

ANNUAL PUBLICATIONS

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

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Oral Pathology

1. Staff and Students

Professor	Akira YAMAGUCHI
Associate Professor (GCOE)	Tadahiro Iimura
Lecturer	Ken-ichi Katsube
Assistant Professor	Kei Sakamoto
Tokunin Assistant Professor	Sadahiro Tamamura
JSPS fellow	Ji-Won Lee
Technician	Miwako Hamagaki
Graduate Students	
Ph.D. Course	Samir Kumar Pal Yuji Makino (Juntendou University) Akiko Himeno (Periodontology) Yuji Matsushita (Maxillofacial Surgery) Zhao Xin Yasuyuki Shimada (Oral and Maxillofacial Surgery) Rumana Khanom Zayar Lin (Implant) Rei Touyama Masita Mandasari Ryousuke Nakamura (Maxillofacial Surgery) Kenji Ogura (Maxillofacial Orthognathics)
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-pathological 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. Himeno-Ando A, Izumi Y, Yamaguchi A, Iimura T: Structural differences in the osteocyte network between the calvaria and long bone revealed by three-dimensional fluorescence morphometry, possibly reflecting distinct mechano-adaptations and sensitivities. *Biochem Bioph Res Co* 417:765-770,2012
2. Sakamoto K, Fujii T, Kawachi H, Miki Y, Omura K, Morita K, Kayamori K, Khanom R, Katsube K, Yamaguchi A: Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lob Invest* 92:688-702:2012
3. Khanom R, Sakamoto K, Pal SK, Shimada Y, Morita K-i, Omura K, Miki Y, Yamaguchi A: Expression of basal cell keratin 15 and keratin 19 in oral squamous cell carcinoma represent diverse pathophysiological. *Histol Histopathol* 27:949-959,2012

4. Aizawa R, Yamada A, Suzuki D, Iimura T, Kassai H, Harada T, Tsukasaki M, Yamamoto G, Tachikawa T, Nakao K, Yamamoto M, Yamaguchi A, Aiba A, Kamijo R: Cdc42 is required for chondrogenesis and interdigital programmed cell death during limb development. *Mech Dev* 129:38-50,2012
5. Michikawa C, Uzawa N, Kayamori K, Sonoda I, Ohyama Y, Okada N, Yamaguchi A, Amagasa T: Clinical significance of lymphatic and blood vessel invasion in oral tongue squamous cell carcinomas. *Oral Oncol* 48:320-324,2012
6. Umehara K, Iimura T, Sakamoto K, Lin Z, Kasugai S, Igarashi Y, Yamaguchi A: Canine oral mucosal fibroblasts differentiate into osteoblastic cells in response to BMP-2. *Anat Rec* 295:1327-1335,2012
7. Watanabe T, Tamamura Y, Hoshino A, Makino Y, Nishimura R, Kamioka H, Yoneda T, Amagasa T, Yamaguchi A, Iimura T: Increasing participation of Sclerostin in postnatal bone development revealed by three-dimensional immunofluorescence morphometry. *BONE* 51:447-458,2012
8. Sakamoto K, Khanom R, Hamagaki M, Yamaguchi A: Ectopic production of hair keratin constitutes Rushton' s hyaline bodies in association with hematogenous deposits. *J Oral Pathol Med* 27:949-959,2012
9. Oue E, Lee JW, Sakamoto K, Iimura T, Aoki K, Kayamori K, Michi Y, Yamashiro M, Yamaguchi A: CXCL2 synthesized by oral squamous cell carcinoma is involved in cancer-associated bone destruction. *Biochem Bioph Res Co* 424:456-461,2012
10. Nishimura R, Wakabayashi M, Hata K, Matsubara T, Honma H, Wakisaka S, Kiyonari H, Shioi G, Yamaguchi A, Tsumaki N, Akiyama H, Yoneda T: Osterix regulates calcification and degradation of chondrogenic matrices through matrix metalloproteinase (MMP13) expression in association with transcription factor Runx2 during endochondral ossification. *J Biol Chem* 287:33179-33190,2012
11. 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* 258:28826-28837,2012
12. 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 1alpha, 25(OH)2D3 and FGF23. *J Nutr Biochem*. 2012 [Epub ahead of print]
13. 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
14. 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

Review

1. Iimura T, Nakane A, Sugiyama M, Sato H, Makino Y, Watanabe T, Takagi Y, Numano R, Yamaguchi A: A fluorescence spotlight on the clockwork development and metabolism of bone. *J Bone Miner Metab*. 30:254-269,2012

Bacterial Pathogenesis

1. Staffs and Students (March 2013)

Professor	Ichiro Nakagawa
Associate Professor	Fumito Maruyama
Assistant Professor(Tenure Truck)	Takashi Nozawa
Postdotoral Student	Chihiro Aikawa
Graduate Student	Takayasu Watanabe
	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. Purpose of 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. Ohtsubo Y, Maruyama F, Mitsui H, Nagata Y, Tsuda M. "Complete Genome Sequence of Acidovorax sp. KKS102, a Polychlorinated Biphenyl-Degrading strain." J. Bacteriol. 194:6970-1 (2012)
2. Jorquera M*, Saavedra N, Maruyama F, Richardson A, Crowley D, Catrilaf R, Henriquez E, Mora M. "Phytate addition to soil induces changes in the abundance and expression of Bacillus β -propeller phytase genes in the

- rhizosphere." FEMS Microbiol. Ecol.83(2):352-60 (2012)
3. Ogawa M, Sugita S, Shimizu N, Watanabe K, Nakagawa I, Mochizuki M. "Broad-range real-time PCR assay for detection of bacterial DNA in ocular samples from infectious endophthalmitis." Jpn J Ophthalmol. 56(6):529-35 (2012)
 4. Nozawa T, Aikawa C, Goda A, Maruyama F, Hamada S, Nakagawa I "The small GTPases Rab9A and Rab23 function at distinct steps in autophagy during Group A *Streptococcus* infection." Cell Microbiol. 14(8):1149-65. (2012)
 5. Aikawa C, Furukawa N, Watanabe T, Minegishi , Furukawa A, Eishi Y, Oshima K, Kurokawa K, Hattori M, Nakano K, Maruyama F**, Nakagawa I and Ooshima T "Complete Genome Sequence of the serotype k *Streptococcus mutans* LJ23." J Bacteriol.194(10):2754-5.(2012)
 6. Nonaka L, Maruyama F, Miyamoto M, Miyakoshi M, Kurokawa K, Masuda M. "Novel conjugative transferable multiple drug resistance plasmid pAQU1 from *Photobacterium damsela* subsp. damsela isolated from marine aquaculture environment." Microb. Environ. 27(3):263-72 (2012)
 7. Okada K, Roobthaisong A, Nakagawa I, Hamada S, Chantaroj S. "Genotypic and PFGE/MLVA analyses of *Vibrio cholerae* O1: geographical spread and temporal changes during the 2007-2010 cholera outbreaks in Thailand." PLoS One Vol.7(1):e30863 (2012)
 8. Aoki A, Shibata Y, Okano S, Maruyama F, Amano A, Nakagawa I, Abiko Y. "Transition metal ions induce carnosinase activity in PepD-homologous protein from *Porphyromonas gingivalis*." Microb Pathog. 52(1):17-24 (2012)

Molecular Immunology

1. Staffs and Students (April, 2012)

Professor	Miyuki AZUMA	
Associate Professor	Yoshiko IWAI	
Assistant Professor	Tatsukuni OHNO	
Adjunct instructor	Hiroshi KIYONO	Masaaki HASHIGUCHI
	Yosuke KAMIMURA	
Graduate Students (Doctor)	Chenyang ZHANG	Arundhati C .BHINGARE
	Siwen KANG(Oct.~)	Syougo MAEKAWA
Graduate Student (Master)	Yuichi KODAMA	
Research Student	Doan Thi TOA(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. Ritprajak P, Hashiguchi M, Akiba H, Yagita H, Okumura K, Azuma M: Antibodies against B7-DC with differential binding properties exert opposite effects. *Hybridoma* 31: 40-47, 2012
2. Hashiguchi M, Inamochi Y, Nagai S, Otsuki N, Piao J, Kobori H, Kanno Y, Kojima H, Kobata T, Azuma M: Human B7-H3 binds to Triggering receptor expressed on myeloid cells-like transcript 2 (TLT-2) and enhances T cell responses. *Open J Immunol* 2:9-16, 2012
3. Yokosuka T, Takamatsu M, Kobayashi-Imanishi W, Hashimoto-Tani A, Azuma M, Saito T: Programmed cell death-1 forms negative costimulatory microclusters that directly inhibit T cell receptor signaling by recruiting phosphatase SHP2. *J Exp Med* 209:935-945, 2012
4. Isoda Y, Takagi M, Piao J, Nakagama S, Sato M, Masuda K, Ikawa T, Azuma M, Morio T, Kawamoto H, Mizutani S: Process for immune defect and chromosomal translocation during early thymocyte development lacking ATM. *Blood* 120: 789-799, 2012
5. Morita H, Arae K, Ohno T, Kajiwarana N, Oboki K, Matsuda A, Suto H, Okumura K, Sudo K, Takahashi T, Matsumoto K, Nakae S: ST2 requires Th2-, but not Th17-, type airway inflammation in epicutaneously antigen-sensitized mice. *Allergol Int* 61:265-73, 2012
6. Ohno T, Morita H, Arae K, Matsumoto K, Nakae S: Interleukin-33 in allergy. *Allergy* 67:1203-14, 2012
7. 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, 2012. doi:10.1002/rji.201242501
8. 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. Doi:10.4049/jimmunol.1201782. Epub 2012 Dec 14.
9. Schmiedel BJ, Neubling 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, doi:10.1158/0008-5472.CAN-12-2280. Epub 2012 Nov 8.

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 synclotron 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. Yoshida E., Yoshimura Y., Uo M., Yoshinari M., Hayakawa T.: Influence of nanometer smoothness and fibronectin immobilization of titanium surface on MC3T3-E1 cell behavior. *J Biomed Mater Res Part A*, 100A, 1556-1564, 2012.
2. Hayakawa T., Yoshida E., Yoshimura Y., Uo M., Yoshinari M.: MC3T3-E1 Cells on Titanium Surfaces with Nanometer Smoothness and Fibronectin Immobilization. *International Journal of Biomaterials*, Vol.2012, Article ID 743465, 6 pages, doi:10.1155/2012/743465, 2012.
3. Tarumi N., Uo M., Yamaga E., Watari F.: SEM observation and wettability of various processed and fractured surface of dental zirconia. *Applied Surface Science*, 262, 253-257, 2012.
4. Hirata E., Akasaka T., Uo M., Takita H., Watari F., Yokoyama A.: Carbon nanotube-coating accelerated cell adhesion and proliferation on poly (L-lactide). *Applied Surface Science*, 262, 24-27, 2012.
5. Furuhashi K., Uo M., Kitagawa Y., Watari F.: Rapid and non-destructive analysis of metallic dental restorations using X-ray fluorescence spectra and light-element sampling tools. *Applied Surface Science*, 262, 13-18, 2012.
6. Yamagata S., Hamba Y., Akasaka T., Ushijima N., Uo M., Iida J., Watari F.: The effect of enhancing the hydrophobicity of OMMT on the characteristics of PMMA/OMMT nanocomposites. *Applied Surface Science*, 262, 56-59, 2012.
7. Wada T., Bando K. K., Miyamoto T., Takakusagi S., Oyama S. T., Asakura K.: Operando QEXAFS studies of Ni₂P during thiophene hydrodesulfurization: direct observation of Ni-S bond formation under reaction conditions. *Journal of Synchrotron Radiation*, 19(2), 205-209, 2012.
8. Wada T., Bando K. K., Oyama S. T., Miyamoto T., Takakusagi S., Asakura K.: Operando Observation of Ni₂P Structural Changes during Catalytic Reaction: Effect of H₂S Pretreatment. *Chemistry Letters* 41(10), 1238-1240, 2012.
9. 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 analysis of a Ni phosphide catalyst under hydrodesulfurization conditions. *Journal of Catalysis*, 286, 165-171, 2012.
10. Miyamoto T., Wada T., Niimi H., Suzuki S., Kato M., Kudo M., Asakura K.: A New Collinear-Type Energy-Filtered X-ray Photoemission Electron Microscope Equipped with a Multi-Pole Aberration-Corrected Air-Core Coil Wien Filter. *Japanese Journal of Applied Physics*, 51(4), 046701-046707, 2012.
11. Koottathape N., Takahashi H., Finger JW., Kanehira M., Iwasaki N., Aoyagi Y.: Quantification of in vitro produced

wear sites on composite resins using contact profilometry and CCD microscopy: A methodological investigation, *Journal of Medical and Dental Sciences*, 59, 53-56, 2012.

12. Koottathape N, Takahashi H, Iwasaki N, Kanehira M, Finger JW.: Morphological features of composite resin surfaces after two- and three-body wear simulation, *World Journal of Dentistry*, 3, 221-228, 2012.
13. Koottathape N., Takahashi H., Iwasaki N., Kanehira M., Finger JW.: Two- and three-body wear of composite resins, *Dental Materials*, 28(12), 1261-1270, 2012.

Diagnostic Oral Pathology

1. Staffs and Students (Apr. 2012)

Associate Professor	Toshiyuki IZUMO		
Visiting Lecturer	Norihiko OKADA,	Kou KAYAMORI	
Hospital Staff	Cheko MICHIKAWA,	Yuuichi YAMADA,	Kiyoko NAGUMO,
	Kana NANBA (IDA),	Akino INOUE,	Kana ENDOU,
	Akiko ASANO,	Mayuko MINAMI,	Yukiko KUROKI
Research Students	Yuka HIROTA		

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 has played two roles, pathology diagnosis and clinical laboratory for clinical examinations which deal with hematological, biochemical, bacteriological and histopathological samples in the dental hospital.

5. Publications

Original Article

1. Michikawa C, Uzawa N, Kayamori K, Sonoda I, Ohyama Y, Okada N, Yamaguchi A, Amagasa T. Clinical significance of lymphatic and blood vessel invasion in oral tongue squamous cell carcinomas. *Oral Oncol.* 2012 Apr;48(4):320-4. doi: 10.1016/j.oraloncology.2011.11.014. Epub 2011 Dec 16.
2. Ida M, Tetsumura A, Kuribayashi A, Okada N and Kurabayashi T: A clinoradiological study of odontogenic carcinomas and their impact on clinical diagnosis. *Dentomaxillofacial Radiology* 41:594-600, 2012.
3. Oue E, Lee JW, Sakamoto K, Imura T, Aoki K, Kayamori K, Michi Y, Yamashiro M, Harada K, Amagasa T, Yamaguchi A. CXCL2 synthesized by oral squamous cell carcinoma is involved in cancer-associated bone destruction. *Biochem Biophys Res Commun.* 2012 Aug 3;424(3): 456-61. doi: 10.1016/j.bbrc.2012.06.132. Epub 2012 Jul 4.
4. Sakamoto K, Fujii T, Kawachi H, Miki Y, Omura K, Morita K, Kayamori K, Katsube K, Yamaguchi A. Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lab Invest.* 2012 May;92(5):688-702. doi: 10.1038/labinvest.2012.9. Epub 2012 Feb 13.
5. Ariyasathitman S, Tsunoda A, Tokumaru T, Kayamori K, Hirooka S, Kishimoto S. Ultrastructural morphology of juvenile psammomatoid ossifying fibroma. *Auris Nasus Larynx.* 2012 Jun;39(3):314-6. doi: 10.1016/j.anl.2011.07.019. Epub 2011 Aug 31.
6. Tsushima F, Sawai T, Kayamori K, Okada N, Omura K. Schwannoma in the floor of the mouth: A case report and clinicopathological studies of 10 cases in the oral region. *Journal of Oral and maxillofacial surgery, Medicine, and Pathology.* 24:175-179, 2012.

Review Articles

1. Izumo T, Kirita T, Ariji E, Ozeki S, Okada N, Okabe N, Okazaki Y, Omura K, Kusama M, Sato T, Shinohara M, Shimozato K, Working Group 1 on the Guidelines for Clinical and Pathological Studies of Oral Cancer, Scientific Committee, Japan Society for Oral Tumors. General rules for clinical and pathological studies on oral cancer: A synopsis. *Jpn J Clin Oncol* 42:1099-1109, 2012. doi: 10.1093/jjco/hys141

Organic Biomaterials

1. Staffs and Students (April, 2012)

Professor	Nobuhiko YUI	
Associate Professor	Yoshihiro SASAKI	
Assistant Professor	Ji-Hun SEO	
Research Assistant Professor	Atsushi TAMURA	
Secretary	Nanae NISHI	
Graduate Student	Yuji TSUCHIDO,	Nanako Yokoyama,
	Hajime TANAKA	

2. Purpose of Education

Courses: Biomaterials, Advanced Medical Materials, Advanced Organic Materials

3. Research Subjects

- 1) Design of Dynamic Biomaterials Surfaces
- 2) Modulation of Cellular Functions by Dynamic Ligand-Polymers
- 3) Design of Intracellularly Functionalizing Biomaterials
- 4) Design of Liposomal Device and Hybrid Nanomaterials

4. Clinical Services

5. Publications

Original Article

1. Inoue Y, Lin Ye, Ishihara K, Yui N. Preparation and surface properties of polyrotaxane-containing tri-block copolymers as a design for dynamic biomaterials surfaces. *Colloids Surf. B* 89(1): 223-227, 2012.
2. Yamada Y, Nomura T, Harashima H, Yamashita A, Yui N. Post-nuclear gene delivery events for transgene expression by biocleavable polyrotaxanes. *Biomaterials* 33(15): 3952-3958, 2012.
3. Yamada Y, Hashida M, Nomura T, Harashima H, Yamasaki Y, Kataoka K, Yamashita A, Katoono R, Yui N. Different mechanisms for nanoparticle formation between pDNA and siRNA using polyrotaxane as the polycation. *ChemPhysChem* 13(5): 1161-1165, 2012.
4. Yamada K, Katoono R, Yui N. Controlled loop and graft formations of water-soluble polymers on SAM for the design of biomaterials surfaces. *Polym J* 44: 286-293, 2012.
5. Seo J-H, Kakinoki S, Inoue Y, Yamaoka T, Ishihara K, Yui N. Designing dynamic surfaces for regulation of biological responses. *Soft Matter* 8: 5477-5485, 2012.
6. Jang S, Lee S, Kim H, Ham J, Seo J-H, Mok Y, Noh M, Lee Y. Preparation of pH-sensitive CaP nanoparticles coated with a phosphate-based block copolymer for efficient gene delivery. *Polymer* 53: 4678-4685, 2012.
7. Jin GW, Kim H, Seo J-H, Ham J, Park JS, Lee Y. Formation of polyion complex micelles with tunable isoelectric points based on zwitterionic block copolymers. *Macromol. Res.*, 20(12): 1249-1256, 2012.
8. Noh M, Mok Y, Lee S, Kim H, Lee SH, Jin GW, Seo J-H, Koo H, Park TH, Lee Y. Novel lower critical solution temperature phase transition materials effectively control osmosis by mild temperature change. *Chem. Comm.* 48: 3845-3847, 2012.
9. Tamura A, Kobayashi J, Yamato M, Okano T. Thermally responsive microcarriers with optimal poly(N-isopropylacrylamide) grafted density for facilitating cell adhesion/detachment in suspension culture. *Acta Biomater* 8: 3904-3913, 2012.
10. Tamura A, Nishi M, Kobayashi J, Nagase K, Yajima H, Yamato M, Okano T. Simultaneous enhancement of cell proliferation and thermally-induced harvest efficiency based on temperature-responsive cationic copolymer-grafted. *Biomacromolecules* 13: 1765-1773, 2012.
11. Tamura A, Kobayashi J, Yamato M, Okano T. Temperature-responsive poly(N-isopropylacrylamide)-grafted microcarriers for large-scale noninvasive harvest of anchorage-dependent cells. *Biomaterials* 33: 3803-3812, 2012.
12. Tamura G, Shinohara Y, Tamura A, Sanada Y, Oishi M, Akiba I, Nagasaki Y, Sakurai K, Amemiya Y. Dependence of Swelling Behavior of pH-responsive PEGylated Nanogel on Cross-link Density. *Polymer Journal*, 44(3):240-244, 2012.

Functional Materials (Material-based Medical Engineering)

1. Staffs and Students

Associate Professor	Yoshinori KADOMA	
Graduate Student	Jun NEGISHI,	Kwang-il KIM,
	Naoko NAKAMURA,	PingLi WU,
	Mitsuki UEKI,	Rie MATSUSHIMA,
	Satoshi Honda,	Ayumi TANZAWA
Research Student	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) Control of cell functions by physical stimuli.

Using physical stimuli such as nano-vibration or pressure, the technology for the control of cell functions such as the proliferation and differentiation is being developed.

5) Development of high functional adhesive

For the development of stable adhesive for precious metal and resin, high functional monomer possessing adhesivity to the precious metal is being developed.

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. Seiichiro Fujisawa, Yoshinori Kadoma. Mechanisms of action of (meth)acrylates in hemolytic activity, in vivo toxicity and dipalmitoylphosphatidylcholine (DPPC) liposomes determined using NMR spectroscopy. *Int J Mol Sci* 13(1): 758-773, 2012.
2. Yoshinori Kadoma, Seiichiro Fujisawa. Radical-scavenging activity of thiols, thiobarbituric acid derivatives and phenolic antioxidants determined using the induction period method for radical polymerization of methyl methacrylate. *Polymers* 4(2): 1025-1036, 2012.
3. Seiichiro Fujisawa, Yoshinori Kadoma. Relationships between base-catalyzed hydrolysis rates or glutathione reactivity for acrylates and methacrylates and their NMR spectra or heat of formation. *Int J Mol Sci* 13(5): 5789-5800, 2012.
4. Yukio Murakami, Akifumi Kawata, Yuya Seki, Teho Koh, Kenji Yuhara, Takehisa Maruyama, Mamoru Machino,

- Shigeru Ito, Yoshinori Kadoma, Seiichiro Fujisawa. Comparative inhibitory effects of magnolol, honokiol, eugenol and bis-eugenol on cyclooxygenase-2 expression and nuclear factor-kappa B activation in RAW264.7 macrophage-like cells stimulated with fimbriae of *Porphyromonas gingivalis*. *In Vivo* 26(6): 941-950, 2012.
5. Jun Negishi, Seiichi Funamoto, Tsuyoshi Kimura, Kwangwoo Nam, Tetsuya Higami, Akio Kishida, Porcine radial artery decellularization by high hydrostatic pressure, *J. Tissue Eng. Regen. Med.*, 2012; DOI: 10.1002/term. 1662
 6. Kwangwoo Nam, Yuuki Sakai, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida, Fabrication of a heterostructural fibrillated collagen matrix for the regeneration of soft tissue function, *Soft Matter* 2012; 8; 472-480.
 7. Kaori Taniguchi, Shinya Takizawa, Tomoya Hirano, Shigeru Murata, Hiroyuki Kagechika, Akio Kishida, Ayumi Ohsaki, Amarastelline A: A Fluorescent Alkaloid from *Quassia amara* and Its Properties in Living Cells, *Chem Plus Chem* 2012; 7(6):427-431.
 8. Ayumi Ohsaki, Masaaki Ozawa, Kanki Komiyama, Akio Kishida, Takahiko Isobe, The cytotoxic activity of diterpenoids from *Isodon* species, *Nat. Prod. Commun.* 2012; 7(8); 977-978.
 9. Toshiyuki Aodai, Toru Masuzawa, Kazuhide Ozeki, Akio Kishida, Tetsuya Higami, Effect of metal surface characteristics on the adhesion performance of the integrated low-level energies method of adhesion, *J. Artif Organs* 2012; 15(4); 386-394.
 10. Kunio Ikemura, Takeshi Endo, Yoshinori Kadoma. A review of the development of multi-purpose primers and adhesives comprising novel dithiooctanoate monomers and phosphonic acid monomers. *Dent Mater J* 31(1): 1-25, 2012.
 11. Seiichiro Fujisawa, Yoshinori Kadoma. Relationship between phenol-induced cytotoxicity and experimental inhibition rate constant or a theoretical parameter. *Mini Rev Med Chem* 12(6): 477-490. 2012.
 12. Seiichiro Fujisawa S, Yoshinori Kadoma. QSAR for the cytotoxicity of tert-butylphenols and 2-methoxyphenols in terms of inhibition rate constant and a theoretical parameter; In: *Recent trends on QSAR in the pharmaceutical perceptions*, Ed. Mahmud Tareq Hassan Khan, Chap. 7, 242-254. Bentham Science Publishers, Netherlands, 2012.

Oral Radiation Oncology

1. Staffs and Students

Professor	Masahiko MIURA	
Tokunin Assistant Professor	Yu DUNG,	Yoko MORI
Graduate Students(Doctor)	Atsushi KAIDA,	Asumi HONDA
	Chisato YAMADA,	Eri TUCHIDA
Graduate Students(Mastor)	Shifumi DEGUCHI,	Itumi OOMORI
Research Associate	Rieko MATSUDA	
International Resercher	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 radioresponse by molecurl imaging
- 2) Tumor radiosensitization and antiangiogenic mechanism by sulfoglycolipids
- 3) Signal transduction of insulin-like growth factor I (IGF-I) receptor
- 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. Honda-Uezono A, Kaida A, Michi Y, Harada K, Hayashi Y, Hayashi Y, Miura M : Unusual expression of red fluorescence at M phase induced by anti-microtubule agents in HeLa cells expressing the fluorescent ubiquitination-based cell cycle indicator (Fucci). *Biochem Biophys Res Commun*, 428:224-229 (2012)
2. Abe S, Hamada K, Miura M, Yamaguchi S. Neural crest stem cell property of apical pulp cells derived from human developing tooth. *Cell Biol Int*, 36: 927-936 (2012)
3. Miyano Y, Tsukuda S, Sakimoto I, Takeuchi R, Shimura S, Takahashi N, Kusayanagi T, Takafusagi Y, Okado M, Matsumoto Y, Takakusagi K, Takeuchi T, Kamisuki S, Nakazaki A, Ohta K, Miura M, Kuraomchi K, Mizushina Y, Kobayashi S, Sugawara F, Sakaguchi K : Exploration of the binding proteins of perfluorooctane sulfonate by a T7 phage display screen. *Bioorg Med Chem*, 20: 3985-3990 (2012)
4. Kaida A, Miura M : Differential dependence on oxygen tension during the maturation process between monomeric Kusabira Orange 2 and monomeric Azami Green expressed in HeLa cells. *Biochem Biophys Res Commun*, 421:855-859 (2012)
5. Kaida A, Miura M : Visualizing the effect of hypoxia on fluorescence kinetics in living HeLa cells using the fluorescent ubiquitination-based cell cycle indicator (Fucci). *Exp Cell Res*, 318:288-297 (2012)
6. Yoshimura R, Shibuya H, Hayashi K, Nakagawa K, Toda K, Watanabe H, Kaida A, Miura M : Repeat brachytherapy for patients with residual or recurrent tumors of oral cavity. *Int J Radiat Oncol Biol Phys*, 83: 1198-1204 (2012).

6. Patent

1. Patent No.5046150 (USA) , Registration date: July 27 2012
2. Patent No.154847(SINGAPORE), Registration date: July 13 2012
3. Patent No.1136601(KOREA) , Registration date: April 6 2012
4. Application No.2012-208816 , Filing date: September 21 2012

Oral and Maxillofacial Surgery

1. Staffs and Students (April, 2012)

Professor	Ken OMURA	
Associate Professor	Hiroyuki HARADA	
Junior Associate Professor	Yusuke NAKAJIMA,	Jinkyō SAKURAI
Assistant Professor	Yuji KABASAWA,	Hiroaki SHIMAMOTO,
	Eriko MARUKAWA,	Fumihiko TSUSHIMA,
	Kae TANAKA,	Hirofumi TOMIOKA
Project Junior Associate Professor	Keiichi MORITA	
Graduate Student	Toshimitsu OSAKO,	Yasuyuki SHIMADA,
	Ichiro HATAKEYAMA,	Sho MATSUKAWA,
	Takahide TAGUCHI,	Shinsuke YAMAMOTO,
	Yukiko TAKAHASHI,	Junpei SHIRAKAWA,
	Atsushi KIMURA,	Pradit RUSHATAMUKAYANUNT,
	Namiaki TAKAHARA,	Aya NAKANO,
	Seiichiro ODA,	Dilruba AKTER

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 early detection of oral cancer by mouth washing.
- 5) Clinical study on skeletal and dental changes after distraction osteogenesis in patients with cleft lip and palate.
- 6) Clinical study on maxillomandibular skeletal and dental changes after orthognatic surgery.
- 7) Study on neurosensory disturbances using the heat flux technique.
- 8) Clinical study on pre-surgical nasoalveolar molding in patients with cleft lip and palate.
- 9) Clinical study on alveolar bone grafting with platelet rich plasma.
- 10) Multidisciplinary treatment of temporomandibular disorders.
- 11) Clinical and experimental studies on bone regeneration using β -TCP and/or platelet rich plasma.
- 12) Development of multidisciplinary treatment of oral mucosal diseases.

4. Clinical Services

The Oral and Maxillofacial Surgery Clinic examines yearly more than 6,000 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. Hanabata Y, Nakajima Y, Morita KI, Kayamori K, Omura K: Coexpression of SGLT1 and EGFR is associated with tumor differentiation in oral squamous cell carcinoma. *Odontology*. 100(2):156-163, 2012.

