawa K, Ebata R, Higashi K, Saji T, Kemmotsu Y, Takatsuki S, Ouchi K, Kishi F, Yoshikawa T, Nagai T, Hamamoto K, Sato Y, Abe J, Seki M, Kobayashi T, Takahashi A, Tsunoda T, Kubo M, Nakamura Y, Hata A, Tanaka T. Variations in ORAI1 gene associated with Kawasaki disease. *American Society of Human Genetics Annual Meeting* Oct, 2013.
3. Ozaki K, Tanaka T. Whole genome association study for atrial fibrillation in a Japanese population. *XXI International Society for Heart Research World Congress* July, 2013
4. Ozaki K, Morizono T, Tsunoda T, Kubo M, Nakamura Y, Tanaka T. Genetic risk factors for atrial fibrillation in the Japanese population. *European Human Genetics Conference* June, 2013

7. Research Funding

1. Tanaka T, a grant from the Naito Foundation
2. Tanaka T, Grant-in-Aid for Scientific Research (B), co-investigator

3. Tanaka T, Grant-in-Aid for Scientific Research (B), co-investigator
4. Tanaka T, Health and Labor Sciences Research Grants, co-investigator
5. Okada Y, a grant from Gout Foundation

8. Award

1. Okada Y, Travel award from The Program in Quantitative Genomics (PQG) at Harvard School of Public Health.
2. Okada Y, ASHG/Charles J. Epstein Trainee Award for Excellence in Human Genetics Research – Finalist.

Applied Regenerative Medicine

1. Staffs

Professor Ichiro SEKIYA
Assistant Professor Masafumi HORIE, Koji OTABE,
Koji FUJITA

2. Purpose of Education

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.

3. Research Subjects

- 1) Development of regenerative medicine with stem cells.
- 2) Realization and industrialization of cell and regenerative therapy.
- 3) Establishment of safety test for regenerative medicine.
- 4) Translational research.

4. Clinical Services

We started transplantation of synovial stem cells to enhance meniscus healing after meniscus suture.

5. Publications

Original Articles

1. Matsukura Y, Muneta T, Tsuji K, Koga H, Sekiya I. (2013) Mesenchymal Stem Cells in Synovial Fluid Increase After Meniscus Injury. *Clin Orthop Relat Res.* May;472(5):1357-64.
2. Atesok K, Doral MN, Bilge O, Sekiya I. (2013) Synovial stem cells in musculoskeletal regeneration. *J Am Acad Orthop Surg.* Apr;21(4):258-9.
3. Ozeki N, Muneta T, Koga H, Katagiri H, Otabe K, Okuno M, Tsuji K, Kobayashi E, Matsumoto K, Saito H, Saito T, Sekiya I. (2013) Transplantation of Achilles tendon treated with bone morphogenetic protein 7 promotes meniscus regeneration in a rat model of massive meniscal defect. *Arthritis Rheum.* Nov; 65(11):2876-86.
4. Katagiri H, Muneta T, Tsuji K, Horie M, Koga H, Ozeki N, Kobayashi E, Sekiya I. (2013) Transplantation of aggregates of synovial mesenchymal stem cells regenerates meniscus more effectively in a rat massive meniscal defect. *Biochem Biophys Res Commun.* Jun;435(4):603-9.
5. Hatsushika D, Muneta T, Horie M, Koga H, Tsuji K, Sekiya I. (2013) Intraarticular injection of synovial stem cells promotes meniscal regeneration in a rabbit massive meniscal defect model. *J Orthop Res.* Sep;31(9):1354-9.
6. Ichinose S, Tagami M, Muneta T, Mukohyama H, Sekiya I. (2013) Comparative sequential morphological analyses during in vitro chondrogenesis and osteogenesis of mesenchymal stem cells embedded in collagen gels. *Med Mol Morphol.* Mar;46(1):24-33.
7. Miyatake K, Tsuji K, Yamaga M, Yamada J, Matsukura Y, Abula K, Sekiya I, Muneta T. (2013) Human YKL39 (chitinase 3-like protein 2), an osteoarthritis-associated gene, enhances proliferation and type II collagen expression in ATDC5 cells. *Biochem Biophys Res Commun.* Feb;431(1):52-7.

[学会]

(海外)

1. Sekiya I, Muneta T. (2013) Arthroscopic Transplantation of synovial MSCs for cartilage regeneration. International Cartilage Repair Society. 2013.9.15. Izmir, Turkey.
2. Ozeki N, Sekiya I, Tsuji K, Saito T, Muneta T. (2013) Weekly intraarticular injections of synovial mesenchymal stem cells delay cartilage degeneration through trophic factors in a rat osteoarthritis model. International Cartilage Repair Society. 2013.9.15-18. Turkey.
3. Nakagawa Y, Sekiya I, Kondo S, Saito R, Yanagisawa K, Tabuchi T, Nagata T, Obara M, Okuaki T, Koga H, Tsuji K, Muneta T. (2013) Comparison of MRI T1rho mapping and histology for normal and torn menisci in a pig model. International Cartilage Repair Society. 2013.9.15-18. Turkey.
4. Udo M, Sekiya I, Tsuji K, Muneta T. (2013) Evaluation of a rat arthritis model induced by various doses of monoiodoacetic acid. International Cartilage Repair Society. 2013.9.15-18.

5. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Fumiaki Ayabe, Tetsuya Matsukawa, Martin K. Lotz, Hiroshi Asahara. (2013) The transcription factor Mohawk plays an important role for maintaining human ACL homeostasis and ligament/tendon differentiation of mesenchymal stem cells. Osteoarthritis Research Society International. 2013.4.18-21. Philadelphia
6. Koji Otabe, Hiroyuki Nakahara, Akihiko Hasegawa, Martin Lotz, Hiroshi Asahara. (2013) Tenogenic effect of transcription factor Mohawk for bone marrow mesenchymal stem cells. ACR/ARHP Annual Meeting. 2013.10.26-30.

<招待講演>

(海外)

1. Ichiro Sekiya. Arthroscopic transplantation of synovial MSCs for cartilage regeneration. Sportsclinic Germany. 2013.9.30. Hannover, Germany
2. Ichiro Sekiya. Arthroscopic transplantation of synovial MSCs for cartilage regeneration. Maartenskliniek Woerden. 2013.10.2 Utrecht, Netherlands
3. Ichiro Sekiya. Cartilage and meniscus regeneration with synovial stem cells. Symposium on Materials and Regenerative Medicine. 2013.11.30. Taipei, Taiwan

JFCR Cancer Biology

1. Staffs

Visiting Professor	Takuro NAKAMURA
Visiting Professor	Kiyotaka SHIBA
Visiting Professor	Akihiro TOMIDA
Visiting Professor	Eiji HARA
Visiting Professor	Toru HIROTA
Visiting Associate Professor	Kengo TAKEUCHI

2. Purpose of Education

The molecular mechanisms of carcinogenesis are the main subjects of the course. Novel findings of the research fields on cellular senescence, cell-of-origin of tumors will be focused. Pathological and genetical approaches to human cancers such as malignant lymphoma and lung cancer are also introduced. The application of nanobiotechnology on cancer diagnostics and development of novel drug therapies are also important topics.

3. Research Subjects

- 1) Development of new cancer diagnostic tools using nanobiotechnology
- 2) Pathological analyses of malignant lymphoma
- 3) Identification of novel human cancer genes including fusion oncogenes.
- 4) Development of novel cancer drugs based on cancer biology
- 5) Development of novel animal models for human cancer
- 6) Regulation of cellular senescence that is important in carcinogenesis
- 7) Understanding of chromosomal instabilities in cancer

4. Publications

Original Articles

1. Yoshimoto S, Loo TM, Atarashi K, Kanda H, Sato S, Oyadomari S, Iwakura Y, Oshima K, Morita H, Hattori M, Honda K, Ishikawa Y, Hara E, Ohtani N. (2013). Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* 499, 97-101.
2. Ushijima M*, Mashima T*, Tomida A*+, Dan S, Saito S, Furuno A, Tsukahara S, Seimiya H, Yamori T, Matsuura M+. (*equally, +corresponding) Development of a gene expression database and related analysis programs for evaluation of anticancer compounds. *Cancer Sci.* 104:360-8, 2013.
3. Migita T, Okabe S, Ikeda K, Igarashi S, Sugawara S, Tomida A, Taguchi R, Soga T, Seimiya H. Inhibition of ATP Citrate Lyase Induces an Anticancer Effect via Reactive Oxygen Species: AMPK as a Predictive Biomarker for Therapeutic Impact. *Am J Pathol.* 182:1800-10, 2013.
4. Sano, K., Miura, A., Yoshii, S., Okuda, M., Fukuta, M., Uraoka, Y., Fuyuki, T., Yamashita, I., and Shiba, K. (2013). Nonvolatile flash memory based on biologically integrated hierarchical nanostructures. *Langmuir* 29, 12483-9.
5. Yuasa, K., Kokubu, E., Kokubun, K., Matsuzaka, K., Shiba, K., Kashiwagi, K., and Inoue, T. An artificial fusion protein between BMP-2 and TBP is functional in vivo. *J Biomed Mater Res A* 102, 1180-6.
6. Ando, K., Ozaki, T., Hirota, T., Nakagawara, A. (2013) NFBD1/MDC1 is phosphorylated by Plk1 and controls G2/M transition through the regulation of Topoisomerase II alpha-mediated decatenation checkpoint. *PLoS One*, 8: e82744
7. Earnshaw, WC., Allshire, RC., Black, BE., Bloom, K., Brinkley, BR., Brown, W., Cheeseman, IM., Choo, KHA., Copenhaver, GP., DeLuca, JG., Desai, A., Diekmann, S., Erhardt, S., Fitzgerald-Hayes, M., Foltz, D., Fukagawa, T., Gassmann, R., Gerlich, DW., Glover, DM., Gorbsky, GJ., Harrison, SC., Heun, P., Hirota, T., Jansen, LET., Karpen, G., Kops, GJP., Lampson, MA., Lens, SM., Losada, A., Luger, K., Maiato, H., Maddox, PS., Margolis, RL., Masumoto, H., McAinsh, AD., Mellone, BG., Meraldi, P., Musacchio, A., Oegema, K., O'Neill, RJ., Salmon, ED., Scott, K., Straight, AF., Stukenberg, PT., Sullivan, BA., Sullivan, KF., Sunkel, CE., Swedlow, JR., Walczak, CE, Warburton, PE., Westermann, S., Willard, HF., Wordeman, L., Yanagida, M., Yen, TJ., Yoda, K., Cleveland, DW. (2013) Esperanto for Histones: CENP-A, not CenH3, is the centromeric histone H3 variant. *Commentary. Chromosome Res.* 21: 101-106.
8. Itoh, G., Sugino, S., Mizuguchi, M., Kanno, S., Amin, MA., Iemura, K., Ikeda, M., Yasui, A., Hirota, T., Tanaka, K. (2013) The nucleoporin Nup188 is required for chromosome alignment in mitosis. *Cancer Sci.* 104: 871-879
9. Kon S, Minegishi N, Tanabe K, Watanabe T, Funaki T, Wong WF, Sakamoto T, Higuchi Y, Kiyonari H, Asano K,

- Iwakura Y, Fukumoto M, Osato M, Sanada M, Ogawa S, Nakamura T, Satake M. (2013). Smad1 deficiency perturbs receptor trafficking and predisposes mice to myelodysplasia. *J Clin Invest.* 123: 1123-1137.
10. Nagamachi A, Matsui H, Asou H, Ozaki Y, Aki D, Kanai A, Takubo K, Suda T, Nakamura T, Wolff L, Honda H, Inaba T. (2013). Haploinsufficiency of SAMD9L, an endosome fusion facilitator, causes myeloid malignancies in mice mimicking human diseases with monosomy 7. *Cancer Cell.* 24: 305-317.

Biomedical Devices and Instrumentation

1. Staffs and Students (April 2013)

Professor	Kohji MITSUBAYASHI	
Assistant Professor	Takahiro ARAKAWA	
Lecturer (part-time)	Kazuyoshi YANO	
Research Staff	Munkhjargal MUNKHBAYAR	
Graduate Student	Elito KAZAWA,	Tomoko GESSEI,
	Kumiko MIYAJIMA,	Ming YE,
	Koji MIZUKOSHI,	Rei SATO,
	Sota YAMASHITA,	Yusuke KUROKI,
	Toshiyuki SATO,	Yurika SUZUKI,
	Hiroyuki TAKAGI,	Daisuke MIKI,
	Hidehisa MORI	

2. Education

We provide opportunity to study advanced biomedical devices and instrumentation. Students in our laboratory are working on the research projects as follows.

3. Research Subjects

1) Soft contact-lens biosensor

Based on advanced polymer microelectromechanical systems (MEMS) techniques, a soft contact-lens biosensor have been developed. The biosensor provides novel biomonitoring such as glucose monitoring in tear fluids.

2) Biological odor measurement and smell communication

High selective gas-sensors “Bio-sniffers” have been constructed with molecular recognition of enzyme in human liver. Potential applications of the bio-sniffer and -nose includes halitosis analysis, breath alcohol & aldehyde measurement, environmental VOC monitoring, etc.

3) Spatiotemporal gas visualization system for imaging of ‘odor’ information

A visualization system for spatial distribution of volatile chemicals have been developed. The visualization system is expected to be used in future medical screening or dental health.

4) ‘Organic engine’ based on chemo-mechanical energy conversion

A novel chemo-mechanical energy conversion system (organic engine) that utilizes enzyme reactions and active transport of chemicals have been constructed. Biomedical applications (chemical pumps, drug release systems, etc.) are also investigated.

4. Publications

Original Article

- Miyajima K, Miki D, Arakawa T, Kudo H, Saito H, Mitsubayashi K, Fiber-optic Fluoroimmunoassay for Determination of Dermatophagoides farinae Allergen by Flow Analysis Technique, *Sensors and Materials*, 25(9), 591-599, 2013.
- Munkhjargal M, Matsuura Y, Hatayama K, Miyajima K, Arakawa T, Kudo H, Mitsubayashi K, Glucose-sensing and glucose-driven “organic engine” with co-immobilized enzyme membrane toward autonomous drug release systems for diabetes, *Sensors and Actuators B: Chemical*, vol. 188, 831-836, 2013.
- Arakawa T, Wang X, Kajiro K, Miyajima K, Takeuchi S, Kudo H, Yano K, Mitsubayashi K, A direct gaseous ethanol imaging system for analysis of alcohol metabolism from exhaled breath, *Sensors and Actuators B: Chemical*, 186, 27-33, 2013.
- Arakawa T, Ando E, Wang X, Miyajima K, Takeuchi S, Kudo H, Saito H, Takahashi M, Mitani T, Mitsubayashi K, Chemiluminescent visualization for evaluation of gaseous ethanol distribution during ‘La France’ pear maturation, *IEEE Sensors Journal*, vol. 13, No. 8, 2842-2848, 2013.
- Kudo H, Yamashita T, Miyajima K, Arakawa T, Mitsubayashi K, NADH-fluorometric Biochemical Gas sensor (bio-sniffer) for Evaluation of Indoor Air Quality, *IEEE Sensors Journal*, vol. 13, No. 8, 2828-2833, 2013.
- Miyajima K, Koshida T, Arakawa T, Kudo H, Saito H, Yano K, Mitsubayashi K, Fiber-Optic Fluoroimmunoassay System with a Flow-Through Cell for Rapid On-Site Determination of Escherichia coli O157:H7 by Monitoring Fluorescence Dynamics, *Biosensors*, 3(1), 120-131, 2013.

Biomedical Information

1. Staffs and Students (April, 2013)

Professor	Kenji YASUDA
Associate Professor	Fumimasa NOMURA
Assistant Professor	Hideyuki TERAZONO
Project Assistant Professor	
Graduate Student	

2. Purpose of Education

Medical instrument (Biomedical information) is a branch of institute of biomaterials and bioengineering which deals with the measurement of epigenetic information and memorization stored in living system such as brain (neural network system), immune system, and cardio systems caused by environmental hysteresis. Main objective of medical instrument in the graduate course is to provide students opportunity to study fusion of latest technologies of nano- and bio-tech, and to develop artificial organ model on chip for drug discovery and toxicology use.

3. Research Subjects

- 1) Studies on Epigenetic Information Stored Living System.
- 2) Constructing "On-chip Organ Model" using Nano-Bio Technology.
- 3) Bio-computing using "Real Neural Network on Chip".
- 4) New Drug Discovery Technology applying Single Molecule Measurement.

4. Publications

Original Articles

1. Yasuda K, Hattori A, Hyonchol K, Terazono H, Hayashi M, Takei H, Kaneko T, Nomura F: Non-destructive on-chip imaging flow cell-sorting system for on-chip cellomics. *Microfluid Nanofluid* 14(6): 907-931, 2013.
2. Yasuda K: On-Chip Cellomics: Single-Cell-Based Constructive Cell-Network Assay for Quasi-In Vivo Screening of Cardiotoxicity. *Proceedings of 35th Annual International Conference of IEEE EMBS* 2825, 2013.
3. Kaneko T, Takizawa E, Nomura F, Hamada T, Hattori A, Yasuda K: On-Chip Single-Cell-Shape Control Technology for Understanding Contractile Motion of Cardiomyocytes Measured Using Optical Image Analysis System. *Jpn J Appl Phys* 52: 06GK06, 2013.
4. Hamada H, Kaneko T, Nomura H, Yasuda K: Physiological Sample Uniformity and Time-Course Stability in Lined-Up Structure of Human Cardiomyocyte Network for In vitro Predictive Drug-Induced Cardiotoxicity. *Jpn J Appl Phys* 52: 06GK05, 2013.
5. Terazono H, Hattori A, Kim H, Takei H, Nomura F, Kaneko T, Yasuda K: Temperature-Shift Speed Dependence of Nonspecific Amplification of Polymerase Chain Reaction Examined by 1480nm Photothermal Transition Speed Controllable High-Speed Polymerase Chain Reaction System. *Jpn J Appl Phys* 52: 06GK02, 2013.
6. Nomura F, Kaneko T, Hamada T, Hattori A, Yasuda K: Advanced Ring-Shaped Microelectrode Assay Combined with Small Rectangular Electrode for Quasi-In vivo Measurement of Cell-to-Cell Conductance in Cardiomyocyte Network. *Jpn J Appl Phys* 52: 06GK07, 2013.
7. Brunell C.A, Jokinen V, Sakha P, Terazono H, Nomura F, Kaneko T, Lauri S.E, Franssila S, Rivera C, Yasuda K, Huttunen H.J: Microtechnologies to fuel neurobiological research with nanometer precision. *J Nanobiotech* 11: 11, 2013.
8. Hamada H, Nomura F, Kaneko T, Yasuda K, Okamoto M: Exploring the implicit interlayer regulatory mechanism between cells and tissue: Stochastic mathematical analyses of the spontaneous ordering in beating synchronization. *BioSystems* 111: 208-215, 2013.

Invited Talks

1. Kenji Yasuda. On-chip cardiomyocyte network screening assay for predictive cardiotoxicity. HESI Cardiac Safety Committee Workshop: Stem Cell-Derived Cardiomyocytes as Models of Cardiac Pathobiology and Toxicity, Cambridge, USA, March 2013
2. Kenji Yasuda. On-chip quasi-in vivo cardiomyocyte network screening assay for predictive cardiotoxicity beyond hERG and QT assays. *Stem Cells & Cell Signaling -2013 Meeting*, Waltham, USA, May 2013

3. Kenji Yasuda. On-chip quasi-in vivo pre-clinical cardiac toxicity: Testing compounds beyond hERG and QT assay using spatiotemporal human cardiomyocytes measurement. Collectis Science seminar “Stem cells in Drug Discovery”, Tokyo, May 2013
4. Kenji Yasuda. On-Chip Cellomics: Single-Cell-Based Constructive Cell-Network Assay for Quasi-In Vivo Screening of Cardiotoxicity. 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC'13), Osaka, Japan, July 2013
5. Kenji Yasuda. On-Chip Quasi-In Vivo iPS Cardiomyocyte Network Screening Assay for Predictive Cardiotoxicity beyond hERG and QT Assays. 5th TMDU International Summer Program Symposium 2013, Tokyo, Japan, August 2013
6. Kenji Yasuda. Development of Screening Technology of Circulating Tumor Cells Using Multi-imaging Cell Sorter. Bio Japan 2013, Tokyo, Japan, October 2013
7. Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Akihiro Hattori. On-chip cellomics technology for studying dynamics of cellular networks. 5th Hiroshima Conference on Education and Science in Dentistry, Hiroshima, Japan, October 2013

Meetings

1. Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Quasi-in Vivo Electrocardiogram Measurement Using Convolution of Field Potential Propagation in the On-Chip Cardiomyocytes Network Circuit. Biophysical Society 56th Annual Meeting, San Diego, USA, Feb. 2012.
2. Tomoyo Hamada, Fumimasa Nomura, Hideyuki Terazono, Akihiro Hattori, Peter Sartipy, Mitsuhiro Edagawa, Thomas Meyer, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (I). Development of spatial conductance fluctuation measurement assay using a human cardiomyocyte line-network cell chip with multielectrode array system for in vitro predictive proarrhythmic cardiotoxicity. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
3. Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (II). Importance of spatial arrangement of cardiomyocyte network for precise and stable in vitro drug screening measurement. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
4. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Tomoyo Hamada, Fumimasa Nomura, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (III): Noninvasive Identification and Purification Method of Target Cardiomyocyte Cells Using Nuclease Digestive Magnet-Beads-Attached ssDNA Aptamers. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
5. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Fumimasa Nomura, Tomoyo Hamada, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (IV): Fabrication of Direction-Controlled Artificial Neuronal Networks Using Agarose-Microetching Method and Single-Cell-Electrodes for Quantitative Evaluation of Neuropsychiatric Disorders. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
6. Yumiko Asahi, Yasuyuki Abe, Kiyoshi Takasuna, Atsushi Sanbuissho, Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada. Evaluation of Fluctuation of Temporal Field Potential Duration and Spatial Conduction Time in Linear Network of Human-iPS Cell Derived Cardiomyocytes for Predictive Cardiotoxicity Measurement. Safety Pharmacology Society 13th Annual Meeting, Rotterdam, Netherlands, Sep. 2013.
7. Hyonchol Kim, Hideyuki Terazono, Hiroyuki Takei, Kenji Yasuda. Fabrication of Cup-Shaped Superparamagnetic Metal Hemispheres for Size-Selective Target Cell Collection. MNC2013, Sapporo, Japan, Nov. 2013.
8. Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Matsu-ura, Hideyuki Terazono, Kenji Yasuda. Importance of Spatial Arrangement of Cell Network Patterns for Precise and Stable Measurement of in Vitro Properties of Cells. MNC2013, Sapporo, Japan, Nov. 7. 2013.
9. Akihiro Hattori, Hyonchol Kim, Kenji Yasuda. Development of On-chip Flow Cytometry System based on Bright Field/Fluorescent Dual-image Analysis. MNC2013, Sapporo, Japan, Nov. 2013.
10. Kenji Matsuura, Akihiro Hattori, Fumimasa Nomura, Tomoyo Hamada, Hideyuki Terazono, Kenji Yasuda. Quantitative Evaluation of Origin of Changes in Electrophysiological Properties of Cells on Micro Electrodes using Impedances Analysis Measurement Setup. MNC2013, Sapporo, Japan, Nov. 2013.
11. Hideyuki Terazono, Hyonchol Kim, Hiroyuki Takei, Akihiro Hattori, Kenji Yasuda. Development of Ultra-high-speed Microfluidic Submicron-droplet PCR Device using Circulating Water System and a photo detector. MNC2013, Sapporo, Japan, Nov. 2013.

Bioelectronics

1. Staffs and Students

Professor	Yuji MIYAHARA	
Associate Professor	Akira MATSUMOTO	
Assistant Professor	Tatsuro GODA	
Project Assistant Professor	Yasuhiro MAEDA	
Project Assistant Professor	Mai SANJOH	
Project Assistant Professor	Miyuki TABATA	
Graduate Student	Eriko YAMADA, Yurika KATAYAMA, Takahiro ARAI,	Daisuke IIZUKA, Keitaro NAGASAKA, Yuuki IMAIZUMI

2. Purpose of Education

- (1) Charge: A part of the lecture of biomedical engineering for master's course, a part of the lecture of bio-intelligence science as a graduate education, and the research guidance of the master and the doctor's course are done.
- (2) Scope: A lot of biochemical components in serum play an important role in the metabolic cycle, and the homeostasis of those concentrations appears as a result of dynamic equilibrium in the living body. When some change takes place in this metabolic pathway, concentration of biochemical component shifts from the reference value. The detection methodology of the biochemical components and control mechanism of their concentration are studied from the viewpoint of integration of the materials science and the device technology, with biological and medical science.
- (3) Knowledge and the technology to be acquired: The processing methods for DNA, proteins, and cells, are acquired. The techniques for measuring the function of the biomolecules and the cells are actually experienced, and the operational theories and principles studied are confirmed. By participating in the on-going research in this laboratory, the meaning of the experiment, how to make the research plan, how to advance the research, and how to analyze the results are learnt.

3. Research Subjects

1. Study on chemical modification and nano-structure formation at the solid/liquid interface for efficient biomolecular recognition
Interaction between materials surfaces and biomolecules, cell, and organisms plays an important role for designing many biosensors, biochips, and biomaterials. In order to realize effective biomolecular recognition on the surface of a substrate material, functional nano-interface is investigated through chemical modification and formation of nano-structures at the solid/liquid interface.
2. Study on signal transduction mechanism for biomolecular and cellular activities
Electrostatic interaction between biomolecules and semiconductor materials and devices is investigated to elucidate mechanism for signal transduction from biomolecular recognition into electrical signals. In order to achieve compatibility between biomolecules and semiconductor materials, functional interface molecules are designed and synthesized at the bio/semiconductor interface for efficient signal transduction. Based on these studies on detection methodologies for biomolecules and cell functions, new types of bio-transistors are studied for medical and pharmaceutical applications.
3. Synthesis of biofunctional polymer and development of bio-regulation system
Through the design of functional polymers that are able to imitate, recognize and feedback information to biology, develop novel materials and devices that assist in medicine and biology. These include alternative materials and devices to insufficiency of the body, nano-materials that realize new mode of pharmacokinetics in cells as well as live cell imaging technologies.
4. Fundamental study on Bioelectronics
Interdisciplinary field between biotechnology and electronics is explored and investigated. Cell-based biotransistors employing signal processing inside cells are investigated for application to life science field. Information processing devices using both electrons and ions as information carriers are investigated for new types of information processing.

4. Publications

Original Articles

1. Deshayes S, Cabral H, Ishii T, Miura Y, Kobayashi S, Yamashita T, Matsumoto A, Miyahara Y, Nishiyama N,

- Kataoka K. Phenylboronic acid-installed polymeric micelles for targeting sialylated epitopes in solid tumors. *J Am Chem Soc* 135(41): 15501-15507, 2013.
2. Goda T, Tabata M, Sanjoh M, Uchimura M, Iwasaki Y, Miyahara Y. Thiolated 2-Methacryloyloxyethyl Phosphorylcholine for an Antifouling Biosensor Platform. *Chem Commun* 49(77): 8683-8685, 2013.
 3. Matsumoto A, Matsumoto H, Maeda Y, Miyahara Y. Simple and Robust Strategy for Potentiometric Detection of Glucose Using Fluorinated Phenylboronic Acid Self-assembled Monolayer. *BBA - Gen. Subjects* 1830(9): 4359-4364, 2013.
 4. Goda T, Singi B A, Maeda Y, Matsumoto A, Torimura M, Aoki H, Miyahara Y. Label-free Potentiometry for Detecting DNA Hybridization using Peptide Nucleic Acid and DNA Probes. *Sensors* 13(2): 2267-2278, 2013.
 5. Goda T, Miyahara Y. Label-free and Reagent-less Protein Biosensing using Aptamer-modified Extended-gate Field-effect Transistors. *Biosens. Bioelectron* 45: 89-94, 2013.

Books and Reviews

1. Goda T, Miyahara Y. Aptamer Nanostructures as Signaling Molecular Switches in Electrochemical Biosensing. In: Nanotechnology, Volume 10 Nanosensing (eds.: N. K. Navaani, S. Sinha, J. N. Govil), Studium Press LLC, USA, Chapter 3, 37-58, 2013.
2. Matsumoto A, Miyahara Y. Current and emerging challenges in field effect transistor based bio-sensing. *Nanoscale*, 5 (22): 10702-10718, 2013.
3. Tabata M, Goda T, Matsumoto A, Miyahara Y. Biotransistor with Functional Nanointerface Containing Biomolecules" (in Japanese), *IEEEJ Transactions on Sensors and Micromachines*, 133(11), B314-B319 (2013)
4. Matsumoto A, Ishii, T, Kataoka K, Miyahara Y. Glucose-Responsive Gel for Self-Regulated Insulin Delivery System" (in Japanese), *Drug Delivery System*, 28-2, 119-126 (2013).

Material-Based Medical Engineering

1. Staffs and Students

Professor	Akio KISHIDA	
Associate Professor	Tsuyoshi KIMURA	
Assistant Professor	Kwangwoo NAM	
Secretary	Naomi HIWATARI	
Graduate Student	Naoko NAKAMURA,	PingLi WU,
	Mitsuki UEKI,	YongWei ZHANG,
	Satoshi HONDA,	Ai ITO,
	Satoshi INADA,	Takuya IWATA

2. Purpose of 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. Research Subjects

1) 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.

2) 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.

3) 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.

4. Clinical Services

The development of functional molecules can provide novel materials for the clinical application such as blood vessel, cornea, skin, or bone. Unlike the conventional materials which have been used in clinics so far, it would be possible to promote or suppress specific biological response using functionalized materials. Furthermore, the screening essential drug compound for certain purpose, it would help the patients to be treated with higher efficiency and less pain.

5. Publications

- 1) Ji-HunSeo, S. Kakinoki, Y. Inoue, K. Nam, T. Yamaoka, K. Ishihara, A. Kishida, N. Yui, The significance of hydrated surface molecular mobility in the control of the morphology of adhering fibroblasts, *Biomaterials* 34(13):3206-3214, 2013.
- 2) N. Murakami, N. Wakabayashi, R. Matsushima, A. Kishida, Y. Igarashi, Effect of high-pressure polymerization on mechanical properties of PMMA denture base resin, *J. Mech. Behav. Biomed. Mater.*20:98-104, 2013.
- 3) N. Katoh, A. T. Kawaguchi, A. Kishida, T. Yamaoka, Static Cardiomyoplasty With Synthetic Elastic Net Suppresses Ventricular Dilatation and Dysfunction After Myocardial Infarction in the Rat: A Chronic Study, *Artif. Organs* 37(7):593-599, 2013.
- 4) T. Kimura, A. Sano, K. Nam, K. Akiyoshi, Y. Sasaki, A. Kishida, Improvement of Antisense Oligonucleotides Delivery Using High Hydrostatic Pressurized Lipoplex, *Proceedings of 2012 MRS fall meeting MRS Proceedings*, vol 1498
- 5) Y. Sawa, E. Tatsumi, T. Tsukiya, K. Matsuda, K. Fukunaga, A. Kishida, T. Masuzawa, G. Matsumiya, A. Myoui, M. Nishimura, T. Nishimura, T. Nishinaka, E. Okamoto, *Journal of Artificial Organs* 2012: the year in review, *Journal of Artificial Organs* 16(1): 1-8, 2013.

Organic and Medicinal Chemistry

1. Staffs and Students (April 2013)

Professor	Hiroyuki KAGECHIKA	
Assistant Professor	Shinya FUJII (-2012 11)	
Assistant Professor	Syuichi MORI	
Assistant Professor	Mari YUASA	
Graduate Student	Takashi FUJIWARA,	Minoru IMAI,
	Takuya SHIRAIISHI,	Shotaro IIHAMA,
	Kanako OSHIRO,	Kasumi OHIRA,
	Toshiki SAITO,	Haruka TSUKADA,
	Kenji, HATTA,	Yohei WATANABE,
	Honoka SUZUYAMA	

2. Purpose of Education

Organic and Medicinal Chemistry covers several aspects of organic chemistry, medicinal chemistry and chemical biology. Through this course, students are expected to understand the fundamental knowledge, recent topics, and experimental techniques related to these fields.

3. Research Subject

1) Medicinal Chemistry of Retinoids

Retinoids regulates various significant biological phenomena, such as cell differentiation, proliferation, morphogenesis, metabolism and homeostasis. We have developed novel synthetic retinoid, Am80 (tamibarotene) as drug for acute promyelocytic leukemia. Novel synthetic retinoids have been developed for clinical use in the field of autoimmune diseases, neurodegenerative diseases, metabolic syndromes.

2) Medicinal Chemistry of Nuclear Receptors

Small hydrophobic molecules such as steroid hormones and activated vitamins A/D control various biological phenomena, including growth, development, metabolism, and homeostasis, by binding to and activating specific nuclear receptors. Nuclear receptors have become one of the most significant molecular targets for drug discovery in the fields of cancer, metabolic syndrome, autoimmune diseases, and so on. In this project, novel ligands of various nuclear receptors have been developed.

3) Development of Novel Functional Fluorescent Molecules for Elucidation of Intracellular Signal Transduction Pathways

Functional fluorescent molecules useful in many fields of scientific research, including analytical chemistry or cell biology have been developed.

4) Aromatic Architecture Based on the Steric Properties of *N*-Methylated Amides

The amide bond structure of amide derivatives often plays a key role in functions such as molecular recognition events or biological activities. In contrast to the extended trans structures of most secondary amides, the corresponding *N*-methylated compounds exist in cis form in the crystals and predominantly in cis form in various solvents. The cis conformational preference is useful as a building block to construct aromatic molecules with unique crystal or solution structures.

4. Publications

Original articles

- Fujii, S., Miyajima, Y., Masuno, H., Kagechika, H. Increased Hydrophobicity and Estrogenic Activity of Simple Phenols with Silicon and Germanium-Containing Substituents. *J. Med. Chem.* 56: 160-166, 2013.
- Ohta, K., Kawachi, E., Shudo, K., Kagechika, H. Structure-activity relationship study on benzoic acid part of diphenylamine-based retinoids. *Bioorg. Med. Chem. Lett.* 23: 81-84, 2013.
- Niwa, H., Handa, N., Tomabechi, Y., Honda, K., Toyama, M., Ohsawa, N., Shirouzu, M., Kagechika, H., Hirano, T., Umehara, T., Yokoyama, S. Structures of histone methyltransferase SET7/9 in complexes with adenosylmethionine derivatives. *Acta Cryst. D*69: 595-602, 2013.
- Matsumura, M., Tanatani, A., Azumaya, I., Masu, H., Hashizume, D., Kagechika, H., Muranaka, A., Uchiyama, M. Unusual conformational preference of an aromatic secondary urea: solvent-dependent open-closed conformational switching of *N,N'*-bis(porphyrinyl)urea. *Chem. Commun.* 49: 2290-2292, 2013.

5. Persaud, S. D., Lin, Y.-W., Wu, C.-Y., Kagechika, H., Wei, L.-N. Cellular retinoic acid binding protein I mediates rapid non-canonical activation of ERK1/2 by all-trans retinoic acid. *Cell. Signal.* 25: 19-25, 2013.
6. Sagara, C., Takahashi, K., Kagechika, H., Takahashi, N. Molecular mechanism of 9-cis-retinoic acid inhibition of adipogenesis in 3T3-L1 cells. *Biochem. Biophys. Res. Commun.* 433: 102-107, 2013.
7. Kanazawa, J., Takita, R., Jankowiak, A., Fujii, S., Kagechika, H., Hashizume, D., Shudo, K., Kaszyński, P., Uchiyama, M. Copper-mediated C-C cross-coupling reaction of monocarba-closo-dodecaborate anion for construction of functional molecules. *Angew. Chem. Int. Ed.*, 52: 8017-8021, 2013.
8. Takeuchi, H., Yokota-Nakatsuma, A., Ohoka, Y., Kagechika, H., Kato, C., Si-Young Song, S.-Y., Iwata, M. Retinoid X Receptor Agonists Modulate Foxp3 + Regulatory T Cell and Th17 Cell Differentiation with Differential Dependence on Retinoic Acid Receptor Activation. *J. Immunol.* 191: 3725-3733, 2013.
9. Mori, T., Kikuchi, E., Watanabe, Y., Fujii, S., Ishigami-Yuasa, M., Kagechika, H., Sohara, E., Rai, T., Sasaki, S., Uchida, S. Chemical library screening for WNK signalling inhibitors using fluorescence correlation spectroscopy. *Biochem. J.* 455: 339-345, 2013.
10. Matsumura, M., Tanatani, A., Kaneko, T., Azumaya, I., Masu, H., Hashizume, D., Kagechika, H., Muranaka, A., Uchiyama, M. Synthesis of porphyrinylamide and observation of N-methylation-induced trans-cis amide conformational alteration. *Tetrahedron* 69: 10927-10932, 2013.
11. Hurst, R. J. M., De Caul, A., Little, M. C., Kagechika, H., Else, K. J. The Retinoic Acid Receptor Agonist Am80 Increases Mucosal Inflammation in an IL-6 Dependent Manner During *Trichuris muris* Infection. *J. Clin. Immunol.* 33: 1386-1394. 2013.
12. Yamada, A., Fujii, S., Mori, S., Kagechika, H. Design and synthesis of 4-(4-benzoylamino-phenoxy)phenol derivatives as androgen receptor antagonists. *ACS Med. Chem. Lett.* 24: 937 – 941, 2013.

Chemical Bioscience

1. Staffs and Students

Professor	Takamitsu HOSOYA	
Assistant Professor	Suguru YOSHIDA,	Yuto SUMIDA
Technical Assistant	Tomoe KATO, Yoshihiro MISAWA, Koji MITSUI	Takako NONAKA, Miyuki OKUYAMA,
Clerical Assistant	Naomi SAITA	
Graduate Students	Ryu HARADA, Junko TANAKA,	Takamoto MORITA, Yasutomo HATAKEYAMA
Graduate Research Students	Keisuke UCHIDA	
Collaborators	Ken SHIMOMORI	

2. Purpose of Education

Acquire specialized knowledge and techniques for developing new organic synthetic methods, new chemical methodologies, and new chemical tools, those are useful for biological and drug discovery researches.

3. Research Subjects

- 1) Development of new generation and application methods of aryne for the synthesis of various aromatic compounds.
- 2) Development of new bioconjugation methods using strained alkynes.
- 3) Target identification of drugs or drug candidates by photoaffinity labeling based on diazido probe method.
- 4) Development of new molecular ligation methods based on new azido chemistry.
- 5) Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
- 6) Design and synthesis of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

4. Publications

Original Articles

1. Yoshida S, Hosoya T. Synthesis of diverse aromatic oxophosphorus compounds by the Michaelis–Arbuzov-type reaction of arynes. *Chem Lett*, 42(6): 583-585, 2013.
2. Sumida Y, Kato T, Hosoya T. Generation of Arynes via Ate Complexes of Arylboronic Esters with an *ortho*-Leaving Group. *Org Lett*, 15(11): 2806-2809, 2013.
3. Inouye S, Sahara–Miura Y, Sato J-i, Iimori R, Yoshida S, Hosoya T. Expression, purification and luminescence properties of coelenterazine-utilizing luciferases from *Renilla*, *Oplophorus* and *Gaussia*: Comparison of substrate specificity for C2-modified coelenterazines. *Protein Expres Purif*, 88(1): 150-156, 2013.
4. Inouye S, Sato J-i, Sahara–Miura Y, Yoshida S, Kurakata H, Hosoya T. C6-Deoxy coelenterazine analogues as an efficient substrate for glow luminescence reaction of nanoKAZ: the mutated catalytic 19 kDa component of *Oplophorus* luciferase. *Biochem Biophys Res Commun*, 437(1): 23-28, 2013.
5. Koyama H, Zhang Z, Ijuin R, Siqin, Son J, Hatta Y, Ohta M, Wakao M, Hosoya T, Doi H, Suzuki M. Pd⁰-mediated rapid coupling of methyl iodide with excess amounts of benzyl- and cinnamylboronic acid esters: efficient method for incorporation of positron-emitting ¹¹C radionuclide into organic frameworks by coupling between two sp³-hybridized carbons. *RSC Adv*, 3(24): 9391-9401, 2013.
6. Miyajima M, Kusuhara H, Takahashi K, Takashima T, Hosoya T, Watanabe Y, Sugiyama Y. Investigation of the effect of active efflux at the blood–brain barrier on the distribution of nonsteroidal aromatase inhibitors in the central nervous system. *J Pharm Sci*, 102(9): 3309-3319, 2013.
7. Tanaka K, Nakamoto Y, Siwu ERO, Pradipta AR, Morimoto K, Fujiwara T, Yoshida S, Hosoya T, Tamura Y, Hirai G, Sodeoka M, Fukase K. Development of bis-unsaturated ester aldehydes as amino-glue probes: Sequential double azaelectrocyclization as promising strategy for bioconjugation. *Org Biomol Chem*, 11(42): 7326-7333, 2013.

Metallic Biomaterials

1. Staffs and Students

Professor	Takao HANAWA	
Associate Professor	Yusuke TSUTSUMI	
Assistant Professor	Hisashi DOI,	Maki ASHIDA
Research Assistant	Osamu FUKUSHIMA	
Project Assistant Professor	Peng CHEN	
Secretary	Toshie NAKANISHI,	Yasuko SEKI
Graduate Student	Takeru NISHISAKA	

2. Purpose of Education

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. Research Subjects

1) Bio-functionalization of metals with electrochemical 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 artifacts 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.

4. Publications

Original Articles

1. Imai H, Tanaka Y, Nomura N, Tsutsumi Y, Doi H, Kanno Z, Ohno K, Ono T, Hanawa T. Three-dimensional quantification of susceptibility artifacts from various metals in magnetic resonance images. *Acta Biomaterialia* 9: 8433-8439, 2013.
2. Zhu S, Xie G, Qin F, Wang X, Hanawa T. Ti particles dispersed Ti-based metallic glass matrix composite prepared by spark plasma sintering. *Materials Transactions* 54: 1335-1338, 2013.
3. Seki I, Umetsu R, Xie G, Nomura N, Wang X, Hanawa T. Cooling rate and composition dependences of magnetic susceptibility for $Zr_{54-x}Cu_{30+x}Al_8Ag_8$ glassy alloys. *Materials Transactions* 54: 1356-1360, 2013.
4. Hieda J, Niinomi M, Nakai M, Kamura H, Tsutsumi H, Hanawa T. Improvement of adhesive strength of segmented polyurethane on Ti-29Nb-13Ta-4.6Zr alloy through H_2O_2 treatment for biomedical application. *Journal of Biomedical Materials Research* 101B: 776-783, 2013.
5. Takaichi A, Suyalatu, Nakamoto T, Joko N, Nomura N, Tsutsumi Y, Migita S, Doi H, Kurosu S, Chiba A, Wakabayashi N, Igarashi Y, Hanawa T. Microstructures and mechanical properties of Co-29Cr-6Mo alloy fabricated by selected laser melting. *The Journal of the Mechanical Behavior of Biomedical Materials* 21: 67-79, 2013.
6. Kaneto M, Namura Y, Tamura T, Shimizu N, Tsutsumi Y, Hanawa T, Yoneyama T. Influence of electrolytic treatment time on the corrosion resistance of Ni-Ti orthodontic wire. *Dental Materials Journal* 32: 305-310, 2013.

7. Kondo R, Shimizu R, Nomura N, Doi H, Suyalatu, Tsutsumi Y, Mitsuishi K, Shimojo M, Noda K, Hanawa T. Effect of cold rolling on the magnetic susceptibility of the Zr-14Nb alloy. *Acta Biomaterialia* 9: 5795-5801, 2013.
8. Tsutsumi Y, Kobayashi E, Ogo M, Suyalatu, Migita S, Doi H, Nomura N, Noda K, Hanawa T. Accelerated calcium phosphate formation on titanium utilizing galvanic current between titanium and gold in Hanks' solution. *Materials Transactions* 54: 149-155, 2013.

Review Articles

1. Hanawa T. Research and development of metals for medical devices based on clinical needs. *Science and Technology of Advanced Materials* 13: 064102, 2013.

Books

1. Hanawa T. Metal-polymer composite biomaterial, *Polymeric Biomaterials. Structure and Function, Volume 1*, (S. Dumitriu, V. Popa Eds.), CRC Press, Boca Raton, FL, USA, 2013.

Molecular Cell Biology

1. Staffs and Students

Professor	Hiroshi Shibuya
Associate Professor	Toshiyasu Goto
Assistant Professor	Atsushi Sato
Graduate Students	Masahiro Shimizu

2. Purpose of Education

Various signaling molecules inducing the cell-growth and differentiation regulate morphogenesis and organogenesis of the vertebrate. The failure of these signal molecules has also been caused with induction of the diseases. Therefore, the elucidation of signal transduction network regulating generation and differentiation is important upon clarifying the mechanism of morphogenesis, organogenesis and diseases. Our research aim is to clarify the signal transduction network regulating the mechanisms of morphogenesis and organogenesis in developmental process. We serve these research and following education to provide graduate students who will become senior scientists in life sciences.

3. Research Subjects

- 1) Roles of WNK protein kinases signaling in early development.
- 2) Roles of IQGAP1 in the canonical Wnt signaling.

5. Publications

1. Sato, A. and Shibuya, H. (2013). WNK Signaling Is Involved in Neural Development via Lhx8/Awh Expression. **PLoS One** 8, e55301.
2. Shimizu, M., Goto, T., Sato, A. and Shibuya, H. (2013). WNK4 is an essential effector of anterior formation in FGF signaling. **Genes Cells** 8, 442-449.
3. Goto T., Michiue T., Ito Y., Asashima M. (2013). Characterization of CXC-type chemokine molecules in early *Xenopus laevis* development. **Int. J. Dev. Biol.** 57, 41-47.
4. Goto, T., Sato, A., Shimizu, M., Adachi, S., Satoh, K., Iemura, S, Natsume, T and Shibuya, H. (2013). IQGAP1 Functions as a Modulator of Dishevelled Nuclear Localization in Wnt Signaling. **PLoS One**, 8, e60865.
5. Goto. T, Sato, A., Adachi, S., Iemura, S., Natsume, T. and Shibuya, H. (2013). IQGAP1 regulates nuclear localization of β -Catenin via importin- β 5 in Wnt signaling. **J. Biol. Chem.**, 288, 36351-36360.

Developmental and Regenerative Biology

1. Staffs and Students (April, 2013)

Professor	Hiroshi NISHINA	
Associate Professor	Jun HIRAYAMA	
Assistant Professor	Yoichi ASAOKA	
Graduate Students	Eiichiro NODA,	Makoto YAMAMOTO

2. Purpose of Education

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.

3. Research Subjects

- 1) Studies on the stress-activated protein kinase (SAPK/JNK) signaling pathway
- 2) Studies on the Hippo signaling pathway
- 3) Studies on the cell differentiation of mouse ES cells
- 4) Studies on liver formation using a small fish, Medaka, *Oryzias Latipes*
- 5) Studies on liver regeneration using mice
- 6) Studies on circadian clock using zebrafish and mice

4. Publications

Original Article

1. Norie Arima¹, Yoshimi Uchida¹, Ruoxing Yu, Koh Nakayama and Hiroshi Nishina (2013) Acetylcholine Receptors Regulate Gene Expression that Is Essential for Primitive Streak Formation in Murine Embryoid Bodies. ***Biochem. Biophys. Res. Commun.*** 435, 447-453 (1Contributed equally)
2. Menno J. Oudhoff, Spencer A. Freeman, Amber L. Couzens, Frann Antignano, Ekaterina Kuznetsova, Paul H. Min, Jeffrey P. Northrop, Bernhard Lehnertz, Dalia Barsyte-Lovejoy, Masoud Vedadi, Cheryl H. Arrowsmith, Hiroshi Nishina, Michael R. Gold, Fabio M.V. Rossi, Anne-Claude Gingras, and Colby Zaph (2013) Control of the Hippo pathway by Set7-dependent methylation of Yap. ***Dev. Cell*** 26, 188-194.

Review Articles

1. Yoichi Asaoka, Shuji Terai, Isao Sakaida and Hiroshi Nishina (2013) [review] The expanding role of fish models in understanding non-alcoholic fatty liver disease (NAFLD). ***Disease Models & Mechanisms*** 6, 905-914.