2. Inomata K, Marukawa E, Takahashi Y, Omura K: The effect of covering materials with open wound in alveolar ridge augmentation using beta-tricalcium phosphate: an experimental study in the dog. *Int J Oral Maxillofac Implants.* 27(6):1413-21, 2012.
3. Izumo T, Kirita T, Arijii E, Ozeki S, Okada N, Okabe S, Okazaki Y, Omura K, Kusama M, Sato T: General rules for clinical and pathological studies on oral cancer: A synopsis. *Jpn J Clin Oncol.* 42(11):1099-1109, 2012.
4. Khanom R, Sakamoto K, Pal SK, Shimada Y, Morita K, Omura K, Miki Y, Yamaguchi A: Expression of basal cell keratin 15 and keratin 19 in oral squamous neoplasms represents diverse pathophysiological. *Histol Histopathol.* 27(7):949-959, 2012.
5. Kugimoto T, Morita K, Omura K: Development of oral cancer screening test by detection of squamous cell carcinoma among exfoliated oral mucosal cells. *Oral Oncol.* 48(9):794-798, 2012.
6. Kuribayashi Y, Tsushima F, Sato M, Morita KI, Omura K: Recurrence patterns of oral leukoplakia after curative surgical resection: important factors that predict the risk of recurrence and malignancy. *J Oral Pathol Med.* 41(9):682-688, 2012.
7. Mochizuki Y, Omura K, Nakamura S, Harada H, Shibuya H, Kurabayashi T: Preoperative predictive model of cervical lymph node metastasis combining fluorine-18 fluorodeoxyglucose positron-emission tomography/computerized tomography findings and clinical factors in patients with oral or oropharyngeal squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 113(2):274-282, 2012.
8. Mochizuki Y, Omura K, Hirai H, Kugimoto T, Osako T, Taguchi T: Chronic mandibular osteomyelitis with suspected underlying synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome: a case report. *J Inflamm Res.* 5:29-35, 2012.
9. Mochizuki Y, Omura K, Nakamura S, Kayamori K, Harada H, Shibuya H: Evaluation of metastatic cervical lymph nodes in patients with oral squamous cell carcinoma using 18F-FDG PET-CT scans and histopathologic correlation. *J Surg Rad.* 3(4):210-215, 2012.
10. Sakamoto K, Fujii T, Kawachi H, Miki Y, Omura K, Morita K, Kayamori K, Katsube K, Yamaguchi A: Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lab Invest.* 92(5):688-702, 2012.
11. Suzuki M, Hatsuse H, Nagao K, Takayama Y, Kameyama K, Kabasawa Y, Omura K, Yoshida M, Fujii K, Miyashita T: Selective haploinsufficiency of longer isoforms of PTCH1 protein can cause nevoid basal cell carcinoma syndrome. *J Hum Genet.* 57(7):422-426, 2012.
12. Tsushima F, Sawai T, Kayamori K, Okada N, Omura K: Schwannoma in the floor of the mouth: A case report and clinicopathological studies of 10 cases in the oral region. *Journal of Oral and maxillofacial surgery, Medicine, and Pathology.* 24:175-179, 2012.

Oral and Maxillofacial Radiology

1. Staffs and Students (April, 2012)

Professor	Tohru KURABAYASHI	
Associate Professor	Hiroshi WATANABE	
Junior Associate Professor	Naoto OHBAYASHI,	Norio YOSHINO
Assistant Professor	Akemi TETSUMURA,	Shin NAKAMURA,
	Kiyoshi OKOCHI,	Ami KURIBAYASHI
Hospital Staff	Natsuko TAKATSUKA,	Tadanobu ARAGAKI
	Yoshikazu NOMURA,	Atsushi KAIDA
Graduate Student	Yosuke KAMIYAMA,	Kretapirom KORNKAMOL,
	Kamrun NAHAR,	Madoka SUZUKI,
	Akira TAKAHASHI,	Yoshihiro OZAKI
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. Fukami K, Shiozaki K, Mishima A, Kuribayashi A, Hamada Y, Kobayashi K. Bifid mandibular canal: confirmation of limited cone beam computed tomography findings by gross anatomical and histological investigations. *Dentomaxillofac Radiol*. 41: 460-5, 2012.
2. Ida M, Tetsumura A, Kuribayashi A, Okada N, Kurabayashi T. A clinicoradiological study of odontogenic carcinomas and their impact on clinical diagnosis. *Dentomaxillofac Radiol* 41: 594-600, 2012.
3. Imaizumi A, Kuribayashi A, Watanabe H, Ohbayashi N, Nakamura S, Sumi Y, Sano T, Kurabayashi T. Non-Hodgkin lymphoma involving the mandible: imaging findings. *Oral Surg Oral Med Oral Pathol Oral Radiol* 113: e33-9, 2012.
4. Kaida A, Miura M. Differential dependence on oxygen tension during the maturation process between monomeric Kusabira Orange 2 and monomeric Azami Green expressed in HeLa cells. *Biochem Biophys Res Commun* 421: 855-859, 2012.
5. Kamiyama Y, Nakamura N, Abe T, Munakata M, Nomura T, Watanabe H, Akiyama M, Kurabayashi T. Linear measurement accuracy of dental CT images obtained by 64-slice multi-detector row CT: the effects of mandibular positioning and pitch factor at CT scanning. *Implant Dentistry* 21: 496-501, 2012.
6. Koyama T, Shimura M, Minemoto Y, Nohara S, Shibata S, Iida Y, Iwashita S, Hasegawa M, Kurabayashi T, Hamada H, Kono K, Honda E, Aoki I, Ishizaka Y. Evaluation of selective tumor detection by clinical magnetic resonance imaging using antibody-conjugated superparamagnetic iron oxide. *J Control Release* 159: 413-418, 2012.
7. Mochizuki Y, Omura K, Nakamura S, Harada S, Shibuya H, Kurabayashi T. Preoperative predictive model of

cervical lymph node metastasis combining fluorine-18-fluorodeoxyglucose positron emission tomography computerized tomography findings and clinical factor in patients with oral or oropharyngeal squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol* 113: 274-282, 2012.

8. Ng IW, Ono T, Inoue-Arai MS, Honda E, Kurabayashi T, Moriyama K. Differential articulatory movements during Japanese /s/ and /t/ as revealed by MR image sequences with tooth visualization. *Arch Oral Biol* 57: 749-759, 2012.
9. Okochi K, Nakamura S, Tetsumura A, Honda E, Kurabayashi T. Magnetic resonance imaging of temporomandibular joint cyst. *Oral Surg Oral Med Oral Pathol Oral Radiol* 113: 827-831, 2012.
10. Qiu L, Haruyama N, Suzuki S, Yamada D, Obayashi N, Kurabayashi T, Moriyama K. Accuracy of orthodontic miniscrew implantation guided by stereolithographic surgical stent based on cone-beam CT-derived 3D images. *Angle Orthod* 82: 284-93, 2012.
11. Tetsumura A, Nakamura S, Yoshino N, Watanabe H, Kurabayashi A, Nagumo K, Okada N, Sasaki T, Kurabayashi T. USPIO-enhanced MRI of highly invasive and highly metastasizing transplanted human squamous cell carcinoma: an experimental study. *Dentmaxillofac Radiol* 41: 55-63, 2012.
12. Yoshimura R, Shibuya H, Hayashi K, Nakagawa K, Toda K, Watanabe H, Kaida A, Miura M. Repeat brachytherapy for patients with residual or recurrent tumors of oral cavity. *Int J Radiat Oncol Biol Phys* 83: 1198-1204, 2012.

Anesthesiology and Clinical Physiology

1. Staffs and Students (April, 2012)

Professor	Haruhisa Fukayama	
Associate Professor	Hikaru Kohase	
Junior Associate Professor	Shigeharu Jinnō	
Assistant Professors	Fumihiko Yoshikawa, Tomoka Matsumura	Tomoyuki Miyamoto,
Hospital Staffs	Kazumasa Kubota, Youhei Fukumori, Haruka Haida, Yuko Takusagawa.	Yuka Oono, Yukiko Baba, Reina Ichikawa,
Graduate Students	Atsushi Nakajima, Tomoko Ebisawa–Matsushita, Takuya Funayama, Yoko Sasaki.	Kanako Saji, Katsuhiko Matsumoto,
Research Students	Manami Yajima,	Hironari Ando.
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. Baba Y, Kohase H, Oono Y, Fujii-Abe K, Arendt-Nielsen L. Effects of dexmedetomidine on conditioned pain modulation in humans. *European Journal of Pain* 16: 1137 – 47, 2012.
2. Haida H, Ando S, Ogami S, Wakita R, Kohase H, Saito N, Yoshioka T, Ikoma T, Tanaka J, Umino M, and Fukayama H. In vitro evaluation of calcium alginate gels as matrix for iontophoresis electrodes. *Journal of Medical and Dental Sciences* 59 (1): 9 – 16, 2012.
3. Wakita R, Kohase H, Fukayama H. Comparison of dexmedetomidine sedation with and without midazolam for dental implant surgery. *Anesthesia Progress* 59 (2): 62 – 8, 2012.
4. Oono Y, Wang K, Svensson P, Arendt-Nielsen L. Conditioned pain modulation evoked by a mechanical craniofacial

stimulus is not influenced by nociceptive stimulation of the temporomandibular joint. *Journal of Orofacial Pain* 26: 105 – 116, 2012.

5. Niimi K, Horie S, Yokosuka M, Kawakami-Mori F, Tanaka K, Fukayama H, Sahara Y. Heterogeneous electrophysiological and morphological properties of neurons in the mouse medial amygdala in vitro. *Brain Research* 1480: 41 – 52, 2012.
6. Matsumoto K, Morita K, Jinno S, Omura K. Sensory changes after tongue reduction for macroglossia. *Oral Surg Oral Med Oral Pathol Oral Radiol*; Aug 15. Epub, 2012.

Congress

1. Fukayama H. A new electric injector for infiltration anesthesia. 30th Myanmar Dental Conference and 10th FDI-MDA Joint Educational Meeting, Yangon, Myanmar, January, 2012.
2. Nakachi S. Titanium implant: The IAT EXA Implant in Japan. 32nd Myanmar Dental Conference and 13th FDI-MDA Joint Educational Meeting, Yangon, Myanmar, January, 2012.
3. Fukayama H, Yoshikawa F, Fujii-Abe K. A new electric injector for infiltration anesthesia. 13th International Congress of Dental Anesthesiology Societies, Hawaii, USA, March, 2012.
4. Yoshikawa F, Nakamura Z, Sumi Y, Togashi K, Nishimura M, Fukayama H. Anesthetic effect of water-soluble edible film containing surface anesthetics, 13th International Congress of Dental Anesthesiology Societies, Hawaii, USA, March, 2012.
5. Nakamura Z, Oe C, Makiyama T, Yoshikawa F, Fukayama H. Anesthetic management in patients with severe motor and intellectual disabilities (SMID) undergoing dental treatment, 13th International Congress of Dental Anesthesiology Societies, Hawaii, USA, March, 2012.
6. Ebisawa T, Nakajima A, Haida H, Ando S, Yoshioka T, Ikoma T, Tanaka J, and Fukayama H. Calcium Alginate gel as electrode material for iontophoresis of lidocaine. The 6th International Conference on the Science and Technology for Advanced Ceramics (STAC-6), June, 2012.
7. Wang K, Oono Y, Atis ES, Luo Y, Arendt-Nielsen L. Human somatosensory perceptions are modulated by skin temperature. The IADR/LAR General Session, Iguazu Falls, Brazil, June, 2012.
8. Kohase, H, Baba Y, Makino K, Fukayama H, Abe-Fujii K, Oono Y. Phenylephrine inhibits conditioned pain modulation in humans. The 14th World Congress on Pain, International Association for the Study of Pain, IASP, Milan, Italy, August, 2012.
9. Oono Y, Baad-Hansen L, Wang K, Arendt-Nielsen L, Svensson P. Effect of trigeminal conditioned pain modulation on somatosensory function evaluated by quantitative sensory testing. The 14th World Congress on Pain, International Association for the Study of Pain, IASP, Milan, Italy, August, 2012.
10. Atis ES, Oono Y, Arendt-Nielsen L, Wang K. EMG-bite force relationships are modulated by experimental low and high cutaneous temperatures. The 14th World Congress on Pain, International Association for the Study of Pain, IASP, Milan, Italy, August, 2012.
11. Ikeda Y, Saji K, Kim W, Shingai Y, Tateno A, Takahashi H, Okubo Y, Fukayama H, Suzuki H. Effects of an NK1 receptor antagonist on reward processing in healthy individuals: a pharmacological fMRI study. The 35th Annual Meeting of the Japan Neuroscience Society. Nagoya, Japan, September, 2012.
12. Yoshikawa F, Tamaki Y, Okumura H, Nakamura Z, Kohase H, Fukayama H. Factors affecting decreasing SpO₂ and delayed recovery in intravenous sedation. iADH 2012, Melbourne, Australia, October, 2012.

Books

1. Oono Y. Conditioned pain modulation (CPM): experimental studies in the craniofacial region in healthy humans. 2012, Aalborg University, Aalborg, Denmark. (ISBN: 978-87-7094-119-8).
2. Oono Y. Conditioned pain modulation (CPM): experimental studies in the craniofacial region in healthy humans. 2012, River Publishers, Aalborg, Denmark. (ISBN: 978-87-92329-51-6).

Editorial Comment

1. Oono Y, Arendt-Nielsen L. Impact of mental stressor on conditioned pain modulation. *Scandinavian Journal of Pain*. 2012; 3: 141.

Orofacial Pain Management

1. Staffs and Students (April, 2012)

Professor	Masahiko SHIMADA	
Assistant Professor	Yoko YAMAZAKI	
Hospital Staff	Tomoko NIIMI,	Yuko ANDOH,
	Daisuke TOMIZAWA	
Graduate Student	Akitoshi HOSODA,	Hiroko IMURA

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 pberipheral nerves including acupuncture and psychotherapies.

5. Publication

Original Article & Clinical report

1. Miyawaki T, Kohjitani A, Maeda S, Shimada M: Combination of midazolam and a cyclooxygenase-2 inhibitor inhibits lipopolysaccharide-induced interleukin-6 production in human peripheral blood mononuclear cells. *Immunopharmacol Immunotoxicol.* 34: 79-83, 2012;
2. Arai Y, Maeda S, Higuchi H, Tomoyasu Y, Shimada M, Miyawaki T.: Effects of midazolam and phenobarbital on brain oxidative reactions induced by pentylenetetrazole in a convulsion model. *Immunopharmacol Immunotoxicol.* 34.: 216-221., 2012
3. Y.Yamazaki, M.Umino, H.Fukayama, M.Shimada, The Effect of Alternating Current Iontophoresis on Rats with the Chronic Constriction Injury to the Infraorbital Nerve. *International Journal of Dentistry* 34: Article ID 405292, 7 pages, 2012.

Pediatric Dentistry

1. Staffs and Students (April, 2012)

Junior Associate Professor	Yoshiaki ONO, Zenzo MIWA	
Assistant Professor	Yoshiaki HASHIMOTO,	Michiyo MIYASHIN,
	Haruko FUJITA,	Mizuho MOTEGI
Hospital Staff	Satoko KAKINO,	Yuki IMAMURA,
	Makiko TAKASHI,	Yukie NAKAJIMA (April~),
	Atsushi OISHI (April~),	Sachi GOTOH
Secretary	Mai INOUE	
Graduate Student	Yukie NAKAJIMA(~March),	Atsushi OISHI(~March),
	Sun MEINA(~March),	Isidro Sharon YAMBAO(~March),
	Seiko OHBA,	Ayako NAKANE,
	Kaori SHOI,	Taki SEKIYA,
	Sachiko ITOH,	Daiki HORIKAWA,
	Tomoki UEHARA (April~)	

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 maxillofacial cranium and the dentition
- 4) Development of the 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. Uehara N, Takagi Y, Miwa Z, Sugimoto K. Objective assessment of internal stress in children during dental treatment by analysis of autonomic nervous activity. *Int J Paediatr Dent.* 22(5):331-41. 2012.
2. Nakajima Y, Shimada Y, Miyashin M, Takagi Y, Tagami J, Sumi Y. Noninvasive cross-sectional imaging of

- incomplete crown fractures (cracks) using swept-source optical coherence tomography. *International Endodontic Journal*. 45: 933-41, 2012.
3. Sasagawa I, Yokosuka H, Ishiyama M, Mikami M, Shimokawa H, Uchida T. Fine structural and immunohistochemical detection of collar enamel in the teeth of *Polypterus senegalus*, an actinopterygian fish. *Cell Tissue Res*. 347(2): 369-81, 2012.
 4. Hayashi N, Kusumoto Y, Yamazaki T, Shinozuka O, Tamura Y, Aoki K, Ohya K, Shimokawa H. Gingival Overgrowth Induced by Phenytoin -Study of the Human Gingival Overgrowth Tissues and Clonal Gingival Cells-. *Disability and Oral Health*. 33(1):16-26, 2012.
 5. Imamura Y, Nakamura M, Nagai A, Takagi Y, Yamashita K. Octacalcium phosphate-mediated cement as a root canal filling material for primary teeth. *Phosphorus Research Bulletin*. Vol. 26: 33-38,2012.
 6. Imamura Y, Horikawa D, Yamashita K, Takagi Y. Effects of Particle size on the Hardening process and Sealing ability of OCP-mediated cement. *Proceeding of 8th biennial conference of PDAA 2012*. p402-408, 2012.
 7. Kanazawa H, Miyashin M, Kudo M, Masaki H, Kitamura M, Kindaichi J, Takagi Y. Prevention of late complications on teeth due to electron beam therapy for children with malignant tumors. *Proceeding of 8th biennial conference of PDAA 2012*. P305-310, 2012.
 8. Tuchihashi N, Uehara N, Takagi Y, Miwa Z, Sugimoto K. Internal stress in children and parental attitude to dental treatment with passive restraint. *Pediatric Dental Journal*. 22(2):170-177, 2012.
 9. Sun M, Ono Y, Takagi Y. Prediction of the upper airway growth in normal children. *Pediatric Dental Journal*. Vol. 22(1): 35-42, 2012.
 10. Isidro S, Ono Y, Takagi Y. Craniofacial Growth changes and dental attrition in the primary dentition. *Pediatric Dental Journal*. Vol. 22(1): 43-49, 2012.
 11. Ohba S, Wang W, Itoh S, Takagi Y, Nagai A, Yamashita K. Acceleration of new bone formation by an electrically polarized hydroxyapatite microgranule/platelet-rich plasma composit. *Acta Biomaterialia*. Vol.8: 2778-2787, 2012.
 12. Ohba S, Wang W, Itoh S, Takagi Y, Nagai A, Yamashita K. Efficacy of platelet-rich plasma gel and hyaluronan hydrogel as carriers of electrically polarized hydroxyapatite micro-granules for accelerating bone formation. *Journal of Biomedical Materials Research Part A*. 100A:3167-3176, 2012.

Orthodontic Science

1. Staffs and Students

Professor	Takashi ONO	
Associate Professor		
Junior Associate Professor	Yoshiro MATSUMOTO,	Zuisei KANNO
Assistant Professor	Sawa KANEKO(-Mar), Kazuo SHIMAZAKI, Satoshi KOKAI,	Jun HOSOMICHI, Ippei WATARI, Ikuo YONEMITSU(Apr-)
Graduate Students	Ikuko HATTORI(-Mar), Chiho KATOU(-Mar), Risa USUMI(-Mar), Takako KANESHIMA, Sachiko KOMORI, Chisa SHITANO, Ayako KAWABE, Rieko ONO, Emina WAKASUGI, Jui-Chin HSU, Toshihiro IMAMURA, Mutsumi MIYAZAKI, Kulthida NUNTHAYANON, Souma KITA(Apr-), Tomomi SAKAGUCHI(Apr-), Hiroyuki YAMAGUCHI(Apr-)	Maya HIRANUMA(-Mar), Mariko MIZUMACHI(-Mar), Haruki IMAI, Sarina KOIKE, Takeru KYURAGI, Yukiha FUNAKI, Hidemasa OKIHARA, Arisa SAWADA, Jutiporn PRIVATANANUPUNT, Yuhei IKEDA, Minami MIYASAKA, Asuka OKITOU, Syuji OISHI(Apr-), Yoichiro KUMA(Apr-), Mio MAKIGUCHI(Apr-)
Graduate School Research Students	Emi SAKO (-Mar), Satomi NAITO(-Mar), Yukiko KURODA, Ikuko HATTORI(Apr-), Chiho KATO(Apr-), Risa USUMI(Apr-Dec), Satoko SHIZUMA(-Mar), Ayako KIRII, Junpei SUZUKI(Apr-), Tomonari MATSUMURA(Apr-), Kyohei YAMADA(Apr-), Yusuke TAKATSU, Daisuke TOMITA,	Yasuhiro SHIMIZU(-Mar), Koji HONDA(-Mar), Keiichi SAKAI, Maya HIRANUMA(Apr-), Mariko MIZUMACHI(Apr-), Hyung Sik YOON (-Mar), Syusuke UESUGI(Apr-), Jin-Gyu AN (-Mar), Wei-Jen LAI(-Mar), Karin Harumi UCHIMA KOECKLIN(Apr-), Satoshi KURUSU, Yumi ARAI(-Mar)

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. Kato C, Fujita K, Naito S, Shibata M, Ishida T, Kokai S, Yabushita T, Ono T: Increased occlusal vertical dimension induces cortical plasticity in the rat face primary motor cortex. *Behav Brain Res* 228: 254-260, 2012.
2. Ng IW, Ono T, Inoue-Arai MS, Honda E, Kurabayashi T, Moriyama K: Differential articulatory movements during Japanese /s/ and /t/ as revealed by MR image sequences with tooth visualization. *Arch Oral Biol* 57: 749-59, 2012.
3. Abbassy MA, Horiuchi M, Harouny NME, Kanno Z, Ono T: Comparative cephalometric study of Class I malocclusion in Egyptian and Japanese adult females. *Orthod Waves* 71: 59-65, 2012.
4. Mizumachi-Kubono M, Watari I, Ishida Y, Ono T: Reduced mechanical stress on the periodontium influences AQP5 expression and distribution in the rat submandibular salivary gland. *Arch Oral Biol* 57: 877-883, 2012.
5. Kure-Hattori I, Watari I, Takei M, Ishida Y, Yonemitsu I, Ono T: Effect of functional shift of the mandible on lubrication of the temporomandibular joint. *Arch Oral Biol* 57: 987-994, 2012.
6. Sakamoto-Ozaki K, Matsumoto Y, Kanno Z, Iida J, Soma K: Development of a surgical procedure for biointegration of a newly designed orthodontic onplant. *Orthodontics* 13: 216-225, 2012
7. Ohmori H, Kirimoto H, Ono T: Comparison of the physiological properties of human periodontal-masseteric reflex evoked by incisor and canine stimulation. *Front Physiol* 3: 233, 2012.
8. Ono T: Orale Dysfunktionen in der kieferorthopädischen Praxis: der Anteil des peripheren und des zentralen Nervensystems auf die Lage der Zunge bei Mundatmung. *Inf Orthod Kieferorthop* 44: 293-301, 2012.

Cariology and Operative Dentistry

1. Staffs and Students (April, 2012)

Professor	Junji Tagami	
Associate Professor	Masayuki Otsuki,	Yoshiyuki Sasaki
Junior Associate Professor	Toru Nikaido,	Masatoshi Nakajima
Assistant Professor	Takako Yoshikawa,	Yasushi Shimada,
	Yuichi Kitasako,	Ryuzo Kishikawa,
	Go Inoue,	Eitetsu Cho,
	Keiichi Hosaka,	Tomohiro Takagaki,
	Naoko Harada	
Specially Appointed Junior Associate Professor (GCOE)		Alireza Sadr
Specially Appointed Junior Associate Professor		Shoji Nakashima
Specially Appointed Assistant Professor		Noriko Hiraishi
Specially Appointed Assistant Professor		NHM Khairul Matin
Hospital Staff	Masahiro Takahashi,	Rena Takahashi,
	Oto Aramaki,	Hidenori Hanba,
	Tomoko Maeda	
Secretary	Shiori Ogi,	Miura Noriyo Miura
Graduate Student	Tomoyuki Takai,	Hamid Nurrohman,
	Amir Nazari,	Ilnaz Hariri,
	Taweesak Prasansuttiporn,	Kanako Imai,
	Yumi Imamura,	Sachiko Utaka,
	Iori Gando,	Masaru Kirihara,
	Emi Kuribayashi,	Wakae Sakano,
	Hitomi Mita,	Turki Abdulsam Bakhsh,
	Gerardo Jose Joves Mendez,	Suppason Thittaweerat,
	Turki Abdulsam Bakhsh,	Azusa Tanaka,
	Kiminori Kinose,	Mona Mohammad Mandura,
	Md. Sofiqul Islam,	Hisaich Nakagawa,
	Haidil Akmla Mahdan,	Ena Lodha,
	Upoma Guha,	Shigeyuki Nagai,
	Naoko Matsui,	Ikumi Wada,
	Yumiko Uesugi,	Nariaki Yoshimine,
	Emi Oshima,	Ornnicha Thanatvarakorn,
	Alaa Turkistani,	Teerapong Mamanee,
	Sahar Jameel Khunkar,	Ka Kyou,
	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
Research Student	Shinji Ogura,	Mineo Kijima,
	Yuichiro Mitsui,	Ayaka Kusanagi
Intern	Masahiro Ono,	Kanako Shida

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

Mechanism of dentin bonding
 Adhesive of resin restoration systems to tooth substance and other restorative materials
 Structure, diagnosis and treatment of dentin caries
 Physic-chemical and manipulative properties of restorative materials
 Durability of restorative materials
 Compensation of resin composite polymerization contraction stress
 Pulpal response to restorative materials
 Improvement of various restorative techniques for direct and indirect restorations
 Improvement of various esthetic treatment techniques
 Caries risk assessment and prevention of recurrent caries
 Development and introduction for clinical works of OCT (Optical coherence tomography)

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. Cantanhede de Sá RB, Carvalho AO, Puppini-Rontani RM, Ambrosano GM, Nikaido T, Tagami J, Giannini M: The effects of water storage on bond strength and dentin sealing ability promoted by adhesive systems. *J Adhes Dent* 14: 543-549, 2012.
2. Carvalho AO, Oliveira MT, Nikaido T, Tagami J, Giannini M: Effect of adhesive system and application strategy on reduction of dentin permeability. *Braz Oral Res* 26: 397-403, 2012.
3. Hamba H, Nikaido T, Sadr A, Nakashima S, Tagami J: Enamel lesion parameter correlations between polychromatic Micro-CT and TMR. *J Dent Res* 91: 586 – 591, 2012.
4. Hariri I, Sadr A, Shimada Y, Tagami J, Sumi Y: Effects of structural orientation of enamel and dentin on light attenuation and local refractive index: an optical coherence tomography study. *J Dent* 40:387-96, 2012.
5. Hariri I, Shimada Y, Sadr A, Ichinose S, Tagami J: The effects of aging on shear bond strength and nanoleakage expression of an etch-and-rinse adhesive on human enamel and dentin. *J Adhes Dent* 14:235-43, 2012.
6. Horie K, Nakajima M, Hosaka K, Kainose K, Tanaka A, Foxton RM, Tagami J: Influence of composite-composite join on light transmission characteristics of layered resin composite. *Dent Mater* 28(2): 204-211, 2012.
7. Ichikawa C, Nikaido T, Inoue G, Sadr A, Tagami J: Ultra-morphologies of the dentin acid-base resistant zone of two-step self-etching systems after long-term storage in water. *J Adhes Dent* 14: 207-213, 2012.
8. Imai K, Shimada Y, Sadr A, Tagami J, Sumi Y: Noninvasive cross-sectional visualization of enamel cracks by optical coherence tomography. *J Endod* 38: 1269-74, 2012.
9. Inoue G, Nikaido T, Sadr A, Tagami J: Morphological categorization of acid-base resistant zones with self-etching primer adhesive systems. *Dent Mater J* 31: 232-238, 2012.
10. Islam S, Hiraishi N, Nassar M, Yiu C, Otsuki M, Tagami J: Effect of natural cross-linkers incorporation in a self-etching primer on dentine bond strength. *J Dent* 40: 1052-1059, 2012.
11. Islam SM, Hiraishi N, Nassar M, Sono R, Otsuki M, Takatsura T, Yiu C, Tagami J: In vitro effect of hesperidin on root dentin collagen and de/re-mineralization. *Dent Mater J* 31: 362-367, 2012.
12. Jamleh A, Sadr A, Nomura N, Yahata Y, Ebihara A, Hanawa T, Tagami J, Suda H: Nano-indentation testing of new

- and fractured nickel-titanium endodontic instruments. *IntEndod J* 45:462-8, 2012.
13. Kambara K, Nakajima M, Hosaka K, Takahashi M, Thanatvarakorn O, Ichinose S, Foxton RM, Tagami J: Effect of smear layer treatment on dentin bond of self-adhesive cements. *Dent Mater J* 31(6): 980-987, 2012.
 14. Kitasako Y, Sadr A, Hamba H, Ikeda M, Tagami J: Gum containing calcium-fluoride reinforces enamel subsurface lesion in situ. *J Dent Res* 91: 370-375, 2012.
 15. Komagamine Y, Kanazawa M, Kaiba Y, Sato Y, Minakuchi S, Sasaki Y: Association between self-assessment of complete dentures and oral health-related quality of life. *J Oral Rehabil* 39(11): 847-857, 2012.
 16. Kuribayashi M, Kitasako Y, Matin K, Sadr A, Shida K, Tagami J: Intraoral pH measurement of carious lesions with qPCR of cariogenic bacteria to differentiate caries activity. *J Dent* 40: 222-228, 2012.
 17. Nakajima M, Arimoto A, Prasansuttiporn T, Thanatvarakorn O, Foxton RM, Tagami J: Light transmission characteristics of dentine and resin composites with different thickness. *J Dent* 40(Suppl 2): e77-e82, 2012.
 18. Momoi Y, Fujitani M, Fukushima M, Hayashi M, Imazato S, Kubo S, Nikaido T, Shimizu A, Unemori M, Yamaki C: Clinical guidelines for treating caries in adults following a minimal intervention policy, Evidence and consensus based report. *J Dent* 40: 95-105, 2012.
 19. Mori F, Hiraishi N, Otsuki M, Tagami J: Effect of mastication on flow and properties of saliva. *Asian Pac J Dent*. 12: 1-5, 2012.
 20. Nakajima Y, Shimada Y, Miyashin M, Takagi Y, Tagami J, Sumi Y: Noninvasive cross-sectional imaging of incomplete crown fractures (cracks) using swept-source optical coherence tomography. *IntEndod J* 45:933-41, 2012.
 21. Nakata K, Nikaido T, Nakashima S, Nango N, Tagami J: An approach to normalizing micro-CT depth profiles of mineral density for monitoring enamel remineralization progress. *Dent Mater J* 31: 533-540, 2012.
 22. Nazari A, Shimada Y, Sadr A, Tagami J: Pre-etching vs. grinding in promotion of adhesion to intact enamel using self-etch adhesives. *Dent Mater J* 31:394-400, 2012.
 23. Nurrohman H, Nikaido T, Takagaki T, Sadr A, Ichinose S, Tagami J: Hydroxyapatite crystal protection against acid-attack beneath resin-dentin interface with four adhesives: TEM and crystallography evidence. *Dent Mater* 28: e89-e98, 2012.
 24. Nurrohman H, Nikaido T, Takagaki T, Sadr A, Waidyasekera K, Kitayama S, Ikeda M, Tagami J: Dentin bonding performance and ability of four MMA-based adhesive resins to prevent demineralization along the hybrid layer. *J Adhes Dent* 14: 339-348, 2012.
 25. Prasansuttiporn T, Nakajima M, Foxton RM, Tagami J: Scrubbing effect of self-etching adhesives on bond strength to NaOCl-treated dentin. *J Adhes Dent* 14(2): 121-127, 2012.
 26. Shimada Y, Sadr A, Nazari A, Nakagawa H, Otsuki M, Tagami J, Sumi Y: 3D evaluation of composite resin restoration at practical training using swept-source optical coherence tomography (SS-OCT). *Dent Mater J* 31: 409-17, 2012.
 27. Takahashi R, Nikaido T, Tagami J, Hickel R, Kunzelmann KH: Contemporary adhesives: marginal adaptation and microtensile bond strength of class II composite restorations. *Am J Dent* 25: 181-188, 2012.
 28. Takai T, Hosaka K, Kambara K, Thitthaweerat S, Matsui N, Takahashi M, Kishikawa R, Nakajima M, Otsuki M, Foxton RM, Tagami J: Effect of air-drying dentin surfaces on dentin bond strength of a solvent-free one-step adhesive. *Dent Mater J* 31: 558-563, 2012.
 29. Tano E, Otsuki M, Kato J, Sadr A, Ikeda M, Tagami J: Effects of 405 nm diode laser on titanium oxide bleaching activation. *Photomed Laser Surg*. 30: 648-654, 2012.
 30. Thitthaweerat S, Nakajima M, Foxton RM, Tagami J: Effect of waiting interval in chemical activation mode of one-step dual-cure adhesives on bonding to root canal dentine. *J Dent* 40: 1109-1118, 2012.
 31. Tsubone M, Nakajima M, Hosaka K, Foxton RM, Tagami J: Color shifting effect at the border of resin composite restorations in human teeth. *Dent Mater* 28: 811-817, 2012.
 32. Waidyasekera K, Nikaido T, Weerasinghe DDS, Nurrohman H, Tagami J: Bonding durability of dual cure composite core material with different self-etching systems in a model complete vertical root fracture reconstruction. *J Adhes Dent* 14: 167-74, 2012.
 33. Yahagi C, Takagaki T, Sadr A, Ikeda M, Nikaido T, Tagami J: Effect of lining with a flowable composite on internal adaptation of direct composite restorations using all-in-one adhesive systems. *Dent Mater J* 31: 481-488, 2012.
 34. Yiu CK, Hiraishi N, Tay FR, King NM: Effect of chlorhexidine incorporation into dental adhesive resin on durability of resin-dentin bond. *J Adhes Dent* 14:355-62, 2012
 35. Yoshikawa T, Wattanawongpitak N, CHO E, Tagami J: Effect of remaining dentin thickness on bond strength of various adhesive systems to dentin. *Dental Materials Journal* 31: 1033-1038, 2012.