Immunology

1. Staffs and Students

Professor	Takeshi TSUBATA, M.D., Ph.D.	
Associate Professor	Takahiro ADACHI, Ph.D.	
Assistant Professor	Mitsuhiro SUZUKI, Ph.D.	
Assistant Professor	Naoko MATSUBARA,	Miduo XU,
	Chizuru AKATSU,	
Lecturer	Ji-Yang WANG	
Researcher	Soha Gomaa Ramadan Abdel SALAM	
Technician	Yukie KURUSU,	Shigeko NAKANO,
	Haruka MIYAKE,	Ai BEPPU
Secretary	Hiroko TAKAHASHI	
Graduate Student	Miao TANG,	Toshitaro TAKATA,
	Aslam MOHAMMAD,	Ayse Ucar KONUSKAN,
	Sumiyo EZAKI,	Xuyang JIAO
Research Student	Nazim MEDZHIDOV	
Undergraduate Student	Mayo YOSHIOKA	

2. Purpose of Education

Lecture course on immunology at the master course aims at giving the students the basic ideas how immune system recognize and respond to the antigens, and how immune system efficiently remove pathogens without responding to self-antigens and environmental antigens. In the lecture course in bioscience at the doctor course, lectures on immune responses are given so that the students are introduced with the current topics in the field of humoral immune responses. Research projects in both master and doctor courses aims at training the students to acquire basic research techniques on immunology, molecular biology and biochemistry, and abilities to conduct cutting-edge research in the field of immunology by themselves under supervision.

3. Research Subjects

The nature of immune responses depends on whether they respond to protein or non-protein antigens because T lymphocytes recognize only protein antigens. Normal immune system removes pathogens and cancer cells but does not respond to non-microbial foreign substances or self-antigens. Immune responses to non-microbial foreign substances and self-antigens cause allergy and autoimmune diseases, respectively. How the immune system distinguishes pathogens from non-microbial antigens and self-antigens is already clarified for protein antigens. However, little is known about such distinction for non-protein antigens. Immune responses to non-protein antigens play crucial roles in host defense against pathogens such as tuberculosis bacilli and meningococci, and autoimmune diseases such as lupus and immuno-neurological disorders. Thus, immune responses to non-protein antigens constitute a remaining frontier in immunology research. Followings are our research subjects.

- 1) Elucidation of the mechanisms for humoral immune responses to glycans, glyco-lipids and nucleic acids-related antigens.
- 2) Elucidation of the role of glycan signals in the regulation of humoral immune responses, and application of glycan signals to therapy.
- 3) Analysis of pathogenesis of lupus and immuno-neurological disorders.

4. Publications

[Original Article]

1. Shimoda, M., Bolduc, A., Takezaki, M., Amtani, Y., Huang, L., Nutt S. L., Kamanaka, M., Flavell, R. A., Mellor A. L., Tsubata, T. and Koni, P. (2013): Constitutively CD40-activated B cells regulate CD8 T cell inflammatory response by IL-10 induction. *J. Immunol.* 190: 3189-3196.
2. Xu, M., Hou, R., Sato-Hayashizaki, A., Man, R., Zhu, C., Wakabayashi, C., Hirose, S., Adachi, T. and Tsubata, T. (2013): *CD72* is a modifier gene that regulates *Fas^{lpr}*-induced autoimmune disease. *J. Immunol.* 190: 5436-5445.
3. Aslam, M., Kishi, Y. and Tsubata, T. (2013): Excess CD40L does not rescue anti-DNA B cells from clonal anergy. *F1000 Research* 2:218.

4. Naito-Matsui, Y., Takada, S., Kano, Y., Iyoda, T., Sugai, M, Shimizu, A., Inaba, K., Nitschke, L., Tsubata, T., Oka, S., Kozutsumi, Y. and Takematsu, H. (2014): Functional evaluation of activation-dependent alterations in the sialoglycan composition of T cells. *J. Biol. Chem.* 289: 1564-1579.

Epigenetics

1. Staffs and Students

Professor	Fumitoshi ISHINO	
Associate Professor	Takashi KOHDA	
Assistant Professor	Ryuichi ONO	
Tokunin Lecturer	Jiyoung LEE	
Tokunin Assistant Professor	Mie NARUSE	
Adjunct Lecturer	Shin KOBAYASHI,	
Secretary	Ikuko MAEDA	
Graduate students	Mami OIKAWA,	Saori TAKAHASHI,
	Miki SOMA,	Kiyotaka TAKAGI,
	Moe KITAZAWA,	Ayumi Matsuzawa

2. Purpose of Education

“Epigenetics” coupled with “Genetics” enables us to elucidate several ‘genomic functions’ in inheritance, development and evolution of organisms including our human beings. Genomic imprinting is one of the mammalian specific gene regulation mechanisms that gives rise to functional differences between paternally- and maternally-derived genomes in development, behavior and growth. Somatic cloned animals give us unique chances to examine ‘genetically identical but epigenetically diverged animals’. These studies show us how Epigenetics is important in mammalian biology. Our department focuses these mammalian specific genomic functions to elucidate how these genomic functions work and how new genomic functions have been evolved during evolution. Our final goal is to contribute to the 21st’s medicine and human biology by novel understanding of genomic functions.

3. Research Subjects

- 1) Genomic imprinting in human and mammalian development.
- 2) Placenta function and its evolution in mammals.
- 3) Somatic cloning: its epigenetic effects and application to regenerative medicine.
- 4) Assisted reproductive technology: its epigenetic effects and safer application.
- 5) Role of retrotransposon-derived genes in mammalian specific genomic functions.

4. Publications

Original Article

1. Wakayama S, Kohda T, Obokata H, Tokoro M, Li C, Terashita Y, Mizutani E, Nguyen VT, Kishigami S, Ishino F and Wakayama T. Successful serial recloning in the mouse over multiple generations. **Cell Stem Cell** 12(3), 293-297 (2013).
2. Oikawa M, Matoba S, Inoue K, Kamimura S, Hirose M, Ogonuki N, Shiura H, Sugimoto M, Abe K, Ishino F and Ogura A. RNAi-mediated Knockdown of Xist Does Not Rescue the Impaired Development of Female Cloned Mouse Embryos. **J Reprod Dev** 59(3), 231-237(2013).
3. Iwasaki S, Suzuki S, Clark H, Ono R, Shaw G, Renfree MB, Kaneko-Ishino T and Ishino F. Identification of novel *PNMA-MSI* in marsupials suggests LTR retrotransposon-derived *PNMA* genes differently expanded in marsupials and eutherians. **DNA Res** 20(5), 425-436 (2013).
4. Nishimoto M, Katano M, Yamagishi T, Hishida T, Kamon M, Nabeshima Y, Nabeshima Y, Katsura Y, Satta Y, Deakin JE, Graves JAM, Kuroki Y, Ono R, Ishino, F, Okazaki Y, Kato H and Okuda A.. *In vivo* function and evolution of the eutherian-specific pluripotency marker *UTF1*. **PLoS One** 8(7):e68119 (2013).
5. Kobayashi S, Totoki Y, Soma M, Matsumoto K, Fujihara Y, Toyoda A, Sakaki Y, Okabe M and Ishino F. Identification of an imprinted gene cluster in the X-inactivation center. **PLoS One** 8(8):e71222 (2013).
6. Kawasaki Y, Lee J, Matsuzawa A, Kohda T, Kaneko-Ishino T and Ishino F. Active DNA demethylation is required for complete imprint erasure in primordial germ cells. **Sci Rep** (in press).

Review Articles

1. Kohda T and Ishino F. Embryo manipulation via assisted reproductive technology and epigenetic asymmetry in mammalian early development. (Review) **Philos Trans R Soc Lond B Biol Sci**, 368(1609):20120353 (2013).
2. Kohda T. Effects of embryonic manipulation and epigenetics. **J Hum Genet** 58(7):416-420. (2013)

Bioinformatics

1. Staffs and Students

Professor:	Hiroshi Tanaka	
Associate Professor:	Yoshihito Niimura (~March)	
Assistant Professor:	Kaoru Mogushi,	Masaki Suimye Morioka (July~)
Project Associate Professor:	Fengrong Ren	
Project Assistant Professor:	Takeshi Hase,	Kumiko Iijima
Graduate Students:	Yoshiyuki Kaneko,	Arihito Endo,
	Eiichi Ueno,	Kyoko Sugimoto,
	Sakiko Ohta,	Yasuha Tanaka,
	Hajime Sawai,	Asami Suzuki,
	Chikako Shimizu,	Shoko Nukaya,
	Hiroaki Hasegawa,	Aw Wanping,
	Noriaki Koizumi,	Akihiko Hoshi,
	Norihiko Inoue,	Tomohisa Maruyama,
	Ko Watanabe,	Sophia Subat,
	Asiya Hapaer,	Kota Koide,
	Jun-ya Hagiwara,	Toshihiro Takahashi,
	Kasumi Otsubo,	Norihiko Satake,
	Hirozumi Nishibe,	Miyo Okubo,
Te-cheng Chang		

2. Purpose of Education

Prof. Tanaka is in charge of the education of medical informatics and bioinformatics. For undergraduates, he teaches “Clinical Informatics”, “Statistics for Health Sciences”, “Practice in Clinical Informatics II”, “Project Research”, and “Basics of Clinical Informatics”. For graduate students, he teaches “Computational Biology”, “Systems Pathology”, “Clinical Informatics”, “Integrated Bioinformatics”, “Integrated Translational Research”, and “Statistics for Nurses”. He also teaches “Cancer Systems Biology” for the “Training Program for Specialists in Cancer”. In addition, Prof. Tanaka supervises 27 graduate students in total (22 PhD and 5 Master course students in Graduate School).

3. Research Subjects

Our mission is “system-level understanding of biological systems” in molecular biology and evolution (systems evolution) and medicine (omics-based medicine, systems pathology). Recently, the whole genome sequences of diverse organisms have become available. Moreover, various “omics” information such as a proteome, transcriptome, and metabolome are currently accumulating. Our goal is to establish a grand-theory of biological sciences from the viewpoint of “evolving networks composed of biological molecules” by integrating omics information. Genomic and omics data are also utilized in the field of medicine. It has been revealed that most diseases are caused by the interaction among abnormalities of multiple genes, those at the tissue level, and environments. It is therefore possible to consider diseases as a system. From this standpoint, we try to establish the omics-based medicine and systems pathology.

1) Protein interaction network analysis of Alzheimer’s disease

Alzheimer’s disease (AD) is the most common cause of dementia. It is characterized by senile plaques (deposits of amyloid-beta) and neurofibrillary tangles (NFTs; accumulations of hyperphosphorylated tau proteins). To date, many experimental drugs for AD have been developed based on amyloid-beta hypothesis. However, they do not show any clear effects, suggesting the presence of cross talks among biological molecules including known proteins. In addition, it is considered that the relationships among various molecules dynamically change with the progression of AD. In order to elucidate how protein interaction networks (PINs) change across Braak NFT stage known to be associated with expansion of NFTs across brain regions, we integrated the human protein interaction datasets and the gene expression profiles of three distinct brain regions (entorhinal cortex, hippocampus and superior frontal gyrus) dissected from postmortem brains of AD patients in each Braak NFT stage. Consequently, we found that the PIN in entorhinal cortex, which is affected in the early stage of AD, significantly collapsed with Braak NFT stage compared to that of normal aging. Furthermore, we identified deubiquitinating enzyme UCHL5 as one of responsible proteins provoking the network perturbation.

2) Analysis of disease mechanism using omics-based approaches

Recent advances in analysis techniques in molecular biology have led to the investigation of genome-wide data such as genome, transcriptome and proteome. In order to reveal the underlying biological mechanisms from such a large amount of “omics” data, integration of biomedical knowledge with multivariate statistical analyses or machine learning methods is one of the most crucial tasks for bioinformatics research. We performed collaborative researches with our university hospital and other institutes mainly based on genome-wide analysis techniques such as DNA microarray and next generation sequencing. Our research activities focus on the following topics: 1) identification of diagnosis markers for prognosis prediction in hepatocellular carcinoma patients, 2) development of predictive markers for metastatic relapse in colorectal cancer, and 3) drug repositioning research in chronic obstructive pulmonary disease.

3) Evolution of olfactory receptor genes in turtles

We participated in the International Turtle Genome Sequencing Consortium, a joint project of RIKEN CDB, BGI in China, Ensembl in UK etc., and performed evolutionary analyses of olfactory receptor (OR) genes in two turtle species, the soft-shell turtle and the green sea turtle. We found that, although the two turtles are aquatic, their genomes contain only group α and γ OR genes, which are specific to terrestrial vertebrates. We also showed that the fraction of group α genes is much higher than other amniotes ever examined and a large number of group α gene duplications have occurred in a turtle-specific manner. These observations may be related with their secondary adaptation to the aquatic life, because group α ORs tend to bind hydrophilic ligands.

4) Development of gene-set meta-analysis for omics data

Due to the advance of high-throughput technologies, researchers have proposed the use of omics data for the interpretation of biological phenomena. To address biological system signature in each omics data, a new method combined gene-set analysis (GSA) and meta-analysis will be promising for omics data, where it can reveal novel data features and improve research performance. We currently develop new omics approaches called gene-set meta-analysis (GSMA), by combining GSA and meta-analyses. Of them, biological system radar (BSR) employs a probability-based method and visualizes results by radar chart. BSR can successfully identify biological system-wide changes among multiple omics data-sets.

5) A network-guided module identification approach towards investigation of potential drug targets

A useful characteristic for identification of drug targets is modular structure in the human protein-protein interaction network. In networks with modular structure, interactions between proteins are much denser within a module than between modules. Proteins in a module have closely related functions with each other. If a module contains target proteins for a disease, proteins and interactions in the module could play important roles in disease mechanisms and may be potential candidate targets for the disease. In order to investigate potential drug targets, we analyzed modules in the human protein-protein interaction networks and found that drugs for different diseases target different modules in the network. For example, target modules for anti-Parkinson's are different from those for cancerous diseases. The listing of proteins and interactions in the modules for a given disease may help us to search more efficiently for drug action mechanisms and novel targets for the disease.

4. Publications

Original Article

1. Kikuchi, M., Ogishima, S., Miyamoto, T., Miyashita, A., Kuwano, R., Nakaya, R., Tanaka, H. (2013). Identification of Unstable Network Modules Reveals Disease Modules Associated with the Progression of Alzheimer's Disease. PLoS ONE, DOI: 10.1371/journal.pone.0076162.
2. Tanaka, Y., Nogata, H., Tanaka, H. (2013). Effect of Music upon Awakening from Nap. Biomedical Soft Computing and Human Sciences, 18(2):29-37.
3. Tanaka, K., Ishihara, T., Sugizaki, T., Kobayashi, D., Yamashita, Y., Tahara, K., Yamakawa, N., Iijima, K., Mogushi, K., Tanaka, H., Sato, K., Suzuki, H., Mizushima, T. (2013). Mepenzolate bromide displays beneficial effects in a mouse model of chronic obstructive pulmonary disease. Nature Communications, 4:2686.
4. Mogushi, K., Tanaka, H. (2013). PathAct: a novel method for pathway analysis using gene expression profiles. Bioinformatics, 9(8):394-400.
5. Ogishima, S., Mizuno, S., Kikuchi, M., Miyashita, A., Kuwano, R., Tanaka, H., Nakaya, J. (2013). A Map of Alzheimer's Disease-Signaling Pathways: A Hope for Drug Target Discovery. Clinical Pharmacology & Therapeutics, 93(5):399-401.
6. Muramatsu, S., Tanaka, S., Mogushi, K., Adikrisna, R., Aihara, A., Ban, D., Ochiai, T., Irie, T., Kudo, A., Nakamura, N., Nakayama, K., Tanaka, H., Yamaoka, S., Arii, S. (2013). Visualization of stem cell features in human hepatocellular carcinoma enlightened in vivo significance of tumor-host interaction and clinical implication. Hepatology, 58(1):218-28.

7. Takahashi, M., Obayashi, M., Ishiguro, T., Sato, N., Niimi, Y., Ozaki, K., Mogushi, K., Mahmut, Y., Tanaka, H., Tsuruta, F., Dolmetsch, R., Yamada, M., Takahashi, H., Kato, T., Mori, O., Eishi, Y., Mizusawa, H., Ishikawa, K. (2013). Cytoplasmic Location of alpha1A Voltage-Gated Calcium Channel C-Terminal Fragment (Cav2.1-CTF) Aggregate Is Sufficient to Cause Cell Death. *PLoS One*, 8(3):e50121.
8. Rotkrua, P., Shimada, S., Mogushi, K., Akiyama, Y., Tanaka, H., Yuasa, Y. (2013). Circulating microRNAs as biomarkers for early detection of diffuse-type gastric cancer using a mouse model. *British Journal of Cancer*, 108(4):932-40.
9. Sato, K., Tanaka, S., Mitsunori, Y., Mogushi, K., Yasen, M., Aihara, A., Ban, D., Ochiai, T., Irie, T., Kudo, A., Nakamura, N., Tanaka, H., Aii, S. (2013). Contrast-enhanced intraoperative ultrasonography for vascular imaging of hepatocellular carcinoma; clinical and biological significance. *Hepatology*, 57(4):1436-47.
10. Mayinuer, A., Yasen, M., Mogushi, K., Obulhasim, G., Xieraili, M., Aihara, A., Tanaka, S., Mizushima, H., Tanaka, H., Aii, S. (2013). Upregulation of Protein Tyrosine Phosphatase type IVA member 3 (PTP4A3/PRL-3) Associated with tumor differentiation and a poor prognosis in human hepatocellular carcinoma. *Annals of Surgical Oncology*, 20:305-17.
11. Sumino, J., Uzawa, N., Okada, N., Miyaguchi, K., Mogushi, K., Takahashi, KI., Sato, H., Michikawa, C., Nakata, Y., Tanaka, H., Amagasa, T. (2013). Gene expression changes in initiation and progression of oral squamous cell carcinomas revealed by laser microdissection and oligonucleotide microarray analysis. *International Journal of Cancer*, 132(3):540-8.
12. Kikuchi, A., Ishikawa, T., Mogushi, K., Ishiguro, M., Iida, S., Mizushima, H., Uetake, H., Tanaka, H., Sugihara, K. (2013). Identification of NUCKS1 as a colorectal cancer prognostic marker through integrated expression and copy number analysis. *International Journal of Cancer*, 132(10):2295-302.
13. Obulhasim, G., Yasen, M., Kajino, K., Mogushi, K., Tanaka, S., Mizushima, H., Tanaka, H., Aii, S., Hino, O. (2013). Up-regulation of dbpA mRNA in hepatocellular carcinoma associated with metabolic syndrome. *Hepatology International*, 7:215-25.
14. Kudo, A., Mogushi, K., Takayama, T., Matsumura, S., Ban, D., Irie, T., Ochiai, T., Nakamura, N., Tanaka, H., Anzai, N., Sakamoto, M., Tanaka, S., Aii, S. (2013). Mitochondrial metabolism in the noncancerous liver determine the occurrence of hepatocellular carcinoma: a prospective study. *Journal of Gastroenterology*, Doi: 10.1007/s00535-013-0791-4.
15. Wang, Z., Pascual-Anaya, J., Zadissa, A., Li, W., Niimura, Y., ..., Zhang, G., Irie, N. (2013). The draft genomes of soft-shell turtle and green sea turtle yield insights into the development and evolution of the turtle-specific body plan. *Nat Genet*. 45: 701-706.
16. Matsumae H, Hamada M, Fujie M, Niimura Y, Tanaka H, Kawashima T. (2013). A methodical microarray design enables surveying of expression of a broader range of genes in *Ciona intestinalis*. *Gene* 519: 82-90.

Reviews

1. Niimura Y. (2013). Identification of chemosensory receptor genes from vertebrate genomes. *Methods Mol Biol*. 1068: 95-105.
2. Niimura Y. (2013). Identification of olfactory receptor genes from Mammalian genome sequences. *Methods Mol Biol*. 1003: 39-49.

Structural Biology

1. Staffs and Students

Professor	Nobutoshi ITO	
Associate Professor	Teikichi IKURA	
Assistant Professor	Nobutaka NUMOTO	
Technical Assistant	Michiko HATTORI,	Marina OHNO
Graduate Students	Kenrou SHINAGAW,	Michika MIYASHITA
Program Semester	Sono ITO	

2. Purpose of Education

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.

3. Research Subjects

- 1) Physicochemical analysis on the mechanism of the signal transduction for activation of T cells
- 2) Structural and functional analysis of bone morphogenetic protein
- 3) Analysis of interactions between tau protein and Pin1
- 4) Structural analyses of potential drug targets
- 5) Improvement in Protein Data Bank

4. Publications

Original Articles

1. Masuno[†] H, Ikura[†] T, Morizono D, Orita I, Yamada S, Shimizu M, Ito N (2013). Crystal structures of complexes of vitamin D receptor ligand-binding domain with lithocholic acid derivatives. *J Lipid Res* 54: 2206-2213. ([†]These authors contributed equally to this work.)
2. Ikura T, Ito N (2013). The peptidyl-prolyl isomerase activity of FK506 binding protein 12 prevents tau peptide from aggregating. *Protein Eng Des Sel*, 26: 539-546.
3. Nakabayashi M, Tsukahara Y, Iwasaki-Miyamoto Y, Mihori-Shimazaki M, Yamada S, Inaba S, Oda M, Shimizu M, Makishima M, Tokiwa H, Ikura T, Ito N (2013). Crystal structures of hereditary vitamin D-resistant rickets-associated vitamin D receptor mutants R270L and W282R bound to 1,25-dihydroxyvitamin D₃ and synthetic ligands. *J Med Chem*, 56: 6745-6760.
4. Higo K, Ikura T, Oda M, Morii H, Takahashi J, Abe R, Ito N (2013). High resolution crystal structure of the Grb2 SH2 domain with a phosphopeptide derived from CD28. *Plos One*, 8, e74482: 1-6.
5. Numoto N, Shimizu K, Matsumoto K, Miki K, Kita A (2013). Observation of the orientation of membrane protein crystals grown in high magnetic force fields. *J Cryst Growth*, 367: 53-56.
6. Nagamatsu Y, Takeda K, Kuranaga T, Numoto N, Miki K (2013). Origin of Asymmetry at the Intersubunit Interfaces of V₁-ATPase from *Thermus thermophilus*. *J Mol Biol*, 425: 2699-2708.

Bio-informational Pharmacology

1. Staffs and Students

Associate Professor Junko KUROKAWA
Graduate Students Min LI

2. Purpose of Education

Bio-informational pharmacology treats diverse area of life sciences by using pharmacological tools. This laboratory focuses on understanding fundamental physiological roles of ion channels and transporters in cardiovascular system. We employ multidisciplinary approach (patch-clamp, cell biology, fluorescent imaging, and comprehensive analysis) in order to seek novel regulatory mechanisms and modulatory molecules/compounds of ion channels and transporters in cardiovascular organs.

Our ultimate goal is to discover novel diagnostic and therapeutic strategy for intractable cardiovascular diseases, such as sudden death, life-threatening arrhythmias, and atherosclerosis, by modulating ion channels and transporters.

3. Research Subjects

- (1) Gender specific medicine in cardiovascular diseases
- (2) Cardiac arrhythmias and iPS cells
 - (A) Cardiac disease models of iPS-derived cardiomyocytes from long QT syndrome patients
 - (B) Drug safety screening system using human iPS cells-derived cardiomyocytes
- (3) New technologies in cardiovascular research
 - (A) In vitro cardiomyocyte contraction assay system using the motion vector technology
 - (B) Generation of 3-D simulator for cardiac electrical activity

4. Clinical Services

None.

5. Publications

Original Articles

1. Asayama M, Kurokawa J, Shirakawa K, Okuyama H, Kagawa T, Okada J, Sugiura S, Hisada T, Furukawa T. Effects of a hERG activator, ICA-105574, on electrophysiological properties of canine hearts. *J Pharmacol Sci*, **2013**,**121**:1-8.

Review articles

1. Kurokawa J, Furukawa T. (2013) Non-genomic action of sex steroid hormones and cardiac repolarization. *Biol. Pharmacol. Bull*, **36**, 8-12.

Books

1. Sasano T, Kurokawa J* (2013) Remodeling of potassium channels in cardiac hypertrophy In: *Molecular Mechanisms of Cardiac Remodeling*. Jugdutt BI, Dhalla NS (Eds): Springer, New York, p31-45.

Therapeutic Genomics

1. Staffs

Associate Professor Ken-ichi Kozaki D.D.S., Ph.D.
 Assistant Professor Jun Inoue Ph.D.