6. Review Articles

1. Nikaido T, Takahashi R, Ariyoshi M, Sadr A, Tagami J: Protection and reinforcement of tooth structures by dental coating materials. *Coatings* 2: 210-220, 2012.

Books

1. Bakhsh TA, Sadr A, Shimada Y, Khunkar S, Tagami J, Sumi Y: Relationship between non-destructive OCT evaluation of resins composites and bond strength in a cavity. *Pros SPIE* 8208:91-98, 2012.
2. Hariri I, Sadr A, Shimada Y, Nakashima S, Sumi Y, Tagami J: Relationship between refractive index and mineral content of enamel and dentin using SS-OCT and TMR. *Proc SPIE* 8208: M1-6, 2012.
3. Sadr A, Nakashima S, Shimada Y, Tagami J, Sumi Y: Longitudinal assessment of subsurface artificial root caries lesions by optical coherence tomography in comparison with transverse microradiography. *Proc SPIE* 8208: H1-7, 2012.

Fixed Prosthodontics

1. Staffs and Students(April, 2012)

Professor	Hiroyuki MIURA	
Associate Professor	Keiichi YOSHIDA	
Junior Associate Professor	Daizo OKADA,	Wataru KOMADA(from May)
Assistant Professor	Wataru KOMADA(to April), Kumiko KAWASHIMA, Yuji FUKUI(to March), Kenichi GOSHIMA, Naosuke KUMAGAE(from April)	Chiharu SHIN, Yuko KIZUKI(to March), Shiho OTAKE, Koichiro YUSA(from April),
Graduate Student	Reiko OGURA, Ning XU, Reina NEMOTO, Yoji UEDA, Tasuku INAGAKI, Hiroyuki OKAMOTO, Fujino OSHIMA,	Naosuke KUMAGAE(to March), Satoshi OMORI, Sachi MAKINO, Izumi KATAOKA, Rie FUJITA, Miho SATO, Kyoshi MATSUKAWA

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. Kumagae N, Komada W, Fukui Y, Okada D, Takahashi H, Yoshida K, Miura H: Influence of the flexural modulus of prefabricated and experimental posts on the fracture strength and failure mode of composite resin cores. *Dent Mater J*, 31(1), 113-119, 2012.
2. Ogura R, Kato H, Okada D, Foxton RM, Ikeda M, Miura H: The relationship between bite force and oral sensation during biting in molars. *Aust Dent J*,57,292-299,2012.

Pulp Biology and Endodontics

1. Staffs and Students (April 2012)

Professor	Hideaki SUDA	
Associate Professor	Chihiro KOBAYASHI,	Mitsuhiro SUNAKAWA
Junior Associate Professor	Atsushi TAKEDA,	Hideharu IKEDA
Assistant Professor	Arata EBIHARA,	Nobuyuki KAWASHIMA,
	Hiroyuki MATSUMOTO,	Reiko WADACHI,
	Noriyuki SUZUKI,	Hitomi HANADA
Clinical staff	Satoshi WATANABE,	Jun KAWAMURA,
	Yu KOIZUMI,	Chizuko KOKUZAWA,
	Toshihiko YOSHIOKA,	Tetsu SATO
Graduate Student	Kouyou TAKIMOTO,	Mengyu ZHOU,
	Ying LI,	Kei KOMATSU,
	Kana MIYARA,	Mioko YAMAMOTO,
	Ahmed Osama JAMLEH,	Jindan PIAO,
	Kazuto HURUHATA,	Saliman AIERKIN,
	Jie GU	

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) Improvement 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) Evidence for an innocuous sensation in the dental pulp
- 16) Lymphangiogenesis in the dental pulp
- 17) Neuro-scientific research for dental pain
- 18) Molecular biological approach to the alveolar bone resorption associated with pulpal diseases
- 19) Three dimensional analysis of periapical bone loss using CBCT
- 20) Effect of motion artifacts on dental CT images
- 21) Global Center of Excellence (GCOE) Program

“International Research Center for Molecular Science in Tooth and Bone 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. Otabe K, Muneta T, Kawashima N, Suda H, Tsuji K, Sekiya I : Comparison of gingiva, dental pulp, and periodontal ligament cells from the standpoint of mesenchymal stem cell properties. *Cell Medicine*. 4. 13-21, 2012.
2. Xu J, Kawashima N, Fujiwara N, Harada H, Ota M, Suda H. : Promotional effects of vasoactive intestinal peptide on the development of rodent Hertwig’s epithelial root sheath. *Congenital Anomalies*. 52(3):162-7. 2012.
3. Sun H, Yang J, Kawashima N, Li Y, Zhang W, Wang P. : A brief comparison of curricula at dental schools in China and Japan. *J Dent Educ*. 76(6):765-73. 2012.
4. Bolortuya G, Ebihara A, Ichinose S, Watanabe S, Anjo T, Kokuzawa C, Saegusa H, Kawashima N, and Suda H. : Effects of Dentin Surface Modifications Treated with Er:YAG and Nd:YAG Laser Irradiation on Fibroblast Cell Adhesion. *Photomedicine and laser surgery*. 30(2):63-70. 2012.
5. Jamleh A, Sadr A , Nomura N, Yahata Y , Ebihara A, Hanawa T, Tagami J. and Suda H. : Nano-indentation testing of new and fractured nickel-titanium endodontic instruments. *International Endodontic Journal*. 45(5):462-8. 2012.
6. Jamleh A, Kobayashi C, Yahata Y, Ebihara A and Suda H. : Deflecting load of nickel titanium rotary instruments during cyclic fatigue. *Dental Materials Journal*. 31(3):389-93. 2012.
7. Kokuzawa C, Ebihara A, Watanabe S, Anjo T, Bolortuya G, Saegusa H, Suda H. : Shaping of the root canal using Er:YAG laser irradiation. *Photomedicine and laser surgery*. 30(7):367-73. 2012.
8. Ikeda H, Suda H : Iatrogenic Pulp Exposure in Paramolar Tubercles Carries the Risk of Pulp or Tooth Loss. *IJDCR* 2(5):66-72, 2012.

Review articles

1. Hideharu Ikeda, Hideaki Suda, *Circulation of the pulp*, Seltzer and Bender's Dental Pulp, Quintessence Pub Co, Second Edition, 109-131. 2012.
2. Kawashima N. : Characterisation of dental pulp stem cells: A new horizon for tissue regeneration?, *Arch Oral Biol*. 57(11):1439-58. 2012.

Removable Partial Denture Prosthodontics

1. Staffs and Students (April, 2012)

Professor	Yoshimasa IGARASHI	
Associate Professor	Noriyuki WAKABAYASHI	
Junior Associate Professor	Masayuki HIDESHIMA,	Kenji FUEKI
Assistant Professor	Masayuki SATO, Ichirou MINAMI, Jyurou WADACHI, Eiko YOSHIDA	Takeshi UENO, Teruyasu NAKAMURA, Syusuke INUKAI,
Hospital Staff	Yuka ABE, Junnichirou WADA, Yuuki IWAKI,	Kouta OKANO, Aiichirou AO, Kengo FUJIKI
Secretary	Yoko FUKI	
Graduate Student	Kazuhito SHOUI, Natsuko MURAKAMI, Yuusuke TOYOSHIMA, Tooru SAITOU, Ryousuke HARAKAWA, Yuuki ARAI, Yuka KAJIMA, Chiaki TSUTSUMI, Kazuyuki HANNDA,	Atsushi TAKAICHI, Takashi SEKINISHI, Ryo HAYASHI, Natsuki SUZUKI, James LEE, Hiroyuki ISHIYAMA, Hayato KUMAGAI, Yasuha NOGAWA, Teisuke AKIMOTO

2. Purpose of Education

Removable partial denture prosthodontics is a branch of Oral Health Science that deals with replacement of missing teeth and oral tissues to restore and maintain oral form, function, appearance, and health. Main objective of removable partial denture prosthodontics is to provide students in the graduate course opportunity to master standard method of diagnosis, technical skill, applied skill in lectures and practical works. Students are also taught on how to adapt removable prosthesis in the mouth with missing teeth from a biological and science and engineering standpoints.

3. Research Subjects

- 1) Evaluation of and factors for jaw movement smoothness.
- 2) Effects of delayed-onset muscle soreness (DOMS) on masticatory function.
- 3) Genetic, psychological, and behavioral factors for sleep bruxism.
- 4) Reproducibility of pocket depth measurement by experimental periodontal probe incorporating optical fiber sensor.
- 5) Dimensional accuracy of optical bite registration in single and multiple unit restorations.
- 6) The influence of mechanical stimulation on osteoclast localization in the mouse maxilla.
- 7) The influence of elastic modulus mismatch between tooth and post and core restorations on root fracture.
- 8) Bone integration capability of surface-treated titanium implants.
- 9) Effects of chromium and nitrogen content on the microstructures and mechanical properties of Co-Cr-Mo alloys.

4. Clinical Services

Patients with missing teeth have increased in step with the aging of the population, so improving their quality life has been required. Dental prosthesis clinic provides removable partial dentures to patients with missing teeth by the best treatment technique. The dentures are individually designed from mobility of dentures, oral sense, pronunciation and aesthetic points of view.

5. Publications

Original Article

1. Ishihata K, Wakabayashi N, Wadach J, Akizuki T, Izumi Y, Takakuda K, Igarashi Y. Reproducibility of pocket depth measurement by experimental periodontal probe incorporating optical fiber sensor. *J Periodontol.* 83: 222-227, 2012.
2. Iwaki Y, Wakabayashi N, Igarashi Y. Dimensional accuracy of optical bite registration in single and multiple unit

- restorations. *Oper Dent*. Epub 2012 Oct 23.
3. 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*. Epub 2012 Jul 7.
 4. Fujiki K, Aoki K, Marcián P, Borák 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. *Biomech Model Mechanobiol*. Epub 2012 May 15.
 5. Kuboki T, Ichikawa T, Baba K, Hideshima M, Sato Y, Wake H, Nagao K, Kodaira-Ueda Y, Kimura-Ono, A, Tamaki K, Tsuga K, Sakurai K, Sato H, Ishibashi K, Yatani H, Ohyama T, Akagawa Y, Hirai T, Sasaki K, Koyano K: A multi-centered epidemiological study evaluating the reliability of the treatment difficulty indices developed by the Japan Prosthodontic Society. *J of Pros Res*. 56: 71-86, 2012.
 6. Yamada M, Ueno T, Tsukimura N, Ikeda T, Nakagawa K, Hori N, Suzuki T, Ogawa T. Bone integration capability of nanopolymeric crystalline hydroxyapatite coated on titanium implants. *Int J Nanomedicine*. 7: 859-73, 2012.
 7. Ueno T, Takeuchi M, Hori N, Iwasa F, Minamikawa H, Igarashi Y, Anpo M, Ogawa T. Gamma ray treatment enhances bioactivity and osseointegration capability of titanium. *J Biomed Mater Res B Appl Biomater*. 100: 2279-87, 2012.
 8. Minami I, Akhter R, Luraschi J, Oogai K, Nemoto T, Peck CC, Murray GM. Jaw-movement smoothness during empty chewing and gum chewing. *Eur J Oral Sci*. 120: 195-200, 2012.
 9. Molenaar WN, Gezelle Meerburg PJ, Luraschi J, Whittle T, Schimmel M, Lobbezoo F, Peck CC, Murray GM, Minami I. The effect of food bolus location on jaw movement smoothness and masticatory efficiency. *J Oral Rehabil*. 39: 639-47, 2012.
 10. Yoshida E, Lobbezoo F, Fueki K, Naeije M. Effects of delayed-onset muscle soreness on masticatory function. *Eur J Oral Sci*. 120: 526-530, 2012.
 11. Abe Y, Suganuma T, Ishii M, Yamamoto G, Gunji T, Clark GT, Tachikawa T, Kiuchi Y, Igarashi Y, Baba K. Association of genetic, psychological and behavioral factors with sleep bruxism in a Japanese population. *J Sleep Res*. 21: 289-96, 2012.
 12. Yoda K, Suyalatu, Takaichi A, Nomura N, Tsutsumi Y, Doi H, Kurosu S, Chiba A, Igarashi Y, Hanawa T. Effects of chromium and nitrogen content on the microstructures and mechanical properties of as-cast Co-Cr-Mo alloys for dental applications. *Acta Biomater*. Epub 2012 Mar 17.

Oral Implantology and Regenerative Dental Medicine

1. Staffs and Students (April 2012)

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,	Hisatomo KONDO,
	Hidemichi KIHARA,	Toru KANAI,
	Maho OZEKI,	Katsuichiro MARUO,
	Daisuke SATO,	Yuki DATE
Dentists in Dental Implant Clinic	Hidemi NAKATA,	Aoi SAKUYAMA,
	Takahiro NAKAMURA,	Hiroshi KOBAYASHI,
	Maho AKATSUKA,	Kazuhisa TSURUMI,
	Ai YAMAMOTO,	Kei FUCHIGAMI,
Specially Appointed Assistant Professor		Osama ZAKARIA
Graduate Students	Shang GAO,	Masahiro SHIMOGISHI,
	Kang CHEN,	Ken YUKAWA,
	Marwa MADI Ibrahim,	Maiko YAMAMOTO,
	Kaori TAKAYA,	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
Clinical research Student	Shuichi KOYAMA,	Takayuki KOMATSU,
	Hitoshi SAITO,	Tadamasa YOSHIDA,
	Takaaki KITAZUME,	Toshimitu SHIGEMATSU,
	Toshihiko MORIKAWA,	Kazuhiko INOUE,
	Takeshi WATANABE,	Noriko OSADA,
	Kensuke FUKUTOMI,	Shuuko TAKEYAMA,
	Hiroko HAYASHI,	Arihiro IWATA,
	Kilwoo AHN,	Narumi SATO,
	Yoshiko YOKOYAMA,	Haruka KUBOTA,
	Chiharu IMAKITA,	Masahiro ISHIWATA,
	Tomoya MATSUMOTO,	Hidekazu KOTAKE,
	Haruka ITOH,	Gou INOUE,
	Seiji OHARA,	Akihiro SUZUKI,
	Tatsuya HOTTA,	Norio AKINO,
	Tomoko NAGAYAMA,	Masaki FUJII,
	Akiko FURUICHI,	Takayuki MIYAHARA,
	Ding LIN	
Foreign research Student	Hao JIA	

Registration Specialist Trainee	Yuki SHIMIZU, Yoshiyuki SASAKI, Yoko YAMAGUTI,	Yuko OYOYABU, Tomoto TERAMAE, Youta IIDA
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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. Noritake K, Kuroda S, Kasugai S : Guided Bone Regeneration: Membrane Characteristics and Future Perspectives. *Nano Biomedicine*. 4(1): 42-46, 2012.
2. Kimura J, Shiota M, Kon K, Fujii M, Sato H, Kasugai S : Effect of Hydroxyapatite Fiber Material with Autogenous Bone Graft on Vertical Bone Augmentation. *J Oral Tissue Engin* 9 (3):136-146 2012.
3. Date Y, Yokoyama Y, Kondo H, Kuroda S, Ohya K, Ota MS, Iseki S, Kasugai S. : Restricted expression of chromatin remodeling associated factor Chd3 during tooth root development. *J Periodontal Res*. 47(2):180-7, 2012.
4. Hao J, Kuroda S, Chen K, Noritake K, Rodriguez R, Pluemsakunthai W, Aoki H, Kasugai S : Bacterial Adhesion Behavior and Bone Formation Effect Of Zoledronic Acid (ZOL) Immobilized Sputtered Hydroxyapatite Implant. *Journal of Bio-Integration* 2(1):103-109, 2012.
5. Madi M, Zakaria O, Noritake K, Fuji M, Kasugai S : Ligature-induced periimplantitis surrounding thin sputtered HA-coated implants. An experimental study in dogs. Clinical and radiographic evaluations. *Journal of Bio-Integration* Vol.2 No.1, 111-117, 2012.
6. Rungsianont S, Dhanesuan N, Swasdison S, Kasugai S : Evaluation of biomimetic scaffold of gelatin-hydroxyapatite crosslink as a novel scaffold for tissue engineering: Biocompatibility evaluation with human PDL Fibroblasts, human mesenchymal stromal cells, and primary bone cells. *Journal of Biomaterials Applications* 27(1):47-54, 2012.
7. Bhargava S, Doi H, Kondo R, Aoki H, Hanawa T, Kasugai S : Effect of sandblasting on the mechanical properties of Y-TZP zirconia. *Biomedical and Material Engineering* 22(6):383-98, 2012.
8. Umehara K, Iimura T, Sakamoto K, Lin Z, Kasugai S, Igarashi Y, Yamaguchi A : Canine oral mucosal fibroblasts differentiate into osteoblastic cells in response to BMP-2. *The Anatomical Redord* 295(8):1327-35, 2012.
9. Zakaria O, Madi M, Kasugai S : Induced osteogenesis using a new periosteal distractor. *Journal of Oral Maxillofacial Surgery* 70(3):225-34, 2012.
10. Murakami I, Murakami Y, Clifford DK, Palacci P, Kasugai S : Panoramic implant notation sytem – A mothod to

denote implant position and prosthodontic modalities. *Journal of Prosthodontic Research* 56(1):65-9, 2012.

11. Zakaria O, Kon K, Kasugai S : Evaluation of a biodegradable novel periosteal distractor. *Journal of Biomedical Materials Research: Part B - Applied Biomaterials* 2012 Apr;100(3):882-9.
12. Zakaria O, Madi M, Kasugai S : A novel osteogenesis technique: The expansible guided bone regeneration. *Journal of tissue engineering*.2012;3(1): 2012 Apr 4.
13. Miyahara T, Dahlin C, Galli S, Parsafar S, Koizumi H, Kasugai S : A novel dual material mouthguard for patients with dental implants. *Dent Traumatol.* 2012 Jul 31.
14. Miyahara T, Nyan M, Shimoda A, Yamamoto Y, Kuroda S, Shiota M, Akiyoshi K, Kasugai S : Exploitation of a novel polysaccharide nanogel cross-linking membrane for guided bone regeneration (GBR). *Journal of Tissue Engineering and Regenerative Medicine* 6(8):666-72, Aug 2012.
15. Madi M, Zakaria O, Noritake K, Fuji M, Kasugai S : Ligature-induced peri-implantitis surrounding thin sputtered HA-coated implants. An experimental study in dogs. Clinical and radiographic evaluations. *Journal of Bio-Integration* Vol.2 No.1 p.111-117, Oct 2012.
16. Nyan M, Hao J, Miyahara T, Noritake K, Rodriguez R, Kasugai S : Feasibility of Alpha Tricalcium Phosphate for vertical bone augmentation. *J Investig Clin Dent.* 2012 Dec 17.
17. Chou J, Green DW, Singh K, Hao J, Ben-Nissan B, Milthorpe B : Adipose Stem Cell Coating of Biomimetic β -TCP Macrospheres by Use of Laboratory Centrifuge. *BioResearch Open Access.* Dec 2012.
18. Kamiyama Y, Nakamura S, Abe T, Munakata M, Nomura Y. Measurement accuracy of dental CT images obtained by 64-slice multi-detector row CT: the effects of mandibular positioning and pitch factor at CT scanning. *Implant Dentistry* 21(6):496-501,2012.
19. Kuroda S, Sumner D, Virdi A : Effects of TGF- β 1 and VEGF-A transgenes on the osteogenic potential of bone marrow stromal cells in vitro and in vivo. *Journal of Tissue Engineering.* 3(1): 2041731412459745, 2012.
20. Madi M, Zakaria O, Kasugai S : Coated vs. Uncoated Implants: Bone Defect Configurations after Progressive Peri-implantitis in Dogs. *Journal of Oral Implantology.* doi:http://dx.doi.org/10.1563/AAID-JOI-D-12-00089

6. Conference Presentation

1. Inoue K, Shiota M, Sato T, Kato R, Imai S, Hanada N, Kasugai S : Microbiologic effects of irrigation with function waters in pri-implant sulcus. *ICOI Asia-Pacific Section Congress, 22-24, June, Ho Chi Minh, Vietnam.*
2. Madi M, Zakaria O, Noritake K, Fujii M, Kasugai S : Progression of Ligature-induced Peri-implantitis around Thin Sputtered HA-coated Implants. *Academy of Osseointegration 27th Annual Meeting, 2012.3.1-3, Phoenix, USA.*
3. Chen K, Hao J, Noritake K, Yamashita Y, Zayer L, Kuroda S, Kasugai S : Effects of Low-intensity Pulsed Ultrasound Stimulation on Bone Healing in A Rat Calvarial Defect Model. *Academy of Osseointegration 27th Annual Meeting, 2012.3.1-3, Phoenix, USA.*
4. Madi M, Zakaria O, Noritake K, Fujii M, Kasugai S : Progression of Ligature-induced Peri-implantitis around Thin Sputtered HA-coated implants. *Academy of Osseointegration 27th Annual Meeting, 2012.3.1-3, Phoenix, USA.*
5. Kasugai S : Novel strategy for bone augmentation: Respecting “mother nature”. *The 11th Stomatology Conference of West China 2012.4.20-23 Chengdu Convention Center, Chengdu (成都) China.*
6. Kasugai S : New approach to bone augmentation: Respecting endogenous key players and providing space for regeneration. *The 15th ICOI Asia Pacific Section Congress 2012.6.23 Intercontinental Hotel, Ho Chi Minh City, Vietnam*
7. Hao J, Chen K, Achaya A, Kuroda S, Kasugai S, Lang N.P. : Synthesis and Evaluation of a novel Strontium Apatite-Gelatin Membrane for Guided Bone Regeneration (GBR). *The 100th Anniversary FDI Annual World Dental Congress, 2012.8.29-9.1, Hong Kong.*
8. Furuichi A, Tachikawa N, Kasugai S : Evaluation of the biological activity of a novel ozonated solution. *100th The FDI Annual World Dental Congress in 2012. 8.29-9.1, Hong Kong.*
9. Madi M, Zakaria O, Kasugai S : Assessment of peri-implantitis bone defects configuration around implants with different surface treatments in a canine model. *100th The FDI Annual World Dental Congress in 2012. 8.29-9.1, Hong Kong.*
10. Kon K, Shiota M, Ozeki M, Kasugai S : Alteration of occlusal force in unilateral free-end and intermediate missing cases by implant prosthesis. *Annual Scientific Meeting of the European Association of Osseointegration. 10-13 October 2012, Copenhagen, Denmark.*
11. Kusumoto Y, Kon K, Munakata M, Nakamura T, Tachikawa N, Shiota M, Kasugai K : Clinical outcome of sinus bone augmentation without graft; radiological analysis. *Annual Scientific Meeting of the European Association of*

Osseointegration. 10-13 October 2012, Copenhagen, Denmark.

12. Yukawa K, Tachikawa N, Akino N, Kon K, Takaya K, Kusumoto Y, Kasugai S : The cell kinetic with porous poly-DL-lactic acid –anatomical insight- . Annual Scientific Meeting of the European Association of Osseointegration. 10-13 October 2012, Copenhagen, Denmark.
13. Bhargava S, Kuroda S, Aoki H, Ohya K, Kasugai S. : Osteoblast differentiation on surface modified zirconia - an in vitro study. Annual Scientific Meeting of the European Association of Osseointegration. 10-13 October 2012, Copenhagen, Denmark.
14. Zakaria O, Madi M, Kasugai S : A Novel guided bone regeneration technique. Annual Scientific Meeting of the European Association of Osseointegration. 10-13 October 2012, Copenhagen, Denmark.
15. Miyahara T, Parsafar S, Dahlin C, Pluemsakunthai W, Palmquist A, Akiyoshi K, Thomsen P, Kasugai S : Novel dry type of cholesterol-bearing pullulan nanogel cross-linking membrane for guided bone regeneration (GBR). Annual Scientific Meeting of the European Association of Osseointegration. 10-13 October 2012, Copenhagen, Denmark.
16. Kasugai S : How to augment bone effectively, safely and less costly. Bangkok Implant Symposium 2012 2012.11.28-30 Pullman Hotel, Bangkok, Thailand.
17. Sato D, Kanazawa M, Minakuchi S, Baba K, Kasugai S, Ozeki M : CAD/CAM Template-Guided flapless surgery for Immediate loading of 2 freestanding implants. mandibular overdentures 40th Indian Prosthodontic Society and 8th Asian Association of Prosthodontics Conference, Chennai, India, December 2012.

Complete Denture Prosthodontics

1. Staffs and Students (April, 2012)

Professor	Shunsuke MINAKUCHI	
Assistant Professor	Tatsuro UCHIDA, Manabu KANAZAWA, Maiko IWAKI	Norihisa AKIBA, Yusuke SATO,
Hospital Staff	Mai OKUBO, Shin TAKESHITA, Sachi MASTUDA,	Yuriko KOMAGAMINE, Hiroshi KATASE, Tomomi ONODERA
Graduate Student	Megumi OCHI, Marie MURATA, Tomonori KAGAWA, Yoshihito HOSHINO, Keisuke KIKUCHI, Mariko TANOUE, Ayami JO, Ayako FUJIMOTO, Hiroyuki TANIMOTO, Taro YOSHIZAKI,	Yohei HAMA, Eijiro YAMAGA, Minoru INOUE, Takeshi HORIE, Shinta YAMAMOTO, Yuri OMURA, Daisuke HIRAYAMA, Toshinari Nakamura, Ken ODA, Yui FUJIMOTO

2. Purpose of Education

Complete denture prosthodontics is a discipline which contributes to better quality of life for edentulous patients by full mouth reconstruction treatments with complete denture prosthesis. The purpose of education is to get the knowledge about the dynamic state of soft tissues around dentures during oral functions, occlusion, and technical skills required to fabricating complete dentures.

3. Research Subjects

- 1) Relationship between denture treatment and body function
- 2) Palatal coverage disturbance in masticatory function
- 3) Stress analyses of implant overdenture
- 4) Factorial analysis of complete denture prosthesis
- 5) Resilient denture lining material
- 6) CAD/CAM system for fabricating complete dentures
- 7) Evaluations of masticatory performance using color-changeable chewing gum

4. Clinical Services

Complete denture prosthodontics clinic provides edentulous patients with planned prosthodontic treatments, and maintains the restored function for long periods. In addition, we set original criteria and objectively evaluate effect of our prosthetic treatments.