2. Purpose of Education

The principal aims of our practice are to understand (1) integrative approaches for genetic and epigenetic analyses using the bio-resources of cancers, lifestyle-related diseases, and genetic diseases, (2) molecular mechanisms underlying these diseases, and (3) therapeutic genomics for Personalized Medicine in these diseases.

3. Research Subjects

1. Functional genomics-based approach for identification of tumor-suppressive microRNAs having potential as therapeutic agents for cancer.
2. Discovery of aberrant DNA methylation specific to pathophysiological conditions during multistep processes with the acquisition of malignant properties in cancer cells.

4. Clinical Services

5. Publications

Original Article

1. Takemura K, Kawachi H, Eishi Y, Kitagaki K, Negi M, Kobayashi M, Uchida K, Inoue J, Inazawa J, Kawano T, Board PG: γ -Glutamylcyclotransferase as a novel immunohistochemical biomarker for the malignancy of esophageal squamous tumors. *Hum Pathol*, 2013 [Epub ahead of print]
2. Yamamoto S, Inoue J, Kawano T, Kozaki K, Omura K, Inazawa J: The impact of miRNA-based molecular diagnostics and treatment of NRF2-stabilized tumors. *Mol Cancer Res*, 2013 [Epub ahead of print]
3. Yamamoto Y, Konishi H, Ichikawa D, Arita T, Shoda K, Komatsu S, Shiozaki A, Ikoma H, Fujiwara H, Okamoto K, Ochiai T, Inoue J, Inazawa J, Otsuji E: Significance of GSTP1 for predicting the prognosis and chemotherapeutic efficacy in esophageal squamous cell carcinoma. *Oncol Rep* 30:1687-94, 2013
4. Harazono Y, Muramatsu T, Endo H, Uzawa N, Kawano T, Harada K, Inazawa J, Kozaki K: miR-655 is an EMT-suppressive microRNA targeting ZEB1 and TGFBR2. *PLoS One* 8:e62757, 2013
5. Furuta M, Kozaki K, Tanimoto K, Tanaka S, Arie S, Shimamura T, Niida A, Miyano S, Inazawa J: The tumor-suppressive miR-497-195 cluster targets multiple cell-cycle regulators in hepatocellular carcinoma. *PLoS One* 8:e60155, 2013

Molecular Genetics (Molecular Genetics)

1. Staffs and Students (April, 2013)

Professor	Yoshio MIKI	
Associate Professor	Akira NAKANISHI	
Graduate Student	Nurmaa DASHZEVEG,	Yuya KAGAMI,
	Shota TESHIROGI	

2. Purpose of 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.

3. Research Subject

- 1) Functional analysis of the BRCA2 gene.
 - ① Synthetic lethality effect for chemotherapy using BRCA2-deficient breast cancers
 - ② Enhancement of the ATPase activity of nonmuscle myosin (NM)-IIC by BRCA2
 - ③ Analysis of intramolecular BRCA2 region concerning the numerical integrity of centrosomes by an automated centrosome counting system
- 2) Regulatory mechanisms of tumor cells in the apoptotic response to DNA damage
 - ① PKCdelta regulates Mdm2 independently negative regulator of p53 in the apoptotic response to DNA damage.
 - ② Identification of Evi-1 as a novel effector of PKCdelta in the apoptotic response to DNA damage.

4. Publication

Original Article

1. Wali N, Hosokawa K, Malik S, Saito H, Miyaguchi K, Imajoh-Ohmi S, Miki Y, Nakanishi A. Centrosomal BRCA2 is a target protein of membrane type-1 matrix metalloproteinase (MT1-MMP). *Biochem Biophys Res Commun* 2014, 443:1148-1154.
2. Wada Y, Matsuura M, Sugawara M, Ushijima M, Miyata S, Nagasaki K, Noda T, Miki Y. Development of detection method for novel fusion gene using GeneChip exon array. *J Clin Bioinforma* 2014, 4:3.
3. Takaoka M, Saito H, Takenaka K, Miki Y, Nakanishi A. BRCA2 Phosphorylated by PLK1 Moves to the Midbody to Regulate Cytokinesis Mediated by Nonmuscle Myosin IIC. *Cancer Res* 2014.
4. Nakamura S, Takahashi M, Tozaki M, Nakayama T, Nomizu T, Miki Y, Murakami Y, Aoki D, Iwase T, Nishimura S, et al. Prevalence and differentiation of hereditary breast and ovarian cancers in Japan. *Breast Cancer* 2013.
5. Mimoto R, Taira N, Takahashi H, Yamaguchi T, Okabe M, Uchida K, Miki Y, Yoshida K. DYRK2 controls the epithelial-mesenchymal transition in breast cancer by degrading Snail. *Cancer Lett* 2013, 339:214-225.
6. Low SK, Takahashi A, Ashikawa K, Inazawa J, Miki Y, Kubo M, Nakamura Y, Katagiri T. Genome-wide association study of breast cancer in the Japanese population. *PLoS One* 2013, 8:e76463.
7. Kawazu M, Ueno T, Kontani K, Ogita Y, Ando M, Fukumura K, Yamato A, Soda M, Takeuchi K, Miki Y, et al. Transforming mutations of RAC guanosine triphosphatases in human cancers. *Proc Natl Acad Sci U S A* 2013, 110:3029-3034.

Epigenetic Epidemiology

1. Staffs and Students (April, 2013)

Professor	Masaaki MURAMATSU	
Associate Professor	Noriko SATO	
Assistant Professor	Shinobu IKEDA	
Adjunct Instructor	Katsuko SUDO,	Fumihiko SATA
Graduate Student	Nay Chi Htun,	Cuneyd Palrayan,
	Atsuko Hiraishi,	Zhao Chen-xi,
	Sariya Dechamethakun,	Mia Sawabe,
	Kaung Si Thu,	Khin Thet Thet Zaw
Research Resident	Tay Zar Kyaw,	Yumie Hiraoka

2. Education

Many common diseases such as diabetes, hypertension, obesity, metabolic syndrome, and atherosclerosis are caused by multiple genetic and environmental factors. We 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. The effects of intrauterine environment on fetal epigenome are investigated using mouse model.

3. Research Subjects

1. Gene-environment interaction that affects the onset of metabolic syndrome and its related phenotypes.
2. Genetic factors that affect the severity of pathological atherosclerosis.
3. Responder vs non-responder of prodrugs and polymorphisms of drug metabolizing enzymes.
4. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
5. The role of epigenetic regulation and fetal programming in common diseases.
6. Likelihood ratio based integrated personal risk assessment of type 2 diabetes.

4. Publications

1. Kengia JT, Ko KC, Ikeda S, Hiraishi A, Mieno-Naka M, Arai T, Sato N, Muramatsu M, Sawabe M. A gene variant in the *Atp10d* gene associates with atherosclerotic indices in Japanese elderly population. *Atherosclerosis*. 231:158-62. 2013
2. Daimon M, Sato H, Kaino W, Tada K, Takase K, Karasawa S, Wada K, Kameda W, Susa S, Oizumi T, Kayama T, Muramatsu M, Kato T. Association of the G-protein $\beta 3$ subunit gene polymorphism with the incidence of cardiovascular disease independent of hypertension: the Funagata study. *J Hum Hypertens*. 27:612-6. 2013
3. Honma N, Mori S, Zhou H, Ikeda S, Mieno MN, Tanaka N, Takubo K, Arai T, Sawabe M, Muramatsu M, Ito H. Association between estrogen receptor- β dinucleotide repeat polymorphism and incidence of femoral fracture. *J Bone Miner Metab*. 31:96-101.2013
4. Honma N, Yamamoto K, Ohnaka K, Morita M, Toyomura K, Kono S, Muramatsu M, Arai T, Ueki T, Tanaka M, Kakeji Y, Maehara Y, Okamura T, Ikejiri K, Futami K, Maekawa T, Yasunami Y, Takenaka K, Ichimiya H, Terasaka R. Estrogen receptor- β gene polymorphism and colorectal cancer risk: effect modified by body mass index and isoflavone intake. *Int J Cancer*. 132:951-8. 2013
5. Yatsuga C, Toyohisa D, Fujisawa TX, Nishitani S, Shinohara K, Matsuura N, Ikeda S, Muramatsu M, Hamada A, Tomoda A. No association between COMT genotype and attention deficit hyperactivity disorder (ADHD) in Japanese children. *Brain Dev*. S0387-7604(13)00258-1 2013
6. Kaniwa N, Sugiyama E, Saito Y, Kurose K, Maekawa K, Hasegawa R, Furuya H, Ikeda H, Takahashi Y, Muramatsu M, Tohkin M, Ozeki T, Mushiroda T, Kubo M, Kamatani N, Abe M, Yagami A, Ueta M, Sotozono C, Kinoshita S, Ikezawa Z, Matsunaga K, Aihara M; Japan Pharmacogenomics Data Science Consortium. Specific HLA types are associated with antiepileptic drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Japanese subjects. *Pharmacogenomics*. 14:1821-31. 2013

RIKEN Molecular and Chemical Somatology

1. Staffs and Students

Visiting Professor	Soichi Kojima	
Visiting Professor	Hiroyuki Osada	
Visiting Professor	Mikiko Sodeoka	
Visiting Professor	Yoshiki Yamaguchi	
Visiting Professor	Takashi Saito	
Visiting Professor	Tsutsuro Toyoda	
Visiting Lecturer	Naoko Imamoto	
Visiting Lecturer	Tamio Saito	
Visiting Lecturer	Masashi Ueki	
Visiting Lecturer	Takeshi Nakano	
Visiting Lecturer	Kenji Ogawa	
Visiting Lecturer	Go Hirai	
Visiting Lecturer	Shinya Hanashima	
Visiting Lecturer	Arata Takeuchi	
Visiting Lecturer	Masamichi Nagae	
Graduate Students	D3 Kenji Hayamizu,	Shuta Hara
	D2 Rajan Shrestha	
	D1 Motonari Sakai,	Sayoko Yamasaki,
	Dulal Hari Prasad	
	M2 Yuka Yamamoto,	Asami Shibuya,
	Kumiko Ugata,	Rin Tokunaga
	M1 Shuntaro Kojima	

2. Purpose of Education

Molecular and Chemical Somatology is an interdisciplinary fields to understand basis of Bioorganic Chemistry, Chemical Biology, Structural Biology, Molecular Immunology, and Integrating Bioinformatics as well as their applications to Medicine and Biology by dealing with variety of molecules that regulate cellular functions including low molecular organic compounds, proteins, sugars, and hormones. Students will hear and discuss about outlines and/or latest topics on discovery, structure, synthesis, biology, and management of these key molecules/factors, and deepen their understanding of this new study field.

3. Research Subjects

- 1) Synthesis, screening, and targets of natural products focusing on microbial metabolites
- 2) Synthesis of bioactive molecules and research on chemical biology based on synthetic organic chemistry
- 3) Clarification of pathogenesis of diseases at molecular and cellular levels using molecules that regulate cellular functions (bioprobes)
- 4) Structural and functional analysis of glycoproteins and lectins.
- 5) Regulatory mechanisms for the lymphocyte activation and immune responses
- 6) Knowledge discoveries through integrating multiple datasets and information by next generation sequencers

4. Publications

Original Articles

1. Sakata, K., Hara, M., Terada, T., Watanabe, N., Takaya, D., Yaguchi, S., Matsumoto, T., Matsuura, T., Shirouzu, M., Yokoyama, S., Yamaguchi, T., Miyazawa, K., Aizaki, H., Suzuki, T., Wakita, T., Imoto, M., and Kojima, S. HCV NS3 protease enhances liver fibrosis via binding to and activating TGF- β type I receptor. *Sci. Rep.* 3:3243. 2013.
2. Wada A, Hara S, Osada H: Ribosome display and photo-crosslinking techniques for in vitro identification of target proteins of bioactive small molecules. *Anal. Chem.* 86: 6768-6773, 2014.
3. Tsuchiya A, Asanuma M, Hirai G, Oonuma K, Muddassar M, Nishizawa E, Koyama Y, Otani Y, Zhang KYJ, Sodeoka M: CDC25A-inhibitory RE Derivatives Bind to Pocket Adjacent to the Catalytic Site. *Molecular BioSystems*, 9: 1026-1034, 2013.

4. Ozawa M, Morita M, Hirai G, Tamura S, Kawai M, Tsuchiya A, Oonuma K, Maruoka K, Sodeoka M: ACS Med. Chem. Lett. 4: 730-735, 2013.
5. Nagae, M., Yamanaka, K., Hanashima, S., Ikeda, A., Morita-Matsumoto, K., Satoh, T., Matsumoto, N., Yamamoto, K., and Yamaguchi, Y.. Recognition of bisecting N-acetylglucosamine: structural basis for asymmetric interaction with the mouse lectin dendritic cell inhibitory receptor 2. J. Biol. Chem., 288: 33598-33610, 2013.
6. Yuasa, N., Koyama, T., Subedi, G.P, Yamaguchi, Y., Matsushita, M., and Fujita-Yamaguchi, Y.. Expression and structural characterization of anti-T-antigen single chain antibodies (scFvs) and analysis of their binding to T-antigen by surface plasmon resonance and NMR spectroscopy. J. Biochem., 154: 521-529, 2013.
7. Tsukumo S, Unno M, Muto A, Takeuchi A, Kometani K, Kurosaki T, Igarashi K, Saito T. Bach2 maintains T cells in a naive state by suppressing effector memory-related genes. Proc Natl Acad Sci U S A. 110: 10735-10740, 2013.

Review Articles

Books

Meetings & Conferences

1. Eda S, Lee E, Hara M, Imoto M, Kojima S, Neovessels contribute to liver fibrosis via providing latent transforming growth factor-beta to be activated by hepatic stellate cells, American Association for the Study of Liver Diseases(Atlanta, USA) Jun, 2013.
2. Hara S, Wada A, Osada H, Development of a new methodology for target identification of bioactive small molecules by using ribosome display. KRIBB-RIKEN Chemical Biology Joint Symposium, (Ochang Korea) May, 2013.
3. Ugata K., Futamura Y., Hayase H., Watanabe N., Osada H., Exploration of novel antimalarial compounds. KRIBB-RIKEN Chemical Biology Joint Symposium, (Ochang Korea) May, 2013.
4. Saito, T. "Dynamic regulation of T cell activation and co-stimulation" 43rd Annual Scientific Meeting Australasian Society for Immunology (ASI ASM 2013) (Wellington, New Zealand) December, 2013
5. Saito, T. "Dynamic regulation and modulation of T cell activation" Immunology 2013, AAI Annual Meeting Symposium (Honolulu, USA) May, 2013

Miscellaneous

<Invited Lectures>

1. Kojima, S. "Non-genomic and genomic actions of acyclic retinoid" 1st International Retinoids Meeting 2013, Calabria, Italy, September, 2013.
2. Yamaguchi Y, Matsumoto K, Hirose K, Nishima W, Re S, Sugita Y, "Experimental and theoretical approaches to understand the conformational differences in isomeric glycan pairs", 22nd International Symposium on Glycoconjugates, Dalian, China, June 27, 2013
3. Osada, H. "Isolation of New Microbial Metabolites for Natural Product Depository (NPDepo)", 2nd Annual Conference ICBS2013, Kyoto, Japan, Oct. 2013.
4. Sodeoka M. "Synthesis and Evaluation of Bioactive Molecules Designed Based on Natural Products" The 23rd French-Japanese Symposium on Medicinal and Fine Chemistry, Nagasaki, Japan, May 2013.
5. Saito T. "Spatiotemporal regulation of T cell activation and co-stimulation" 2012 Gordon Research Conference -Immunochemistry & Immunobiology, Les Diablerets, Switzerland, June 2012.

Molecular Biomedicine

1. Staffs and Students (April, 2013)

Associate Professor	Wataru NOMURA	
Graduate Student	Yosuke NONAKA,	Shohei TAKETOMI,
	Atsushi ITO,	Taisuke KOSEKI,
	Takuya KOBAYAKAWA,	Hikaru TAKANO,
	Yuki HIROTA,	Daichi MATSUMOTO,
	Yu IRAHARA,	Tsugunori OKABE,
	Ryosuke KOBAYASHI,	Sho SAKAMOTO,
	YUZUNA HONDA	

2. Purpose of Education

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.

3. Research Subjects

- 1) Development of applications of zinc finger protein for gene therapy and nanotechnology.
- 2) Development of conformational-constrained templates for drug discovery.
- 3) Development of bio-probes, bio-sensing, medicinal chemistry towards chemical biology.
- 4) Structural analysis of the interactions between receptors/enzymes and their ligands.

4. Publications

Original Article

- 1) Hashimoto C, Narumi T, Otsuki H, Hirota Y, Arai H, Yoshimura K, Harada S, Ohashi N, Nomura W, Miura T, Igarashi T, Matsushita S, Tamamura H. A CD4 Mimic as an HIV Entry Inhibitor: Pharmacokinetics. *Bioorg Med Chem* 21(24): 7884–7889, 2013.
- 2) Hashimoto C, Nomura W, Narumi T, Fujino M, Nakahara T, Yamamoto N, Murakami T, Tamamura H. CXCR4-derived Synthetic Peptides Inducing Anti-HIV-1 Antibodies. *Bioorg Med Chem* 21(22): 6878–6885, 2013.
- 3) Nomura W, Aikawa H, Ohashi N, Urano E, Metifiot M, Fujino M, Maddali K, Ozaki T, Nozue A, Narumi T, Hashimoto C, Tanaka T, Pommier Y, Yamamoto N, Komano J, Murakami T, Tamamura H. Cell-Permeable Stapled Peptides Based on HIV-1 Integrase Inhibitors Derived from HIV-1 Gene Product. *ACS Chem Biol* 8(10): 2235–2244, 2013.
- 4) Hashimoto C, Nomura W, Narumi T, Fujino M, Tsutsumi H, Haseyama M, Yamamoto N, Murakami T, Tamamura H. Anti-HIV-1 Peptide Derivatives Based on the HIV-1 Co-receptor CXCR4. *ChemMedChem* 8(10): 1668–1672, 2013.
- 5) Nomura W, Hashimoto C, Suzuki T, Ohashi N, Fujino M, Murakami T, Yamamoto N, Tamamura H. Multimerized CHR-derived Peptides as HIV-1 Fusion Inhibitors. *Bioorg Med Chem* 21(15): 4452–4458, 2013.
- 6) Narumi T, Arai H, Yoshimura K, Harada S, Hirota Y, Ohashi N, Hashimoto C, Nomura W, Matsushita S, Tamamura H. CD4 Mimics as HIV Entry Inhibitors: Lead Optimization Studies of the Aromatic Substituents. *Bioorg Med Chem* 21(9): 2518–2526, 2013.
- 7) Narumi T, Aikawa H, Tanaka T, Hashimoto C, Ohashi N, Nomura W, Kobayakawa T, Takano H, Hirota Y, Murakami T, Yamamoto N, Tamamura H. Low Molecular Weight CXCR4 Ligands with Variable Spacers. *ChemMedChem* 8(1): 118–124, 2013.

Books

- 1) Nomura W, Tanaka T, Aikawa H, Narumi T, Tamamura H. Development of Cell-Penetrating ZIP Tag-Probe Systems for Fluorescent Imaging of Protein Dynamics in Cells. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 113–114, 2013
- 2) Masuda A, Nomura W, Tamamura H. Quantitative Analysis of Sequence-Specific Reactions by Artificial DNA Recombinases. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 21–22,

2013

- 3) Hashimoto C, Nomura W, Komano JA, Tamamura H. Synthesis of an Artificial gp41-C34 Trimer as an HIV-1 Fusion Inhibitor. in "Peptide Science 2012," ed. by Kazuhisa Sugimura, The Japanese Peptide Society, Osaka, pp. 45-46, 2013
- 4) Nomura W, Ohashi N, Narumi T, Tamamura H. Tag-Probe System for Imaging of Intracellular Proteins. Proceedings of the 23rd American Peptide Symposium, Michal Lebl (Ed.), American Peptide Society, Hawaii, pp. 174-175, 2013.
- 5) Nomura W, Tanaka T, Aoki T, Narumi T, Tamamura H. Biological Effects of Bivalent-Type CXCR4 Ligands with Rigid Linkers. Proceedings of the 23rd American Peptide Symposium, Michal Lebl (Ed.), American Peptide Society, Hawaii, pp. 176-177, 2013.

Review

- 1) Ohashi N, Nomura W, Narumi T, Tamamura H. Peptide-based Ligand Screening and Functional Analysis of Protein Kinase C. Biopolymers: Peptide Science 100(6): 613-620, 2013..

Department of Pharmacovigilance

1. Staffs and Students (April, 2013)

Professor	Masayoshi Harigai	
Associate Professor	Ryuji Koike	
Assistant Professor	Ryoko Sakai,	Hayato Yamazaki,
	Waka Yokoyama	
Graduate Student	Fumio Hirano,	Mari Kihara
Research Pharmacist	Marie Yajima	
Secretary	Tomoko Takahashi	

2. Purpose of Education

Department of Pharmacovigilance has established since 2005 and dedicated to pharmacovigilance activity in the field of rheumatology. Main objective of Department of Pharmacovigilance in the graduate course is to provide students opportunity to study basics of pharmacoepidemiology including clinical statistics and to implement epidemiological studies in pharmacovigilance using some databases which have been maintained by this department.

3. Research Subjects

1. Registry of Japanese rheumatoid arthritis patients on biologics for long-term safety (REAL study)
2. Clinical outcomes of Japanese rheumatoid arthritis patients in real world commencing targeted therapy (CORRECT)
3. Safety of biologics in clinical use in Japanese patients with rheumatoid arthritis in long-term (SECURE study)
4. Identification of susceptibility genes associated with anti-neutrophil cytoplasm antibody-associated vasculitis in Japanese
5. Effectiveness and safety in clinical practice of abatacept in Japanese patients with rheumatoid arthritis
6. A prospective cohort study of early arthritis in clinical practice evaluating development of rheumatoid arthritis (PRECEDE)
7. Population-based study of comorbidities and safety in patients with rheumatoid arthritis using Japanese health insurance database
8. Clinical epidemiological study of treat-to-target strategy in rheumatoid arthritis patients with moderate to high disease activity
9. Efficacy and safety of programmed intensive treatment with methotrexate in patients with active rheumatoid arthritis
10. A randomized clinical trial on the efficacy and tolerability of dose reduction and escalation regimen of Trimethoprim/Sulfamethoxazole (TMP/SMX) in patients with rheumatic diseases (A study on dose reduction and escalation regimen of TMP/SMX).
11. Rheumascan Pilot Study
12. Efficacy and safety of treatment with moderate doses of corticosteroid and immunosuppressants in rheumatoid arthritis patients with interstitial lung diseases

4. Clinical Service

Most of the members of Department of Pharmacovigilance are rheumatologists and engaged in clinical services in the field of rheumatology as specialists.

5. Publications

Original Article

1. Miyabe C, Miyabe Y, Miura NN, Takahashi K, Terashima Y, Toda E, et al. Am80, a retinoic acid receptor agonist, ameliorates murine vasculitis through the suppression of neutrophil migration and activation. *Arthritis Rheum.* 2013; 65(2):503-12.
2. Nanki T, Onoue I, Nagasaka K, Takayasu A, Ebisawa M, Hosoya T, et al. Suppression of elevations in serum C reactive protein levels by anti-IL-6 autoantibodies in two patients with severe bacterial infections. *Ann Rheum Dis.* 2013; 72(6):1100-2.
3. Kawasaki A, Inoue N, Ajimi C, Sada KE, Kobayashi S, Yamada H, Furukawa H, Sumida T, Tohma S, Miyasaka N, Matsuo S, Ozaki S, Hashimoto H, Makino H, Harigai M, Tsuchiya N. Association of IRF5 polymorphism with MPO-

- ANCA-positive vasculitis in a Japanese population. *Genes Immun.* 2013; 14:527-9.
4. Koike T, Harigai M, Inokuma S, Ishiguro N, Ryu J, Takeuchi T, Tanaka Y, Yamanaka H, Hirose T, Yoshinaga T, Suzukawa M. Safety and effectiveness of 6 months' etanercept monotherapy and combination therapy in Japanese patients with rheumatoid arthritis: effect of concomitant disease-modifying antirheumatic drugs. *J Rheumatol.* 2013; 40:1658-68.
 5. Watanabe K, Sakai R, Koike R, Sakai F, Sugiyama H, Tanaka M, Komano Y, Akiyama Y, Mimura T, Kaneko M, Tokuda H, Iso T, Motegi M, Ikeda K, Nakajima H, Taki H, Kubota T, Kodama H, Sugii S, Kuroiwa T, Nawata Y, Shiozawa K, Ogata A, Sawada S, Matsukawa Y, Okazaki T, Mukai M, Iwahashi M, Saito K, Tanaka Y, Nanki T, Miyasaka N, Harigai M. Clinical characteristics and risk factors for *Pneumocystis jirovecii* pneumonia in patients with rheumatoid arthritis receiving adalimumab: a retrospective review and case - control study of 17 patients. *Mod Rheumatol.* 2013; 23:1085-93
 6. Harigai M, Takamura A, Atsumi T, Dohi M, Hirata S, Kameda H, Nagasawa H, Seto Y, Koike T, Miyasaka N. Elevation of KL-6 serum levels in clinical trials of tumor necrosis factor inhibitors in patients with rheumatoid arthritis: a report from the Japan College of Rheumatology Ad Hoc Committee for Safety of Biological DMARDs. *Mod Rheumatol.* 2013; 23:284-96

Department of Nanomedicine

1. Staffs and Students

Associate Professor Motohiro KOMAKI, D.D.S., Ph.D.
Assistant Professor Kengo IWASAKI, D.D.S., Ph.D

2. Purpose of Education

Understand the mechanisms of wound healing process and connect the knowledge to the regenerative medicine.