5. Publications

Original Article

1. Komagamine Y, Kanazawa M, Kaiba Y, Sato Y, Minakuchi S, Sasaki S. Association between self-assessment of complete dentures and oral health-related quality of life. *J Oral Rehabil.* 2012; 39: 847-57.
2. Inokoshi M, Kanazawa M, Minakuchi S. Evaluation of a complete denture trial method applying rapid prototyping. *Dent Mater J.* 2012; 31(1): 40-6.
3. Sato Y, Kaiba Y, Yamaga E, Minakuchi S. Reliability and validity of a Japanese version of the Oral Health Impact Profile for edentulous subjects. *Gerodontology.* 2012; 29:e1033-e1037.
4. Inokoshi M, Kameyama A, Munck JD, Minakuchi S, Van Meerbeek B. Durable bonding to mechanically and/or chemically pre-treated dental zirconia. *Journal of Dentistry (in press).* *J Dent.* 2012 Nov 5. [Epub ahead of print]

Plastic and Reconstructive surgery

1. Staffs and Students (April, 2012)

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

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. Yano T, Okazaki M, Tanaka K, Iida H, Aoyagi M, Tsunoda A, Kishimoto S. A New Concept for Classifying Skull Base Defects for Reconstructive Surgery. *Journal of Neurological Surgery* 73: 125-131, 2012
2. Okazaki M, Tanaka K, Kodaira S, Homma T, Miyashita H. One stage transfer of 2 paddles of thoracodorsal artery perforator flap with 1 pair of vascular anastomoses for Barraquer-Simons syndrome. *J Craniofac Surg* 23: 883-885, 2012
3. Aini H, Ochi H, Iwata M, Okawa A, Koga D, Okazaki M, Sano A, Asou Y. Procyanidin B3 prevents articular cartilage degeneration and heterotopic cartilage formation in a mouse surgical osteoarthritis model. *PLoS One* 7: e37728, 2012
4. Okochi M, Okazaki M, Asato H. Oral antithrombotic treatment and postoperative thrombotic complications after head and neck reconstruction using free flaps. *J Plast Surg Hand Surg* 46: 163-166, 2012
5. Kurita M, Okazaki M, Kaminishi-Tanikawa A, Niikura M, Takushima A, Harii K. Differential expression of wound fibrotic factors between facial and trunk dermal fibroblasts *Connect. Tissue Res* 53: 349-354, 2012

Head and Neck Surgery

1. Staff s and Students

Professor	Seiji Kishimoto	
Assistant Professor	Yosuke Ariizumi(~March),	Takuro Sumi(April~)
Hospital Staff	Fuminori Nomura,	Takao Tokumaru(April~)
Secretary	Mariko Tosa	
Graduate Student	Masakazu Miyazaki,	Zenda Sadamoto,
	Toru Sasaki,	Fuminori Nomura,
	Tatsuo Masubuchi,	Yosifumi Fukushima,
	Takao Tokumaru(April~)	
Foreign student	Paiboon Sureepong(April~)	

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 conference is 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 cance.

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. M Yamada, A Tsunoda, K Hagino, M Aoyagi, Y Kawano, T Yano, K Tanaka, S Kishimoto : Surgical management of a case of large juvenile nasopharyngeal angiofibroma invading the infratemporal fossa with intracranial extra dural parasellar involvement in an 8-year-old boy. *Auris Nasus Laynx* 39:341-344,2012
2. T Yano, M Okazaki, K Tanaka, H Iida, M Aoyagi, A Tsunoda, S Kishimoto : A new concept for classifying skull base defects for reconstructive surgery. *Journal of Neurological Surgery-Part B*:125-131,2012
3. Sumi T, Watanabe I, Tsunoda A, Nishio A, Komatsuzaki A, Kitamura K : Lonitudinal study of 29 patients with Meniere's disease with follow-up of 10 years or more(In commemoration of Professor Emeritus Isamu Watanabe). *Acta Otolaryngol* 132:10-15, 2012.
4. Hamahata A, Saitou T, Kubo K, Beppu T, Yamaki T, Sakurai H. : Usefulness of Harmonic Focus during Anterolateral Thigh Flap Elevation. *J Reconstr Microsurg*. Nov;28(9):615-8, 2012
5. Hamahata A, Saitou T, Ishikawa M, Beppu T, Sakurai H. : Lower Lip Reconstruction Using a Combined Technique of the Webster and Johanson Methods. *Ann Plast Surg*. 2012 Nov 1. [Epub ahead of print]
6. T Yano, K Tanaka, H Iida, S Kishimoto, M Okazaki : Usabitiy of the Middle Temporal Vein as a Recipient Vessel for Free Tissue Transeconstruction, *Ann Plastic Surg* 68:286-289,2012
7. T Yano, M Olazaki, : New Classification Concept for Classifying Skull base defects for recpmstrictive surgery. *J Neurological Surgery-Part B skull Base* 73:125-131,2012

International Congress

1. T Sugimoto, S Kishimoto, Y Ariizumi, T Tokumaru, F Nomura, Y Kiyokawa : Symposium. Recent advances in head

- and neck surgery : The diagnosis and management of parapharyngeal tumors: from the perspective of predictive factors of malignancy. 14th Japan-Korea Joint Meeting of Otorhinolaryngology-Head and Neck Surgery, Kyoto, April, 2012
2. S Kishimoto, A Tsunoda, T Sugimoto, T Yano, K Tanaka, S Aoyagi, Y Kawano, : Facial dismasking approach for craniofacial lesion. 6th International Congress of the World Federation of Skull Base Societies, Brighton, May, 2012
 3. A Tsunoda, T Sumi, S Shirakura. S Kishimoto, S Aoyagi, Y Kawano, : Otitis media with effusion and skull base lesions. 6th International Congress of the World Federation of Skull Base Societies, Brighton, May, 2012
 4. T Yano, M Okazaki, K Tanaka, A Tsunoda, S Aoyagi, S Kishimoto : Feasibility and stability of pericranial flaps for skull base reconstruction combined with facial dismasking flap approach. 6th International Congress of the World Federation of Skull Base Societies, Brighton, May, 2012
 5. T Yano, M Okazaki, K Tanaka, A Tsunoda, S Aoyagi, S Kishimoto : Strategies of reconstructive procedures for craniofacial meningioma. 6th International Congress of the World Federation of Skull Base Societies, Brighton, May, 2012
 6. S Kishimoto : Lecture: Future of Neck Dissection with Proposals from a Japanese Neck Dissection Study Group. International ENT Conference, Shanghai, 2012, July
 7. T Sugimoto, S Kishimoto, Y Ariizumi, T Tokumaru, Y Kiyokawa, F Nomura : Transoral partial hypopharyngectomy using a curved distending laryngoscope for early stage hypopharyngeal cancer. 8th International Conference on Head and Neck Cancer, Tronto, 2012, July
 8. S Kishimoto, A Tsunoda, K Ohno : Surgical treatment of pediatric sarcomas in the skull base and other head and neck regions. 8th International Conference on Head and Neck Cancer, Tronto, 2012, July
 9. S Yoshimoto, T Nakashima, K Nibu , S Kamata, T Fujii, K Matsuura, N Otsuki, S Kishimoto, S Fukuda, Y Hasegawa, M Sugasawa, N Kohno, T Asakage, Y Fujimoto, N Hanai, A Homma, N Monden, K Okami : Board Certification for Head and Neck Surgeons in Japan. 8th International Conference on Head and Neck Cancer, Tronto, 2012, July
 10. T Yano, M Okazaki, K Tanaka, M Aoyagi, S Kishimoto : A flap binding technique to prevent postoperative titanium mesh exposure for the skull base reconstruction. 4th Congress of the World Union of Wound Healing Societies, Yokohama, 2012, September
 11. T Sugimoto, S Kishimoto : Round Table Video Session (Robotic Surgery in Head and Neck). 2nd International Robotic Surgery Symposium, Seoul, 2012. October
 12. S. Kishimoto : Lecture : Locally extended juvenile angiofibromas. Workshop on new technologies and approaches to skull base : An interdisciplinary challenge, Rome, December, 2012
 13. S. Kishimoto : Hands-On Dissection Course. Lecture : Cranio-facial approaches to anterior and middle cranial base. Workshop on new technologies and approaches to skull base:An interdisciplinary challenge (Rome, December,2012
 14. S Kishimoto : Chairman Oral session. Rhinology, tumor, 14th Japan-Korea Joint Meeting of Otorhinolaryngology-Head and Neck Surgery, Kyoto, April, 2012
 15. Kawada K, Sugimoto T, Okada T, Jiwarat Swangsri, Kawano T : Endoscopic treatment for the superficial squamous cell carcinoma for the Head and Neck region. The 4th Annual Japan/Mongolia International Cancer Symposium, Ulaanbaatar, September 6-7, 2012
 16. Kawada K, Saito K, Fujiwara N, Ryotokuji T, Ohta S, Okada T, Miyawaki Y, Hoshino A, Jirawat S, Tokairin Y, Nakajima Y, Nishikage T, Nagai K, Sugimoto T, Kawano T : Endoscopic diagnosis of superficial oral cavity and laryngopharyngeal carcinoma using a transnasal ultrathin endoscope with FICE system The 20th United European gastroenterology week, Amsterdam, October 20-24, 2012

Diagnostic Radiology and Oncology

1. Staff and Students (2012)

Professor	Hitoshi Shibuya	
Associate Professors	Isamu Ohashi and Ichiro Yamada	
Lecturers	Kaoru Hanafusa and Mitsuhiro Kishino,	
Research Associates	Ryoichi Yoshimura(~Jul), Rin Chaou(~Feb), Yoshio Kitazume, Tomoko Makino, Keiji Hayashi, Akira Toriihara, Kaori Okazawa(Nov.~)	
Hospital Staff members	Kaori Okazawa(~Oct.), Keiko Nakagawa, Naoki Harata, Rina Fujisawa(~Sep.), Masashi Nakadate, Runa Kakubari(Apr.~)	
Resudent	Tomoyuki Fujioka	
Graduate Students	Youichi Machida, Satoko Hayashi, Mais M Abd-Alamear	
Research Students	Kiyomi Amemiya(~Mar.), Syuichi Yanai	

2. Purpose of Education

The Diagnostic Radiology and Oncology section covers the fields of diagnostic radiology, nuclear medicine, radiation oncology and biology, and radiation physics. The objectives of our institution of the graduate course are to study radiological medicine from the area of human anatomy and pathology, physiology, and clinical medicine. Our section is composed of over 70 members; about 45 of them are serving as heads or rotating staff members of general hospitals in the metropolitan area and approximately another 20 of them are studying and working as members of the university and/or university hospital staff. Postgraduate courses are made to study basic/clinical radiation medicine in order to obtain license as a specialist from the Japan Radiological Society (JRS). JRS specialist licenses are granted in two fields: diagnostic radiology and radiation oncology. Doctors of our section are also expected to obtain PH.D. and 34 students had obtained a degree of PH.D. under the guidance of Prof. Shibuya and staff.

3. Clinical Services and Research Subjects

A. Diagnostic Radiology

CT section:

After the introduction of two sets of multi-slice CT machines (MDCT: 64 arrays), number of patients examined has been markedly increased, and MDCT has enabled CT angiography of coronary artery as well as the cerebral artery. MDCT has offered a chance of on the day examination and early image diagnosis of disease. The clinical CT studies for liver diseases have offered the chance to get doctor degree for three doctors.

MRI section:

Three sets high speed MRI (1.5T and 3T) are enable to detect early findings of cerebral infarction by DWI (diffusion weighted image). Calculation of apparent diffusion coefficients (ADCs) of the kidney and liver has provided data for studying the physiology and pathology of these parenchymatous organs.

Interventional Radiology:

TAE (trans-catheter arterial embolization) for liver cell carcinoma and PTA (percutaneous trans-catheter angioplasty) for peripheral arterial occlusive disease have been routinely done to-date. Emergency angiography can be carried out at any time at any time as occasion calls.

Ultrasonography:

Breast disease and soft tissue ultrasonography is performed in the radiological center. Combined ultrasonography and MRI examinations have provided precise information for the diagnosis and treatment of breast cancer.

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 rememed Linear accelerating machines this year, and we had three Linear accelerating machines equipped IMRT intersiting-modulated radiation therapy and IGRT(image-guided radiation therapy).

4. Manuscript

1. Ryu Y, Yoshida K, Suzuki Y, Nakadate M, Umehara I, Tomita M, Shibuya H. Long-term changes of aortic (18)F-FDG uptake and calcification in health-screening subjects. *Ann Nucl Med*. 2012 Dec 23.
2. Okazawa K, Yuasa-Nakagawa K, Yoshimura RI, Shibuya H. Permanent interstitial re-irradiation with Au-198 seeds in patients with post-radiation locally recurrent uterine carcinoma *J Radiat Res*. 2012 Oct 15.
3. Yoshimura R, Shibuya H, Keiji H, Nakagawa K, Toda K, Watanabe H, Kaida A, Miura M. Repeat brachytherapy for patients with residual or recurrent tumors of oral cavity. *Int J Radiat Oncol Biol Phys*. 83: 1198-1204, 2012.
4. Toriihara A, Taniguchi Y, Negi M, Kubota K, Makino T, Shibuya H. FDG PET/CT of a benign ovarian Brenner tumor. *Clin Imaging* 2012;36:650-653
5. Machida Y, Kubota K, Katayama T, Toriihara A, Shibuya H. Diagnostic performance of fluorodeoxyglucose-positron emission tomography/computed tomography combined with ultrasonography-guided fine needle aspiration cytology for identifying axillary lymph node status in patients with breast cancer. *Eur JSurg Oncol*. 2013 Jan;39(1):26-30.
6. Matsuhisa A, Toriihara A, Kubota K, Makino T, Mizusawa H, Shibuya H. Utility of F-18 FDG PET/CT in screeing for paraneoplastic neurological syndromes. *Clin Nucl Med*. 2012 Jan;37(1):39-43.
7. Suzuki S, Yasumoto M, Matsumoto R, Andoh A. MR findings of ruptured endometrial cyst comparison with tubo-ovarian abscess. *Eur J Radiol*. Nov;81(11): 3631-7: 2012
8. Murakami N, Suzuki S, Ito Y, Yoshimura R, Inaba K, Kuroda Y, Morota K, Ohtomo K, Itami J. ¹⁰⁶Ruthenium plaque therapy (RPT) for retinoblastoma. *Int J Radiat Oncol Biol Phys*. 84: 59-65, 2012
9. Uezato A, Yamamoto N, Kurumaji A, Toriihara A, Umezaki Y, Toyofuku A, Nishikawa T. Improvement of asymmetrical temporal blood flow in refractory oral somatic delusion after successful electroconvulsive therapy. *J ECT* 2012;28:50-51

5. Congress

1. Kishino M, Takeguchi Y, Takeguchi T, Himeno Y, Yamada I, Shibuya H. Renal artery stenosis associated with Moyamoya disease: angiographic findings and interventional management. The 27th Annual Meeting of the Cardiovascular and Interventional Radiological Society of Europe (CIRSE 2012), Lisbon, Portugal, September 2012
2. M. Kishino, Y. Takeguchi, T. takeguchi, Y. Himeno, I. Yamada, H. Shibuya Renal artery stenosis associated with Moyamoya disease: angiographic findings and interventional management. CIRSE September 2012 Lisbon Portugal
3. M. Kishino, Y. Takeguchi, T. Takeguchi, A. Matsuhisa, Y. Himeno, H. Shibuya The diagnostic value of super-selective left adrenal venous sampling for primary aldosteronism. CIRSE September 2012 Lisbon Portugal
4. M. Kishino, Y. Takeguchi, T. Takeguchi, H. Shibuya Balloon occluded retrograde pulmonary venous sampling for diagnosing ectopic ACTH-secreting small lung tumor. CIRSE September 2012 Lisbon Portugal
5. Yoshimura R, Shibuya H, Miura M, Watanabe H, Hayashi K, Nakagawa K, Harata N, Kaida A. Results of low-dose-rate interstitial brachytherapy using Au-198 grains in T1-2 tongue cancer patients. 54th ASTRO, November 2012, Boston, USA.
6. Kubota K, Machida Y, Katayama T, Okazawa K, Fujioka T, Gomi N, Shibuya H. Preoperative Ultrasonography for Mapping of Breast Cancer: With Reference to the MR Mammography and 4D Ultrasound. RSNA 2012 annual meeting, Chicago, Nov 2012
7. Yoshio Kitazume, Isamu Ohashi, Shinichi Taura, Osamu Noguchi, Hitoshi Shibuya. Diffusion weighted imaging for focal liver lesions: Is there difference in the diagnostic capability using the apparent diffusion coefficient measurement between b- value 1500 and 1000 s/mm² ? The 63rd Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). Boston, USA, November 9-13 2012
8. Takagi Y, Toriihara A, Hosomi Y, Nakahara Y, Akahane M, Okuma Y, Iguchi M, Okamura T, Shibuya M. Does eligibility for bevacizumab (BV) lead to selection bias? 37th ESMO Congress, Vienna, Austria 2012.09.28-10.02

9. Takahashi Ken, Mitsuhiro Kishino, Yoshio Kitazume, Hitoshi Shibuya. Bleeding from autologous iliaco-hepatic bypass graft due to pancreatic fluid leakage; Complete recovery with covered stents designed for biliary duct. APCCVIR 2012 JSIR & ISIR, May 30 - June 2 2012, Kobe, Japan.
10. Yuko Takeguchi, Mitsuhiro Kishino, Yoshio Himeno, Hitoshi Shibuya. Superselective embolization for colonic diverticular bleeding: The impact of MDCT on detecting hemorrhage on angiography and technical success of transcatheter embolization. APCCVIR, JSIR / ISIR May 2012. Kobe.
11. Yuko Takeguchi, Mitsuhiro Kishino, Yoshio Himeno, Hitoshi Shibuya. Unusual complicated congenital bronchial artery-pulmonary artery malformation: how should we embolize? CIRSE 2012. Lisbon, Portugal
12. Nakagawa K, Yoshimura R, Shibuya H, Miura M, Watanabe H, Kishimoto S, Omura K, Okada N. Risk factors for survival in patients with neck metastasis of early stage SCC of the oral tongue. 31st ESTRO, May 2012, Barcelona, Spain.

Maxillofacial Anatomy

1. Staffs and Students (April, 2012)

Professor	Shunichi SHIBATA	
Associate Professor	Tatsuo TERASHIMA	
Assistant Professor	Shun-ichi SHIKANO,	Tatsuhiko ABE

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) Morphological researches on *Sinus maxillaris*.
- 10) Studies on regeneration of jaw bone.

4. Publications

Original Article

1. Kim J H, Abe S, Shibata S, Asakawa S, Maki H, Murakami G, Cho B H: Dense distribution of macrophages in flexor aspects of the hand and foot of mid-term human fetuses. *Anat Cell Biol*, 2012; 45: 259-267.
2. Kamiyama Y, Nakamura S, Abe T, Munakata M, Nomura Y, Watanabe H, Akiyama M, Kurabayashi T: Linear measurement accuracy of dental CT images obtained by 64-slice multidetector row CT: the effects of mandibular positioning and pitch factor at CT scanning. *Implant Dent*; 21 (6) : 496-501, 2012 Dec.
3. Katori Y, Shibata S, Kawase T, Cho B H, Murakami G: Transient appearance of Tyrosine hydroxylase immunoreactive cells in the midline epithelial seam of the human fetal secondary palate. *Cleft Palate-Craniofac J*, 49(4): 414-424, July 2012.
4. Munakata K, Ookata K, Doi H, Baba O, Terashima T, Hirose S, Kato A: Histological demonstration of glucose transporters, fructose-1, 6-bisphosphatase, and glycogen in gas gland cells of the swim bladder: is a metabolic futile cycle operating? *Biochem. Biophys. Res. Commun.*, 417:564-569, 2012.
5. Oshiro A, Iseki S, Miyauchi M, Terashima T, Kawaguchi Y, Ikeda Y, Shinomura T: Lipopolysaccharide induces rapid loss of follicular dendritic cell-secreted protein in the junctional epithelium. *Journal of Periodontal Research*, 47:689-694, 2012.
6. Shibata S, Fukuoka H, Sato R, Abe T, Suzuki Y: An in situ hybridization study of the insulin-like growth factor system in developing condylar cartilage of the fetal mouse mandible. *Eur J Histochem* 2012; volume 56:e23, page 142-148, 2012.
7. Suzuki Y, Obara N, Shibata S: Gene expression of insulin-like growth factor family during tooth development of the mouse. *Dent J Health Sci Univ Hokkaido*, 31(1): 1-9, 2012.6.
8. Suzuki Y, Tsunekawa H, Obara N, Irie K, and Shibata S: Expression and activation of β -catenin in developing and denervated taste buds. *Dent J Health Sci Univ Hokkaido*, 31(2): 63-72, 2012.12.

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	
Researcher	Chisato Yamate,	Mayumi Yamamoto

2. Purpose of Education

----For D3 course students

1. Lectures of unit “Nerve and Sense”

A series of lectures on the conduction/transmission of neuronal excitation, somatic sensation, vision, gustation, olfaction, audition, and sense of equilibrium will be taught. Basic mechanisms of the nervous system and the mechanisms of sensation and perception will be learned.

2. Lectures of unit “Motor System”

A series of lectures on the mechanisms of muscle contraction, its regulation and the related reflexes will be taught. Basic structure of the skeletal muscle and the physiological mechanism of its contraction, together with the deep sensation and skeletal muscular reflexes will be learned.

3. Lectures of unit “Central Nervous System”

A series of lectures on the behavior, emotion, sleep and higher brain functions will be taught. Functions of the central nervous system will be learned.

4. Lectures of unit “Biology of Mastication and Deglutition”

A series of lectures on the neural mechanisms of mastication and deglutition will be taught. Regulatory mechanisms of the mastication system will be learned.

5. Lecture of unit “Eating, Digestion, and Absorption”

A series of lectures on the mechanisms of salivation as well as those of the motility, digestion, and absorption of digestive organs will be taught. Functions of a series of digestive organs starting with the oral cavity will be learned.

6. 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.

----For D2 course students

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

See above.

3. Research Subjects

1. Neural Mechanisms of motor control.

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. Yamashita A, Fuchs E, Taira M, Yamamoto T, Hayashi M. Somatostatin-immunoreactive senile plaque-like structures in the frontal cortex and nucleus accumbens of aged tree shrews and Japanese macaques. *J Med Primatol* 41(3):147-157, 2012.
2. Ojima H, Taira M, Kubota M, Horikawa J. Recognition of non-harmonic natural sounds by small mammals using competitive training. *PLoS One*. Dec 7(12):e51318. 2012.

Review articles

1. Schreiner CE, Kanold PO, Ojima H, Shamma SA, and Lomber SG: Auditory cortical functions: Insights from current approaches. *Acoustics Today*. 8(2):42-50. 2012.

Books

1. Ojima H. Primary Auditory Cortex as a node of the ascending, descending, and local connectivity. In: Elhilali M ed. *Auditory cortex: Anatomy, functions and disorders*. New York:NOVA Biomedical; 2012 (ISBN 978-1-62100-685-5).

Molecular Craniofacial Embryology

1. Staffs and Students

Professor	Sachiko Iseki
Associate Professor	Masa-Aki Ikeda
Lecturer	Masato Ota
Part-time lecturers	Hirofumi Doi, Shumpei Yamada, Shigeru Okuhara
Visiting Researcher	Yoichiro Ninomiya
Graduate Students	Teng Ma (until May), Widya Lestari (until May) Khandakar Abu Shameem MD Saadat (until May), Tomoko Nagayama (Oral Implantology and Regenerative Dental Medicine) (until May), Akihiko Machida (Maxillofacial Surgery), Prasitsak Thanit, Endrawan Pratama, Zhang Kui (Oral Implantology and Regenerative Dental Medicine), Ryohei Takahashi, Masako Fujioka (The University of Tokushima) (until October)
Research Student	Toshiko Furutera (from April)
Foreign Researcher	Khandakar Abu Shameem MD. Saadat (from April)
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 the mechanism of their stemness
- 4) Regulation of gene expression in cell growth and stress response
- 5) Nuclear architecture and function in regulating gene expression
- 6) Dysregulation of tumor suppressors in oral cancer

3. Publications

Original articles

1. Date Y, Yokoyama Y, Kondo H, Kuroda S, Ohya K, Ota MS, Iseki S, Kasugai S. Restricted expression of chromatin remodeling associated factor Chd3 during tooth root development. *J. Periodontal Res.* 47(2):180-7, 2012.
2. Suzuki H., Suda N., Shiga M., Kobayashi Y., Nakamura M., Iseki S., Moriyama K. Apert syndrome mutant FGFR2 and its soluble form reciprocally alter osteogenesis of primary calvarial osteoblasts. *J. Cell. Physiol.* 227 (9): 3267-77, 2012.
3. Nagaoka R., Okuhara S., Sato Y., Amagasa T., Iseki S. Effects of embryonic hypoxia on lip formation. *Birth Defects Res. A Clin. Mol. Teratol.* 94:215-222, 2012.
4. Taki A., Abe M., Oku K., Iseki S., Mizutani S., Morita I. Expression of angiogenesis-related factors and inflammatory cytokines in placenta and umbilical vessels in pregnancies with preeclampsia and chorioamnionitis/funisitis. *Congenit. Anom. (Kyoto)* 52(2):97-103, 2012.
5. Oshiro A., Iseki S., Miyauchi M., Terashima T., Kawaguchi Y., Ikeda Y., Shinomura T. Lipopolysaccharide induces rapid loss of follicular dendritic cell-secreted protein in the junctional epithelium. *J. Periodontal Res.* (in press). 2012
6. Fujioka-Kobayashi M., Ota M.S., Shimoda A., Nakahama K., Akiyoshi K., Miyamoto Y., Iseki S. Cholesteryl group- and acryloyl group-bearing pullulan nanogel to deliver BMP2 and FGF18 for bone tissue engineering. *Biomaterials* 33(30):7613-20, 2012.
7. Kameda Y., Saitoh T., Nemoto N., Katoh T., Iseki S. Hes1 Is Required for the Development of the Superior Cervical Ganglion of Sympathetic Trunk and the Carotid Body. *Dev. Dyn.* 241(8):1289-300, 2012.
8. Chung YM, Park S-H, Tsai W-B, Wang S-Y, Ikeda MA, Berek JS, Chen DJ, Hu MC FOXO3 signalling links ATM to the p53 apoptotic pathway following DNA damage. *Nature Communications* 3, 1000, 2012.
9. Lestari W, Ichwan SJA, Otsu M, Yamada S, Iseki S, Shimizu S, Ikeda MA Cooperation between ARID3A and p53 in the transcriptional activation of p21WAF1 in response to DNA damage. *Biochem. Biophys. Res. Commun.* 417, 710-716, 2012.

10. Ma, T, Yamada S, Ichwan SJA, Ohtani K, Iseki S, Otsu M, Ikeda MA Inability of p53-Reactivating compounds Nutlin-3 and RITA to overcome p53 resistance in tumor cells deficient for p53Ser46 phosphorylation. *Biochem. Biophys. Res. Commun.* 417, 931-937, 2012.
11. Wimardhani SY, Sunia DF, Freisleben H-J, Septelia Wanandi SI, Ikeda MA: Cytotoxic effect of chitosan against oral cancer cell lines is molecular-weight-dependent and cell-type-specific. *Int. J. Oral Res.* 3; e1, 2012.
12. Xu J, Kawashima N, Fujiwara N, Harada H, Ota MS, Suda H. Promotional effects of vasoactive intestinal peptide on the development of rodent Hertwig's epithelial root sheath. *Congenit Anom (Kyoto)*. 52(3):162-7. 2012.