3. Research Subject

In our department, you would know current topics of stem cell therapy. In addition to general biochemical analysis methodology, you can learn stem cell culture, bio-imaging using FACS and confocal fluorescence microscopy, animal models for intrauterine infection, skin decubitus ulcer, hind limb ischemia, and periodontal-/bone- defect.

What we do in our laboratory are;

- 1) Identification of stem cells from various human tissues.
- 2) Investigation of MSC-conditioned medium and its effects.
- 3) Isolation of stem cell derived-exosomes and evaluate their effects.
- 4) Treatment of periventricular leukomalacia using stem cells and stem cell derived factors.
- 5) The regeneration of periodontal tissues by transplanting stem cells using cell-transfer technology or by local application of MSC-conditioned medium.

4. Clinical Services

Our department members are working in periodontology clinic of Tokyo Medical and Dental University Dental hospital (Periodontics). We provide periodontal treatments to patients and instruction for dental hygienist and dentist as periodontal specialist.

5. Publications

1. Gingival tissue healing following Er:YAG laser ablation compared to electrosurgery in rats. Sawabe M, Aoki A, [Komaki M](#), [Iwasaki K](#), Ogita M, Izumi Y. *Lasers Med Sci*. 2013 Nov 16. [Epub ahead of print]
2. Periodontal Regeneration Using Periodontal Ligament Stem Cell-Transferred Amnion. [Iwasaki K](#), [Komaki M](#), Yokoyama N, Tanaka Y, Taki A, Honda I, Kimura Y, Takeda M, Akazawa K, Oda S, Izumi Y, Morita I. *Tissue Eng Part A*. 2013 Dec 9. [Epub ahead of print]
3. Periodontal Ligament Stem Cells Possess the Characteristics of Pericytes. [Iwasaki K](#), [Komaki M](#), Yokoyama N, Tanaka Y, Taki A, Kimura Y, Takeda M, Oda S, Izumi Y, Morita I. *J Periodontol*. 2013 Oct;84(10):1425-33.

6. Conferences

(Domestic)

1. Periodontal regeneration by using PDLSC-conditioned medium. ○[Iwasaki K](#), [Komaki M](#), Akazaaw K, Yokoyama N, Ayame H, Nagata M, Kimura Y, Toyi M, Izumi Y, and Ikuo M. 56th Annual meeting of the Japanese Society of Periodontology (Autum) September 22nd, 2013 Maebashi-city, Gunma.
2. Rutus periodontal tissue regeneration by using PDLSC-conditioned medium ○[Iwasaki k](#), [Komaki M](#), Yokoyama N, Ayame H, and Morita I. 34th Annual meeting of Japanese Society of Inflammation and Regeneration July 2-3rd, 2013. Kyoto-city, Kyoto.
3. Changes in morphology and differentiation capacity of PDLSC during cell culture. ○[Iwasaki K](#), [Komaki M](#), Akazaaw K, Yokoyama N, Ayame H, Kimura Y, Toyi M, Izumi Y, and Ikuo M. 56th nnuual meeting of the Japanese Society of Periodontology (Spring) May 31st, 2013, Tokyo.

7. Others

Invited speaker (International)

- 1 Mesenchymal stem cell therapy for periodontal regeneration: Cell transfer technique to paracrine factors. [Motohiro Komaki](#), Tokyo Medical and Dentai University Taipei Medical University Symposium on Advances of Biomaterials and Regenerative medicine Taipei, Taiwan, Nov 30th, 2013.

Invited speaker (Domestic)

1. Novel periodontal regeneration using MSC-derived paracrine factors. ○Komaki M., Iwasaki K., and Morita I. 34th Annual meeting of Japanese Society of Inflammation and Regeneration (Symposium) July 2-3rd, 2013. Kyoto-city, Kyoto.

Patents

1. 細胞のリプログラミングのための組成物
2. 歯周組織形成用材料
3. レーザープローブ（生検用コンタクトチップ（本学整理番号：P13-012））
4. 組織切除用受け台（手術器具（本学整理番号：P13-013））

Department of Liver Disease Control

1. Staffs and Students

Professor	Yasuhiro ASAHINA	
Senior Associate Professor	Sei KAKINUMA	
Graduate Student (collaboration with Department of Gastroenterology and Hepatology in TMDU)	Miyako MURAKAWA,	Kouhei YOSHINO,
	Junko FUJIKI,	Fukiko KAWAI,
	Hideto YAMANAKA,	Satoshi OHTANI,
	Fumio GOTOH,	Shun KANEKO (04/2013-),
	Hiroko NAGATA (04/2013-),	

2. Education Principles

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 liver failure. Because of a serious shortage of donors, 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 chronic liver diseases has been essential. Our section is a department collaborating with the Department of gastroenterology and hepatology in TMDU.

We believe that the central role of clinical departments in the graduate school 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 primary goal is to train highly educated and experienced clinician-researchers in the field of hepatology. In the clinical section, we pursue development and application of highly advanced technologies, including novel procedures, for sophisticated diagnosis and treatment of liver diseases. In basic 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. Based on these concepts, we are running research projects to prevent progression of chronic liver diseases, by expanding our distinct basic research findings in the area of virology, immunology, stem cell biology, and cell biology 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 hepatologist, and also a leading expert in the field of hepatology.

3. Basic Research Projects

- Analysis of molecular mechanisms for interferon-resistance of hepatitis C virus.
- Analysis of molecular mechanisms for proliferation and differentiation of hepatic stem/progenitor cells.
- Exploration of liver disease-related genes essential for disease progression.
- Regenerative medical science of liver.

4. Expert Areas in Clinical Practice

- Prevention of chronic hepatitis progression to hepatocellular cancer and liver failure, by virology-based treatment strategy.
- Clinical trial of innovative treatment for hepatocellular carcinoma.

5. Publications

1. Asahina Y, Tsuchiya K, Nishimura T, Muraoka M, Suzuki Y, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nakagawa M, Kakinuma S, Watanabe M, Izumi N: α -fetoprotein levels after interferon therapy and risk of hepatocarcinogenesis in chronic hepatitis C. *Hepatology*. 58(4):1253-1262, 2013
2. Kiyohashi K, Kakinuma S, Kamiya A, Sakamoto N, Nitta S, Yamanaka H, Yoshino K, Fujiki J, Murakawa M, Kusano-Kitazume A, Shimizu H, Okamoto R, Azuma S, Nakagawa M, Asahina Y, Tanimizu N, Kikuchi A, Nakauchi H, Watanabe M: Wnt5a signaling mediates biliary differentiation of fetal hepatic stem/progenitor cells. *Hepatology*. 57(6):2502-2513, 2013
3. Nitta S, Sakamoto N, Nakagawa M, Kakinuma S, Mishima K, Kusano-Kitazume A, Kiyohashi K, Murakawa M, Nishimura-Sakurai Y, Azuma S, Tasaka-Fujita M, Asahina Y, Yoneyama M, Fujita T, Watanabe M: Hepatitis C

- virus NS4B protein targets STING and abrogates RIG-I-mediated type-I interferon-dependent innate immunity. *Hepatology*. 57(1):46-58, 2013
4. Asahina Y, Hayashi N, Hiramatsu N, Izumi N, Koike K, Kumada H, Oketani M, Suzuki F, Takikawa H, Tanaka A, Tsubouchi H, Yotsuyanagi H: Editors of the Drafting Committee for Hepatitis Management Guidelines: The Japan Society of Hepatology: Guidelines for the Management of Hepatitis C Virus Infection. *Hepatol Res*. 43(1):1-34, 2013
 5. Asahina Y, Nakagawa M, Kakinuma S, Watanabe M: Polymorphism Near the Interleukin-28B Gene and anti-Hepatitis C viral Response. *J Clin Transl Hepatol*. 1:39-44, 2013
 6. Asahina Y, Tsuchiya K, Nishimura T, Muraoka M, Suzuki Y, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nakagawa M, Kakinuma S, Watanabe M, Izumi N: Genetic variation near interleukin 28B and the risk of hepatocellular carcinoma in patients with chronic hepatitis C. *J Gastroenterol*. (Epub ahead of print), 2013
 7. Nakagawa M, Sakamoto N, Watanabe T, Nishimura-Sakurai Y, Onozuka I, Azuma S, Kakinuma S, Nitta S, Kiyohashi K, Kusano-Kitazume A, Murakawa M, Yoshino K, Itsui Y, Tanaka Y, Mizokami M, Watanabe M, Ochanomizu Liver Conference Study Group: Association of ITPA gene variant and serum ribavirin concentration with blood cells decline in pegylated interferon-alfa plus ribavirin therapy for chronic hepatitis C. *Hepatol Int*. 7(1):153-161, 2013.
 8. Tsuchiya K, Asahina Y, Matsuda S, Muraoka M, Nakata T, Suzuki Y, Tamaki N, Yasui Y, Suzuki S, Hosokawa T, Nishimura T, Ueda K, Kuzuya T, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Izumi N: These authors contributed equally to this study: Changes in plasma vascular endothelial growth factor at 8 weeks after sorafenib administration as predictors of survival for advanced hepatocellular carcinoma. *Br J Cancer*. (in press), 2013
 9. Izumi N, Asahina Y, Kurosaki M, Yamada G, Kawai T, Kajiwara E, Okamura Y, Takeuchi T, Yokosuka O, Kariyama K, Toyoda J, Inao M, Tanaka E, Morikawa H, Adachi K, Katsushima S, Kudo M, Takaguchi K, Hiasa Y, Chayama K, Yatsuhashi H, Oketani M, Kumada H: Inhibition of hepatocellular carcinoma by PegIFN α 2a in patients with chronic hepatitis C: a nationwide multi-center cooperative study. *J Gastroenterol*. 48(3):382-390, 2013
 10. Kurosaki M, Tanaka Y, Nishida N, Sakamoto N, Enomoto N, Matsuura K, Asahina Y, Nakagawa M, Watanabe M, Sakamoto M, Maekawa S, Tokunaga K, Mizokami M, Izumi N: Model incorporating the ITPA genotype identifies patients at high risk of anemia and treatment failure with pegylated-interferon plus ribavirin therapy for chronic hepatitis C. *J Med Virol*. 85(3):449-458, 2013
 11. Nakanishi H, Kurosaki M, Nakanishi K, Tsuchiya K, Noda T, Tamaki N, Yasui Y, Hosokawa T, Ueda K, Itakura J, Anami K, Asahina Y, Enomoto N, Higuchi T, Izumi N: Impaired brain activity in cirrhotic patients with minimal hepatic encephalopathy. *Hepatol Res*. (Epub ahead of print), 2013
 12. Tamaki N, Kurosaki M, Matsuda S, Nakata T, Muraoka M, Suzuki Y, Yasui Y, Suzuki S, Hosokawa T, Nishimura T, Ueda K, Tsuchiya K, Nakanishi H, Itakura J, Takahashi Y, Matsunaga K, Taki K, Asahina Y, Izumi N: Prospective comparison of real-time tissue elastography and serum fibrosis markers for the estimation of liver fibrosis in chronic hepatitis C patients. *Hepatol Res*. (Epub ahead of print), 2013
 13. Tamaki N, Kurosaki M, Tanaka K, Suzuki Y, Hoshioka Y, Kato T, Yasui Y, Hosokawa T, Ueda K, Tsuchiya K, Nakanishi H, Itakura J, Asahina Y, Izumi N: Noninvasive estimation of fibrosis progression overtime using the FIB-4 index in chronic hepatitis C. *J Viral Hepat*. 20: 72-76, 2013.
 14. Toyoda J, Ozeki I, Asahina Y, Izumi N, Takahashi S, Kawakami Y, Chayama K, Kamiya N, Aoki K, Yamada I, Suzuki Y, Suzuki F, Kumada H: Virologic response and safety of 24-week telaprevir alone in Japanese patients infected with hepatitis C virus subtype 1b. *J Viral Hepat*. 20(3):167-173, 2013
 15. Yasui Y, Kudo A, Kurosaki M, Matsuda S, Muraoka M, Tamaki N, Suzuki S, Hosokawa T, Ueda K, Matsunaga K, Nakanishi H, Tsuchiya K, Itakura J, Takahashi Y, Tanaka S, Asahina Y, Enomoto N, Arai S, Izumi N: Reduced organic anion transporter expression is a risk factor for hepatocellular carcinoma in chronic hepatitis C patients: A propensity score matching study. *Oncology*. (in press), 2013

Department of Advanced Therapeutics for GI Diseases

1. Staffs and Students (2013)

Associate Professor	Ryuichi OKAMOTO, Kiichiro TSUCHIYA	Tetsuya NAKAMURA,
Medical Fellow	Tomohiro MIZUTANI	
Graduate Student	Masayoshi FUKUDA, Taichi MATSUMOTO, Shuji HIBIYA, Hiromichi SHIMIZU, Satoru FUJII,	Kengo NOZAKI, Nobukatsu HORITA, Keita FUKUSHIMA, Go ITO, Toru NAKATA

2. Education Principles

The fundamental concept of the department is “Establishment of novel and challenging therapeutic strategies that can be spread worldwide from Japan”. Our main interest is set to analysis and treatment of inflammatory bowel diseases, and thus has organized inflammatory bowel disease-oriented researchers, supported by a number of companies from different areas. We have first established this department on April 2007, and since then, we have succeeded to gain a number of outstanding scientific achievements, including publishment of high-quality papers. In addition, in the clinical field, we have directed and played a major role in nation-wide survey and multi-center researches of inflammatory bowel diseases, which was funded by the Japanese Ministry of Health, Labor and Welfare (Chief researcher; Prof. Mamoru Watanabe).

Main principle of our department upon graduate school education is to promote students to become unique and outstanding clinician-researcher, especially engaged in conquering refractory inflammatory bowel diseases. We share the basic research concepts with Department of Gastroenterology and Hepatology, and collaborate to pursue “clinical science”, a research started from, and always coming back to, clinical findings and problems. Also we strongly promote interchange of ideas and personnel between labs, institutes and foreign countries, and thereby facilitate students and researchers to become cross-sectional, distinguished leaders in the field of inflammatory bowel disease research.

3. Basic Research Projects

- Elucidating pathophysiology of inflammatory bowel diseases, and establishment of novel treatments by disease-specific immune-regulation.
- Research and development of regenerative medicine in gastrointestinal diseases.
- Identification of the molecular mechanism promoting regeneration of inflamed mucosa, and application of molecular-targeted mucosal regeneration therapy in inflammatory bowel diseases.
- Establishment of cell- or tissue-transplantation therapy for refractory GI ulcers.
- Analysis of crosstalk between epithelial cells and micro-organisms, and establishment of novel immunomodulating therapy for inflammatory bowel diseases.

4. Expert Areas in Clinical Practice

- Immunomodulating treatment of inflammatory bowel diseases.
- Establishing improved treatment protocol of immunomodulators by pharmacokinetic analysis.
- 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.

5. Publications

1. Murano T, Okamoto R, Ito G, Nakata T, Hibiya S, Shimizu H, Fujii S, Kano Y, Mizutani T, Yui S, Akiyama-Morio J, Nemoto Y, Tsuchiya K, Nakamura T, Watanabe M: Hes1 promotes the IL-22-mediated antimicrobial response by enhancing STAT3-dependent transcription in human intestinal epithelial cells. **Biochem Biophys Res Commun** 2013; 443(3):840-846.
2. Fujii T, Naganuma M, Kitazume Y, Saito E, Nagahori M, Ohtsuka K, Watanabe M: Advancing MR imaging in Crohn's disease. **Digestion**. (in press), 2013
3. Ito G, Okamoto R, Murano T, Shimizu H, Fujii S, Nakata T, Mizutani T, Yui S, Akiyama-Morio J, Nemoto Y, Okada E, Araki A, Ohtsuka K, Tsuchiya K, Nakamura T, and Watanabe M: Lineage-specific expression of Bestrophin-2 and Bestrophin-4 in human intestinal epithelial cells. **PLoS One**. 8(11):e79693, 2013

4. Kano Y, Tsuchiya K, Zheng X, Horita N, Fukushima K, Hibiya S, Yamauchi Y, Nishimura T, Hinohara K, Gotoh N, Suzuki S, Okamoto R, Nakamura T, Watanabe M: The acquisition of malignant potential in colon cancer is regulated by the stabilization of Atonal homolog 1 protein. *1:432(1):175-181, Biochem Biophys Res Commun*, 2013
5. Nemoto Y, Kanai T, Takahara M, Oshima S, Nakamura T, Okamoto R, Kiichiro T, Watanabe M: Bone marrow-mesenchymal stem cells are a major source of interleukin-7 and sustain colitis by forming the niche for colitogenic CD4+ memory T cells. *Gut*. 62(8):1142-1152, 2013
6. Nemoto Y, Kanai T, Takahara M, Oshima S, Okamoto R, Tsuchiya K, Matsumoto S, Watanabe M: Th1/Th17-Mediated Interstitial Pneumonia in Chronic Colitis Mice Independent of Intestinal Microbiota. *J Immunol*. 190:6616-6625, 2013
7. Okada E, Araki A, Suzuki S, Watanabe H, Ikeda T, Watanabe T, Kurata M, Eishi M, Watanabe M: Histological diagnosis of follicular lymphoma by biopsy of small intestinal normal mucosa. *Digestive Endoscopy*. 39(5):544-546, 2013
8. Okamoto R, Nagahori M, Watanabe M: Perspectives for IBD in Japan. *AGA Perspectives*. 9(2):18-19 2013
9. Saito E, Nagahori M, Fujii T, Otsuka K, Watanabe M: Efficacy of salvage therapy and its effect on operative outcomes in patients with ulcerative colitis, *Digestion JGA Special Issue 2014*. (in press), 2013
10. Takahara M, Nemoto Y, Oshima S, Matsuzawa Y, Kanai T, Okamoto R, Tsuchiya K, Nakamura T, Yamamoto K, Watanabe M: IL-7 promotes long-term in vitro survival of unique long-lived memory subset generated from mucosal effector memory CD4+ T cells in chronic colitis mice. *Immunol Lett*. 156:82-93, 2013
11. Watanabe M, Hanai H, Nishino H, Yokoyama T, Terada T, Suzuki Y: Comparison of QD and TID Oral Mesalazine for Maintenance of Remission in Quiescent Ulcerative Colitis: A Double - blind, Double - dummy, Randomized Multicenter Study. *Inflamm Bowel Dis*. 19(8):1681-1690, (Epub ahead of print), 2013
12. Watanabe M, Nishino H, Sameshima Y, Ota A, Nakamura S, Hibi T: Randomised clinical trial: evaluation of the efficacy of mesalazine (mesalamine) suppositories in patients with ulcerative colitis and active rectal inflammation -a placebo- controlled study. *Aliment Pharmacol Ther*. 38(3):264-273, 2013
13. Fordham RP, Yui S, Hannan NR, Soendergaard C, Madgwick A, Schweiger PJ, Nielsen OH, Vallier L, Pedersen RA, Nakamura T, Watanabe M, Jensen KB :Establishment of Fetal Enteric Progenitors as a Source for Transplantation . *Cell Stem Cell*. 13:734-744, 2013
14. Fukata N, Okazaki K, Omiya M, Matsushita M, Watanabe M: Hematologic malignancies in the Japanese patients with inflammatory bowel disease. *J Gastroenterol*. (Epub ahead of print), 2013
15. Hibi T, Sakuraba A, Watanabe M, Motoya S, Ito H, Sato N, Yoshinari T, Motegi K, Kinouchi Y, Takazoe M, Suzuki Y, Matsumoto T, Kawakami K, Matsumoto T, Hirata I, Tanaka S, Ashida T, Matsui T: C- reactive protein is an indicator of serum infliximab level in predicting loss of response in patients with Crohn's disease. *J Gastroenterol*. (Epub ahead of print), 2013
16. Hisabe T, Hirai F, Matsui T, Watanabe M: Evaluation of diagnostic criteria for Crohn's disease in Japan. *J Gastroenterol*. (Epub ahead of print), 2013
17. Kiyohashi K, Kakinuma S, Kamiya A, Sakamoto N, Nitta S, Yamanaka H, Yoshino K, Fujiki J, Murakawa M, Kusano-Kitazume A, Shimizu H, Okamoto R, Azuma S, Nakagawa M, Asahina Y, Tanimizu N, Kikuchi A, Nakauchi H, Watanabe M: Wnt5a signaling mediates biliary differentiation of fetal hepatic stem/progenitor cells. *Hepatology*, 57(6):2502-2513, 2013
18. Kuwahara E, Asakura K, Nishiwaki Y, Inoue N, Watanabe M, Hibi T, Takebayashi T: Effects of family history on inflammatory bowel disease characteristics in Japanese patients. *J Gastroenterol*. 47(9):961-968, 2012
19. Naganuma M, Fujii T, Kunisaki R, Yoshimura N, Takazoe M, Takeuchi Y, Saito E, Nagahori M, Asakura K, Takebayashi T, Watanabe M: Incidence and characteristics of the 2009 influenza (H1N1) infections in inflammatory bowel disease patients. *Journal of Crohn's & colitis*. 7(4):308-318, (Epub ahead of print), 2013
20. Naganuma M, Kunisaki R, Yoshimura N, Takeuchi Y, Watanabe M: A prospective analysis of the incidence and risk factors for opportunistic infections in patients with inflammatory bowel disease. *J Gastroenterol*. 48(5):595-560, 2013
21. Naganuma M, Nagahori M, Fujii T, Morio J, Saito E, Watanabe M: Poor recall of prior exposure to varicella zoster, rubella, measles, or mumps in patients with IBD. *Inflamm Bowel Dis*. 19(2):418-422, (Epub ahead of print), 2013
22. Ohyagi M, Ohkubo T, Yagi Y, Ishibashi S, Akiyama J, Nagahori M, Watanabe M, Yokota T, Mizusawa H: Chronic inflammatory demyelinating polyradiculoneuropathy in a patient with crohn's disease. *Intern Med*. 52(1):125-128, 2013
23. Ueno F, Matsui T, Matsumoto T, Matsuoka K, Watanabe M, Hibi T, on behalf of the guideline project group of intractable Inflammatory Bowel Disease granted by the Ministry of Health, Labour and Welfare of Japan and the

Guidelines Committee of the Japanese: Evidence-based clinical practice guidelines for Crohn's disease, integrated with formal consensus of experts in Japan. **J Gastroenterol.** 48(1)31-72, 2013

24. Watanabe K, Sasaki I, Fukushima K, Futami K, Ikeushi H, Sugita A, Nezu R, Mizushima T, Kamoka S, Kusunoki M, Yoshioka K, Funayama Y, Watanabe T, Fujii H, Watanabe M: Long-term Incidence and Characteristics of Intestinal Failure in Crohn's disease:A Japanese Multicenter Study. **J Gastroenterol.** (in press), 2013

Department of Sleep Modulatory Medicine

1. Staff and Students

Professor	Naohiko INASE (Department of Integrated Pulmonology)
Associate Professor	Meiyo TAMAOKA
Assistant Professor	Mizue HOBO

2. Purpose of Education

We are engaged in lectures and training of sleep disorder including sleep-disordered breathing for residents and students in our university hospital.