Review Articles

1. Ichwan SJA, Bakhtiar MT, Ohtani K, Ikeda MA: Therapeutic Targeting of p53-Mediated Apoptosis Pathway in Head and Neck Squamous Cell Carcinomas: Current Progress and Challenges, *Tumor Suppressor Genes*, Yue Cheng (Ed.), ISBN: 978-953-307-879-3, InTech. 6, 129-144 (2012)

Cellular Physiological Chemistry

1. Staffs and Students (April, 2012)

Professor	Ikuo Morita	
Associate Professor	Ken-ichi Nakahama	
Junior Associate Professor	Hiroshi Fujita, Mayumi Abe,	Takako Hase, Chieko Yokoyama
Assistant Professor	Kotaro Kato	
Tokuninn Assistant Professor (GCOE)	Olga Safronava	
Tokuninn Assistant Professor	Masako Akiyama,	Jinying Wang
Graduate Student	Praween Wayakanon,	Takeshi Watanabe,
Research Student	Yukihiko Hashida, Yu Hatano, Bowen Xu, Keiko Akasawa, Asuka Okitoh, Kensuke Kojima,	Kaori Shimizu, Izumi Honda, Chikako Morioka, Masayuki Tooï, Kazuki Aisaka, Naoyuki Hirota
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. Komaki M, Iwasaki K, Arzate H, Narayanan AS, Izumi Y, Morita I. Cementum protein 1 (CEMP1) induces a cementoblastic phenotype and reduces osteoblastic differentiation in periodontal ligament cells. *J Cell Physiol.* 2012 Feb; 227(2) : 649-57.
2. Wang J, Ohno-Matsui K, Morita I. Cholesterol enhances amyloid β deposition in mouse retina by modulating the activities of $A\beta$ -regulating enzymes in retinal pigment epithelial cells. *Biochem Biophys Res Commun.* 2012, 10;424(4):704-9
3. Moriyama M, Ohno-Matsui K, Modegi T, Kindo J, Takahashi Y, Tomiyama M, Tokoro T, Morita I. Quantitative analyses of high-resolution 3D MR images of highly myopic eyes to determine their shapes. *Invest Ophthalmol Vis Sci.* 2012, 3;53(8):4510-8
4. Li X, Akiyama M, Nakahama K, Koshiishi T, Takeda S, Morita I. Role of intercellular adhesion molecule-2 in osteoclastogenesis. *Gene Cells.* 2012, 17(7):568-75
5. Wang J, Ohono Matsui K, Morita I. Elevated amyloid β production in senescent retinal pigment epithelium, a possible mechanism of subretinal deposition of amyloid β in age-related macular degeneration. *Biochem Biophys Res Commun.* 2012, 22;423(1):73-8
6. Wayakanon P, Bhattacharjee R, Nakahama K, Morita I. The role of the Cx43 C-terminus in GJ plaque formation and internalization. *Biochem Biophys Res Commun.* 2012 6;420(2):456-61

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*. 2012 Dec 14. [Epub ahead of print]
8. Taki A, Abe M, Komaki M, Oku K, Iseki S, Mizutani S, Morita I. Expression of angiogenesis-related factors and inflammatory cytokines in placenta and umbilical vessels in pregnancies with preeclampsia and chorioamnionitis/funisitis. *Congenit Anom*. 2012 Jun ; 52(2) : 97-103.
9. Fujita H, Nishimura S, Hazama Y, Moriyama A, Daibo K, Ohtake C, Shinozuka K, Fujimoto S, and Kamesaki M. Coagulopathy and transfusion product usage in relation to ruptured abdominal aortic aneurysm scoring systems in a tertiary care centre in the metropolitan Tokyo area in Japan. *Blood Transfusion*, 10 : 393-395. 2012.
10. Fujita H, Sakuma R, Fujimoto S, Hazama Y, Ohtake C, Moriyama A, Kuhara K, and Nishimura S Nafamostat mesilate, a non-calcium compound, as an anticoagulant induces calcium-dependent haemolysis when infused with packed erythrocytes. *Transfusion Medicine*. 22:186-191.2012
11. Yakushiji F, Funaki Y, Yamakawa K, Kudo A, Fujita H, Yasuda M, Nishimura A, Nagasawa K, Ishido H, Yoshikawa T and Kinoshita H. The AutoShield pen needle is useful for preventing accidental puncture while administering insulin to others by injection. *J Diabetes Sci Technol*. 2012.
12. Fujita H, Hamaki T, Handa N, Ohwada A, Tomiyama J, and Nishimura S. Hypocholesterolemia in patients with polycythemia vera. *J Clin Exp Hematopathol*. 52(2):85-89. 2012.
13. Nishimura S, Yamamoto E, Daibo K, Fujimoto S, Moriyama A, Hazama Y, Hoshino M, Fujita H. Development of Clinical Index for Appropriate Hyperoncotic Albumin Use. *Int J Pharamacol*. 10(1):
14. Fujita H, Tomiyama J and Nishimura S. High contact pressure resulting from bone marrow puncture. *Open J Blood Diseases*. 2:56-58. 2012.
15. Somogyi-Ganss E, Nakayama Y, Iwasaki K, Nakano Y, Stolf D, McKee MD, Ganss B. Comparative Temporospacial Expression Profiling of Murine Amelotin Protein during Amelogenesis. *Somogyi-Ganss Cells Tissues Organs*. 195(6):535-49. 2012

Metals

1. Staffs and Students

Professor	Takao HANAWA	
Associate Professor	Naoyuki NOMURA	
Assistant Professor	Hisashi DOI,	Yusuke TSUTSUMI
Research Assistant	Osamu FUKUSHIMA	
Project Assistant Professor	SUYALATU,	Satoshi MIGITA
Secretary	Toshie NAKANISHI,	Yasuko SEKI
Graduate Student	Ryota KONDO,	Takahiro SAKAI

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. Jamleh A, Sadr A, Nomura N, Yahata Y, Ebihara A, Hanawa T, Tagami J, Suda H. Nano-indentation testing of new and fractured NiTi Endodontic Instruments. *International Endodontic Journal* 45:462-468, 2012.
2. Tsutsumi Y, Niinomi M, Nakai M, Tsutsumi H, Doi H, Nomura N, Hanawa T. Micro-arc oxidation treatment to improve the hard-tissue compatibility of Ti-29Nb-13Ta-4.6Zr alloy. *Applied Surface Science* 262:34-38, 2012.
3. Ma C, Nagai A, Yamazaki Y, Toyama T, Tsutsumi Y, Hanawa T, Wang W, Yamashita K. Electrically polarized micro-arc oxidized TiO₂ coatings with enhanced surface hydrophilicity. *Acta Biomaterialia* 8:860-865, 2012.
4. Hieda J, Niinomi M, Nakai M, Kamura H, Tsutsumi H, Hanawa T. Effect of terminal functional groups of silane layers on adhesive strength between biomedical Ti-29Nb-13Ta-4.6Zr alloy and segment polyurethanes. *Surface and Coatings Technology* 206(13):3137-3141, 2012.
5. Yoda K, Suyalatu, Takaichi A, Nomura N, Tsutsumi Y, Doi H, Kurosu S, Chiba A, Igarashi Y, Hanawa T. Effects of chromium and nitrogen content on the microstructures and mechanical properties of as-cast Co-Cr-Mo alloys for dental applications. *Acta Biomaterialia* 8(7):2856-2862, 2012.
6. Nagai A, Tsutsumi Y, Suzuki Y, Katayama K, Hanawa T, Yamashita K. Characterization of air-formed surface oxide film on a Co-Ni-Cr-Mo alloy (MP35N) and its change in Hanks f solution. *Applied Surface Science* 258(14):5490-5498, 2012.

7. Tsutsumi Y, Bartakova S, Prachar P, Suyalatu, Migita S, Doi H, Nomura N, Hanawa T. Long-term corrosion behavior of biocompatible β -type Ti alloy in simulated body fluid. *Journal of the Electrochemical Society* 159(10):C435-C440, 2012.
8. Hastuty S, Tsutsumi Y, Nishikata A, Tsuru T. Pitting corrosion of type 430 stainless steel in the process of drying of chloride solution layer. *ISIJ International* 52(5):863-867, 2012.
9. Murata M, Akazawa T, Yuasa T, Okayama M, Tazaki J, Hanawa T, Arisue M, Mizoguchi I. Quantitative analysis on orientation of human bone integrated with midpalatal implant by micro X-ray diffractometer. *Applied Surface Science* 262: 222-226, 2012.
10. (Supplement) Nam K, Tsutsumi Y, Yoshikawa C, Tanaka Y, Fukaya R, Kimura T, Hanawa T, Kishida A. Preparation of novel polymer-metal oxide nanocomposites with nanophase separated hierarchical structure. *Bulletin of Material Science* 34(7):1289-1296, 2011.

Biodesign (Medical and Dental Device Technology Incubation Center)

1. Staffs and Students

Professor	Kazuo TAKAKUDA	
Assistant Professor	Wei WANG	
Research Assistants	Shukan OKANO	
Graduate Students	Takao IRIBE,	Yuki SAITO,
	Hazuki KOSHITOMAE,	Ryo KOKUBUN,
	Yutaka FUKUDA,	Masahiro WATANABE,
	Atsushi MITA,	Tetsuro WATANABE,
	Kimihiko 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. Ishihata K, Wakabayashi N, Wadachi J, Akizuki T, Izumi Y, Takakuda K, Igarashi Y. Reproducibility of probing depth measurement by an experimental periodontal probe incorporating optical fiber sensor. *J Periodontol.* 2012;83(2):222-227.
2. 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.* 2012 Dec 20
3. 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.* 2012 Oct 3

Presentations

1. Uezono M, Takakuda K, Kikuchi M, Suzuki S, Moriyama. The Coating for Enhanced Osseointegration of Subperiosteal Anchorage Device. The 6th International Conference on the Science and Technology for Advanced Ceramics. Jun 2012, Yokohama, Japan

Maxillofacial Surgery

1. Staffs and Students (2012)

Professor	Kiyoshi HARADA(from April)	
Emeritus Professor	Teruo AMAGASA	
Clinical Professor	Hiroshi IWAKI	
Junior Associate Professor	Masashi YAMASHIRO,	Narikazu UZAWA
Assistant Professor	Satoshi YAMAGUCHI,	Yutaka SATO,
	Hiroyuki YOSHITAKE,	Yasuyuki MICHI,
	Kazuto KUROHARA,	Kouichi NAKAKUKI
Hospital Staff	Itaru SONODA,	Kunihiro MYO (from April),
	Shigehiro ABE(until March),	Miho SUZUKI,
	Misa MISHINA(HOSOKI),	Chikako HAYASHI(until September),
	Mayuko MURASHIMA(until March),	Aya KAWAMATA(until March),
	Kenichiro TAKAHASHI,	Junichi TSUGAWA(until March),
	Nobuyoshi TOMOMATSU,	Junya KUMAGAI(from April),
	Hiroyuki NAKACHI(from April),	Erika OUE(from April),
	Jun SUMINO(from April)	
Graduate Student	Hironori ENDO(until March),	Daisuke MIYAJIMA(until March),
	Yoshimi NAKATA(until March),	Erika OUE(until March),
	Jun SUMINO(until March),	Takashi WATANABE(until March),
	José-María SHINDOI,	Yuki MATSUSHITA,
	Yosuke HARAZONO,	Akihiko MACHIDA,
	Asumi UEZONO(HONDA),	Akira GOUDA,
	Norihiko HASHIDA,	Yujiro MORIYA,
	Eri TSUCHIDA,	Ryosuke NAKAMURA,
	Takayuki YAMADA,	Li KEI,
	Uyangga ENKHBOLD(from April),	Takuma MORITA(from April),
	Chihiro YOSHIDA(from April),	Takeshi OKAMURA(from April),
	Masahiko TERAUCHI(from April),	Hirokazu KACHI(from April),
	Kouhei OKUYAMA(from April),	Sou WAKE(from April),
	Yuuta KONDOU(from April)	
Student	Junya KUMAGAI(AOYAGI) (until March),	
	Ryosuke NAGAOKA (until March),	Nami OGAWA(until March),
	Chika MIURA(until September),	Yumi KOUNO(until March),
	Machiko KOSUGI,	Yasuhiro ARAKI(from April),
	Reiko HOSHI(from April)	
Post graduate trainee	Ming-Chin Mark CHANG(until February)	

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.

5. Publication

Original Article

1. Kurasawa Y, Kozaki K, Pimkhaokham A, Muramatsu T, Ono H, Ishihara T, Uzawa N, Imoto I, Amagasa T, Inazawa J: Stabilization of phenotypic plasticity through mesenchymal-specific DNA hypermethylation in cancer cells. *Oncogene* 31(15): 1963-1974 (2012).
2. Michikawa C, Uzawa N, Kayamori K, Sonoda I, Ohyama Y, Okada N, Yamaguchi A, Amagasa T: Clinical significance of lymphatic and blood vessel invasion in oral squamous cell carcinomas. *Oral oncology* 48(4): 320-324 (2012).
3. Miyaguchi K, Uzawa N, Mogushi K, Takahashi K, Michikawa C, Nakata Y, Sumino J, Okada N, Mizushima H, Fukuoka Y, Tanaka H: Loss of NKX3-1 as a potential marker for an increased risk of occult lymph node metastasis and poor prognosis in oral squamous cell carcinoma. *Int. J. Oncol* 40(6): 1907-1914 (2012).
4. Kurohara K, Uzawa N, Michi Y, Harada K: A Neuroendocrine Tumor in the Maxilla. *J Oral Maxillofac Surg* 70(11): 679-682 (2012).
5. Nakachi H, Aoki K, Tomomatsu N, Alles N, Nagano K, Yamashiro M, Zhang H, Murali R, Greene M I, Ohya K, Amagasa T: A structural modulator of tumor necrosis factor type 1 receptor promotes bone formation under lipopolysaccharide-induced inflammation in a murine tooth extraction model. *Eur J Pharmacol* 679(1-3):132-138(2012).
6. Nagaoka R, Okuhara S, Sato Y, Amagasa T, Iseki S: Effects of embryonic hypoxia on lip formation. *Birth Defects Research Part A Clinical and Molecular Teratology* 94(4):215-222, (2012).
7. Honda-Uezono A, Kaida A, Michi Y, Harada K, Hayashi Y, Hayashi Y, Miura M: Unusual expression of red fluorescence at M phase induced by anti-microtubule agents in HeLa cells expressing the fluorescent ubiquitination-based cell cycle indicator (Fucci). *Biochemical and Biophysical Research Communications* 428: 224–229, (2012).
8. Nozawa T, Aikawa C, Goda A, Maruyama F, Hamada S, Nakagawa I: The small GTPases Rab9A and Rab23 function at distinct steps in autophagy during Group A Streptococcus infection. *Cell Microbiol* 14(8):1149-65. (2012).
9. Miyajima D, Hayata T, Suzuki T, Henmi H, Nakamoto T, Notomi T, Amagasa T, Böttcher R T, Costell M, Fässler R, Ezura Y, Noda M: Profilin1 Regulates Sternum Development and Endochondral Bone Formation. *J Biol Chem* 287(40):33545-53, (2012).
10. Ohyama Y, Katafuchi M, Almeahadi A, Venkitapathi S, Jaha H, Ehrenman J, Morcos J, Aljamaan R, Mochida Y: Modulation of matrix mineralization by Vwc2-like protein and its novel splicing isoforms. *Biochem Biophys Res Commun* 418(1):12-6, (2012).
11. Oue E, Lee J W, Sakamoto K, Iimura T, Kayamori K, Michi Y, Yamashiro M, Harada K., Aamagasa T, Yamaguchi A: CXCL2 synthesized by oral squamous cell carcinoma is involved in cancer-associated bone destruction. *Biochemical and Biophysical Research Communications* 424(3):456-61, (2012).
12. Watanabe T, Tamamura Y, Hoshino A, Makino Y, Kamioka H, Amagasa T, Yamaguchi A, Iimura T : Increasing participation of sclerostin in postnatal bone development, revealed by three-dimensional immunofluorescence morphometry. *Bone* 51(3):447-58, (2012).
13. Tomomatsu N, Uzawa N, Michi Y, Kurohara K, Okada N, Amagasa T: Clinical study of keratocystic odontogenic tumors. *J Korean Assoc Oral Maxillofac Surg* 38:55-63, (2012).

Maxillofacial Orthognathics

1. Staffs and Students (April, 2012)

Professor	Keiji MORIYAMA	
Associate Professor	Shoichi SUZUKI	
Junior Associate Professor	Tatsuo KAWAMOTO,	
Assistant Professor	Michiko TSUJI,	Takuya OGAWA,
	Norihisa HIGASHIHORI,	Jun MIYAMOTO,
	Hiroki FUKUOKA	
GCOE Research Associate Professor	Naoto HARUYAMA	
Hard Tissue Genome Research Center, Research Assistant Professor	Yukiho KOBAYASHI	
Graduate Student	Yousuke ITO,	Naomi KAWAKUBO,
	Jympei MORITA,	Yuko KOMAZAKI,
	Chiho WATANABE,	Masayoshi UEZONO,
	Ryo MARUOKA,	Masako YOSHIZAKI,
	Carolina DUARTE,	Paveenarat AUKKARASONGSUP,
	Takayuki UMEZAWA,	Kenji OGURA,
	Keiko MURAMOTO,	Naomi YAMAMOTO,
	Thunyaporn SURAPORNSAWASD,	
	Seiei RYU,	Kouhei YAHIRO,
	Maki Morishita,	Naoki Kouda,
	Akitsu Ikeda,	Tsasan Tumurkhuu

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) Basic and clinical studies of cleft lip and/or palate and other congenital craniofacial conditions
- 2) Morphological and physiological studies of facial deformity
- 3) Physiological study about control mechanism of stomatognathic function
- 4) Functional MRI study in the craniofacial region
- 5) Clarify the factors of malocclusion with epidemiological technique

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. Tsuji-Takechi K, Negishi-Koga T, Sumiya E, Kukita A, Kato S, Maeda T, Pandolfi PP, Moriyama K, Takayanagi H.

- Stage-specific functions of leukemia/lymphoma-related factor (LRF) in the transcriptional control of osteoclast development. *Proc Natl Acad Sci USA*. 109:2561-6, 2012.
2. Okamoto N, Hayashi S, Masui A, Kosaki R, Oguri I, Hasegawa T, Imoto I, Makita Y, Hata A, Moriyama K, Inazawa J. Deletion at chromosome 10p11.23-p12.1 defines characteristic phenotypes with marked midface retrusion. *J Hum Genet*. 57:191-6, 2012.
 3. Suzuki H, Suda N, Shiga M, Kobayashi Y, Nakamura M, Iseki S, Moriyama K. Apert syndrome mutant FGFR2 and its soluble form reciprocally alter osteogenesis of primary calvarial osteoblasts. *Journal of Cellular Physiology* 227 (9) : 3267-77, 2012.
 4. Suzuki S, Haruyama N, Nishimura F, Kulkarni AB. Dentin sialophosphoprotein and dentin matrix protein-1: Two highly phosphorylated proteins in mineralized tissues. *Arch Oral Biol*. 57(9):1165-75, 2012.
 5. Qiu L, Haruyama N, Suzuki S, Yamada D, Obayashi N, Kurabayashi T, Moriyama K. Accuracy of orthodontic miniscrew implantation guided by stereolithographic surgical stent based on cone-beam CT derived 3D images. *Angle Orthod*. 82(2):284-93, 2012.
 6. Komazaki Y, Fujiwara T, Ogawa T, Sato M, Suzuki K, Yamagata Z, Moriyama K. Prevalence and gender comparison of malocclusion among Japanese adolescents: A population-based study. *J World Fed Orthod*, 1:67-72, 2012.
 7. Suda N, Tominaga N, Niinaka Y, Amagasa T, Moriyama K. Orthognathic treatment for a patient with facial asymmetry associated with unilateral scissors-bite and a collapsed mandibular arch. *Am J Orthod Dentofacial Orthop*. 141(1):94-104, 2012.
 8. Ng IW, Ono T, Inoue-Arai MS, Honda E, Kurabayashi T, Moriyama K. Differential articulatory movements during Japanese /s/ and /t/ as revealed by MR image sequences with tooth visualization. *Arch Oral Biol*. 57(6):749-59, 2012.
 9. Watanabe K, Kuroda S, Takahashi T, Kijima T, Torikai K, Moriyama K, Tanaka E. Segmental distraction osteogenesis with modified LeFort II osteotomy for a patient with craniosynostosis. *Am J Orthod Dentofacial Orthop*. 142(5):698-709, 2012.
 10. Tokugawa Y, Kubota M, Nishimura M, Haruyama N, Igarashi K. Bone regeneration of canine artificial alveolar clefts using bone-marrow-derived mesenchymal stromal cells and β -tricalcium phosphate: A preliminary study. *Orthod Waves*. 71(2):51-58, 2012.
 11. Tanimoto Y, Veistinen L, Alakurtti K, Takatalo M, Rice DP. Prevention of premature fusion of calvarial suture in GLI-Kruppel family member 3 (Gli3)-deficient mice by removing one allele of Runt-related transcription factor 2 (Runx2). *J Biol Chem*. 15:287(25):21429-38, 2012.
 12. Veistinen L, Takatalo M, Tanimoto Y, Kesper DA, Vortkamp A, Rice DP. Loss-of-Function of Gli3 in Mice Causes Abnormal Frontal Bone Morphology and Premature Synostosis of the Interfrontal Suture. *Front Physiol*. 3:121, 2012.
 13. Shibata S, Fukuoka H, Sato R, Abe T, Suzuki Y. An in situ hybridization study of the insulin-like growth factor system in developing condylar cartilage of the fetal mouse mandible. *Eur J Histochem*. 23:56(2):e23, 2012.

Books

1. Kuroda T, Ohyama K, Motohashi N, Moriyama K. Atlas of orthodontic treatment for patients with birth defect. Needham Press, 2012.
2. Takeda S, Haga N, Moriyama K. Clinical correlate: cleidocranial dysplasia. p59-63, Mineralized tissues in oral and craniofacial science, WILEY-BLACKWELL, 2012.

Maxillofacial Prosthetics

1. Staffs and Students (April, 2012)

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

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 and treatment for patients with maxillofacial defects
2. *In vivo* application of modal analysis for maxillofacial prosthodontics
3. Acoustic analysis of speech
4. Medical and dental art

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. Yuka I. Sumita, Takafumi Otomaru, Hisashi Taniguchi. Effects of a denture adhesive in edentulous patients after maxillectomy. *Gerodontology* 29, 645-649, 2012.
2. Takafumi Otomaru, Yuka I. Sumita, Jien Morimata, Hisashi Taniguchi. Effectos of using denture adhesive with a dento-maxillary prosthesis on food mixing ability in post-maxillectomy patients with edentulous maxillae. *Maxillofacial Prosthetics* 35, 8-13, 2012.
3. Naoko MINAMISAWA, Toshiaki IIDA, Taiji HOSHIAI and Hisashi TANIGUCHI. Assessment of Oral Stereognostic Ability in the Post-maxillectomy Patient. *Maxillofacial Prosthetics* 35, 47-53, 2012.

Books

1. Ken Inohara, Yuka I. Sumita and Shuichi Ino. Extraction of Airway in Computed Tomography, *Computed Tomography - Clinical Applications*, Luca Saba (Ed.), ISBN: 978-953-307-378-1, InTech, Available from: <http://www.intechopen.com/articles/show/title/extraction-of-airway-in-computed-tomography>. 137-148, 2012.

Cell biology

1. Staffs and students (April 2012)

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

2. Purpose of Education

We teach histology to 2nd and 3rd 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

1. Tomohiro Ishii, Toshiyuki Kakumoto, Takao Nakata. Photo-regulation of intracellular Ca²⁺ signals. Workshop on Neural basis of olfactory information processing : From Odors to Neural Circuits and Behavior (Comprehensive Brain Science Network), University of Tokyo, Japan. 2012.9.15.

Medical Biochemistry

1. Staffs and Students (April, 2012)

Professor	Yutaka Hata
Assistant Professor	Kentaro Nakagawa
Assistant Professor	Mitsunobu Ikeda
Assistant Professor	Hiroaki Iwasa
Other two staffs and seven students	

2. Purpose of Education

1) Undergraduate

We organize "Medical Biochemistry". The students are requested to obtain a comprehensive integrated knowledge of medical 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 the components lead to oncogenesis and organ malformation. Several recent studies suggest that this pathway is implicated in inflammation and cell differentiation such as adipogenesis, osteogenesis, myogenesis, 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. For more information, please visit our Web site (<http://www.tmd.ac.jp/english/mbc/index.html>).

3. Research Subjects

- 1) Study of the mammalian Hippo pathway
- 2) Study of cancer stem cells
- 3) Study of RASSF proteins
- 4) Study of sarcopenia

4. Clinical Services

N/A

5. Publications

1. 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.* Epub Oct 26 (2012)
2. Kudo T, Ikeda M, Nishikawa M, Yang Z, Ohno K, Nakagawa K, Hata Y. The RASSF3 candidate tumor suppressor induces apoptosis and G1/S cell cycle arrest via p53. *Cancer Res.* 72(11):2901-2911 (2012)
3. Nishio M, Hamada K, Kawahara K, Sasaki M, Noguchi F, Chiba S, Mizuno K, Suzuki S, Dong Y, Tokuda M, Morikawa T, Hikasa H, Eggenschwiler J, Yabuta N, Nojima H, Nakagawa K, Hata Y, Nishina H, Mimori K, Mori M, Sasaki T, Mak TW, Nakano T, Itami S, Suzuki A. Cancer susceptibility and embryonic lethality in Mob1A/1B double mutant mice. *J. Clin. Invest.* 122(12):4505-4518 (2012)
4. Withanage K, Nakagawa K, Ikeda M, Kurihara H, Kudo T, Yang Z, Sakanae A, Sasaki T, Hata Y. Expression of RASSF6 in kidney and the implication of RASSF6 and the Hippo pathway in the sorbitol-induced apoptosis in renal proximal tubular epithelial cells. *J. Biochem.* 152(1):111-119 (2012)
5. Hata S, Hirayama J, Kajihira H, Nakagawa K, Hata Y, Katada T, Furutani-Seiki M, Nishina H. A novel acetylation cycle of the transcription co-activator Yes-associated protein that is downstream of the Hippo pathway is triggered in response to SN2 alkylating agents. *J. Biol. Chem.* 287(26):22089-22098 (2012)
6. Hirai S, Miwa A, Ohtaka-Maruyama C, Kasai M, Okabe S, Hata Y, Okado H. RP58 controls neuron and astrocyte differentiation by downregulating the expression of Id1-4 genes in the developing cortex. *EMBO J.* 31(5):1190-202 (2012)

Joint Surgery and Sports Medicine

1. Staffs and Students

Professor	Takeshi MUNETA	
Professor	Ichiro SEKIYA (Department of Cartilage Regeneration)	
Associate Professor	Tomoyuki MOCHIZUKI (Department of Joint Reconstruction)	
Junior Associate Professor	Kunikazu Tsuji (GCOE)	
Assistant Professor	Hideyuki KOGA	
Assistant Professor	Toshifumi Watanabe (Department of Cartilage Regeneration)	
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

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. Otabe K, Muneta T, Kawashima N, Suda H, Tsuji K, Sekiya I. Comparison of Gingiva, Dental Pulp, and Periodontal Ligament Cells From the Standpoint of Mesenchymal Stem Cell Properties. *Cell Medicine* 4(1): 13-21, 2012
2. 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 Surgery, Sports Traumatology, Arthroscopy* (in press)
3. Nakamura T, Sekiya I, Muneta T, Hatsushika D, Horie M, Tsuji K, Kawarasaki T, Watanabe A, Hishikawa S, Fujimoto Y, Tanaka H, Kobayashi E. Arthroscopic, histological and MRI analyses of cartilage repair after a

- minimally invasive method of transplantation of allogeneic synovial mesenchymal stromal cells into cartilage defects in pigs. *Cytotherapy*. 14(3): 327-338, 2012.
4. Horie M, Driscoll MD, Sampson HW, Sekiya I, Caroom CT, Prockop DJ, Thomas DB. Implantation of allogenic synovial stem cells promotes meniscal regeneration in a rabbit meniscal defect model. *J Bone Joint Surg Am*. 18;94(8):701-12, 2012.Apr.
 5. Horie M, Choi H, Lee RH, Reger RL, Ylostalo J, Muneta T, Sekiya I, Prockop DJ. Intra-articular injection of human mesenchymal stem cells (MSCs) promote rat meniscal regeneration by being activated to express Indian hedgehog that enhances expression of type II collagen. *Osteoarthritis Cartilage*. 20(10):1197-207, 2012.Oct.
 6. Tsukada S, Hoshino A, Cho S, Ikeda H. Intraoperative soft tissue tension and postoperative range of motion in posterior stabilized total knee arthroplasty. *Arch Orthop Trauma Surg*. Published online; 02 November, 2012 (in press)
 7. Akiyama H, Hoshino A, Iida H, et al. A pilot project for the Japan arthroplasty register. *J Orthop Sci*. 17(4): 358-369, 2012.
 8. Muneta T, Koga H, Ju YJ, Mochizuki T, Sekiya I. Hyaluronan injection therapy for athletic patients with patellar tendinopathy. *J Orthop Sci*. 17(4):425-31, 2012.Jul.
 9. 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*, 2012 Apr 28. [Epub ahead of print]
 10. Mochizuki T, Nimura A, Tateishi T, Yamaguchi K, Muneta T, Akita K. Anatomic study of the attachment of the medial patellofemoral ligament and its characteristic relationships to the vastus intermedius. *Knee Surg Sports Traumatol Arthrosc*. (in press)
 11. 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*. (in press)
 12. Kato A, Nimura A, Yamaguchi K, Mochizuki T, Sugaya H, Akita K. An anatomical study of the transverse part of the infraspinatus muscle that is closely related with the supraspinatus muscle. *Surg Radiol Anat*. 34: 257-265, 2012.
 13. Nimura A, Kato A, Yamaguchi K, Mochizuki T, Okawa A, Sugaya H, Akita K. The superior capsule of the shoulder joint complements the insertion of the rotator cuff. *J Shoulder Elbow Surg*. 21: 867-872, 2012.
 14. Sekiya I, Ojima M, Suzuki S, Yamaga M, Horie M, Koga H, Tsuji K, Miyaguchi K, Ogishima S, Tanaka H, Muneta T. Human mesenchymal stem cells in synovial fluid increase in the knee with degenerated cartilage and osteoarthritis. *J Orthop Res*. 30(6):943-9, 2012.
 15. Yamauchi Y, Jinno T, Koga D, Asou Y, Morita S, Okawa A. Comparison of Different Distal Designs of Femoral Components and Their Effects on Bone Remodeling in 1-Stage Bilateral Total Hip Arthroplasty. *J Arthroplasty* (8):1538-43, 2012.Sep.27.
 16. Suzuki S, Muneta T, Tsuji K, Ichinose S, Makino H, Umezawa A, Sekiya I. Properties and usefulness of aggregates of synovial mesenchymal stem cells as a source for cartilage regeneration. *Arthritis Res Ther*.;14(3):R136, 2012.
 17. Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. Surgical management of grade 3 medial knee injuries combined with cruciate ligament injuries. *Knee Surg Sports Traumatol Arthrosc* 20(1):88-94, 2012.
 18. Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. The effect of graft fixation angles on anteroposterior and rotational knee laxity in double-bundle anterior cruciate ligament reconstruction: evaluation using computerized navigation. *Am J Sports Med* 40(3):615-623, 2012.
 19. Koga H, Muneta T, Yagishita K, Watanabe T, Mochizuki T, Horie M, Nakamura T, Okawa A, Sekiya I. Arthroscopic Centralization of an Extruded Lateral Meniscus: a Technical Note. *Arthroscopy Techniques* (in press).
 20. 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* (in press).
 21. Yamaga M, Tsuji K, Miyatake K, Yamada J, Abula K, Ju YJ, Sekiya I, Muneta T. Osteopontin level in synovial fluid is associated with the severity of joint pain and cartilage degradation after anterior cruciate ligament rupture. *PLoS ONE* In Press.
 22. Kokabu S, Gamer L, Cox K, Lowery J, Tsuji K, Raz R, Economides A, Katagiri T, Rosen V. BMP3 suppresses osteoblast differentiation of bone marrow stromal cells via interaction with Acvr2b. *Mol Endocrinol* 26, 87-94, 2012.
 23. Futami I, Ishijima M, Kaneko H, Tsuji K, Ichikawa-Tomikawa, N., Sadatsuki R, Muneta T, Arikawa-Hirasawa, E, Sekiya I, Kaneko K. Isolation and characterization of multipotential mesenchymal cells from the mouse synovium. *PLoS One* 7, e45517, 2012.

24. 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*. (in print)
25. Watanabe T, Ishizuki M, Muneta T, Banks SA. Matched comparison of kinematics in knees with mild and severe varus deformity using fixed- and mobile-bearing total knee arthroplasty. *Clin Biomech*. 27(9):924-8, 2012.
26. 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*. 2012: (in print)

Biostructural Science

1. Staffs and Students (as of April, 2012)

Professor	Yoshiro TAKANO	
Associate Professor	Makoto J TABATA	
Assistant Professor	Otto BABA	
Technician	Hachiro ISEKI	
Graduate Student	Ravindra Kumar RATNAYAKE,	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 3rd-year dental education curriculum and are expected to build solid basis for future studies of advanced dental science and clinical medicine.

In addition to the current curriculum, a novel curriculum also started from April 1, 2012 in which most of the subjects listed above had been transferred to the 2nd-year program where dental students and medical students are supposed to study together.

[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. Nomura Y, Ishikawa M, Yashiro Y, Sanggarnjanavanich S, Yamaguchi T, Arai C, Noda K, Takano Y, Nakamura Y, Hanada N: Human periodontal ligament fibroblasts are the optimal cell source for induced pluripotent stem cells. *Histochem Cell Biol.* 137(6): 719-732, 2012.
2. Atukorala ADS, Inohaya K, Baba O, Tabata MJ, Ratnayake RARK, Abduweli D, Kasugai S, Mitani H, Takano Y: Scale- and tooth phenotypes in medaka with mutated ectodysplasin-A receptor: implication in evolutionary origin of oral- and pharyngeal teeth. *Arch Histol Cytol* 73: 139-148, 2010/2011.
3. Munakata K, Ookata K, Doi H, Baba O, Terashima T, Hirose S, Kato A: Histological demonstration of glucose transporters, fructose-1, 6-bisphosphatase, and glycogen in gas gland cells of the swimbladder: Is a metabolic futile cycle operating? *Biochem Biophys Res Commun* 417: 564-569, 2012.
4. Ida-Yonemochi H, Nakatomi M, Harada H, Takata H, Baba O, Ohshima H: Glucose uptake mediated by glucose transporter 1 is essential for early tooth morphogenesis and size determination of murine molars. *Dev Biol* 363: 52-61, 2012.
5. Zeng L, Wang Y, Baba O, Zheng P, Liu Y, Liu Y: Laforin is required for the functional activation of malin in endoplasmic reticulum stress resistance in neuronal cells. *FEBSJ* 279:2467-2478, 2012 .

Abstracts

1. Abduweli D, Takano Y: Tooth Replacement and Stem Cell Niche in Medaka Pharyngeal Dentition, 41st Annual Meeting & Exhibition of the AADR, Tampa, Fla., USA, March 21-24, 2012.
2. Tabata MJ, Iseki H, Ikegame M, Miyashita K, Maruyama Y, Ohmori K, Endoh M, Baba O, Hattori A: Experiments in space using scale of Gold fish – Ultrastructure analysis of the osteoclasts cultured in micro gravity. The 117th Annual Meeting of the Japanese Association of Anatomists. Kofu, March 26-28, 2012.
3. Baba O, Atukorala ADSL, Inohaya K, Tabata MJ, Mitani H, Takano Y: Differential effect of aberrant expression of ectodysplasin-A receptor (edar) on scales and jaw and pharyngeal dentition of medaka. The 117th Annual Meeting of the Japanese Association of Anatomists. Kofu, March 26-28, 2012.
4. Mishima H, Hattori A, Suzuki N, Tabata MJ, Kakei M, Miake Y, Suzuki M: The connection between the periodicity of incremental lines in the tooth dentin and the regulation by melatonin. European Calcified Tissue Society 39th meeting, Stockholm, May 21, 2012
5. Kamrun N, Tetsumura A, Nomura Y, Baba O, Nakamura S, Watanabe H, Kurabayashi T. Visualization of the superior and inferior borders of the mandibular canal: comparison between digital panoramic radiographs and dental CT images. The 53th Annual Meeting of the Japanese Society for Oral and Maxillofacial Radiology, Morioka, June 1-3, 2012.
6. Kozawa Y, Baba O, Terashima T: Meaning of the pulpal horn in dental pulp. The 54th Annual Meeting of Japanese Association for Oral Biology, Koriyama, September 14-16, 2012.
7. Takano Y: Ultrastructural views of the mechanisms underlying the induction of large-sized enamel crystals during the maturation process of amelogenesis. The 68th Annual Meeting of Japanese Society of Microscopy, Tsukuba International Congress Center, May 14-16, 2012.
8. Hanada, N, Nomura Y, Ishikawa M, Yagi Y, Arai C, Yamaguchi T, Murata T, Noda K, Takano Y, Nakamura Y: PDL- derived iPS cells using retro vectors: Studies on establishment of standards for the evaluation of its safeness. The 54th Annual Meeting of Japanese Association for Oral Biology, Koriyama, September 14-16, 2012.
9. Ratnayake RARK, Abduweli D, Takano Y. Organic Anion Transporters in Rat Enamel Formation, 100th Annual Meeting of the Kanto Branch of the Japanese Association of Anatomist, Toho University, Tokyo, October 13, 2012.
10. Takano Y: Dynamic Events at the Cell-Matrix Interface in Amelogenesis: Contribution to Matrix Processing and Crystal Growth, 11th Annual Meeting of Korean Basic Dental Science Societies Association, Seoul, Korea, Nov. 23, 2012.
11. Jayawardena CK, Walpola V, Nandasena T, Nanayakakara D, Takano Y, Organic Anion Transporters Play Roles in Human Enamel Formation, 60th Annual Meeting of JADR, Niigata Convention Center, December 14-15, 2012.
12. Mishima H, Inonue M, Hattori A, Suzuki N, Tabata MJ, Kakei M, Matsumoto T, Satomura K, Miake Y: The connection between the periodicity of incremental lines in the tooth dentin and the secretion rhythm of melatonin. The 7th Workshop of Bio-Mineralization, Tokyo, Dec 1, 2012

[Invited Lectures]

1. Takano Y: Ultrastructural views of the mechanisms underlying the induction of large-sized enamel crystals during the maturation process of amelogenesis. Symposium: Application of cutting-edge microscopy and analytical methods for hard tissue biology. The 68th Annual Meeting of Japanese Society of Microscopy, Tsukuba International Congress Center, May 14-16, 2012
2. Takano Y: Amelogenesis and Enamel Structure, Kyung Hee University, Seoul, Sept 10, 2012.
3. Takano Y: Cell and Matrix Regulation of Amelogenesis Kyung Hee University Graduate School Seminar, Seoul, Sept 11, 2012.
4. Takano Y: Dynamic Events at the Cell-Matrix Interface in Amelogenesis: Contribution to Matrix Processing and Crystal Growth, 11th Annual Meeting of Korean Basic Dental Science Societies Association, Seoul, Korea, Nov. 23, 2012.
5. Baba O: Phylogeny of tooth root and periodontal tissue. In Satellite symposium 5: Serendipity of the Tooth – Periodontal Tissue Complex. The 54th Annual Meeting of Japanese Association for Oral Biology, Koriyama, September 14, 2012.

Pharmacology

1. Staffs and Students(April, 2012)

Professor	Keiichi OHYA
Associate Professor	Kazuhiro AOKI
Assistant Professor	Yukihiko TAMURA
Foreign Researcher (JSPS)	Chrisman Neil Roshan Alexander ALLES
Researcher (JSPS)	Noriko KOMATSU (Cell Signaling)
Researcher	Miki MAEDA, Kenichi NAGANO, Kengo FUJIKI (Removable Prosthodontics), Nobuyoshi TOMOMATSU (Maxillofacial Surgery), Yasuhiro SHIMIZU (Orthodontic Science)
Graduate Student	Toshimi SATO, Md. Abdulla Al Masud KHAN(GCOE Advanced Super Student), Md. Abdullah Al MAMUN, Atsushi KIMURA (Oral and Maxillofacial Surgery), Genki KATO, Yasutaka SUGAMORI, Makiri KAWASAKI (Molecular Pharmacology)

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 body 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. Hayashi N, Tamura Y, Kusumoto Y, Shimokawa H, Aoki K, Ohya K, Yamazaki T, Shinozuka O. Gingival Overgrowth Induced by Phenytoin-Study of the Human Gingival Overgrowth Tissues and Clonal Gingival Cells. **Disability and Oral Health** 33, 16-25, 2012
2. Seo Y, Fukushima H, Maruyama T, Kuroishi KN, Osawa K, Nagana K, Aoki K, Wejh F, Doi T, Zhang M, Ohya K, Katagiri T, Hosokawa R, Jimi E. Accumulation of p100, a Precursor of NF- κ B2, Enhances Osteoblastic Differentiation *in Vitro* and Bone Formation *in Vivo* in *aly/aly* Mice. **Mol Endocrinol** 26, 414-422, 2012
3. Aoki K, Alles N, Soysa N, Ohya K. Peptide-based delivery to bone. **Advanced Drug Delivery Reviews** 64, 1220-1238, 2012
4. Nakachi H, Aoki K, Tomomatsu N, Alles N, Nagano K, Yamashiro M, Zhang H, Merali R, Greene M.I, Ohya K, Amagasa T. A structural modulator of tumor necrosis factor type 1 receptor promotes bone formation under lipopolysaccharide-induced inflammation in a murine tooth extraction model. **European J Pharmacology** 679, 132-138, 2012
5. Soysa N.S, Alles N, Aoki K, Ohya K. Osteoclast formation and differentiation: An overview. **J Med Dent Sci** 59, 65-74, 2012
6. Muguruma M, Ahhmed A.M, Kawahara A, Kusumegi K, Hishinuma T, Ohya K, Nakamura T. A combination of soybean and skimmed milk reduces osteoporosis in rats. **J Functional Foods** 4, 810-818, 2012
7. Oue E, Lee J-W, Sakamoto K, Iimura T, Aoki K, Kayamori K, Michi Y, Yamashiro M, Harada K, Amagasa T, Yamaguchi A. CXCL2 synthesized by oral squamous cell carcinoma is involved in cancer-associated bone

- destruction. **Biochemical and Biophysical Research Communications** 424, 456-461, 2012
8. Furuta H, Osawa K, Shin M, Ishikawa A, Matsuo K, Khan M, Aoki K, Ohya K, Okamoto M, Tominaga K, Takahashi T, Nakahashi O, Jimi E. Selective inhibition of NF- κ B suppresses bone invasion by oral squamous cell carcinoma *in vivo*. **Int J Cancer** 131 E625-E635, 2012
 9. Fujiki K, Aoki K, Marcián P, Borák 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. **Biomech Model Mechanobiol** DOI 10.1007/s10237-012-0401-z, 2012

Connective Tissue Regeneration

1. Staff (April, 2011)

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 novel genes actively expressed in periodontal tissues.
- 3) Study on the molecular dynamics of extracellular matrix in connective tissues.

4. Publications

Original Articles

1. Shinomura, T., Ito, K., Höök, M., and Kimura, J. H. A Newly Identified Enhancer Element Responsible for Type II Collagen Gene Expression. *J. Biochem.* **152** 565-575 (2012)
2. Oshiro A., Iseki S., Miyauchi M., Terashima T., Kawaguchi Y., Ikeda Y., and Shinomura T. Lipopolysaccharide induces rapid loss of follicular dendritic cell-secreted protein in the junctional epithelium. *J. Periodont. Res.* **47** 689-694 (2012)
3. Hatano S., Kimata K., Hiraiwa N., Kusakabe M., Isogai Z., Adachi E., Shinomura T., and Watanabe H. Versican/Pg-M is essential for ventricular septal formation subsequent to cardiac atrioventricular cushion development. *Glycobiology* **22** 1268-1277 (2012)
4. Podyma-Inoue K. A., Hara-Yokoyama M., Shinomura T., Kimura T., and Yanagishita M. Syndecans Reside in Sphingomyelin-Enriched Low-Density Fractions of the Plasma Membrane Isolated from a Parathyroid Cell Line. *PLoS ONE* **7** e32351 (2012)
5. Wasa J., Nishida Y., Shinomura T., Isogai Z., Futamural N., Urakawa H., Arai E., Kozawa E., Tsukushi S., and Ishiguro N. Versican V1 isoform regulates cell-associated matrix formation and cell behavior differentially from aggrecan in Swarm rat chondrosarcoma cells. *Int. J. Cancer* **130** 2271-2281 (2012)

Biochemistry

1. Staffs and student (April, 2012)

Professor	Masaki Yanagishita
Associate Professor	Miki Yokoyama
Junior Associate Professor	Yasuhiro Kumei
Assistant Professor	Katarzyna Anna Podyma-Inoue
Research Assistant Professor, Global Center of Excellence Program	Hiroyuki Nakamura
Technical staff	Kazue Terasawa
Part-time instructor	Akira Asari
Graduate student	Hiroko Yamanokuchi, Rajapakshe Mudiyansele Anupama Rasadari Rajapakshe

2. Purpose of education

Extracellular matrix is a critical constituent of multicellular organisms by functioning as scaffold for body structures and providing internal environment for cell activities. Our section focuses on the research and education on molecular composition, biological functions and pathological processes involving extracellular matrices.

3. Research subjects

- Studies on the biological functions of heparan sulfate proteoglycans
- Roles of sphingolipid metabolism on cell death progression
- Cell-surface assembly of transmembrane proteins on the plasma membrane
- Sensing and response mechanisms of cells toward gravity

4. Publications

[Original Article]

- Miki Hara-Yokoyama, Mutsuko Kukimoto-Niino, Kazue Terasawa, Satoru Harumiya, Katarzyna A. Podyma-Inoue, Nobumasa Hino, Kensaku Sakamoto, Satsuki Itoh, Noritaka Hashii, Yoko Hiruta, Nana Kawasaki, Chiemi Mishima-Tsumagari, Yoko Kaitsu, Tomoko Matsumoto, Motoaki Wakiyama, Mikako Shirouzu, Takeshi Kasama, Hiroshi Takayanagi, Nakako Utsunomiya-Tate, Kiyoshi Takatsu, Toshiaki Katada, Yoshio Hirabayashi, Shigeyuki Yokoyama and Masaki Yanagishita, *Structure* 20, 1585-1595 (2012)
- Katarzyna A. Podyma-Inoue, Miki Yokoyama, Tomoko Kimura and Masaki Yanagishita, *Syndecans Reside in Sphingomyelin-enriched Low Density Fractions of the Plasma membrane Isolated from a Parathyroid Cell Line*, *PLOS ONE*, 7:3 e3231 (2012)
- Seisuke Kusano, Mutsuko Kukimoto-Niino, Nobumasa Hino, Noboru Ohsawa, Masashi Ikutani, Satoshi Sakaki, Kensaku Sakamoto, Miki Hara-Yokoyama, Mikako Shirouzu, Kiyoshi Takatsu, Shigeyuki Yokoyama, *Structural basis of interleukin-5 dimer recognition by its α receptor*, *Protein Science*, 21, 850-864 (2012)
- Hiroko Yamanokuchi, *Effects of Hyaluronan Tetrasaccharide on Neural Cells*, *Journal of the Stomatological Society, Japan*, 79, 100-109 (2012)
- Jorge L. Zeredo, Kazuo Toda, Masaaki Matsuura, Yasuhiro Kumei, "Behavioral responses to partial-gravity conditions in rats" *Neuroscience Let.* 529: 108-111, 2012

4. Presentation at Meetings

- S. Takehara, M. Yanagishita, K. A. Podyma-Inoue, M. Ueno, K. Shinada and Y. Kawaguchi, *Proteolytic Degradation of Human Salivary MUC5B and MUC7*, Annual Meeting of International Association for Dental Research, San Diego, March 16-19, 2012
- Miki Yokoyama, *Abnormality of Intercellular Interactions in Spermatogenesis in Glycolipid (β 1,4GalNAc-T) Defective Mouse*, Seminar in National Institute for Environmental Studies, June 15, 2012
- Katarzyna A. Podyma-Inoue, Miki Yokoyama and Masaki Yanagishita, *Association of heparan sulphate proteoglycan with trypsin-accessible membrane domains*, Gordon Research Conference on Proteoglycan, Andover, NH, USA, July 7-13, 2012
- Privatananupunt Jutiporn, Watari Ippei, Podyma-Inoue Katarzyna A., Kubono Mariko, Hattori Ikuko, Honda Koji, Ishida Yuji, Yanagishita Masaki, and Ono Takashi, *Expression of GIP and its receptor in the rat major salivary*

- glands, 71st Annual Meeting of the Japanese Orthodontic Society, Morioka, September 26-28, 2012
5. Yasuhiro Kumei, Katsuya Hasegawa, Tsunenori Suganuma, Jorge L. Zeredo, and Shuji Aou “X-ray movie analysis of mice adaptation to lunar/Martian and micro gravity”, ESA Life in Space for Life on Earth symposium, Aberdeen-UK, June, 2012
 6. Shuji Aou, Yuuki Watanabe, Akira Masuda, Katsuya Hasegawa, Tomomi Kawasaki, Yasuhiro Kumei “Reproductive and social behaviours of mice in 0.3G and 0.15G parabolic flight conditions”, ESA Life in Space for Life on Earth symposium, Aberdeen-UK, June, 2012
 7. Yasuhiro Kumei, Katsuya Hasegawa, Shuji Aou, Jorge L. Zeredo, Kimiya Narikiyo, Katarzyna A. Inoue, Yukio Maezawa, and Yuuki Watanabe “A novel centrifuge for animal physiological researches in hypergravity and variable gravity forces”, 39th COSPAR Scientific Assembly, Mysore - India, July, 2012
 8. Shuji Aou, Kimiya Narikiyo, Jorge L. Zeredo, Katarzyna Inoue, Yuuki Watanabe, Katsuya Hasegawa and Yasuhiro Kumei, “Social and sexual behaviours of mice in partial gravity”, Mysore - India, July, 2012
 9. Yasuhiro Kumei “Life sciences for missions to the moon and Mars”, 9th Japan-China-Korea Space symposium, Guilin-China, October, 2012
 10. Yasuhiro Kumei “Noninvasive monitoring of rodent muscle/skeletal and visceral movement by X-ray photo imaging in low gravity”, 28th ASGSR, New Orleans-LA, December, 2012

Cell Signaling

1. Staffs and Students

Professor	Hiroshi TAKAYANAGI (~May)	
Assistant Professor	Masahiro SHINOHARA (~Sep)	
	Tomoki NAKASHIMA,	Satoru HARUMIYA
	Kazuo OKAMOTO (~May)	
Research Associate Professor	Masatsugu OHORA (~Sep)	
Visiting Assistant Professor	Takako KOGA	
Adjunct Junior Associate Professor	Mikihiro HAYASHI,	Yusuke NAGAI,
	Eriko SUMIYA	
Postdoctoral Fellow	Noriko KOMATSU,	Ayako SUEMATSU,
	Asuka TERASHIMA,	Matteo GUERRINI,
	Lynett DANKS	
Graduate Student	Abdul Alim AL-BARI(~Sep), Takehito ONO	

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 and osteoblasts, but also on the osteoimmunology, which is a new integrated field of bone homeostasis and immunology. 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) Function and transcriptional regulation of NFATc1, a master regulator of osteoclast differentiation
- 2) Transcriptome and Proteome of cytokine-induced genes
- 3) Regulation of bone homeostasis by immunoglobulin receptors
- 4) Identification of bone-derived systemic regulatory factors (osteokines)
- 5) Mechanism of sensing and adapting to mechanical stress
- 6) Functional analysis of genes by gene manipulations, RNAi and gene-disrupted mice
- 7) Development of clinical application by experimental animal disease models

4. Publications

【Original Article】

1. Miyazaki T, Iwasawa M, Nakashima T, Mori S, Shigemoto K, Nakamura H, Katagiri H, Takayanagi H, Tanaka S.: Intracellular and extracellular ATP coordinately regulate the inverse correlation between osteoclast survival and bone resorption. *J Biol Chem.* 287(45), 37808-23 (2012).
2. Shinohara M, Nakamura M, Masuda H, Hirose J, Kadono Y, Iwasawa M, Nagase Y, Ueki K, Kadowaki T, Sasaki T, Kato S, Nakamura H, Tanaka S, Takayanagi H.: Class IA phosphatidylinositol 3-kinase regulates osteoclastic bone resorption through Akt-mediated vesicle transport. *J Bone Miner Res.* 27(12):2464-75 (2012).
3. Hara-Yokoyama M, Kukimoto-Niino M, Terasawa K, Harumiya S, Podyma-Inoue KA, Hino N, Sakamoto K, Itoh S, Hashii N, Hiruta Y, Kawasaki N, Mishima-Tsumagari C, Kaitsu Y, Matsumoto T, Wakiyama M, Shirouzu M, Kasama T, Takayanagi H, Utsunomiya-Tate N, Takatsu K, Katada T, Hirabayashi Y, Yokoyama S, Yanagishita M.: Tetrameric Interaction of the Ectoenzyme CD38 on the Cell Surface Enables Its Catalytic and Raft-Association Activities. *Structure.* 20(9):1585-95 (2012).
4. Hayashi M, Nakashima T, Taniguchi M, Kodama T, Kumanogoh A, Takayanagi T.: Osteoprotection by Semaphorin 3A. *Nature.* 485(7396): 69-74 (2012).
5. Otero K, Shinohara M, Zhao H, Cella M, Gilfillan S, Colucci A, Faccio R, Ross FP, Teitelbaum SL, Takayanagi H, Colonna M.: TREM2 and β -Catenin Regulate Bone Homeostasis by Controlling the Rate of Osteoclastogenesis. *J Immunol.* 188(6):2612-21 (2012).
6. Fujita K, Iwasaki M, Ochi H, Fukuda T, Ma C, Miyamoto T, Takitani K, Negishi-Koga T, Sunamura S, Kodama T,

Takayanagi H, Tamai H, Kato S, Arai H, Shinomiy, K, Itoh H, Okawa A, Takeda S: Vitamin E decreases bone mass by stimulating osteoclast fusion. *Nat Med*. 18(4):589-94 (2012).

7. Tsuji-Takechi K, Negishi-Koga T, Sumiya E, Kukita A, Kato S, Maeda T, Pandolfi PP, Moriyama K, Takayanagi H: Stage-specific functions of leukemia/lymphoma-related factor (LRF) in the transcriptional control of osteoclast development. *Proc Natl Acad Sci USA*. 109(7): 2561-6 (2012).

[Review Article]

1. O'Brien CA, Nakashima T, Takayanagi H: Osteocyte control of osteoclastogenesis. *Bone*. in press (2012).
2. Nakashima T, Hayashi M, Takayanagi H: New insights into osteoclastogenic signaling mechanisms. *Trends Endocrinol Metab*. 23(11): 582-90 (2012).
3. Takayanagi H: New developments in osteoimmunology. *Nat Rev Rheumatol*. 8(11):684-9 (2012).
4. Nakashima T, Takayanagi H. RANK and RANKL. *Encyclopedia of Signaling Molecules* (Book; Springer New York, Editor Sangdum Choi) 1581-1589, (2012).
5. Komatsu N, Takayanagi H: Inflammation and bone destruction in arthritis: synergistic activity of immune and mesenchymal cells in joints. *Front Immunol*. 3:77 (2012).
6. Komatsu N, Takayanagi H: Autoimmune Arthritis: The Interface Between the Immune System and Joints. *Adv Immunol*. 115:45-71 (2012).

[Presentation]

1. Tomoki Nakashima, Mikihito Hayashi, Hiroshi Takayanagi: Osteocyte-derived RANKL in bone remodeling. American Society for Bone and Mineral Research 2012 Annual Meeting. 2012.10.13, Minneapolis USA.
2. Mikihito Hayashi, Tomoki Nakashima, Hiroshi Takayanagi: Semaphorin 3A inhibits osteoclastogenesis and promotes osteoblastogenesis synchronously. American Society for Bone and Mineral Research 2012 Annual Meeting. 2012.10.15, Minneapolis USA.
3. Hiroshi Takayanagi: Mouse genetics in osteoimmunology. EMBO Practical Course on Anatomy and Embryology. 2012.9.10, Split, Croatia.
4. Hiroshi Takayanagi: Bone cell communications. Annual Scientific Meeting ANZBMS and Asia-Pacific Bone and Mineral Research Meeting. 2012.9.22, Perth, Australia.
5. Hiroshi Takayanagi: Molecular basis for communication among bone cells. 4th International Conference on Osteoimmunology, 2012.6.21, Corfu, Greece.
6. Tomoki Nakashima: Osteoprotection by semaphoring 3A. Annual Scientific Meeting ANZBMS and Asia-Pacific Bone and Mineral Research Meeting. 2012.9.22, Perth, Australia.
7. Takako Koga, Eriko Sumiya, Masahiro Shinohara, Hiroshi Takayanagi: Regulation of bone remodeling by osteoclastic expression of semaphorin 4D. 4th International Conference on Osteoimmunology, 2012.6.20, Corfu, Greece.
8. Tomoki Nakashima: Osteocyte-derived RANKL in bone remodeling. 4th International Conference on Osteoimmunology, 2012.6.20, Corfu, Greece.
9. Mikihito Hayashi, Tomoki Nakashima, Hiroshi Takayanagi: Semaphorin 3A drives bone formation phase in bone remodeling. 4th International Conference on Osteoimmunology, 2012.6.20, Corfu, Greece.
10. Hiroshi Takayanagi: Molecular mechanism of osteoclast differentiation. Cold Spring Harbor Asia conferences, 2012.6.12, Suzhou, China.
11. Hiroshi Takayanagi: Immune Signalling in Osteoclasts. 15th International and 14th European Congress of Endocrinology (ICE / ECE 2012), 2012.5.6, Florence, Italy.

[Award]

1. Tomoki Nakashima: 2012 The Japanese Society for Bone and Mineral Research. Research Encouragement Award 2012, July
2. Mikihito Hayashi: 012 The Japanese Society for Bone and Mineral Research. Young Investigator Award 2012, July
3. Matteo Guerrini: 4rd Osteoimmunology Travel Award 2012, Jun
4. Mikihito Hayashi: 4rd Osteoimmunology Travel Award 2012, Jun

Inorganic Biomaterials

1. Staffs and Students

Professor	Kimihiro Yamashita	
Associate Professor	Akiko Nagai	
Assistant Professors	Miho Nakamura,	Nahohiro Horiuchi,
	Kosuke Nozaki	
Students	Seiko Oba,	Yu Tsuchiya

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 bio-ceramics, 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. Ma C., Nagai A., Yamazaki Y., Toyama T., Tsutsumi Y., Hanawa T., Wei W., Yamashita K., Electrically Polarized Micro-arc Oxidized TiO₂ Coatings with Enhanced Surface Hydrophilicity. *Acta Biomater.* 8(2):860-865, 2012.
2. Nakamura M., Soya T., Okabayashi R., Nagai A., Hashimoto K., Morita I., Yamashita K., Endothelial Migration and Morphogenesis on Silk Fibroin Scaffolds Including Hydroxyapatite Electret. *J. Biomed. Mater. Res. A*, 100A (4):969-977, 2012.
3. Nagai, A. Tsutsumi Y., Suzuki Y., Katayama K., Hanawa T., Yamashita K., Characterization of the Air-Formed Surface Oxide Film on a Co-Ni-Cr-Mo Alloy (MP35N) and its Change in Hanks Solution, *Appl. Surf. Sci.*, 258(14):5490-5498, 2012.
4. Nakamura M., Hiratai R., Yamashita K., Bone Mineral as an Electric Energy Reservoir, *J. Biomed. Mater. Res. A*, 100A(5):1368-1374, 2012.

5. Ohba S., Wang W., Itoh S., Takagi Y., Nagai A., Yamashita K., Acceleration of New Bone Formation by an Electrically Polarized Hydroxyapatite Microgranule/Platelet-rich Plasma Composite, *Acta Biomater.*, 8(7):2778-2787, 2012.
6. Nagai A., Yamazaki Y., Ma C., Nozaki K., Toyama T., Yamashita K., Response of Osteoblast-like MG63 Cells to TiO₂ Layer Prepared by Micro-arc Oxidation and Electric Polarization, *J. Euro. Ceram. Soc.*, 32(11):2647-2652, 2012.
7. Mukougawa K, Wada N, Horiuchi N, Nakamura M, Nagai A, Yamashita K. Surface Properties of Hydroxyapatite Electrets. *Phosphorus Res. Bull*, 26:6-7, 2012.
8. Imamura Y., Nakamura M., Nagai A., Takagi Y., Yamashita K., Octacalcium Phosphate-Mediated Cement as a Root Canal Filling Material for Primary Teeth, *Phosphorus Res. Bull.*, 26:33-38, 2012.
9. Nakamura M., Inuzuka M., Hashimoto K., Nagai A., Yamashita K., Polarized Yttria-Stabilized Zirconia Improves Durability and Apatite Formation in Simulated Body Fluid, *Phosphorus Res. Bull.*, 26:77-80, 2012.
10. Watarai T., Nakamura M., Horiuchi N., Nagai A., Hashimoto K., Yamashita K., Sintering and Osteoclast Behaviors of Carbonate Apatite Ceramics, *Phosphorus Res. Bull.*, 27:45-49, 2012.
11. Wada N, Horiuchi N, Wei W, Hiyama T, Nakamura M, Nagai A, Yamashita K. Electrical Conduction and Polarization of Calcite Single Crystals. *Phy Chem Miner*, 39:761-768, 2012.
12. Ohba S., Wang W., Itoh S., Nagai A., Takagi Y., Nagai A., Yamashita K., Efficacy of Platelet-rich Plasma Gel and Hyaluronan Hydrogel as Carriers of Electrically Polarized Hydroxyapatite Microgranules for Accelerating Bone Formation, *J. Biomed. Mater. Res. A*, 100A(11):3167-3176, 2012.
13. Horiuchi N, Nakamura M, Nagai A, Katayama K, Yamashita K. Proton Conduction Related Electrical Dipole and Space Charge Polarization in Hydroxyapatite. *J. Appl. Phys.* 112(7):074901, 2012.
14. Okura T., Kawada K., Yoshida N., Monma H., Yamashita K., Synthesis and Na⁺ Conduction Properties of Nasicon-Type Glass-Ceramics in the System Na₂O-Y₂O₃-X₂O₃-SiO₂ (X=B, Al, Ga) and Effect of Si Substitution, *Solid State Ionics*, 225:367-370, 2012.
15. Shinonaga T., Tsukamoto M., Nishii R., Ito Y., Nagai A., Yamashita K., Hanawa T., Matsushita N., Guoqing X., Abe N., Formation of Periodic Nanostructures on Titanium Dioxide Film by Femtosecond Laser Irradiation, *Trans. Join. Meld. Res. Inst.*, 41(1):25-28, 2102.
16. Iwahara Y., Nagai A., Yoshiki N., Igarashi K., Ishikawa T., Harada T., Yamashita K., Kubota T., Expression of Heme Oxygenase in the Eutopic and Ectopic Endometrium in Patients with Adenomyosis, *Gynecol. Endocrinol.*, 28(11):892-896, 2012.
17. Nagai A., Ma C., Kishi S., Inuzuka M., Nakamura M., Horiuchi N., Nishio K., Yamashita K., Surface Properties of Al₂O₃-YSZ Ceramic Composites Modified by a Combination of Biomimetic Coatings and Electric Polarization, *Appl. Surf. Sci.*, 262, 45-50 (2012).
18. Horiuchi N, Yamashita K. Physical and Chemical Properties of Apatite Electrets for Biomedical and Energy Applications. *Ceram. Trans.* 233:39-44. 2012.
19. Tsuchiya Y, Horiuchi N, Nakamura M, Nozaki K, Nagai A, Hashimoto K, Yamashita K. Effect of Polarization Treatment Time on Inhibition of Low Temperature Degradation in Y-Doped ZrO₂. *Key. Eng. Mater.* 529-530:601-4, 2012
20. Horiuchi N, Wada N, Nakamura M, Nagai A, Yamashita K. Inhibition of Low-Temperature Degradation and Biocompatibility on Surface of Yttria-Stabilized Zirconia by Electric Polarization. *Ceram. Trans.* 237:183-190, 2012.
21. Nakamura M., Yamashita K., Polarization Effect on Wettability of Bioceramic Electrets, *IEEE Trans. Dielectr. Electr. Insul.*, 19(4):1247-1253, 2012.
22. Nakamura M, Soya T, Hiratai R, Nagai A, Hashimoto K, Morita I, Yamashita K. Polarized Endothelial Cell Migration and Morphogenesis on Silk Fibroin Scaffolds Including Hydroxyapatite Electret. *J. Biomed. Mater. Res. A*, 100A: 969-977, 2012.
23. Nakamura M, Horiuchi N, Nagai A, Yamashita K. Electrical Polarization Depresses Low Temperature Degradation and Promotes Bioactivity of Chemically Treated Yttria-Stabilized Zirconia. *Key. Eng. Mater.*, 493-494:11-15, 2012.
24. Hiratai R, Nakamura M, Nagai A, Yamashita K. The Storing Properties of Electric Energy in Bone. *Key. Eng. Mater.*, 493-494:170-174, 2012.