3. Research Subjects

- 1) Effects of NMDA-type glutamate receptor co-agonist on gamma oscillations and sleep in schizophrenia.
- 2) Open-label trial of ramelteon for diabetes mellitus with sleep disorder.
- 3) The effect of chronotherapy with the angiotensin-antagonist in hypertension with sleep apnea syndrome.
- 4) The efficacy of home-oxygen therapy in patients with sleep apnea and pulmonary fibrosis.
- 5) Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
- 6) Open-label trial of hyperbaric oxygen therapy on sleep quality
- 7) The heart rate and T-wave variability in sleep apnea syndrome

4. Clinical Services

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. Tsutsui (Pulmonary Medicine)
	PM	Dr. Fujie (Pulmonary Medicine)
Tuesday:	AM	Dr. Hirai (Psychiatry)
Wednesday:	AM & PM	Dr. Miyazaki (Health Service Center)
Thursday:	AM & PM	Dr. Tamaoka (Sleep Modulatory Medicine)
Friday:	AM	Dr. Uezato (Psychiatry)
	AM & PM	Dr. Tateishi (Pulmonary Medicine)

Department of Women's Health

1. Staffs

Associate Professor	Masakazu Terauchi
Assistant Professor	Kimio Wakana (concurrent)

2. Education

As a branch of the Department of Obstetrics and Gynecology, we shared responsibility in the education of Obstetrics and Gynecology and Human Genetics, as well as in the training of medical students on clinical clerkship.

3. Research Subjects

Our research, mainly focusing on the relationship between food and women's health, deals with a variety of topics listed below in 2013, summarized as "the effects of nutrients and other bioactive substances contained in food and drugs on women's physical and mental aging".

- Effects of grape seed extract on middle-aged women's health-related quality of life
- Effects of hormone therapy and keishibukuryogan on blood pressure in perimenopausal and postmenopausal women
- Effects of nonbenzodiazepine, melatonin receptor agonist, and Kampo medication on sleep disturbances in perimenopausal and postmenopausal women
- Effects of selective serotonin reuptake inhibitors on subjective and objective sleep parameters in middle-aged women with depression
- Effects of oral contraceptive pills on sleep disturbances in young women with primary dysmenorrhea
- Effects of tomato juice on cardiovascular risk markers in middle-aged women
- Effects of soy isoflavone aglicone on middle-aged women's health-related quality of life
- Menopausal hormone therapy: route of administration and platelet-derived microparticles

4. Clinical Services

As a branch of the Department of Obstetrics and Gynecology, we provide a comprehensive diagnosis, treatment and disease management solution for women suffering from:

- menopausal symptoms
 - premature ovarian insufficiency
 - postmenopausal osteoporosis
 - dyslipidemia
 - hypertension
 - pelvic organ prolapse
 - lower urinary tract syndrome
 - depression
 - anxiety disorder
 - insomnia
 - dysmenorrhea
 - premenstrual syndrome
- etc.

5. Publications

Original Articles

1. Terauchi M, Hiramitsu S, Obayashi S, Akiyoshi M, Owa Y, Kato K, Matsushima E, Kubota T. Associations among Depression, Anxiety, and Somatic Symptoms in Peri- and Post-Menopausal Women. *J Obstet Gynaecol Res* 39(5): 1007-1013, 2013
2. Hiramitsu S, Terauchi M, Kubota T. The effects of Dickkopf-4 on the proliferation, differentiation, and apoptosis of osteoblasts. *Endocrinology* 154(12):4618-4626, 2013
3. Terauchi M, Horiguchi N, Kajiyama A, Akiyoshi M, Owa Y, Kato K, Kubota T. Effects of Grape Seed Proanthocyanidin Extract on Menopausal Symptoms, Body Composition, and Cardiovascular Parameters in Middle-aged Women: A Randomized, Double-blind, Placebo-controlled, Pilot Study. *Menopause* (online publication)
4. Terauchi M, Hiramitsu S, Akiyoshi M, Owa Y, Kato K, Obayashi S, Matsushima E, Kubota T. Effects of the

Kampo Formula Tokishakuyakusan on Headaches and Concomitant Depression in Middle-aged Women. Evid-Based Compl Alt (online publication)

Review

1. Terauchi M. Which is worse: old or obese? *Menopause* 20(8): 802-803, 2013

Oral Presentation

1. Masakazu Terauchi, Shiro Hiramitsu, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Satoshi Obayashi, Eisuke Matsushima, Toshiro Kubota. "Effects of a Kampo formula Tokishakuyakusan on headaches and concomitant depression in middle-aged women". 17th International Congress of the International Society of Psychosomatic Obstetrics and Gynaecology (ISPOG). Berlin, 2013-05-22
2. Masakazu Terauchi, Noe Horiguchi, Asuka Kajiyama, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Toshiro Kubota. "The effects of grape seed extract proanthocyanidin on menopausal symptoms". 5th Scientific Meeting of the Asia Pacific Menopause Federation. Tokyo, 2013-10-18

Poster Presentation

1. Masakazu Terauchi, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Asuka Kajiyama, Shiro Hiramitsu, Satoshi Obayashi, Eisuke Matsushima, Toshiro Kubota. "Prevalence and Determinants of Lower Urinary Tract Symptoms in Peri- and Postmenopausal Women". 5th Scientific Meeting of the Asia Pacific Menopause Federation. Tokyo, 2013-10-18

Department of Advanced Surgical Technology Research and Development

1. Staff

Project Associate Professor Katsuhiro OHUCHI
Associate Professor Tomohiro MIZUNO

2. Purpose of Education

The missionary work of our department is to advance the state-of-the-art of surgical technology and to drive surgical education and training. To satisfy the increasing need for surgical training and training in the area of modern surgery, we will pursue the training platform for advanced surgery.

3. Research Subjects

- 1) Research and Development of Advanced Surgical Technologies
- 2) Research and Development of Innovative Medical Devices
- 3) Surgical Training and Training Program Development

4. Publications

Original Articles

1. Fujita S, Arai H, Tomita M, Mizuno T, Kawaguchi S, Manabe S, Hachimaru T, Miyagi N. Proposal of a Novel Index for Selection of Optimal Annuloplasty Ring Size for Tricuspid Annuloplication. *Circulation Journal* 2013 Oct; 77(10): 2505-2513

Department of Arteriosclerosis and Vascular Biology

1. Staff

Associate Professor Shohei SHINOZAKI
 Assistant Professor Kenji TOYOSHIMA

2. Purpose of Education

In accordance with aging and westernization of diet, atherosclerotic disease has been increasing in Japan. Recently, the chronic inflammation has been focused as the mechanism of arteriosclerosis. It has been demonstrated that inflammation is deeply involved in the initial stage of atherosclerosis. However, treatments with anti-inflammatory drugs, such as NSAIDs, for atherosclerosis generally have not been successes. Thus we consider that there are some unknown mechanisms between development of arteriosclerosis and inflammation. Our course's education policy is to obtain basic research skills for elucidating pathogenesis of atherosclerosis.

3. Research Subject

- Basic research on arteriosclerosis
- Search and identification for novel S-nitrosylated protein
- Molecular mechanism of metabolic syndromes through S-nitrosylation

4. Publications

- 1) [Shinozaki S](#), Chiba T, Kokame K, Miyata T, Kaneko E, Shimokado K. (2013). **A deficiency of Herp, an endoplasmic reticulum stress protein, suppresses atherosclerosis in apoE knockout mice by attenuating inflammatory responses.** *PlosOne*. 28;8(10):e75249.
- 2) Sips PY, Irie T, Zou L, [Shinozaki S](#), Sakai M, Shimizu N, Nguyen R, Stamler JS, Chao W, Kaneki M, Ichinose F. (2103). **Reduction of cardiomyocyte S-nitrosylation by S-nitrosoglutathione reductase protects against sepsis-induced myocardial depression.** *Am J Physiol Heart Circ Physiol*. 15;304(8):H1134-46.
- 3) Kaneki M, Fukushima Y, [Shinozaki S](#), Fukaya M, Habiro M, Shimizu N, Chang K, Yasuhara S, Martyn JA. (2013). **iNOS inhibitor, L-NIL, reverses burn-induced glycogen synthase kinase-3 β activation in skeletal muscle of rats.** *Metabolism*. Mar;62(3):341-6.

5. Grants

- Shohei Shinozaki: Grant-in-Aid for Young Scientists (B), MEXT KAKENHI Grant Number 25860231; The role of S-nitrosylation in pathogenesis of metabolic syndrome.
- Shohei Shinozaki: Takeda Science Foundation for Medical Research, Identification of the missing link between chronic inflammation and pathogenesis of metabolic syndrome.

Clinical Laboratory

1. Staffs

General Manager (Junior Associate Professor)

Naoko Tojo

Associate Manager (Associate Professor)

Shuji Tohda

Assistant Professor

Naomi Murakami

Tadashi Kanouchi

Ryoko Azuma

2. Purpose of Education

Main purpose of education in the clinical laboratory is to provide students the opportunity to study clinical laboratory medicine and medical technology. The staffs lecture on clinical laboratory medicine and give technical training on clinical laboratory tests to not only the medical students and medical technologist students in the faculty of medicine of the university but also those in the another vocational schools for medical technologists.

Besides the students, eight residents of the medical hospital of our university had a general training for clinical laboratory medicine, including ultrasonography. Hands-on seminars of Gram staining, abdominal ultrasonography and so on have been repeatedly held for young doctors in the hospital. One clinical laboratory technicians in the other hospital was also given a short term of practical training in our clinical laboratory.

3. Research Subjects

- 1) Evidence-based laboratory medicine
- 2) Standardization of respiratory function tests.
- 3) Development of molecular diagnostic tests for hematological diseases.
- 4) Development of electrophysiological diagnostic tests for peripheral neuropathies.
- 5) Clinical and electrophysiological study for amyotrophic lateral sclerosis.

4. Clinical Services

High quality and advanced laboratory tests are being done speedily in the clinical laboratory all day all the time. Blood-taking is started at 8:05, 30 minutes earlier than before. It results in shortening the waiting time of patients and in more speedy reporting the test results. Items of emergency laboratory tests have been in increase, including smear test for tubercle bacillus and cell counting of the cerebrospinal fluid. The results of physiological examinations are online reported quickly and accurately. The updated information on antibiotic sensitivity of the pathogens in each ward is also provided online regularly. In the night time, the laboratory also provides appropriate blood products for transfusion, in cooperation with blood transfusion service of the hospital. Our clinical laboratory is going to acquire ISO15189 certification.

5. Publications

Original Article

1. Ono A, Oike R, Okuhashi Y, Takahashi Y, Itoh M, Nara N, **Tohda S**. Comparative effects of PP242 and rapamycin on mTOR signalling and NOTCH signalling in Leukemia cells. *Anticancer Res* 2013; 33: 809-814.
2. Yonekura S, Itoh M, Okuhashi Y, Takahashi Y, Ono A, Nara N, **Tohda S**. Effects of the HIF1 inhibitor, echinomycin, on growth and NOTCH signalling in leukaemia cells. *Anticancer Res* 2013; 33: 3099-3103.
3. Okuhashi Y, Itoh M, Nara N, **Tohda S**. *NOTCH* Knockdown affects the proliferation and mTOR signaling of leukemia cells. *Anticancer Res* 2013; 33: 4293-4298.
4. Watanabe R, **Azuma RW**, Suzuki J, Ogawa M, Itai A, Hirata Y, Komuro I, Isobe M. Inhibition of NF- κ B activation by a novel IKK inhibitor reduces the severity of experimental autoimmune myocarditis via suppression of T-cell activation. *Am J Physiol Heart Circ Physiol* 2013; 305: H1761-H1771.

Department of Blood Transfusion Medicine

1. Staffs

Director (Lecturer) Michiko KAJIWARA
 Assistant Director (Medical Technologist)
 Naoki OHTOMO

2. Purpose of Education

Transfusion therapy is a supplementation of the blood component, but it also has aspects of cell therapy and transplantation. So, it is important to practice safe and appropriate transfusion therapy. Clinical tests of transfusion, such as blood type test, are most basic immunological test technique. The accurate understanding and practice of these tests is also necessary for the safety of medical treatment. From this point of view, we educate the students of school of medicine, school of allied health sciences, graduate school of medical and dental sciences, medical doctors, and co-medicals.

3. Research Subjects

- 1) Practice of safe and appropriate transfusion therapy (including prevention of medical accident related transfusion)
- 2) Basic and clinical research of hematopoietic stem cell transplantation

4. Clinical Services (The result of 2013)

1) The amount of blood products used

Red cell component products	11,661	Units	(5,938 bags)
Platelet concentration	28,575	Units	(2,442 bags)
Fresh frozen plasma	6,773	Units	(3,199 bags)

2) Autologous blood collection and transfusion

Autologous blood collection	395	cases	(500times, 967Units)
Autologous blood transfusion	361	cases	(857Units)

3) The number of clinical tests of transfusion

Blood typing	8,719
Anti red blood cell antibody test	3,668
Cross match	9,748

4) Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest	16 cases	18 times
Allogenic peripheral blood stem cell harvest	4 cases	7 times
Autologous peripheral mononuclear cell harvest	1 case	1 time
Allogenic bone marrow harvest	16 cases	16 times

(Including Japan Marrow Donor Program donors)

5) Hematopoietic stem cell transplantation

(The evaluation and preservation of the stem cells were done in our department)

Autologous peripheral blood stem cell transplantation	15 cases	15 times
Allogenic peripheral blood stem cell transplantation	4 cases	4 times
Autologous peripheral mononuclear cell transplantation	1 case	1 time
Allogenic bone marrow transplantation	15 cases	15 times
Allogenic umbilical cord blood transplantation	4 cases	4 times

5. Publications

Original articles

1. Miyawaki Y, Imoto I, Tokairin Y, Kawada K, Nakajima T, Nishikage T, Nagai K, Kajiwara M, Inazawa J, Kawano T. Esophageal squamous cell carcinoma developed 11 years after allogenic bone marrow transplantation for acute lymphoblastic leukemia. *Jpn J Clin Oncol* 43:69-73, 2013.
2. Isoda T, Mitsuiki N, Ohkawa T, Kaneko S, Endo A, Ono T, Aoki Y, Tomizawa D, Kajiwara M, Araki S, Nagasawa M, Morio T, Takagi M, Mizutani S. Irreversible leukoencephalopathy after reduced-intensity, stem cell transplantation in a dyskeratosis congenita patient with TINF2 mutation. *J Pediatr Hematol Oncol* 35:178-182, 2013.

3. Nagasawa M, Ohkawa T, Endo A, Mitsui N, Ono T, Aoki Y, Isoda T, Tomizawa D, Takagi M, Kajiwara M, Morio T, Mizutani S. Early coagulation disorder after allogeneic stem cell transplantation is a strong prognostic factor for transplantation-related mortality, and intervention with recombinant human thrombomodulin improves the outcome: a single-center experience. *Int J Hematol* 98:533-542, 2013.

Department of Hemopurification

Associate Professor	Tatemitsu RAI	
Assistant Professor	Nofumi YUI,	Hidenori NISHIDA
Hospital Staff	Mayuko NOZAKI,	Haruna AZETSU

(1) Education

The Department of Hemopurification has been engaged in such educational activities as follows.

- 1) Clinical clerkship of 6th year students of Medical School
- 2) Preclinical lectures of 5th year students of Medical School
- 3) Lectures of 4th year students of Medical School
- 4) Lectures of students of Dental School
- 5) Hospital training of postgraduate master course students of Medical School
- 6) Hospital training of clinical engineering technologists and nurses (2 trainees)

(2) Research

The Department of Hemopurification has been engaged in such research activities as follows.

- 1) Pathophysiology and treatment of chronic renal failure
- 2) Pathophysiology and treatment of acute renal failure
- 3) New techniques in blood purification

(3) Clinical Services

The achievements of clinical services of The Department of Hemopurification in 2013 are as follows:

Total number of blood purification sessions	5156
Number of hemodialysis (HD) sessions	4510
Number of plasma exchange (PE) sessions	128
Number of plasma adsorption sessions	84
Number of continuous hemodiafiltration (CHDF) sessions	339
Number of leukapheresis sessions	47
Number of endotoxin adsorption sessions	35
Number of cell-free concentrated ascites reinfusion (CART) sessions	9

(4) Publications

【Original articles】

1. Ando F, Okado T, Sohara E, Rai T, Uchida S, Sasaki S. Development of minimal-change glomerular disease and Hashimoto's thyroiditis during the treatment of sarcoidosis. *CEN Case Rep.* 2: 248-51, 2013.
2. Ando F, Sohara E, Ito E, Okado T, Rai T, Uchida S, Sasaki S. Acute poststreptococcal glomerulonephritis with acute interstitial nephritis related to streptococcal pyrogenic exotoxin B. *Clin Kidney J.* 6 : 347-348, 2013.
3. Iimori S, Noda Y, Okado T, Naito S, Toda T, Chida Y, Kuwahara M, Ando R, Nishio Y, Maeda Y, Tanaka H, Tamura T, Kimoto S, Kanda E, Inoshita S, Yoshikawa M, Okutsu R, Tajima M, Kusaura T, Kobayashi K, Rai T, Uchida S, Sasaki S. Baseline characteristics and prevalence of cardiovascular disease in newly visiting or referred chronic kidney disease patients to nephrology centers in Japan: a prospective cohort study. *BMC Nephrol.* 14: 152, 2013.
4. Inoue R, Sohara E, Rai T, Satoh T, Yokozeki H, Sasaki S, Uchida S. Immunolocalization and translocation of aquaporin-5 water channel in sweat glands. *J Dermatol Sci.* 70: 26-33, 2013.
5. Ishimoto I, Sohara E, Ito E, Okado E, Rai T, Uchida S. Fibronectin glomerulopathy. *Clin Kidney J.* 6 : 513-515, 2013.
6. Isobe K, Mori T, Asano T, Kawaguchi H, Nonoyama S, Kumagai N, Kamada F, Morimoto T, Hayashi M, Sohara E, Rai T, Sasaki S, Uchida S. Development of enzyme-linked immunosorbent assays for urinary thiazide-sensitive Na-Cl cotransporter (NCC) measurement. *Am J Physiol Renal Physiol.* 305: F1374-81, 2013.
7. Mori T, Kikuchi E, Watanabe Y, Fujii S, Ishigami-Yuasa M, Kagechika H, Sohara E, Rai T, Sasaki S, Uchida S. Chemical library screening for WNK signalling inhibitors using fluorescence correlation spectroscopy. *Biochem J.* 455: 339-45, 2013.
8. Mori Y, Wakabayashi M, Mori T, Araki Y, Sohara E, Rai T, Sasaki S, Uchida S. Decrease of WNK4 ubiquitination by disease-causing mutations of KLHL3 through different molecular mechanisms. *Biochem Biophys Res Commun.* 439:

30-4, 2013.

9. Nomura N, Kamiya K, Ikeda K, Yui N, Chiga M, Sohara E, Rai T, Sasaki S, Uchida S. Treatment with 17-allylamino-17-demethoxygeldanamycin ameliorated symptoms of Bartter syndrome type caused by mutated *Bsmd* in mice. *Biochem Biophys Res Commun.* 441: 544-49, 2013.
10. Ohkubo A, Kurashima N, Nakamura A, Miyamoto S, Iimori S, Rai T. Solute Removal Capacity of High Cut-Off Membrane Plasma Separators. *Ther Apher Dial.* 17: 484-9, 2013.
11. Sasaki S, Chiga M, Kikuchi E, Rai T, Uchida S. Hereditary nephrogenic diabetes insipidus in Japanese patients: analysis of 78 families and report of 22 new mutations in *AVPR2* and *AQP2*. *Clin Exp Nephrol.* 17: 338-344, 2013.
12. Takahashi D, Mori T, Wakabayashi M, Mori Y, Susa K, Zeniya M, Sohara E, Rai T, Sasaki S, Uchida S. *KLHL2* interacts with and ubiquitinates *WNK* kinases. *Biochem Biophys Res Commun.* 437: 457-62, 2013.
13. Wakabayashi M, Mori T, Isobe K, Sohara E, Susa K, Araki Y, Chiga M, Kikuchi E, Nomura N, Mori Y, Matsuo H, Murata T, Nomura S, Asano T, Kawaguchi H, Nonoyama S, Rai T, Sasaki S, Uchida S. Impaired *KLHL3*-mediated ubiquitination of *WNK4* causes human hypertension. *Cell Rep.* 3: 858-68, 2013.
14. Zeniya M, Sohara E, Kita S, Iwamoto T, Susa K, Mori T, Oi K, Chiga M, Takahashi D, Yang SS, Lin SH, Rai T, Sasaki S, Uchida S. Dietary salt intake regulates *WNK3*-*SPAK*-*NKCC1* phosphorylation cascade in mouse aorta through angiotensin II. *Hypertension.* 62: 872-878, 2013.

【Scientific meetings】

1. Iimori S, Naito S, Okado T, Noda Y, Rai T, Uchida S, Sasaki S. Baseline characteristics and prevalence of cardiovascular disease in newly visiting or referred chronic kidney disease patients to nephrology centers in Japan. 50th European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Congress, Istanbul, May, 2013.
2. Iimori S, Naito S, Okado T, Noda Y, Rai T, Uchida S, Sasaki S, CKD-ROUTE Study Group. Baseline characteristics and prevalence of cardiovascular disease in newly visiting or referred chronic kidney disease patients to nephrology centers in Japan. 2nd Chronic Kidney Disease Frontier Meeting, Nagoya, Japan, Feb, 2013.
3. Inoue Y, Sohara E, Kobayashi K, Rai T, Ishibashi K, Horie S, Su X, Zhou J, Sasaki S, Uchida S. Aberrant Glycosylation and Localization of Polycystin-1 Cause Polycystic Kidney in *AQP11*-Knockout Mice. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
4. Ishigami J, Tajima M, Motomura A, Rai T, Uchida S, Sasaki S. Association between Mortality Risk and Severity of Acute Kidney Injury among Critical-care Patients from Remote Islands: A Single Center Prospective Cohort Study. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
5. Ishimoto I, Sohara E, Ito E, Chiga M, Iimori S, Okado T, Rai T, Uchida S, Sasaki S. A case of fibronectin glomerulopathy with rapidly progressive, severe nephrotic syndrome leading to end-stage renal disease. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
6. Isobe K, Mori T, Sohara E, Rai T, Sasaki S, Uchida S. Clinical Significance of Urinary Thiazide-Sensitive Na-Cl Cotransporter (NCC) Measurement by Newly Development Enzyme-Linked Immunosorbent Assays. The 46th Annual meeting of American Society of Nephrology, Atlanta, November, 2013.
7. Kurashima N, Ohkubo A, Yui N, Rai T. Recombinant human soluble thrombomodulin administration improves septic shock requiring continuous renal replacement therapy: A retrospective cohort study. 46th Annual Meeting of American Society of Nephrology, Atlanta, USA, November, 2013.
8. Mori T, Eriko K, Sohara E, Rai T, Sasaki S, Uchida S. Chemical library screening for *WNK* signaling inhibitors by using fluorescent correlation spectroscopy. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
9. Mori Y, Wakabayashi M, Mori T, Araki Y, Sohara E, Rai T, Sasaki S, Uchida S. Analyses of *KLHL3* mutants that cause Pseudohypoaldosteronism type II. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
10. Naito S, Iimori S, Okado T, Noda Y, Rai T, Uchida S, Sasaki S. Evaluation of blood pressure control of chronic kidney disease patients prior to nephrologist care in Japan. 50th European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Congress, Istanbul, May, 2013.
11. Ohkubo A, Kurashima N, Nakamura A, Miyamoto S, Seshima H, Iimori S, Yui N, Rai T. Therapeutic plasma exchange using high cut-off membrane plasma separator. The 46th Annual Meeting of American Society of Nephrology, Atlanta, USA, November, 2013.
12. Okado T, Iimori S, Noda Y, Yamamura C, Kihira H, Yui N, Rai T, Uchida S, Sasaki S. Anemia status of middle stage

- CKD patients on their first visit to the nephrology clinic in Japan. 50th ERA-EDTA Congress, Istanbul, Turkey, May, 2013.
13. Susa K, Sohara E, Zeniya M, Rai T, Sasaki S, Uchida S. Low salt intake decreased transcription and protein level of KLHL3 in mouse kidney. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
 14. Takahashi D, Mori T, Wakabayashi M, Mori Y, Susa K, Zeniya M, Sohara E, Rai T, Sasaki S, Uchida S. KLHL2 interacts with and ubiquitinates WNK kinases. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
 15. Tanaka H, Iimori S, Naito S, Okado T, Rai T, Uchida S, Sasaki S, CKD-ROUTE Study Group. Cardiovascular events and mortality in a prospective cohort of CKD patients in Japan: effects of underlying kidney diseases. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
 16. Wakabayashi M, Mori T, Isobe K, Sohara E, Susa K, Araki Y, Chiga M, Kikuchi E, Nomura N, Mori Y, Rai T, Sasaki S, Uchida S. Impaired KLHL3-mediated ubiquitination of WNK4 activates OSR1 and SPAK kinases-NaCl cotransporter (NCC) signaling and causes hypertension. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.
 17. Zeniya M, Sohara E, Kita S, Iwamoto T, Susa K, Mori T, Oi K, Chiga M, Takahashi D, Yang SS, Lin SH, Rai T, Sasaki S, Uchida S. WNK3 Regulates Blood Pressure Through the Regulation of Vascular OSR1/SPAK-NKCC1 Phosphorylation Cascade. The 46th Annual Meeting of American Society of Nephrology, Atlanta, November, 2013.