Books

1. Horiuchi N, Nakamura M, Nagai A, Yamashita K. Manipulation of Interfaces on Vector Materials. Chapter 17, Biological Interactions with surface charge Biomaterials, RSC Nanoscience & Nanotechnology No.21, Edited by Tofail Syed, Royal Society of Chemistry 2012.

Conferences

■Invited

1. Nakamura M. Improvement of wettability and osteoblastic adhesion by surface electric fields of polarized hydroxyapatite. 244th American Chemical Society National Meeting & Exposition. Philadelphia, PA, U.S.A., August 2012
2. Nagai A., Nozaki K., Yamashita K., Electrical Polarization on Titania-Coated Titanium and Its Application. AMDI-3, Toyohashi, Japan, Nov., 2012.
3. Yamashita K., Potentiality of Polarized Bioceramic electrets as *living biomaterials*. 2012 Asian Bioceramics symposium, Tainan, Taiwan, Nov., 2012.

■General

1. Nakamura M, Hentunen T, Nagai A, Yamashita K. Surface Electric Fields of Apatite Electret Promote Osteoblast Behaviors. 9th World Biomaterials Congress, Chengdu, China, June 2012.
2. Nagai, K. Igarashi, H. Miyazaki, K. Katayama, K. Yamashita. Electrically Polarized Hydroxyapatite Modulates Phenotype of SK-LMS-1 cells. 9th WBC, Chengdu, China, Jun., 2012.
3. Nozaki K., Nagai A., Yamashita K., Effect of Polarization Method on Osseointegration around Ti Implants. 9th World Biomaterials Congress, Chengdu, China, Jun., 2012.
4. Tsuchiya Y, Horiuchi N, Nakamura M, Nozaki K, Nagai A, Hashimoto K, Yamashita K., Effect of Polarization Treatment Time on Low Temperature Degradation of Yttria Stabilized Zirconia. The 6th International Conference on the Science and Technology for Advanced Ceramics (STAC-6), Yokohama, Jun., 2012.
5. Horiuchi N, Nozaki K, Nakamura M, Nagai A, Yamashita K. Influence of Defect Concentration on Dielectric and Polarization Property in Hydroxyapatite. 4th International Congress on Ceramics, Chicago, Illinois, Jul., 2012.
6. Tsuchiya Y, Horiuchi N, Nakamura M, Nozaki K, Nagai A, Hashimoto K, Yamashita K. Effect of Polarization Treatment Time on Inhibition of Low-temperature Degradation in Y-doped ZrO₂. Bioceramics 24, Fukuoka, Oct., 2012.
7. Koizumi H., Nozaki K., Nagai A., Okura T., Yamashita K., Application of Electrical Polarization on Dental Glassceramics. The 11th International Symposium on Advanced Technology, Tokyo, Oct., 2012.
8. Nozaki K., Nagai A., Yamashita K., Effect of Polarization Method on Bone Formation around Ti Implants. AMDI-3, Toyohashi, Japan, Nov., 2012.
9. Andoh H, Nakamura M, Horiuchi N, Nagai A, Toyama T, Yamashita K. Effects of Apatite Electret Fields on Osteocyte-to-osteoclast Interaction. The 12th Asian BioCeramics Symposium, Tainan, Taiwan, Nov., 2012.
10. Nakamura M, Kobayashi A, Nozaki K, Horiuchi N, Nagai A, Yamashita K. Improvement of Osteoblast Adhesion through Polarization of Plasma-sprayed Hydroxyapatite Coating on Titanium. 4th PCGMR-NCKU Symposium on Nano-Technology/Material for Bio-Medical Application, Tainan, Taiwan, Nov., 2012.
11. Hattori T., Nagai A., Aizawa M., Tamamura H., Yamashita K., Polarized Hydroxyapatite Modulates Cell Cycle and Promotes Differentiation of SK-LMS-1 Cells. 2012 Asian Bioceramics symposium, Tainan, Taiwan, Nov., 2012.
12. Hattori T., Nagai A., Aizawa M., Tamamura H., Yamashita K., Polarized Hydroxyapatite Inhibits Proliferation of SK-LMS-1 Cells. 4th PCGMR-NCKU Symposium on "Nano-Technology/Material for Bio-Medical application" Tainan, Taiwan, Nov., 2012.
13. Mukougawa K., Wada N., Horiuchi N., Hiyama T., Nakamura M., Nagai A., Okura T., Yamashita K., Properties of Surface Electric Field due to Hydroxyapatite Electret and its Application. The 11th International Symposium on Advanced Technology, Tokyo, Nov., 2012.
14. Nagai, A. Horiuchi N., Nakamura M., Yamashita K.. Quantitative Evaluation of the Hydrophilic Properties of Polarized Hydroxyapatite. MS&T' 12, Pittsburgh, USA, Oct., 2012.
15. Nakamura M, Hentunen T, Salonen J, Nagai A, Yamashita K. Recognition and Resorption of Synthesized Inorganic Substrata by Human Osteoclasts. Annual Meeting of The Korean Society for Biomaterials, Korea, Nov., 2012.

Periodontology

1. Staffs and Students

Professor	Yuichi IZUMI	
Associate Professor	Hisashi WATANABE	
Lecturer	Satsuki HAGIWARA,	Akira AOKI
Research Associate	Shinichi ARAKAWA(~June), Yasuo TAKEUCHI, Sayaka KATAGIRI(~April), Tomonari SUDA(Aug.~)	Hiroaki KOBAYASHI, Tatsuya AKIZUKI, Koji MIZUTANI(July~)
GCOE AI Supper Students	Azusa YAMADA, Mayumi OGITA, Ye CHANGCHANG,	Chui CHANTHOEUN, Norihiko ASHIGAKI, Supreda SUPHANANTACHAT
Graduate Students	Bhati PARIKSHA (~Sep.), Masanori SAWABE, Kaori FUJIWARA, Yasuo ITO, Asuka SEKINISHI, Yasuyuki KIMURA, Noriko MARUYAMA, Takahiko SHIBA, Shogo MAEKAWA, Takashi HOSHI, Masayuki TOI(April~), Takahiro IKAWA(April~), Masaru ONIZUKA(April~), Misa GOKYU(April~), Taicheng Lin(April~)	Marika TAKAHASHI, Naho KOBAYASHI, Tomoya HANATANI(~Sep.), Kenichiro EJIRI, Yuichi IKEDA, Akiko ENDO, Akiko TSUNO, Kuniha KONUMA, Takanori MATSUURA, Keiko AKAZAWA(April~), Masahiro NODA(April~), Ayano UEKUBU(April~), Makoto KANEKO(April~), Yuka SHIHEIDO(April~),

Hospital Staff: 7, Research Student: 18, Registered dentist: 33

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 CO₂ lasers. *Lasers Med Sci* (e-pub May 15th, 2012).
2. Aoyama N, Suzuki J, Ogawa M, Watanabe R, Kobayashi N, Hanatani T, Yoshida A, Ashigaki N, Izumi Y, Isobe M. Clarithromycin Suppresses the Periodontal Bacteria-Accelerated Abdominal Aortic Aneurysms in Mice. *J Periodontol*

Res. 47(4):463-469;2012

3. Belal MH, Watanabe H, Ichinose S, Ishikawa I. Effect of PDGF-BB combined with EDTA gel on adhesion and proliferation to the root surface. *Odontology* 100(2):206-214, 2012 .
4. Chui C, Hiratsuka K, Aoki A, Takeuchi Y, Abiko Y, Izumi Y. Blue LED Inhibits the Growth of *Porphyromonas gingivalis* by Suppressing the Expression of Genes Associated with DNA Replication and Cell Division. *Lasers Surg Med* 44:865-864, 2012.
5. Hamaya R, Ogawa M, Kobayashi N, Suzuki J, Itai A, Hirata Y, Nagai R, Isobe M. A novel IKK inhibitor prevents progression of restenosis after arterial injury in mice. *Int Heart J.* 53(2):133-138, 2012.
6. Hanatani T, Suzuki J, Ogawa M, Aoyama N, Kobayashi N, Hirata Y, Nagai R, Izumi Y, Isobe M. The periodontal pathogen *Aggregatibacter actinomycetemcomitans* deteriorates ventricular remodeling after myocardial infarction in mice. *Int Heart J* 53(4):253-256, 2012.
7. Himeno-Ando A, Izumi Y, Yamaguchi A, Iimura T. Structural differences in the osteocyte network between the calvaria and long bone revealed by three-dimensional fluorescence morphometry, possibly reflecting distinct mechano-adaptations and sensitivities. *Biochem Biophys Res Commun* 417(2):765-770, 2012.
8. Ito H, Numabe Y, Sekino S, Murakashi E, Iguchi H, Hashimoto S, Sasaki D, Yaegashi T, Kunimatsu K, Takai H, Maezawa 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* DOI 10.1007/s10266-012-0090-1 Published online: November 22nd, 2012.
9. Katagiri S, Nagasawa T, Kobayashi H, Takamatsu H, Bharti P, Izumiyama H, Uchimura I, Tagami T, Suzuki T, Nanbara H, Taniguchi Y, Hayakumo S, Koyanagi T, Himeno-Ando A, Goto M, Kajio H, Takahashi Y, Izumi Y, Noda M. Improvement of glycemic control after periodontal treatment by resolving gingival inflammation in type 2 diabetic patients with periodontal disease. *J Diabetes Invest* 3(4): 402-409, 2012
10. Kobayashi N, Suzuki J, Ogawa M, Aoyama N, Hanatani T, Hirata Y, Nagai R, Izumi Y, Isobe M. *Porphyromonas gingivalis* accelerates neointimal formation after arterial injury. *J Vasc Res.* 49(5):417-424. 2012.
11. Komaki M, Iwasaki K, Arzate H, Narayanan AS, Izumi Y, Morita I. Cementum protein 1 (CEMP1) induces a cementoblastic phenotype and reduces osteoblastic differentiation in periodontal ligament cells. *J Cell Physiol* 227:649-657, 2012
12. Mima A, Hiraoka-Yamamoto J, Li Q, Kitada M, Li C, Gerald P, Matsumoto M, Mizutani K, Park K, Cahill C, Nishikawa SI, Rask-Madsen C, King GL. Protective Effects of GLP-1 on Glomerular Endothelium and Its Inhibition by PKC β Activation in Diabetes. *Diabetes.* ([Epub ahead of print] Aug 3rd. 2012.)
13. Mima A, Kitada M, Gerald P, Li Q, Matsumoto M, Mizutani K, Qi W, Li C, Leitges M, Rask-Madsen C, King GL. Glomerular VEGF resistance induced by PKC δ /SHP-1 activation and contribution to diabetic nephropathy. *FASEB J.* 26(7):2963-74. 2012.
14. Nanbara H, Wara-aswapati N, Nagasawa T, Yoshida Y, Yashiro R, Bando Y, Kobayashi H, Khongcharoensuk J, Hormdee D, Pitiphat W, Boch JA, Izumi Y. Modulation of Wnt5a expression by periodontopathic bacteria. *PLoS One.* 2012;7(4):e34434. Epub Apr 2nd, 2012.
15. Rajakaruna GA, Umeda M, Uchida K, Furukawa A, Yuan B, Suzuki Y, Ebe N, Izumi Y, Eishi Y. Possible translocation of periodontal pathogen into the lymph nodes draining the oral cavity. *J Microbiol* 50(5):827-836, 2012
16. Sekinishi A, Suzuki J, Aoyama N, Ogawa M, Watanabe R, Kobayashi N, Hanatani T, Ashigaki N, Hirata Y, Nagai R, Izumi Y, Isobe M. A periodontal pathogen *Aggregatibacter actinomycetemcomitans* deteriorates pressure overload-induced myocardial hypertrophy in mice. *Int Heart J* 53(5):324-330, 2012
17. Takeuchi Y, Nagasawa T, Katagiri S, Kitagawara S, Kobayashi H, Koyanagi T, Izumi Y. Salivary levels of antibacterial peptide (LL-37/hCAP-18) and cotinine in periodontitis patients. *J Periodontol* 83(6):766-772, 2012.
18. Taniguchi Y, Aoki A, Mizutani K, Takeuchi Y, Ichinose S, Takasaki AA, Schwarz F, Izumi Y. Optimal Er:YAG laser irradiation parameters for debridement of microstructured fixture surfaces of titanium dental implants. *Lasers Med Sci* (e-pub Aug 11th, 2012).

Book

1. Koyanagi T, Takeuchi Y, Taniguchi Y, Izumi Y. Peri-implant disease and bacterial infection. WCOI Year Book 2001 –CD version- 1st Edition, Year Book Committee Publication, World Congress for Oral Implantology, Published in June 25th, Tokyo, Japan, pp26-32, 2012. (Short communication)
2. Taniguchi Y, Aoki A, Koyanagi Y, Takeuchi Y, Izumi Y, Oda S. Current Status of Various Approaches for Treatment of Peri-implant disease. WCOI Year Book 2001 –CD version- 1st Edition, Year Book Committee

Publication, World Congress for Oral Implantology, Published in June 25th, Tokyo, Japan, pp33-40, 2012. (Short communication)

3. Yuichi Izumi, Kozue Hasegawa-Nakamura, Kazuyuki Noguchi, Yasushi Furuichi. AT THE FOREFRONT IIIustrated Topics in Dental Research and Clinical Practice Edited by Hiromasa Yoshie, Quintessence publishing Co, Inc, pp.27-30, 2012

Health Promotion

1. Staffs and Students

Professor	Takehito Takano	
Assistant Professor	Masashi Kizuki,	Masafumi Watanabe
Graduate Student	Satoshi Suyama,	Pham Luu Hong (till September),
	Stephen Kibusi Mathew (till September),	
	Chau Darapheak,	Mari Uchimura,
	Aya Anzai,	Musafer Ajmal Pardis,
	Miho Ito,	Azusa Okada
Research Student	2 students	

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. 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. *Injury prevention*. 2013 Jan 15.
2. Nyambayar K, Nakamura K, Ohnishi M, Nakajima R, Urnaa V, Takano T. Purchase of Antimicrobials in Retail Pharmacies When a Prescription is Not Required. *Journal of rural medicine*. 2012 Nov;7(2):51-58.
3. Pichenda K, Nakamura K, Morita A, Kizuki M, Seino K, Takano T. Non-hospital DOT and early diagnosis of tuberculosis reduce costs while achieving treatment success. *The international journal of tuberculosis and lung disease*. 2012 Jun;16(6):828-34.
4. 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 Promotion International*. 2012 Jul 6.

Environmental Parasitology

1. Staffs and Students

Professor	Nobuo Ohta	
Associate Professor	Nobuaki Akao	
Assistant Professor	Takashi Kumagai, Mitsuko Suzuki,	Rieko Shimogawara, Takenori Seki
Project Professor	Takashi Suzuki	
Senior Technical staff	Misato Tomoda	
Graduate Student (PhD)	Takenori Seki, Keisuke Nakayama, Yuki Miyazawa, Katsumi Maezawa, Nobuhide Hata, Ripa Jamal	Toshie Taniguchi, Toshihiro Tokiwa, Katarina Macuhova, Toshio Arai, Francis Ekow Dennis,
Graduate Student (Master)	Masafumi Yamabe,	Emi Wada

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 helminthiases, 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 helminthiases, 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: Special

4. Clinical Services

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

5. Publications

Original articles

1. Seki T, Kumagai T, Kwansa-Bentum B, Furushima-Shimogawara R, Anyan WK, Miyazawa Y, Iwakura Y, Ohta N. Interleukin-4(IL-4) and IL-13 suppress excessive neutrophil infiltration and hepatocyte damage during acute murine schistosomiasis japonica. *Infect Immun*, 80: 159-168, 2012.
2. Kong QM, Lu SH, Tong QB, Lou D, Chen R, Zheng B, Kumagai, T, Wen LY, Ohta N, Zhou XN. Loop-mediated isothermal amplification (LAMP): early detection of *Toxoplasma gondii* infection in mice. *Parasit Vectors*, 5;2, 2012.
3. Tokiwa T, Harunari T, Tanikawa T, Komatsu N, Koizumi N, Tung KC, Suzuki J, Kadosaka T, Takada N, Kumagai T, Akao N, Ohta N. Phylogenetic relationships of rat lungworm, *Angiostrongylus cantonesis*, isolated from different

- geographical regions revealed widespread multiple lineages. *Parasitol Int.* 61: 431-436, 2012.
4. Fukae J, Kawanabe T, Akao N, Kado M, Tokoro M, Yokoyama K, Hattori N. Longitudinal myelitis caused by visceral larve migrans associated with *Toxocara cati* infection: case report. *Clin Neurol Neurosurg.* 114(7): 1091-1094, 2012
 5. Kitamura K, Kishi-Itakura C, Tsuboi T, Sato S, Kita K, Ohta N, Mizushima. Autophagy-related Atg8 localizes to the apicoplast of the human malaria parasite *Plasmodium falciparum*. *Plos One*, 7(8)e42977, 2012.
 6. El-Malky MA, Lu SH, El-Beshbishi SN, Saady NS, Ohta N. Effect of Mirazid in *Shistosoma japonicum*-infected mice: parasitological and pathological assessment. *Parasitol Res*, 112:373-377, 2012.
 7. N. Koizumi, C. Nakajima, T. Harunari, T. Tanikawa, T. Tokiwa, E. Uchimura, T. Furuya, C. Mingala, M. Villanueva, M. Ohnishi, and Suzuki Y. A new loop-mediated isothermal amplification method for rapid, simple, and sensitive detection of *Leptospira* spp. in urine. *Journal of Clinical Microbiology*, 50: 2072-2074, 2012
 8. 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, Jaapn. *J Helminthol*, 13:1-6, 2012.

Book

(None)

Forensic Medicine

1. Staff and Students

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

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. Aki T, Nara A, Uemura K. Cytoplasmic vacuolization during exposure to drugs and other substances. *Cell Biol Toxicol.* 2012;28(3):125-131.
2. Unuma K, Uozaki H, Kuroda R, Uemura K, Yoshida K. Death from axillary haemorrhage during haemodialysis in a patient with a history of microscopic polyangiitis. *BMJ Case Rep* 2012;doi:10.1136/bcr.11.2011.5194
3. Bessho M, Unuma K, Nara A, Uemura K. A case in which a bone fragment caused by a bullet made a second channel in addition to the bullet channel. *Leg Med (Tokyo).* 2012 July; 14(4):188-190.
4. Noritake K, Aki T, Funakoshi T, Unuma K, Nara A, Kato C, Uemura K. Critical roles of Rho-associated kinase in membrane blebbing and mitochondrial pathway of apoptosis caused by 1-butanol. *Toxicol in vitro.* 2012; 26(6):849-855.
5. Nara A, Aki T, Funakoshi T, Unuma K, Uemura K. Hyperstimulation of macropinocytosis leads to lysosomal dysfunction and cell death during exposure to methamphetamine in differentiated SH-SY5Y cells. *Brain Res.* 2012; 1466:1-14.
6. 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. *Hepatology Res.* 2012;doi: 10.1111/j.1872-034X.2012.01049.x
7. Unuma K, Aki T, Matsuda S, Funakoshi T, Yoshida K, Uemura K. Elimination and active extrusion of liver mitochondrial proteins during LPS administration in rat. *Hepatology Res.* 2012;doi: 10.1111/j.1872-034X.2012.01084.x

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	[Public Health Leaders Course] Suresh Babu Munuswamy, MD, MPH; Molina Honeyfaith Alteza, MPH; Al Rifai Rami Hani, DVM; Adam Izzeldin Fadl, MSc; Ghadah Al-khulaidi, MA; Mosiur Rahman MPH, Nguyen huu Chan Duc, MD Rasheed Abdul, MD Rakprasit Jutarat, MPH; Shagdarsuren Tserendulam, MA

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. Pichenda K, Nakamura K, Morita A, Kizuki M, Seino K, Takano T. Non-hospital DOT and early diagnosis of tuberculosis reduce costs while achieving treatment success. *International Journal of Tuberculosis and Lung Disease* 2012; 16: 828-834.
2. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and use of reproductive health services among married women: evidence from a national Bangladeshi sample. *BMC Public Health*. 2012; 12: 913.
3. Rahman M, Nakamura K, Seino K, Kizuki M. Intimate partner violence and chronic under nutrition among married Bangladeshi women of reproductive age: are the poor uniquely disadvantaged? *European Journal of Clinical Nutrition*. 2012; DOI:10.1038/ejcn.2012.202.
4. 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. *European Journal of Contraception and Reproductive Health Care* 2012; DOI: 10.3109/13625187.2012.745932.
5. Silatolu A, Nakamura K, Seino K, Kizuki M. Greater adherence to mass drug administration against lymphatic filariasis through traditional village forums in Fiji. *Journal of Rural Medicine*. 2012; 7(2): 65-72.
6. Nyambayar K, Nakamura K, Ohnishi M, Nakajima R, Urnaa V, Takano T. Purchase of antimicrobials in retail pharmacies when a prescription is not required. *Journal of Rural Medicine*. 2012; 7(2): 51-58.
7. Kibushi S , 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. *Injury Prevention*.
8. Rahman M, Poudel KC, Yasuoka J, Otsuka K, Yoshikawa K, Jimba M. Maternal exposure to intimate partner violence and the risk of undernutrition among children younger than 5 Years in Bangladesh. *American Journal of Public Health*. 2012;102(7):1336-45
9. Rahman M, Islam MT, Mostofa MG, Reza MS. Men's role in women's antenatal health status: evidence from rural Rajshahi, Bangladesh. *Asia Pacific Journal of Public Health*. 2012; DOI: 10.1177/1010539512437603
10. Naariyong S, Poudel KC, Rahman M, Yasuoka J, Otsuka K, Jimba M. Quality of antenatal care services in the Birim North District of Ghana: contribution of the community-based health planning and services program. *Maternal and Child Health Journal*. 2012 ;16(8):1709-17
11. Haque SE, Rahman M, Mostofa MG, Sarwar Zahan. Reproductive health care utilization among young mothers in Bangladesh: does autonomy matter? *Women's Health Issues*. 2012; 22(2):e171-80.
12. Roussan D, Shaheen I, Totanji W, Khawaldeh G, Al-Rifai R. Simultaneous Detection of *Clostridium perfringens* and *Clostridium colinum* by duplex-polymerase chain reaction. *Poultry Science*. 2012; 91(12): 3080-3085.
13. Roussan D, Shaheen I, Khawaldeh G, Totanji W, Al-Rifai R. Simultaneous detection of astrovirus, rotavirus, reovirus and adenovirus type I in broiler chicken flocks. *Polish Journal of Veterinary Sciences*. 2012; 15(2)337-344.

[Review Articles]

1. Nakamura K. Residential environment and Healthy Cities: Social design to nurture community support. *Universal Design* 2012; 33: 18-25.

[Books]

1. Mercado S, Havermann K, Nakamura K. Addressing health vulnerabilities of the urban poor in the 'new urban settings' of Asia. In: *The Urban Transformation: Health Shelter and Climate Change* (eds. Scar D, Volavka-Close N, Brown P) Taylors & Francis / Routledge, Abingdon, 2012.
2. Nakamura K. A model of community re-development. In: *Proposals for Restoration and Reconstruction following the Great East Japan Earthquake*. Giho-do, 2012.

[Conferences]

1. Nakamura K. Global Panel: Healthy Cities Movement for Healthy Futures around the World. Fifth Global Conference of the Alliance for Healthy Cities, Brisbane, Australia, October 2012.
2. Nakamura K. Healthy Active Transport. Fifth Global Conference of the Alliance for Healthy Cities, Brisbane, Australia, October 2012.
3. Iizuka A, Seino S. Strategic formulation of a reconstruction plan by applying the "Healthy Cities" approach to a municipality affected by the Great East Japan Earthquake. American Public Health Association 140th Annual Meeting Oct 29, 2012, San Francisco.
4. Rahman M. Economic inequality and utilization of reproductive health services in Vanuatu. The 71th Annual Meeting of the Japan Association of Public Health, Yamaguchi, October 2012.
5. Molina H. Improvements in maternal health services use in the Philippines from 1993 to 2008. The 71th Annual Meeting of the Japan Association of Public Health, Yamaguchi, October 2012.
6. Nakamura K, Takano T. Community development to protect health and lives. 17th Academic Conference of Japanese Association for Disaster Medicine, Kanazawa, February 2012.
7. Nakamura K. A model of community re-development. Japan Association of Planning Administration, Tokyo, July 2012.
8. Nakamura K. Healthy Cities and Healthy Settings Programs. Health and Hot Spring Forum, Tokyo, December 2012.

[International collaboration in research/education]

1. Nakamura K. Assessment of environmental conditions under rapid urbanization in Mongolia. Darkhan, Mongolia, March 2012.
2. Nakamura K. Healthy urban planning: Integrating infrastructural development and community efficacy. Korea Healthy Cities Workshop, Wonju, ROK, May, 2012.
3. Nakamura K. Application of Healthy Cities approach from a community diagnosis to a comprehensive city's plan: public-private-academic collaboration to witness the solid fact of progress. Meeting on national accreditation of Healthy City, Seoul, ROK, June, 2012.

[Collaboration with international organizations]

1. Nakamura K. Preparatory Meeting for Global Conference of the Alliance for Healthy Cities. WHO Western Pacific Regional Office, Manila, Philippines, March 2012.
2. Nakamura K. 13th Steering Committee Meeting of the Alliance for Healthy Cities. Brisbane, Australia, October 2012.
3. Nakamura K. 14th Steering Committee Meeting of the Alliance for Healthy Cities. Brisbane, Australia, October 2012.
4. Nakamura K, Seino K. *International Healthy Cities Symposium Looking 30 years ahead from the Great East Japan Earthquake*. Steering Committee of Healthy Cities, WHO Centre for Health Development, Tokyo, November 2012.
5. Nakamura K. Secretariat of the Alliance for Healthy Cities. January - December 2012.

[Collaboration with local and national public health programs]

1. Nakamura K. Commission on optimal application of Healthy Cities in Owariasahi City, Owariasahi City
2. Nakamura K. Healthy Cities in the world. Ichikawa WHO Wayo Group, January 2012.
3. Nakamura K. Community re-development and Healthy Cities. Community Development Forum in Wakuya, Wakuya, May 2012.
4. Nakamura K. Japan Chapter of the Alliance for Healthy Cities, Yamato, August 2012.
5. Nakamura K. WHO approach towards a Health City. Kasama, August 2012.

[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, 2012)

Professor	Kazuo KAWAHARA	
Assistant Professor	Makiko SUGAWA (December~)	
Graduate Student	Hidehito TAKENAKA,	Daiske IKEDA,
	Youichi SHIMA,	Eiko SHIMIZU,
	Souichirou MOCHIZUKI,	Takeo NIGA,
	Mutsumi UESUGI,	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	

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) Local healthcare system
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. Takashi Kawai, Kazuo Kawahara. A suggestion for changing the Act on Welfare of Physically Disabled Person regarding total hip and knee arthroplasty for osteoarthritis. (Japanese Journal of Joint Diseases. Vol 31(1), pp.21-32, 2012.)

International conference

1. Tareque, M. I., Kawahara, K., Islam, T. M., Sugawa, M., Takenaka, H., Ikeda, D., Kikuchi, M. and Ide, K.: Correlates of Self-rated Health at Old Ages in Rajshahi District of Bangladesh, presented in the 71st Japanese Society of Public Health Meeting, Venue: Shimin Kaikan Exhibition Hall in Yamaguchi Prefecture, Japan, Poster Session, October 24-26, 2012.
2. Tareque, M. I., Saito Y. and Kawahara, K.: Application of Health Expectancy Research on DHS data: A Case of Bangladesh, presented in the 24th REVES meeting, Venue: Chung Shan Medical University, Taichung, Taiwan, Paper Session, May 25-27, 2012.
3. Tareque, M. I., Hoque M. N. Islam, T. M., Kawahara, K. and Sugawa, M.: Active Aging Index and Healthy Life Expectancy in Rajshahi District of Bangladesh, presented in 2012 Annual Meeting of Population Association of America (PAA), Venue: The Hilton San Francisco Union Square, CA, USA, Poster Session, May 3-5, 2012.
4. Tareque, M. I., Hoque M. N. Islam, T. M., Kawahara, K. and Sugawa, M.: Rural-urban Differentials in Socio-economic Status of the Aging Population and Elderly Abuse in Rajshahi District of Bangladesh, presented in the 2012 Applied Demography Conference (ADC), Venue: Crown Plaza Riverwalk Hotel, San Antonio, Texas, USA, International Perspectives Session, January 8-12, 2012.