Hyperbaric Medical Center

1. Staffs

Center Chief and Junior Associate Professor

Kazuyoshi YAGISHITA

Tokunin Junior Associate Professor Mitsuhiko ENOMOTO

Medical Staff

Takashi HIRAI,

Hidetoshi KABURAGI

Tokunin Assistant Professor

Seiichiro TOGAWA,

Yasushi KOJIMA

Researcher

Masaharu SHIBAYAMA,

Masaki HORIE,

Manabu SHIMODA,

Kazuo YAMAMOTO,

Naoko SUZUKI

Secretary

Kiyomi ITOH

Professor Emeritus

Yoshihiro MANO

2. Purpose of Education

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.

3. Research Subjects

- 1) Soft tissue injuries related with sports activities
- 2) HBO for conditioning in sports activities
- 3) Diving medicine
- 4) Hyperbaric oxygen therapy

4. Clinical Services

Hyperbaric Medical Center in Tokyo Medical and Dental University hospital is the center institute of hyperbaric oxygen therapy and research in Japan, and one of the largest hyperbaric oxygen chamber in the world is set up in Hyperbaric Medical Center, which can contain the maximum number of 16 persons.

As described above, 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. In 2012, 5,117 times hyperbaric oxygen therapy (HBO) in 580 patients were performed in our university hospital. In addition, for the purpose of rapid recovery from injury, we now perform HBO aggressively for soft tissue injury related with sports activities including compartment syndrome, ankle sprain, knee ligament injury, and muscle contusion.

5. Publication

Original articles

1. Enomoto M, Bunge MB, Tsoulfas P. A multifunctional neurotrophin with reduced affinity to p75NTR enhances transplanted Schwann cell survival and axon growth after spinal cord injury. *Exp Neurol*. 2013, 248:170-182
2. Aizawa J, Masuda T, Hyodo K, Jinno T, Yagishita K, Nakamaru K, Koyama T, Morita S. Ranges of active joint motion for the shoulder, elbow, and wrist in healthy adults. *Disability & Rehabilitation* 2013, 35(16):1342-1349
3. Sekiya I, Koga H, Muneta T, Yagishita K, Ju YJ, Mochizuki T, Horie M, Nakamura T, Okawa A. Effect of Posterolateral Bundle Graft Fixation Angles on Graft Tension Curves and Load Sharing in Double-Bundle Anterior Cruciate Ligament Reconstruction Using a Transtibial Drilling Technique. *Arthroscopy*. 2013, 29(3):529-538.
4. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Sekiya I. Effect of femoral tunnel position on graft tension curves and knee stability in anatomic double-bundle anterior cruciate ligament

- reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2013. [Epub ahead of print]
5. Koga H, Muneta T, Yagishita K, Ju YJ, Mochizuki T, Horie M, Nakamura T, Okawa A, Sekiya I. Effect of posterolateral bundle graft fixation angles on graft tension curves and load sharing in double-bundle anterior cruciate ligament reconstruction using a transtibial drilling technique. *Arthroscopy.* 2013, 29(3):529-38.
 6. Hirai T, Enomoto M, Kaburagi H, Sotome S, Yoshida-Tanaka K, Ukegawa M, Kuwahara H, Yamamoto M, Tajiri M, Miyata H, Hirai Y, Tominaga M, Shinomiya K, Mizusawa H, Okawa A, Yokota T. Intrathecal AAV Serotype 9-mediated Delivery of shRNA Against TRPV1 Attenuates Thermal Hyperalgesia in a Mouse Model of Peripheral Nerve Injury. *Mol Ther.* 2013. [Epub ahead of print]
 7. Arai Y, Hirai T, Yoshii T, Sakai K, Kato T, Enomoto M, Matsumoto R, Yamada T, Kawabata S, Shinomiya K, Okawa A. A Prospective Comparative Study of Two Minimally Invasive Decompression Procedures for Lumbar Spinal Canal Stenosis: Unilateral Laminotomy for Bilateral Decompression (ULBD) Versus Muscle-preserving Interlaminar Decompression (MILD). *Spine (Phila Pa 1976).* 2013. [Epub ahead of print]
 8. Yoshii T, Yuasa M, Sotome S, Yamada T, Sakaki K, Hirai T, Taniyama T, Inose H, Kato T, Arai Y, Kawabata S, Tomizawa S, Enomoto M, Shinomiya K, Okawa A. Porous/dense composite hydroxyapatite for anterior cervical discectomy and fusion. *Spine (Phila Pa 1976).* 2013, 38(10):833-40.
 9. Taniyama T, Hirai T, Yamada T, Yuasa M, Enomoto M, Yoshii T, Kato T, Kawabata S, Inose H, Okawa A. Modified K-line in magnetic resonance imaging predicts insufficient decompression of cervical laminoplasty. *Spine (Phila Pa 1976).* 2013, 38(6):496-501.
 10. Horie M, Enomoto M, Shimoda M, Okawa A, Miyakawa S, Yagishita K. Enhancement of satellite cell differentiation and functional recovery in injured skeletal muscle by hyperbaric oxygen treatment. *J Appl Physiol.* 2014, 116(2):149-55.

Center for Cell Therapy

1. Staffs and Students

Director	Tomohiro Morio (Department of Pediatrics)
Vise Director	Ichiro Sekiya (Department of Orthopedic Surgery)
Quality control manager	Michiko Kajiwara (Chief Administrator, Department of Blood Transfusion Medicine)
Product manager	Norio Shimizu (Division of Virology, Medical Research Institute)
Technicians	Yuri Kohno, Naomi Terada, Akane Miyasaka(to June 2013)
Technicians (From Collaborative Research)	Takashi Kosaka(to March 2013), Nakaba Ochiai(from April 2013)
Clerical Assistant	Akiko Hoshikawa, Jun Kusano

2. Purpose of Education

Our center is the first ISO9001:2000(2008)-certified cell processing center in Japan. We provide assistance to prepare standard operation procedure (SOP) and also offer on-the-job training for cell processing/manipulating procedures and that for quality assurance at the center.

3. Research Subjects

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 a novel sensitive technique to detect mutation in genes that are involved in genetic instability and tumor progression
4. Clinical study on *ex-vivo* expanded donor T-cell infusion for patients who underwent hematopoietic stem cell transplantation (HSCT)
5. Development of multi-virus specific T lymphocytes for adoptive immunotherapy
6. Development of short tandem repeat method as a molecular ID for personal identification
7. Research on a regeneration system of the cartilage bone from the synovial membrane (Department of Orthopedic Surgery)
8. Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia (Department of Immunotherapeutics)

Those researches are supported by JST project for development and facilitation of regenerative medicine and by grants from the ministry of health, labour, and welfare and from the ministry of engineering, technology, and industry.

4. Clinical Services

Our center has four independent cell processing rooms (class 10,000 clean rooms) and has received ISO9001:2000(2008) certificate. 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.

The cell products prepared in our centers include

- #1 *Ex-vivo* expanded T-lymphocytes
- #2 Synovium-derived mesenchymal stem cells
- #3 Bone marrow-derived mesenchymal stem cells
- #4 Processed peripheral blood stem cells

The center offers our novel detection system for 12 different viruses in rapid and sensitive manner for the doctors in our medical hospital. We also measure virus loads of the detected virus using a real time PCR system. We measured 1,846 samples in year 2013 in total.

5. Publications

Original articles

1. Nagasawa M, Ohkawa T, Endo A, Mitsuiki N, Ono T, Aoki Y, Isoda T, Tomizawa D, Takagi M, **Kajiwara M**.

- Morio T**, Mizutani S. Early coagulation disorder after allogeneic stem cell transplantation is a strong prognostic factor for transplantation-related mortality, and intervention with recombinant human thrombomodulin improves the outcome: a single-center experience. *Int J Hematol.* **98**:533-42, 2013.
2. Kumaki S, Sasahara Y, Kamachi Y, Muramatsu H, **Morio T**, Goi K, Sugita K, Urabe T, Takada H, Kojima S, Tsuchiya S, Hara T. B-cell function after unrelated umbilical cord blood transplantation using a minimal-intensity conditioning regimen in patients with X-SCID. *Int J Hematol.* **98**:355-60, 2013.
 3. Machida S, Tomizawa D, Tamaichi H, Okawa T, Endo A, Imai K, Nagasawa M, **Morio T**, Mizutani S, Takagi M. Successful Treatment of Diffuse Large B-Cell Lymphoma in a Patient With Ataxia Telangiectasia Using Rituximab. *J Pediatr Hematol Oncol.* **35**:482-5, 2013.
 4. Sugita S, Ogawa M, Shimizu N, **Morio T**, Ohguro N, Nakai K, Maruyama K, Nagata K, Takeda A, Usui Y, Sonoda K, Takeuchi M, Mochizuki M. Use of a comprehensive polymerase chain reaction system for diagnosis of ocular infectious diseases. *Ophthalmology.* **120**:1761-8, 2013.
 5. Unno J, Takagi M, Piao J, Sugimoto M, Honda F, Maeda D, Masutani M, Kiyono T, Watanabe F, **Morio T**, Teraoka H, Mizutani S. Artemis-dependent DNA double-strand break formation at stalled replication forks. *Cancer Sci.* **104**:703-10, 2013.
 6. Wada T, Muraoka M, Toma T, Imai T, Shigemura T, Agematsu K, Haraguchi K, Moriuchi H, Oh-Ishi T, Kitoh T, Ohara O, **Morio T**, Yachie A. Rapid Detection of Intracellular p47phox and p67phox by Flow Cytometry; Useful Screening Tests for Chronic Granulomatous Disease. *J Clin Immunol.* **33**:857-864, 2013.
 7. Isoda T, Mitsuiki N, Ohkawa T, Kaneko S, Endo A, Ono T, Aoki Y, Tomizawa D, Kajiwarra M, Araki S, Nagasawa M, **Morio T**, Takagi M, Mizutani S. Irreversible Leukoencephalopathy After Reduced-intensity Stem Cell Transplantation in a Dyskeratosis Congenita Patient With TINF2 Mutation. *J Pediatr Hematol Oncol.* **35**:e178-82, 2013.
 8. Fukuda S, Nanki T, **Morio T**, Hasegawa H, Koike R, Miyasaka N. Recurrent mitral valve regurgitation with neutrophil infiltration in a patient with multiple aseptic abscesses. *Mod Rheumatol.* 2013 (in press)
 9. Shimizu M, Kanegane H, Wada T, Motoyoshi Y, **Morio T**, Candotti F, Yachie A. Aberrant glycosylation of IgA in Wiskott-Aldrich syndrome and X-linked thrombocytopenia. *J Allergy Clin Immunol.* **131**:587-590, 2013.
 10. Yoshimi A, Kamachi Y, Imai K, Watanabe N, Nakadate H, Kanazawa T, Ozono S, Kobayashi R, Yoshida M, Kobayashi C, Hama A, Muramatsu H, Sasahara Y, Jakob M, **Morio T**, Ehl S, Manabe A, Niemeyer C, Kojima S. Wiskott-Aldrich syndrome presenting with a clinical picture mimicking juvenile myelomonocytic leukaemia. *Pediatr Blood Cancer.* **60**:836-41, 2013.
 11. Miyabe C, Miyabe Y, Miura NN, Takahashi K, Terashima Y, **Morio T**, Yamagata N, Ohno N, Shudo K, Suzuki J-I, Isobe M, Matsuhima K, Tsuboi R, Miyasaka N, and Nanki T. Am80, a retinoic acid receptor agonist, ameliorates murine vasculitis through the suppression of neutrophil migration and activation. *Arthritis Rheumatism.* **65**:503-512, 2013.
 12. Kamae C, Nakagawa N, Sato H, Honma K, Mitsuiki N, Ohara O, Kanegane H, Pasic S, Pan-Hammerstrom Q, van Zelm MC, **Morio T**, Imai K, Nonoyama S. Classification of common variable immunodeficiency by quantification of T cell receptor and Ig kappa-deleting recombination excision circles. *J Allerg Clin Immunol.* **131**:1437-1440, 2013.
 13. Park TY, Kim SH, Shin YC, Lee NH, Lee RK, Shim JH, Glimcher LH, Mook-Jung I, Cheong E, Kim WK, Honda F, **Morio T**, Lim JS, Lee SK. Amelioration of neurodegenerative diseases by cell death-induced cytoplasmic delivery of humanin. *J Control Release.* **166**:307-315, 2013.
 14. Kawasaki Y, Toyoda H, Otsuki S, Iwasa T, Iwamoto S, Azuma E, Itoh-Habe N, Wada H, Fujimura Y, **Morio T**, Imai K, Mitsuiki N, Ohara O, Komada Y. A novel Wiskott-Aldrich syndrome protein mutation in an infant with thrombotic thrombocytopenic purpura. *Eur J Haematol.* **290**:164-8, 2013.
 15. Kobayashi Z, Akaza M, Numasawa Y, Ishihara S, Tomimitsu H, Nakamichi K, Saijo M, **Morio T**, **Shimizu N**, Sanjo N, Shintani S, Mizusawa H. Failure of mefloquine therapy in progressive multifocal leukoencephalopathy: report of two Japanese patients without human immunodeficiency virus infection. *J Neurol Sci.* **324**:190-4, 2013.
 16. Matsukura Y, Muneta T, Tsuji K, Koga H, **Sekiya I**. Mesenchymal Stem Cells in Synovial Fluid Increase After Meniscus Injury. *Clin Orthop Relat Res.* 2013 Dec 13.
 17. Ozeki N, Muneta T, Koga H, Katagiri H, Otabe K, Okuno M, Tsuji K, Kobayashi E, Matsumoto K, Saito H, Saito T, **Sekiya I**. Transplantation of Achilles tendon treated with bone morphogenetic protein 7 promotes meniscus regeneration in a rat model of massive meniscal defect. *Arthritis Rheum.* 2013 Nov;65(11):2876-86.
 18. Katagiri H, Muneta T, Tsuji K, Horie M, Koga H, Ozeki N, Kobayashi E, **Sekiya I**. Transplantation of aggregates of synovial mesenchymal stem cells regenerates meniscus more effectively in a rat massive meniscal defect. *Biochem*

Biophys Res Commun. 2013 Jun 14;435(4):603-9.

19. Hatsushika D, Muneta T, Horie M, Koga H, Tsuji K, Sekiya I. Intraarticular injection of synovial stem cells promotes meniscal regeneration in a rabbit massive meniscal defect model. *J Orthop Res*. 2013 Sep;31(9):1354-9.
20. Ichinose S, Tagami M, Muneta T, Mukohyama H, Sekiya I. Comparative sequential morphological analyses during in vitro chondrogenesis and osteogenesis of mesenchymal stem cells embedded in collagen gels. *Med Mol Morphol*. 2013 Mar;46(1):24-33.
21. Miyatake K, Tsuji K, Yamaga M, Yamada J, Matsukura Y, Abula K, Sekiya I, Muneta T. Human YKL39 (chitinase 3-like protein 2), an osteoarthritis-associated gene, enhances proliferation and type II collagen expression in ATDC5 cells. *Biochem Biophys Res Commun*. 2013 Feb 1;431(1):52-7.
22. Atesok K, Doral MN, Bilge O, Sekiya I. Synovial stem cells in musculoskeletal regeneration. *J Am Acad Orthop Surg*. 2013 Apr;21(4):258-9.
23. Yan J, Ng SB, Tay JL, Lin B, Koh TL, Tan J, Selvarajan V, Liu SC, Bi C, Wang S, Choo SN, Shimizu N, Huang G, Yu Q, Chng WJ.: EZH2 overexpression in natural killer/T-cell lymphoma confers growth advantage independently of histone methyltransferase activity. *blood* **121**: 4512-4520(2013)
24. Tachikawa R, Tomii K, Seo R, Nagata K, Otsuka K, Nakagawa A, Otsuka K, Hashimoto H, Watanabe K, Shimizu N.: Detection of Herpes Viruses by Multiplex and Real-Time Polymerase Chain Reaction in Bronchoalveolar Lavage Fluid of Patients with Acute Lung Injury or Acute Respiratory Distress Syndrome. *Respiration*, [Epub ahead of print] (2013)
25. Ito K, Shimizu N, Watanabe K, Saito T, Yoshioka Y, Sakane E, Tsunemine H, Akasaka H, Kodaka T, Takahashi T.: Analysis of viral infection by multiplex polymerase chain reaction assays in patients with liver dysfunction. *Internal Medicine*. 52(2):201-11 (2013)

Cleanroom

1. Staffs and Students (April, 2013)

Associate Professor Mitsuhiro SUNAKAWA
 Assistant Professor Hiroyuki MATSUMOTO

2. Purpose of Education

The improvement of the nosocomial infection control system in the University Hospital, Faculty of Dentistry, Tokyo Medical and Dental University to spread the actual infection control method to all staff and clinical course students.

3. Research Subjects

- 1) The development of disposal, hygienic materials for dental use.
- 2) The survey for the oral diseases in patients with HIV.
- 3) The survey for the relationship between the consciousness of the staff and students with hospital and the need accident.

[Articles]

1. Kaneko T, Chokechanachaisakul U, Kawamura J, Yamanaka Y, Ito T, Sunakawa M, Suda H, Okiji T: Up-regulation of p38 Mitogen-activated Protein Kinase during Pulp Injury-induced Glial Cell/Neuronal Interaction in the Rat Thalamus. *Journal of Endodontics*, 39(4):488 – 492, 2013.

[Meeting]

1. Kawamura J, Kaneko T, Chokechanachaisakul U, Yamanaka Y, Ito T, Sunakawa M, Okiji T, Suda H: Glial Cell/neuronal Interaction in Thalamus following Dental Pulp Inflammation. 91st IADR, Poster, IADR Program book, 207, Washington State Convention Center, Seattle, USA, 2013/3/23-24.
2. Sunakawa M, Suda H: Treatment of Teeth Possibly with Iatrogenic Neuropathic Pain. The 9th World Endodontic Congress, Poster, Tokyo International Forum, Tokyo, 2013/5/26.
3. Matsumoto H, Sunakawa M, Suda H: Alterations of Periodontal Mechanoreceptive Afferents' Activities by MO-induced Pulpal Inflammation. The 9th World Endodontic Congress, Poster, Tokyo International Forum, Tokyo, 2013/5/26.
4. Kawamura J, Kokuzawa C, Sunakawa M, Suda H: A case of Maxillary First Molar with Unique Morphology. IFEA, The 9th World Endodontic Congress, Tokyo International Forum, Tokyo 2013/5/25.
5. Kawamura J, Kaneko T, Yamanaka Y, Ito T, Sunakawa M, Okiji T, Suda H: Analysis of Glial Cell-related Genes in Rat Thalamus following Dental Pulp Inflammation. Abstract Book 89, The 2nd IADR Asia Pacific Region (IADR-APR), Bangkok, Thailand, 2013/8/21.

Center for Development of Devices and Drugs in Dentistry

1. Staffs

Director	Junji TAGAMI	
Co-Director	Hidekazu TAKAHASHI,	Hideki HARASAWA,
	Naoko HARADA	
Member	Miwako WAGAI (CRC),	Kazuko KOJIMA (CRC)

2. Overview

Center for development of devices and drugs in dentistry was established in April, 2004 and is committed to a wide range of activities, such as education, consultation for new devices and drugs application, and support for clinical trials in University Hospital of Dentistry.

3. Purpose of Education

We provide a program for the 3rd year students of the School of Dentistry, also for the 2nd year students of the School of Oral Health Care Sciences majoring in Oral Health Engineering to help them to gain fundamental knowledge of Pharmaceutical Affairs Act which is required for development and application of dental devices.

Collaborating with the Institute of Biomaterials and Bioengineering, we lecture the 1st year students in Master's Program at Graduate School of Medical and Dental Sciences on issues and systems related to the mission that many outcomes from studies about innovative dental devices and materials will be put into use without "device-lag".

4. Clinical trial supporting Services

In order to accomplish clinical trials successfully, we manage and support from planning, paper work to patient care as a main office of clinical trials in University Hospital of Dentistry.

5. Consultation Services

We provide consultation services about various issues concerning the Pharmaceutical Affairs Act, not only for pharmaceutical and dental companies but also for dentists and researchers in our University.

By the supporting services of clinical trials, we hope that applicant will be able to form a protocol adequately and effectively, and to start the clinical trial swiftly.

6. Achievements

Consultation

As of today, one clinical trial and one clinical research (study) are ongoing (from January 1 to December 31, 2013).

The 130 consultation services concerning dental devices were performed in 2013.

7. Publications

Original Article

Review Article

Book

Center of Sports Medicine and Sports Dentistry

1. Staffs

○Clinical Center of Sports Medicine

Center Chief and Junior Associate Professor

Kazuyoshi YAGISHITA

Tokunin Junior Associate Professor Mitsuhiro ENOMOTO

Tokunin Assistant Tomomasa NAKAMURA

Chief of Athletic Rehabilitation Junya AIZAWA

Physiotherapist Shunsuke OHJI

○Sports Medicine/Dentistry

Associate Professor Toshiaki UENO

Assistant Professor Toshiyuki TAKAHASHI, Hiroshi CHUREI

Hospital Staff Sachiko FUJINO, Katsuhide KUROKAWA

Graduate Student Keisuke ABE, Sharika SHAHRIN,
Ruman Uddin CHOWDHURY, Takayuki ISHIGAMI,
Kairi HAYASHI, Mai TANABE,
Akihiro MITSUYAMA, Sintaro FUKASAWA,
Abhishekhi SHRESTHA

2. Purpose of Education

Center of Sports Medicine and Sports Dentistry is 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.

3. Research Subjects

○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

4. Clinical Services

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 April to December, 2012)

Section of out-patient clinic: 712

Section of athletic rehabilitation: 1,154

○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.

5. Publications

Original article

1. Enomoto M, Bunge MB, Tsoulfas P. A multifunctional neurotrophin with reduced affinity to p75^{NTR} enhances transplanted Schwann cell survival and axon growth after spinal cord injury. *Exp Neurol*. 2013, 248:170-182
2. Nakagawa Y, Muneta T, Tsuji K, Ichinose S, Hakamatsuka Y, Koga H, Sekiya I. β -Tricalcium Phosphate Micron Particles Enhance Calcification of Human Mesenchymal Stem Cells In Vitro. *Nanostructured Bioceramics*. 2013.
3. Abe K, Takahashi H, Churei H, Iwasaki N, Ueno T: Flexural properties and shock absorbing capabilities of new face guard materials reinforced with fiberglass cloth. *Dent Traumatol*. 2013, 29(1):23-28.
4. Aizawa J, Masuda T, Hyodo K, Jinno T, Yagishita K, Nakamaru K, Koyama T, Morita S. Ranges of active joint motion for the shoulder, elbow, and wrist in healthy adults. *Disability & Rehabilitation* 2013, 35(16):1342-1349
5. Sekiya I, Koga H, Muneta T, Yagishita K, Ju YJ, Mochizuki T, Horie M, Nakamura T, Okawa A. Effect of Posterolateral Bundle Graft Fixation Angles on Graft Tension Curves and Load Sharing in Double-Bundle Anterior Cruciate Ligament Reconstruction Using a Transtibial Drilling Technique. *Arthroscopy*. 2013, 29(3):529-538.
6. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Sekiya I. Effect of femoral tunnel position on graft tension curves and knee stability in anatomic double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2013. [Epub ahead of print]
7. Koga H, Muneta T, Yagishita K, Ju YJ, Mochizuki T, Horie M, Nakamura T, Okawa A, Sekiya I. Effect of posterolateral bundle graft fixation angles on graft tension curves and load sharing in double-bundle anterior cruciate ligament reconstruction using a transtibial drilling technique. *Arthroscopy*. 2013, 29(3):529-38.
8. Hirai T, Enomoto M, Kaburagi H, Sotome S, Yoshida-Tanaka K, Ukegawa M, Kuwahara H, Yamamoto M, Tajiri M, Miyata H, Hirai Y, Tominaga M, Shinomiya K, Mizusawa H, Okawa A, Yokota T. Intrathecal AAV Serotype 9-mediated Delivery of shRNA Against TRPV1 Attenuates Thermal Hyperalgesia in a Mouse Model of Peripheral Nerve Injury. *Mol Ther*. 2013. [Epub ahead of print]
9. Arai Y, Hirai T, Yoshii T, Sakai K, Kato T, Enomoto M, Matsumoto R, Yamada T, Kawabata S, Shinomiya K, Okawa A. A Prospective Comparative Study of Two Minimally Invasive Decompression Procedures for Lumbar Spinal Canal Stenosis: Unilateral Laminotomy for Bilateral Decompression (ULBD) Versus Muscle-preserving Interlaminar Decompression (MILD). *Spine (Phila Pa 1976)*. 2013. [Epub ahead of print]
10. Fukuda T, Takeda S, Xu R, Ochi H, Sunamura S, Sato T, Shibata S, Yoshida Y, Gu Z, Kimura A, Ma C, Xu C, Bando W, Fujita K, Shinomiya K, Hirai T, Asou Y, Enomoto M, Okano H, Okawa A, Itoh H. *Sema3A* regulates bone-mass accrual through sensory innervations. *Nature*. 2013, 497(7450):490-3.
11. Yoshii T, Yuasa M, Sotome S, Yamada T, Sakaki K, Hirai T, Taniyama T, Inose H, Kato T, Arai Y, Kawabata S, Tomizawa S, Enomoto M, Shinomiya K, Okawa A. Porous/dense composite hydroxyapatite for anterior cervical discectomy and fusion. *Spine (Phila Pa 1976)*. 2013, 38(10):833-40.
12. Taniyama T, Hirai T, Yamada T, Yuasa M, Enomoto M, Yoshii T, Kato T, Kawabata S, Inose H, Okawa A. Modified

- K-line in magnetic resonance imaging predicts insufficient decompression of cervical laminoplasty. *Spine (Phila Pa 1976)*. 2013, 38(6):496-501.
13. Muneta T, Koga H, Ju YJ, Horie M, Nakamura T, Sekiya I. Remnant volume of anterior cruciate ligament correlates preoperative patients' status and postoperative outcome. *Knee Surg Sports Traumatol Arthrosc*. 2013, 21(4):906-13.
 14. Horie M, Muneta T, Yamazaki J, Nakamura T, Koga H, Watanabe T, Sekiya I. A modified quadrant method for describing the femoral tunnel aperture positions in ACL reconstruction using two-view plain radiographs. *Knee Surg Sports Traumatol Arthrosc*. 2013. [Epub ahead of print]
 15. Horie M, Enomoto M, Shimoda M, Okawa A, Miyakawa S, Yagishita K. Enhancement of satellite cell differentiation and functional recovery in injured skeletal muscle by hyperbaric oxygen treatment. *J Appl Physiol*. 2014, 116(2):149-55.
 16. Reza F, Churei H, Takahashi H, Iwasaki N, Ueno T. Flexural impact force absorption of mouthguard materials using film sensor system. *Dent Traumatol*. 2013 Sep 18. [Epub ahead of print]
 17. Shahrin S, Takahashi T, Chowdhury RU, Chowdhury NU, Toyoshima Y, Ueno T. General and oral injuries of the cricketers and field hockey players in Bangladesh. *Int J Sports Dent*. 2013, 6(1):13-23.
 18. Tanabe M, Takahashi T, Shimoyama K, Toyoshima Y, Ueno T. Effects of rehydration and food consumption on salivary flow, pH and buffering capacity in young adult volunteers during ergometer exercise. *J Int Soc Sports Nutr*. 2013, 10(1):49-54.

Lifetime Oral Health Care Science

1. Staffs and Students (April, 2013)

Professor Shinichi ARAKAWA

Junior Associate Professor Keiko KONDO

2. Purpose of 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.

3. Research Subjects

- 1) Clinical and basic studies on Ozone nano-bubble water (NBW3)
- 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

4. Clinical Services

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.

5. Publications

Original article

1. Sae Hayakumo, Shinichi Arakawa, Yoshihiro Mano, Yuichi Izumi. Clinical and microbiological effects of ozone nano-bubble water irrigation as an adjunct to mechanical subgingival debridement in periodontitis patients in a randomized controlled trial. *Clin Oral Invest.* 2013; 17: 379-388.
2. Akiko FURUICHI, Shinichi ARAKAWA, Yoshihiro MANO, Ikuo MORITA, Noriko TACHIKAWA, Yuuichi YAMADA and Shohei KASUGAI. Comparative analysis of efficacy of ozone nano bubble water (NBW3) with established antimicrobials. Bactericidal efficacy and cellular response. An in vitro study. *Journal of Oral Tissue Engineering* 2013;10(3): 131-141.
3. Hidetomo Onishi, Munehiko Ro, Joichiro Hayashi, Junichi Tatsumi, Namba Satomi, Kazuhiro Yatabe, Shinichi Arakawa, Yuichi Izumi, Kitetsu Shin. Modification of forsythia detaching factor by gingival crevicular fluid in periodontitis. *Archives of Oral Biology.* 2013; 58(8): 1007-1013.
4. Sunaga M, Kondo K, Adachi T, Miura Y, Kinoshita A. Development and evaluation of a new dental model at Tokyo Medical and Dental University for the practice of periodontal pocket probing. *J Dent Educ.* 2013 Sep;77(9):1185-1192.

Oral Care for Systemic Health Support

1. Staffs and Student(April,2013)

Professor	Hidemi YOSHIMASU	
Junior Associate Professor	Mitsue ONODERA	
Graduate Students	Yuhei MATSUDA,	Rina USUI
	Mika TSUNO,	Ai OHSATO

2. Purpose of Education

“Oral care for systemic health support” is a branch of oral health care sciences.

Students are taught oral health diagnosis, nutritional sciences, diet education, introduction to care nursing, oral and maxillofacial surgery, and oral health care of medically compromised patient.

3. Research Subjects

- 1) Oral health care of patients with oral cancer, cleft lip and palate and other oral diseases
- 2) Oral health related QOL of patients with oral cancer, cleft lip and palate, dry mouth..
- 3) Basic research of tooth brush, peeling sponge and tooth paste
- 4) Morphological, functional research, and oral health of patients with cleft lip and palate
- 5) Research for safety in supplements in oral functions
- 6) Basic research for pathophysiological roles of gap junction

4. Clinical Services

- 1) High quality oral cleaning programs in collaboration with dental hygienists at Oral Health Care Clinic in Dental Hospital and at wards in Medical Hospital.
- 2) Diagnosis and treatment of patients with oral and maxillofacial diseases at Oral and Maxillofacial Surgery Clinic.

5. Publications

Preventive Oral Health Care Science

1. Staffs and Students (2012)

Professor	Kayoko SHINADA	
Associate Professor	Keiko ENDO	
Assistant Professor	Hiromi OTSUKA	
Part-time Lecturer	Chizuru TAZAWA,	Noriko IIDA,
Graduate Students Master Course	Yuka SHIZUMA,	Ayako KUBOTA,
	Kyoko AKIYAMA,	Kanako TODA,
	Mio NAITO	

2. Purpose of Education

In order to cultivate students' abilities to prevent and notice 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.

3. Research Subjects

- 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 the dental hygiene students.
- 3) Development of new assessment programs (self assessment, achievement assessment) in technical education for dental hygienist students.

4. Clinical Services

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.

5. Publications

Original article

1. S.Takeuchi,M.Ueno,S.Takehara,T.A.V.Pham,C.Hakuta,S.Morishima,K.Shinada,Y. Kawaguchi:The relationship between turbidity of mouth – rinsed water and oral health status,Acta Odontologica Scandinavica, 71:183-188,2013.
2. Ueno M, Takeuchi S, Samnieng P, Morishima S, Shinada K, Kawaguchi Y: Turbidity of mouthrinsed water as a screening index for oral malodor,Oral Surg Oral Med Oral Pathol Oral Radiol. 116(2):203-9, 2013.

Oral Health Care Science for Community and Welfare

1. Staffs and Student

Professor	Chiyoko Hakuta
Junior Associate Professor	Keiko Endo
Student	Rena Nakayama
	Maki Sirobe (April,2013)

2. Purpose of Education

In this course, our lectures will be focused on oral health hygiene for community and welfare. Through these lectures, students as dental hygienists will be able to learn how to create own oral health care and welfare programs based on each community's circumstances.

Furthermore, because of progressing of the aged society in recent years, the healthcare professionals who are in charge of health and medical services need to have extremely close cooperation of each other. Therefore, dental healthcare workers also need to gain enough social welfare knowledge and skills, and they need to understand and support people from both aspects of health and living. Under these circumstances, in addition to conventional social dentistry study, we have had the 4 weeks on-the-spot training in various welfare fields for our students, so that they could experience how to support people from social and welfare point of view. As faculties of this course, we would pay a visit and give our students some instructions and advices for meeting with success of their practical training.

3. Our research

Followings are our researches;

1. Development of education & educational materials for community health activities
2. Upbringing & improving oral cavity function (from infant to elderly)
3. Health education and behavior changes in community
4. Development of the program to promote community health from both health and welfare point of view
5. Preventive long-time care in day care services
6. Adult guardian system for highly advanced functional disorder
7. Special diet to preserve elderly people's health

Oral Health Care Education

1. Staffs and Students (April, 2013)

Professor

Kayo TERAOKA

2. Purpose of 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 national 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. Research Subjects

- 1) Oral health promotion program.
- 2) Oral health and long-term preventive care for the elderly.
- 3) Oral care management system for hospitalized person.
- 4) Oral health administration system in local communities.

Basic Sciences of Oral Health Care

1. Staffs

Professor Akira Yamaguchi
 Junior Associate Professor Yujiro Sakamoto

2. 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:

3. Research Subjects

- 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

4. Publications

Original Articles

1. Sakamoto Y. Gross anatomical observations of attachments of the middle pharyngeal constrictor. *Clinical Anatomy*. In Press. 2013.
2. Shibata S, Sakamoto Y, Baba O, Qin C, Murakami G, Cho BH. An immunohistochemical study of matrix proteins in the craniofacial cartilage in midterm human fetuses. *European Journal of Histochemistry*. 57: 262-270, 2013.
3. Sakamoto Y. Interrelationships between the innervations from the laryngeal nerves and the pharyngeal plexus to the inferior pharyngeal constrictor. *Surgical and Radiologic Anatomy*. 35: 721-728, 2013.
4. Hoshino A, Ueha S, Hanada S, Imai T, Ito M, Yamamoto K, Matsushima K, Yamaguchi A, Iimura T. Roles of chemokine receptor CX3CR1 in maintaining murine bone homeostasis through the regulation of both osteoblasts and osteoclasts. *J Cell Sci* 126: 1031-1045, 2013.
5. Tanabe R, Haraikawa M, Sogabe N, Sugimoto A, Kawamura Y, Takasugi S, Nagata M, Nakane A, Yamaguchi A, Iimura T, Masae Goseki-Sone. Retention of bone strength by feeding of milk and dairy products in ovariectomized rats; involvement of changes in serum levels of Ialpha, 25(OH)2D3 and FGF23. *J Nutr Biochem*. 24: 1000-1007, 2013.
6. Makino Y, Takahashi Y, Tanabe R, Tamamura Y, Watanabe T, Haraikawa M, Hamagaki M, Hata K, Kanno J, Yoneda T, Saga Y, Goseki-Sone M, Kaneko K, Yamaguchi A, Iimura T. Spatiotemporal disorder in endochondral ossification during axial skeleton development in the Mesp2-null mouse: A developmental etiology of spondylocostal dysostosis and spondylothoracic dysostosis. *BONE* 53: 248-258, 2013.
7. Matsumoto T, Iimura T, Ogura K, Moriyama K, Yamaguchi A. The role of osteocytes in bone resorption during orthodontic tooth movement. *J Dent Res* 92: 340-345, 2013.
8. Pal KS, Sakamoto K, Aragaki T, Akashi T, Yamaguchi A. The expression profiles of acidic epithelial keratins in Ameloblastoma. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* 115: 523-531, 2013.
9. Sato K, Lee JW, Sakamoto K, Iimura T, Kayamori K, Yasuda H, Shindoh M, Ito M, Omura K, Yamaguchi A. RANKL synthesized by both stromal cells and cancer cells plays a crucial role in osteoclastic bone resorption induced by oral cancer. *Am J Pathol* 182: 1890-1899, 2013.
10. Matsushita Y, Sakamoto K, Tamamura Y, Shibata Y, Minamizato T, Kihara T, Ito M, Katsube K, Hiraoka S, Koseki H, Harada K, Yamaguchi A. CCN3 protein participates in bone regeneration as an inhibitory factor. *J Biol Chem* 288: 19973-19985, 2013.

11. Shimada Y, Katsube K, Kabasawa Y, Morita K, Omura K, Yamaguchi A, Sakamoto K. Integrated genotypic analysis of hedgehog-related genes identifies subgroups of keratocystic odontogenic tumor with distinct clinicopathological features. *Plos One* 8: e70995, 2013.
12. Lee JW, Yamaguchi A, Iimura T. Functional heterogeneity of osteocytes in FGF23 production: The possible involvement of DMP1 as a direct negative regulator. *BoneKEy Reports*, In Press.

Review Articles

1. Makino Y, Kaneko K, Yamaguchi A, Iimura T. Developmental biology and etiology of axial skeleton: Lessons from a mouse model of spondylocostal dysostosis and spondylothoracic dysostosis. *J Oral Biosci* 55: 175-179, 2013.

5. International meetings

1. Sakamoto Y. Morphological interrelations between the scaleni posterior and medius. The 30th annual meeting American Association of Clinical Anatomists, Denver, USA, July 9-13, 2013.
2. Sakamoto Y. Gross anatomical observations on the attachments of the middle pharyngeal constrictor. European Joint Congress of Clinical Anatomy 2013. Lisbon, Portugal, June 26-29, 2013.

6. Invited Lectures

1. Yamaguchi A. Role of CCN3 in osteoblast differentiation and bone regeneration. 7th International CCN Workshop, Nice, France, October 18, 2013.

Basic Oral Health Science

1. Staffs and Students

Professor

Kumiko Sugimoto

2. Purpose of Education

Fundamental oral health care science is a section of oral health care sciences which deals with the basic oral health sciences to perform evidence-based oral health care and to support people to attain healthy and happy living. Main objective of fundamental oral health care science in the undergraduate course is to provide students opportunity to study the structure and function of the human body as well as stomatognathic region, pharmacology, laboratory practice of physiology and research process.

3. Research Subjects

- 1) Changes in autonomic nerve and brain activities induced by taste stimulation
- 2) The sensitivities to taste, olfactory and capsaicin stimulations in the patients of congenital insensitivity to pain with anhidrosis
- 3) Evaluation of oral care for the elderly by dental professionals
- 4) Oral health problems relevant to menopause
- 5) Objective assessment of internal stress during dental treatment by analyses of autonomic nervous activities and electroencephalogram

Comprehensive Oral Health Engineering

1. Staff

Associate Professor

Meiko Oki

2. Purpose of Education

The goal of the education program in Comprehensive Oral Health Engineering is to provide the knowledge and skills of the figurative arts, design, and the health welfare for oral health engineering students.

The first grade oral health engineering students participate in the tutorial lessons of general knowledge of oral health and specialists, and are introduced to clinical dentistry visiting the hospital clinics, dental technical laboratory, and dental material corporation. Scientific English was provided to learn basic dental terms. The second grade students attend lectures of health promotion, the tutorial lessons of general knowledge of oral and health promotion, Japanese and world dental technic situations, and statistic data analysis. Process device engineering was provided the outlines of 3D CAD/CAM/CAE, especially about 3D printer. The third grade students attend lectures and clinical laboratories to acquire a broad range of general knowledge and skills of a wide variety of maxillofacial defects, cleft lip and palate, oral appliances to support masticatory, swallowing and speech, and involvement of treatment procedures, by means of the high-advanced dental and medical cares. Scientific English II provides to read some English papers about prosthodontics.

3. Research Subjects

- 1) The fabrication of facial prostheses using three dimensional rapid manufacturing method
- 2) Clinical studies of treatments for patients with maxillofacial defects
- 3) Development of materials for facial prostheses

4. Clinical Services

In the Maxillofacial Prosthetic Clinic, I treat patients with cleft lip and/or palate, maxillary defect, mandibular defect, tongue defect, and facial defect, to improve their masticatory and swallowing functions, speech, and esthetic problems with the Maxillofacial Prosthetic staffs in the University Dental Hospital.

Oral Clinical Science

1. Staffs and Students

Lecturer

Masaomi Ikeda

2. Purpose of Education

This course provides education for students to become professional dental technologists with the ability to apply newly developed materials and technologies to clinical dentistry and contribute not only to community dental medicine but also to dental research or educational institution internationally. At present, the latest technologies such as dental implant, dental CAD/DAM, etc are becoming more popular because of the progress of dental materials and technologies. Therefore, it is important to learn about new materials and technologies, and acquire skills in order to perform laboratory works properly. Communication skills are important because giving the information about materials and technologies to dentists and dental hygienists is necessary for the best outcome of dental treatment. Goal of this course is to produce dental technicians with extensive knowledge, high skill, and communication ability.

3. Research Subjects

- 1) Application of antibacterial materials to dental materials
- 2) Evaluation of adhesive systems
- 3) Traceability and quality control of restorative materials

5. Publications

Original Articles

1. Kirihara M, Inoue G, Nikaido T, Ikeda M, Sadr A, Tagami J. Effect of fluoride concentration in adhesives on morphology of acid-base resistant zones. *Dent Mater J.* 32(4), 578-84, 2013.
2. Utaka S, Nakashima S, Sadr A, Ikeda M, Nikaido T, Shimizu A, Tagami J. Cariotester, a new device for assessment of dentin lesion remineralization in vitro. *Dent Mater J.* 32(2), 241-7, 2013.
3. Gando I, Ariyoshi M, Ikeda M, Sadr A, Nikaido T, Tagami J. Resistance of dentin coating materials against abrasion by toothbrush. *Dent Mater J.* 32(1), 68-74, 2013.
4. Thanatvarakorn O, Nakashima S, Sadr A, Prasansuttiporn T, Ikeda M, Tagami J. In vitro evaluation of dentinal hydraulic conductance and tubule sealing by a novel calcium-phosphate desensitizer. *J Biomed Mater Res B Appl Biomater.* 101(2), 303-9, 2013.

Oral Health Information Technology

1. Staffs and Students

Professor	Tetsuya SUZUKI
Assistant Professor	Shingo KAMIJO

2. Purpose of Education

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.

3. Research Subjects

- 1) Relation of "medical care to support life" and the dental technician.
- 2) The education of dental technician which utilized computer simulation training.

Oral Biomaterials Engineering

1. Staffs and Students

Professor	Hidekazu TAKAHASHI
Assistant Professor	Naohiko IWASAKI
Special guest researcher	Sasipin Lauvahutanon

2. Purpose of Education

Dental material science is not only one of basic medical and dental science but also one of clinical dental science. In our department, we will educate students to obtain practical knowledge of the dental materials and devices used in dentistry and to improve skill how to deal with these materials and devices. Our goals of education are to achieve high quality of dental practice with well-understanding dental material and devices.

The aim for education is to obtain the basic knowledge of dental material science and technology. The lecture is simultaneously provided with the laboratory instructions within the limit of the possible.

3. Research Subjects

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

4. Publication

Original articles

1. Nagata K, Wakabayashi N, Takahashi H, Vallittu PK, Lassila LV. Fracture resistance of CAD/CAM manufactured FRC denture retainers. *Inter J Prosthodont* 2013; 26(4): 381-383
2. Shiozawa M, Takahashi H, Finger WJ, Iwasaki N. Effects of the space for wash materials on sulcus depth reproduction with addition-curing silicone using two-step putty-wash technique. *Dent Mater J* 2013; 32(1): 150-5
3. Bakry AS, Takahashi H, Otsuki M, Tagamie J. The durability of phosphoric acid promoted bioglass-dentin interaction layer. *Dent Mater* 2013; 29(4): 357-64
4. Wang Fu, Takahashi H, Iwasaki N. Translucency of dental ceramics with different thicknesses. *J Prosthet Dent*. 2013; 110(1): 14-20
5. Abe K, Takahashi H, Churei H, Iwasaki N, Ueno T. Flexural properties and shock-absorbing capabilities of new face guard materials reinforced with fiberglass cloth. *Dent Traumatol* 2013; 29(1): 23-28
6. Asakawa Y, Takahashi H, Kobayashi M, Iwasaki N. Effect of components and surface treatments of fiber-reinforced composite posts on bond strength to composite resin. *J Mech Behav Biomed Mater* 2013; 26: 23-33
7. Jiangkongkho P, Kamonkhantikul K, Takahashi H, Arksornnukit M. Fracture resistance of endodontically treated teeth using fiber posts with an elastic modulus similar to dentin. *Dent Mater J* 2013; 32(5): 781-6
8. Shiozawa M, Takahashi H, Iwasaki N., Uo M. Effect of calcium chloride solution immersion on surface hardness of restorative glass ionomer cements. *Dent Mater J* 2013; 32(5): 828-33.
9. Shiozawa M, Takahashi H, Iwasaki N., Uo M. Fluoride release and mechanical properties after 1-year water storage of recent restorative glass ionomer cements. *Clin Oral Investig* 2013; Aug 22. [Epub ahead of print]
10. Reza F, Churei H, Takahashi H, Iwasaki N. Impact force absorption of mouthguard materials using film sensor system. *Dent Traumatol*. 2013 Sep 18. [Epub ahead of print]

Fixed Prosthetic Engineering

1. Staffs and Students

Junior Associate Professor Tohru Yasue

2. Purpose of Education

Our instruction will include provision of knowledge and technical training of dental laboratory techniques necessary for dental crown restorative procedures to solve morphological, functional and esthetics problems that have been accompanied with eventual loss of tooth substance and body in the oral tissues. Intensive learning of tooth morphology that should be fundamental to every phase of dental laboratory techniques will be scheduled by practical courses based on the science of shape recognition construction. And our teaching will refer to not only provision of forms and occlusal functions to be best suited for individual patients in crown restoration engineering and plate denture engineering, but also fabrication techniques of restorations with highly color matching together with prosthetic restoration methods using most advanced materials.

3. Research Subjects

From the technicians' viewpoint of fabricating dental crown restorations, our research and development will be ready in an approach toward a new technology of dental laboratory engineering and a new material science, especially in the study of advanced restorative engineering using digital equipments.

4. Clinical Services

As far as crown restorations are concerned in dental esthetics based on Zirconia materials with CAD/CAM machining, functional efficiency and durability will be identified in the oral cavity environment, and crown restorations with highly demanding esthetics will be fabricated.

Oral Prosthetic Engineering

1. Staffs and Students (April, 2013)

Professor Tetsuya SUZUKI
Research Associate Kouichi FUKAWA

2. Purpose of Education

Oral Prosthetic Engineering is one of the dental sciences which propose to restore and maintain oral function, form and health for partially and/or complete edentulous patients. Main object of Oral Prosthetic Engineering is to provide students to obtain the basic knowledge and technical skill of complete denture prosthodontics, removable partial denture prosthodontics and dental occlusion.

3. Research Subjects

1. Standardization of education for dental technicians
2. Optimal occlusion for removable dentures.
3. Evaluation of various denture materials.
4. Evaluation of oral function in elderly.
5. Influence of masticatory function on brain activity.

4. Publication

Original articles

1. Wakabayashi N, Suzuki T. Title: Patient-specific finite element analysis of viscoelastic masticatory mucosa. Journal: Journal of Dental Biomechanics 4:1-7, 2013.