Review Article

None

Book

None

Molecular Epidemiology

1. Staffs and Students

Professor	Masaaki MURAMATSU	
Associate Professor	Noriko SATO	
Assistant Professor	Shinobu IKEDA	
Adjunct Instructor	Katsuko SUDO	
Graduate Student	Miki Yamada,	Kyi Chan Ko,
	Nay Chi Htun,	Cuneyd Palrayan,
	Atsuko Hiraishi,	Sae Masuda,
	Zhao Chen-xi,	Sariya Dechamethakun,
	Mia Sawabe,	Kaung Si Thu,
Research Students	Khin Thet Thet Zaw,	Azusa Sengoku

2. Education

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

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. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
4. The role of epigenetic regulation and fetal programming in common diseases.
5. Application of personal genome to preemptive & preventive medicine.

4. Publications

1. Ikeda S, Tanaka N, Arai T, Chida K, Muramatsu M, Sawabe M. Polymorphisms of LTA, LGALS2, and PSMA6 genes and coronary atherosclerosis: a pathological study of 1503 consecutive autopsy cases. *Atherosclerosis*. 221:458-60 (2012)
2. Ko MK, Ikeda S, Mieno-Naka M, Arai T, Zaidi SA, Sato N, Muramatsu M, Sawabe M. J *Atheroscler Thromb. Association of COMT gene polymorphisms with systemic atherosclerosis in elderly Japanese*.19:552-8 (2012)
3. Xi C, Miyaki K, Ikeda S, Song Y, Sinbo T, Muramatsu M. Association of GLUT4 gene variants with HbA1c level in Japanese men. *Endocr J*.59:677-84 (2012)
4. Ishii T, Hagiwara K, Kamio K, Ikeda S, Arai T, Mieno MN, Kumasaka T, Muramatsu M, Sawabe M, Gemma A, Kida K. Involvement of surfactant protein D in emphysema revealed by genetic association study. *Eur J Hum Genet*.20:230-5 (2012)
5. Ishii T, Hagiwara K, Ikeda S, Arai T, Mieno MN, Kumasaka T, Muramatsu M, Sawabe M, Gemma A, Kida K. Association between genetic variations in surfactant protein d and emphysema, interstitial pneumonia, and lung cancer in a Japanese population. *COPD* 9:409-16 (2012)
6. 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 Epub* 2012 Jul 3
7. 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.Epub* 2012 Sep 5

Research Development

1. Staffs and Students (April, 2012)

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)	Haruhisa INABA, Taku SAWANOBORI, Tomomi YOSHIMURA	Kazushige ENDO, Yasunori MATSUZAKI,

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, 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 Care Informatics

1. Staffs and Students (April, 2012)

Professor	Kiyohide FUSHIMI	
Graduate Student	Daisuke SATO,	Sayuri SHIMIZU,
	Takahiro INOUE,	Chihiro TAKAHASHI,
	Ayako ODA,	Kenjiro MATSUFUJI,
	Asako TUKASAKI,	Tsuyoshi KANEKO,
	Kyoko SHINODA,	Ayako MATSUO,
	Motoko SANO,	Toshihiro TAMAKI,
	Shiho OHAMA	

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. Sato, D., Fushimi, K. Impact of teaching intensity and academic status on medical resource utilization by teaching hospitals in Japan. *Health Policy*. 2012; 108(1): 86-92.
2. Imai, H., Fushimi, K. Factors associated with the use of institutional long-term care in Japan. *Geriatr Gerontol Int*. 2012; 12(1): 72-79.
3. Yasunaga H, Horiguchi H, Matsuda S, Fushimi K, Hashimoto H, Ohe K, Kokudo N. Relationship between hospital volume and operative mortality for liver resection: data from the Japanese Diagnosis Procedure Combination database. *Hepatol Res*. 2012; 42(11):1073-1080.
4. Yasunaga H, Horiguchi H, Hashimoto H, Matsuda S, Fushimi K. The Burden of Clostridium difficile-Associated Disease following Digestive Tract Surgery in Japan. *J Hosp Infect*. 2012; 82(3):175-80.
5. Sugihara T, Yasunaga H, Horiguchi H, Fujimura T, Ohe K, Matsuda S, Fushimi K, Homma Y. Impact of surgical intervention timing on Fournier's gangrene case fatality: an analysis of 379 cases. *BJU Int*. 2012; 110(11):E1096-100.
6. Kuwabara K, Hagiwara A, Matsuda S, Fushimi K, Ishikawa KB, Horiguchi H, Fujimori K: A community-based comparison of trauma patient outcomes between d- and l-lactate fluids. *The American journal of emergency medicine*. 2012; 31(1):206-214.
7. Kuwabara K, Matsuda S, Fushimi K, Ishikawa KB, Horiguchi H, Fujimori K. Contribution of the administrative database and the geographical information system to disaster preparedness and regionalization. *American Journal of Disaster Medicine*. 2012; 7(2):95-104.
8. Kuwabara K, Matsuda S, Fushimi K, Ishikawa K.B, Horiguchi H, Fujimori K Comparative Study on the Difference in Functional Outcomes at Discharge between Proximal and Total Gastrectomy. *Case Reports in Gastroenterology*. 2012; 6(2):400-409.
9. Okumura, Y., Shimizu, S., Ishikawa, K.B., Matsuda, S., Fushimi, K., Ito, H. Characteristics, procedural differences, and costs of inpatients with drug poisoning in acute care hospitals in Japan. *General Hospital Psychiatry*. 2012; 34(6):681-5.

Life Sciences and Bioethics (Bioethics Research Center)

1. Staffs and Students (April, 2012)

Director & Professor	Masayuki YOSHIDA	
Junior Associate Professor	Masumi AI, Yuka OZASA	
Assistant Professor	Mizuko OSAKA	
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, Shunsuke ITO, Hakubun KYO,	Katsuhiko HAMADA, Yûya MATSUE, 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 Metabolic Syndrome
- 2) A role of YY1 in atherosclerosis
- 3) Anti-atherosclerotic effect of lactotripeptide
- 4) A role of lipid absorption in intestine and subsequent metabolic pathways

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 cytogenic 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. Matsue Y, Suzuki M, Nagahori W, Ohno M, Matsumura A, Hashimoto Y, 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.* 2012 <http://dx.doi.org/10.1016/j.ijcard.2012.09.021>
2. 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 Intensive Lipid-Lowering Therapy With Rosuvastatin on Progression of Carotid Intima-Media Thickness in Japanese Patients. *Circ J.* 76: 221-229 (2012)
3. Van Himbergen TM, **Ai M.** Beiser AS, Seshadri S, Otokoza S, Au R, Wolf PA, Schaefer EJ. Biomarkers for insulin resistance and inflammation and the risk for all-cause dementia and alzheimer's disease: results from the Framingham Heart Study. *Arch Neurol.* 2012;69:594-600.
4. 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. A multicenter study on the precision and accuracy of homogeneous assays for LDL-cholesterol: comparison with beta-quantification method using fresh serum obtained from non-diseased and diseased subjects. *Atherosclerosis* 2012;225:208-15.

5. **Kanda E**, Yoshida M, Sasaki S. Applicability of fibroblast growth factor 23 for evaluation of risk of vertebral fracture and chronic kidney disease-mineral bone disease in elderly chronic kidney disease patients. *BMC Nephrol.* 26: 13: 122, 2012.

Oral/Poster Presentation

1. Ito S, Yagi Y, Yamato H, Osaka M, Yoshida M. INDOXYL SULFATE INCREASES Ly-6C^{hi} MONOCYTES AND NEOINTIMA FORMATION. ERA-EDTA Congress 2012, Paris, France, 2012.
2. Ito S, Goto S, Yamato H, Osaka M, Yoshida M. Chronic Kidney Disease-related Monocytes Inflammation Was Reduced by AST-120 Treatment. *Kidney week 2012: San Diego, USA, 2012.*
3. Ito S, Yagi Y, Goto S, Yamato H, Osaka M, Yoshida M. Indoxyl Sulfate Increases Ly6C^{high} Inflammatory Monocytes and Enhanced Neointima Formation in Response to Vessel Injury. *AHA Scientific Session 2012, Los Angeles, USA, 2012.*
4. Kataoka H, Nitta K, Osaka M, Yoshida M. Serotonin Antagonist Inhibits Leukocyte-Endothelial Interactions in Vivo and in vitro: Potential Contribution of Pkc-Dependent Pathway. *AHA Scientific Session 2012, Los Angeles, USA, 2012.*
5. Toyozaki M, Osaka M, Yoshida M, Kondo K. Fat loading enhances immuno-inflammatory reaction in mesenteric lymphocytes in vivo. *XVI International Symposium on Atherosclerosis 2012, Sydney, Australia, 2012.*
6. Ai M, Tomonaga O, Ogawa T, Tomie N, Tanaka A, Okazaki M, Yoshida M. Relationship between serum concentrations of cholesterol in 20 lipoprotein subfractions and cholesterol absorption and synthesis markers in patients with hypercholesterolemia *XVI International Symposium on Atherosclerosis. Sydney, Australia March, 2012.*
7. Ai M, Yoshida M, Tomonaga O, Ogawa T, Yamazaki M, Okazaki M, Tanaka A. The Effects of Ezetimibe on 20 lipoprotein subfractions in hyperlipidemic patients with or without type 2 diabetes mellitus (Results from the E-CAP Study) *Philadelphia, USA June, 2012.*
8. Yuka Ozasa, Miwa Suzuki, Naoko Nii, Masumi Ai, Masayuki Yoshida. Consideration about the Decision Making Process of the Molecular Genetics Predictive Test, *International Society Of Nurses in Genetics 25th annual conference, Philadelphia, October 2012.*
9. Yuka Ozasa, Miwa Suzuki, Naoko Nii, Masumi Ai, Eiichiro Kanda, Masayuki Yoshida. Current Cognition about Biobanks in Japan. *Public Responsibility in Medicine & Research, San Diego, December, 2012.*
10. Uno T, Akazawa M, Nishigaki K, Kuyama T, Yoshida S, Kanda E, Maeda Y. Cell population in peritoneal dialysis effluent reflects peritoneal membrane damage. *49th European Renal Association - European Dialysis and Transplant Association Congress, Paris, May, 2012.*
11. Akazawa M, Uno T, Kanda E, Maeda Y. Malnutrition and inflammation affect the viability of peritoneal mesothelial cells in peritoneal dialysis patients. *49th European Renal Association - European Dialysis and Transplant Association Congress, Paris, May, 2012.*
12. Kanda E, Yoshida M, Sei S. Rate of Change in Fibroblast Growth Factor 23 Level Predicts the Progression of Chronic Kidney Disease in Elderly Patients. *The 45th Annual Meeting of American Society of Nephrology, San Diego, October, 2012.*
13. Kanno Y, Kanda E, Sakamoto K, Nakajima K, Matsumoto Y, Watanabe S, Muneyuki T, Hirayama T. Estimating Daily Protein Intake by Urea Nitrogen Concentration in Spot Urine. *The 45th Annual Meeting of American Society of Nephrology, San Diego, October, 2012.*
14. Kanda E, Ai M, Maeda Y, Okazaki M, Sasaki S, Yoshida M. A New High-Performance Liquid Chromatography Showed That Icodextrin Dialysate Favorably Improved Lipid Profiles in Peritoneal Dialysis Patients. *The 45th Annual Meeting of American Society of Nephrology, San Diego, October, 2012.*
15. Akazawa M, Kanda E, Uno T, Maeda Y, Sasaki S. The Size and Viability of Mesothelial Cells Affect Peritoneal Membrane Functon. *The 45th Annual Meeting of American Society of Nephrology, San Diego, October, 2012.*

Invited Speaker

1. Yoshida M: Current Bioethical Issues Surrounding Biobanks in Japan *APREC2012 Singapore, March 2012*

Health Care Economics

1. Staffs and Students (April, 2012)

Professor	Koichi KAWABUCHI
Assistant Professor	Isao IGARASHI
Graduate Students	Mohammad Touhidul ISLAM, James Tumaini KENGIA, Masae AOTA
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) Economical analysis of the prevention program for metabolic syndrome and counter-programs against onset and progress of age-related conditions
- 2) Study on measurement of non-market output of the service industry (healthcare)
- 3) Quantitative analysis of big data in healthcare and review of related policies
- 4) Research on cost-effectiveness analysis of proton radiotherapy for pediatric tumor such as medulloblastoma
- 5) Impact assessment of OTC use on healthcare cost and the society

4. Publications

Original Articles

1. Kazumitsu Nawata, Koichi Kawabuchi: An Analysis of the New Japanese Payment System for Cataract Operations. *Public Health Frontier*, 1(1), 1-6, 2012.
2. Xuanxiu Liu: The efficiency of healthcare facilities providing PET cancer screening in Japan. *Japanese Journal of Radiology*, 30(3), 198-205, 2012.
3. Mohammad Touhidul Islam, Isao Igarashi, Koichi Kawabuchi: The impact of Gonoshasthaya Kendra's Micro Health Insurance plan on antenatal care among poor women in rural Bangladesh. *BioScience Trends*, 6(4), 165-175, 2012.
4. Akiko Kondo, Koichi Kawabuchi: Evaluation of the introduction of a diagnosis procedure combination system for patient outcome and hospitalisation charges for patients with hip fracture or lung cancer in Japan. *Health Policy*, 107(2-3), 184-193, 2012.

Review Article

1. Koichi Kawabuchi: The issues and future of the healthcare delivery system in Japan. *Japan Hospitals*, 31: 39-43, 2012.

Dental Education Development

1. Staff and Students

Professor	Ikuko MORIO
Junior Associate Professor	Jun TSURUTA
Graduate Student	Rei MUROGA, Akira TAKINAGA, Chinatsu MATSUKAWA (since April 2012)

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 PBL-tutorial, the students' research project, and the electives including various English courses for dental students.

3. Research Subjects

- 1) Comparative study of medical/dental education in Japan and overseas.
- 2) Study of research projects for medical/dental students
- 3) Development of English education programs for medical/dental students
- 4) Development of multimedia teaching materials for medical/dental students
- 5) Development of Japanese language learning materials for international students

4. Clinical Services

Clinic of Oral Diagnosis and General Dentistry (Dr. Tsuruta)

5. Publications

- 1) Tsuruta J, Morio I: A Report on Dental Education in Indonesia. JJDEA 28(2), 38-42, August 2012 (in Japanese).
- 2) Morio I, Tsuruta J, Takehara S, Kawaguchi Y: Dental Education in the Republic of Korea- White Paper on its 11 Dental Schools-. JJDEA 28(2), 43-55, August, 2012 (in Japanese).
- 3) Tsuruta J, Morio I: Quality Assurance System of Australian Dental Education. Jpn J. Dent. Prac. Admin. 47(3), 210-219, November 2012 (in Japanese).

Oral Health Promotion

1. Staffs and Students

Professor	Yoko Kawaguchi	
Associate Professor	Masayuki Ueno	
Assistant Professor	Takashi Zaitu (~March),	Sayaka Furukawa (April~)
Project Assistant Professor	Sachiko Takehara (~November)	
Hospital Staff	Mari Ohnuki	
Registered Resident	Hiromi Nishiyama,	Yukiko Fujishiro
Part-time Lecturer	Akiko Ohshiro (October~)	
Graduate Student	Akiko Ohshiro(~March),	Susumu Takeuchi(~March),
	Melissa Adiatman(~September),	
	Ayumi Takayama(~March),	Haslina Binti Rani,
	EiEi Aung(April~),	Anastasiya Blizniuk (October~)
Research Student	Motoko Ariake,	EiEi Aung(~March),
	Anastasiya Blizniuk (April~September)	

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) Graduate School, International Oral Health Cooperation

The educational purpose is to foster dental professionals who can conduct innovative, academic and international research that can contribute to health promotion in an international society, and can work as a leader of the international health cooperation.

3) 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. M Ueno, Y Izumi, Y Kawaguchi, A Ikeda, H Iso, M Inoue, S Tsugane : Pre-diagnostic Plasma Antibody Levels to Periodontopathic Bacteria and Risk of Coronary Heart Disease for the JPHC Study Group International Heart Journal, July 2012; 209-214
2. Adiatman M, Masayuki U, Mari O, Hakuta C, Shinada K, Kawaguchi Y: Functional Tooth Units and Nutritional Status of Older People in Care Homes in Indonesia, Gerodontology, online 20 May 2012.
3. Ueno M, Shinada K, Zaitso T, Yokoyama S, Kawaguchi Y: Effects of an oral health education program targeting oral malodor prevention in Japanese senior high school students, Acta Odontologica Scandinavica, 2012; 70: 426-431
4. 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 Scadinavica, 2012; Early Online, 1-6
5. A.Oshiro, S. Iseki, M. Miyauchi, T. Terashima, Y. Kawaguchi, Y. Ikeda, T. Shinomura: Lipopolysaccharide induces rapid loss of follicular dendritic cell-secreted protein in the junctional epithelium,Journal of Periodontal Research, 47; 6; 687-694, 2012
6. Pham TAV, Ueno M, Shinada K, Kawaguchi Y: Comparison between self-perceived and clinical oral malodor, Oral Surg Oral Med Oral Pathol Oral Padio 2012; 113: 70-80
7. M Ueno, K Shinada, T Zaitso, S Yokoyama, Y Kawaguchi. Effects of an oral health education program targeting oral malodor prevention in Japanese senior high school students, Acta Odontologica Scandinavica, 2012; 70: 426-431.
8. P. Samnieng, et al: Daily variation of oral malodor and related factors in community-dwelling elderly Thai, Gerodontology, 29(2) 964-971, 2012.
9. 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, online, 2012
10. Pham TAV, Ueno M, Shinada K, Kawaguchi Y: Factors affecting oral malodor in periodontitis and gingivitis patients, Journal of Investigative and Clinical Dentistry 2012, 3, 284-290
11. M Ueno, S Ohara, M Inoue, S Tsugane, Y Kawaguchi. Association between education level and dentition status in Japanese adults: Japan public health center-based oral health study, Community Dentistry and Oral Epidemiology, 40(6): 481-487, 2012.
12. Chisato Mori, Chiyoko Hakuta, Keiko Endo, Tadashi Nariai, Masayuki Ueno, Kayoko Shinoda, Yoko Kawaguchi: The effects of professional oral health care on patients in the subacute stage of emergent neurosurgical disorders. Spec Care Dentist 2012; 32(6): 259-264.

Sports Medicine/Dentistry

1. Staffs and Students (April. 2012)

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

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) Nakajima K, Takeda T, Kurokawa K, Hasegawa K, Narimatsu K, Kajima T, Sato T, Shimada A, Kondo Y, Ishigami K : Influence of mouthguard on single-tooth root distortion. *Int J Sports Dent* 5: 7-12, 2012.
- 2) Mishima O, Amemiya A, Kurokawa K, Nakajima K, Takeda T, Ishigami K : Effect of clenching and pinching force on activation on cortex involved in motor brain activity: an fMRI study. *Int J Sports Dent* 5: 35-43, 2012.

6. Presentations

Public Health

- 1) Mitsuyama A, Abe K, Churei H, Hayashi K, Ishigami T, Chowdhury RU, Sharika S, Ueno T: Clinical useful fabrication technique of custom faceguard for safely return to football after nasal bone fracture. Japan-China Dental Conference 2012, Chengdu, China, April 26-28, 2012.
- 2) Hayashi K, Churei H, Fujino S, Abe K, Ishigami T, Mitsuyama A, Chowdhury RU, Sharika S, Tanabe M, Ueno T: Clinical assessment of faceguards provided for football players sustained maxillofacial bone fractures. Japan-China Dental Conference 2012, Chengdu, China, April 26-28, 2012.
- 3) Sharika S, Chowdhury RU, Toyoshima Y, Takahashi T, Ueno T: A survey of dental traumatic injury among elite cricketers in Bangladesh. 100th FDI Annual World Dental Congress, Hong Kong, China, Aug 29 - Sep 1, 2012.
- 4) Chowdhury RU, Churei H, Takahashi H, Sharika S, Ueno T: Mouthguard design for sports-active person with spaced dentition. 100th FDI Annual World Dental Congress, Hong Kong, China, Aug 29 - Sep 1, 2012.

7. Grants and Fellowships

- 1) JSPS Grant-in-Aid for Scientific Research (Japan Society for the Promotion of Science, 2009.4-12.3). Ueno T, Takahashi T.
- 2) JSPS Grant-in-Aid for Scientific Research (Japan Society for the Promotion of Science, 2011.4-14.3). Takahashi T, Kato G, Ueno T.
- 3) Research Grant for Special Project (MEXT, 5 years from 2011). Yagishita K, Enomoto M, Ueno T, Takahashi T, et al.
- 4) 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.

8. Awards and Honors

N/A

9. Volunteer activities and International exchange, etc

- 1) Churei H, Sharika S, Chowdhury RU, Hayashi K, Mitsuyama A, Fujino S, Ueno T: Information of dental injury prevention, mouthguard and oral health care. 5th Rugby festival in Ichikawa city with Kubota Spears and NTT communications ShiningArcs, Ichikawa, Chiba, March 25, 2012.
- 2) Sharika S: Country introduction of Bangladesh. Bunkyo-ku International Cultural Exchange Festa 2012. Bunkyo Civic Center, Tokyo, Feb 18, 2012.
- 3) Ueno T, Churei H: Dental support. TOYOTA presents FIFA Club World Cup Japan 2012. Tokyo & Nagoya, Nov 26 – Dec 17, 2012.

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	Hirono KIKUCHI,	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. K. Sano, K. Tonami, S. Ichinose, K. Araki, Effects of ArF Excimer Laser Irradiation of Dentin on the Tensile Bonding Strength to Composite Resin, *Photomedicine and Laser Surgery*, 30(2), 71-76, 2012.

Educational Media Development

1. Staffs and Students

Professor	Astuhiko KINOSHITA
Assistant Professor	Masayo SUNAGA
Assistant Professor on Special Assignment	Yoko HAGIYA Izumi KIKUCHI

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 and Second-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. N Yoshida, T Aso, T Asaga, Y Okawa, H Sakamaki, T Masumoto, K Matsui, and A Kinoshita: Introduction and evaluation of computer-assisted education in an undergraduate dental hygiene course. *International Journal of Dental Hygiene* 10(1), p61-66, 2012.

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	Yasuko USHIO,	Mizuki IWAMA,
	Rie MASUDO,	Norihiko IZUMIMOTO,
	Ayumi TOBA,	Kae ITO,
	Tomomi HAKAMADA,	Yuki KISHIMOTO,
	Ryo NAKAYAMA,	Keita TAKAHASHI

2. Purpose of Education

- 1) Undergraduate education of medical students with a particular emphasis on geriatrics
- 2) Development of ability to conduct the 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. Iwama M, Amano A, Shimokado K, Maruyama N, Ishigami A. Ascorbic acid levels in various tissues, plasma and urine of mice during aging. *J Nutr Sci Vitaminol (Tokyo)*. 2012;58:169-74.
2. Iwama M, Kondo Y, Shimokado K, Maruyama N, Ishigami A. Uric acid levels in tissues and plasma of mice during aging. *Biol Pharm Bull*. 2012;35:1367-70
3. Sugita M, Sugita H, Kim M, Mao J, Yasuda Y, Habiro M, Shinozaki S, Yasuhara S, Shimizu N, Martyn JA, Kaneki M. Inducible nitric oxide synthase deficiency ameliorates skeletal muscle insulin resistance but does not alter unexpected lower blood glucose levels after burn injury in C57BL/6 mice. *Metabolism*. 2012;61:127-36
4. Ito K, Inagaki H, Okamura T, Shimokado K, Awata S. Factors associated with mental health well-being of urban community-dwelling elders in Japan: comparison between subjects with and without long-term care insurance certification. *Nihon Ronen Igakkai Zasshi*. 2012;49:82-9. Japanese

Rehabilitation Medicine

1. Staffs and Students (April, 2012)

Associate Professor	Sadao MORITA	
Graduate Student	Kazuhisa INOUE,	Akihito KUBOTA,
	Tomoko ARAKI,	Junya AIZAWA,
	Keisuke KAJI,	Risa NAKAYAMA,
	Kashitarou HYOUDOU,	Kinei BOKU,
	Chisato TAKADA,	Maierhaba AILIXIDING,
	Takanori KOKUBUN	

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. Yamauchi Yuki, Jinno Tetsuya, Koga Daisuke, Asou Yoshinori, Morita Sadao, Okawa Atsushi. Comparison of different distal designs of femoral components and their effects on bone remodeling in 1-stage bilateral total hip arthroplasty. *J Arthroplasty* 27: 1538-43, 2012.
2. Keisuke Kaji, Munenori Katoh, Koji Isozaki, Junya Aizawa, Tadashi Masuda, Sadao Morita. The Effect of Mastication on Reaction Latency to Unanticipated External Disturbances in the Standing Position. *Journal of Medical and Dental Sciences* 59: 2012.
3. Nakamaru K, Vernon H, Aizawa J, Koyama T, Nitta O. Cross-Cultural Adaptation, Reliability and Validity of the Japanese Version of the Neck Disability Index. *Spine* 37: 1343-1347, 2012.

Gerodontology

1. Staffs and Students

Professor	Hiroshi UEMATSU (~2012.3)	
Associate Professor	Tsuneto OHWATARI	
Junior Associate Professor	Ken' ichi KOBAYASHI,	Toshiaki SEKITA
Assistant Professor	Kazuo MOTOMURA, Shino MURATA, Syyuhei TAKEUCHI	Ayako NAKANE, Shinya MIKUSHI (~2012.3),
Project Assistant Professor	Satoshi TERANAKA, Yoshiko UMEDA,	Nobuhiro INOKUCHI, Kazuki TAKAHASHI (2012.4~),
Graduate Student	Ayako NOMURA (~2012.3), Souichi SHIBANO (~2012.3), Hiroshi MAEDA, Bai Doug Ying, Hirotaka SHOJI, Akemi HOSODA, Nami OGAWA (2012.4~),	Yousuke AKIMOTO(~2012.3), Hideo SAKAGUCHI, Chieko KUBOTA, Yu YOSHIZUMI, Sachiko OBA, Yu Su, Eiji Yoshii (2012.4~)

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

Most of medically compromised elderly patients have poor hemodynamic stability. Medical emergencies, such as hypertensive crisis, heart attack and severe arrhythmias, frequently occur in their dental practice. The prevention and prediction of medical emergencies are essential. The purpose of our research is to develop a noninvasive prediction system of medical emergencies in dental practice of medically compromised elderly. For this purpose, our research subjects are as follows: (1) Epidemiological study of medical history, medication and physical examination data in the medically compromised elderly patients, (2) Analysis of hemodynamic changes of those undergoing open heart surgery, (3) Analysis of arrhythmia during invasive dental treatment, (4) Linear and nonlinear analysis of biological signals, (5) Systemic identification analysis of closed loop circulatory system for the prediction of hypertensive crises, (6) Investigation of etiology and risk factors of medical emergencies during dental practice.

2. New Examination Method for Dry Mouth

Construction of an optical fiber oral fluid measurement system and development of oral moisture measurement devices are underway to provide new methods for examining dry mouth in elderly patients.

3. Oral Stereognosis Ability in the Elderly

We used near infra-red spectroscopy to measure brain activity of elderly people in an oral stereognosis ability test (OSA test). Furthermore, the OSA test is currently being reformed and examined for practical application as a screening test for dementia.

4. Threshold of Mucous Membrane under Denture Base in Elderly Oral Mucosa Patients

Using Semmes-Weinstein monofilaments we measured the pain threshold of the mucous membrane under the denture base and examined the change in pain threshold based on the number of remaining teeth or occlusal pattern. Furthermore, we examined possible causes of change in oral pain threshold.

5. State of the art Lasers in Zirconia Prosthetic Processing and Pain-free Treatment

With the goal of establishing a "ceramic crown digital process", we manufactured 3D CAD data for crowns and combined nanosecond lasers and femtosecond lasers and tested 3D high-speed laser processing of fully sintered

zirconia. We also examined the efficacy of natural teeth with a non-thermal femtosecond laser with an extremely small processing reaction force.

6. Denture Mobility

We have developed a inertial measurement unit device for the measurement of denture mobility. This system is composed of a accelerometer, a magnetometer, and a gyro.

7. Deglutition in Elderly Patients Requiring Nursing Care

We studied swallowing function in elderly patients in long-term nursing care facilities and the dietary planning and oral maintenance in those facilities.

We also examined the influence on food intake and swallowing function of foods with added fat that were developed to improve both ease of eating and nutrient levels.

8. Eating and Swallowing Rehabilitation in Post-Oral Tumor Surgery Patients

Our study focused on the swallowing dynamics of pills and the effects of the reclined position, with respect to eating and swallowing disability following oral tumor surgery. We also created a clinical pathway for them and are studying effective rehabilitation methods in order to speed up food intake.

9. Dysphagia of Medullary Infarction Patients

There are cases of lateral medullary syndrome patients in which food predominantly passes through the affected side, and the cause has been thought to be the laterality of the pharyngeal contraction during the swallowing reflex. Therefore we researched, compared and examined the laterality of the side of the pharynx on which food passes and the number of days after onset of condition, the presence of laterality of pharyngeal contraction, and the point position of food during the swallowing reaction.

10. Dental Approaches to Dysphagia

Coping methods for food intake and swallowing disability are primarily physical therapy approaches. By clarifying the effects of specific approaches from dental care practitioners, in order to clarify the importance of our existence in this field, we are studying Palatal Augmentation Prosthesis (PAP), Palatal Lift Prosthesis (PLP) and specialty oral care.

11. Screening Methods of Silent Aspiration

The majority of food intake and swallowing disability screening methods up until now used coughing during accidental swallowing as an index. So we examined the usefulness of a cough test as a screening method for silent aspiration in which there is no coughing. Furthermore, we are conducting research to increase the precision of screening without increasing the difficulty of evaluation.

12. Swallowing Dynamics and Brain Activity

Using optical topography devices we analyzed which regions of the brain were active during swallowing and application of food intake and swallowing rehabilitation methods.

4. Clinical Services

We manage the outpatient special care and the outpatient dysphagia rehabilitation.

1. Outpatient special care for department elderly:

Comprehensive dental treatment is given to patients who are 65 years and older with diseases spanning multiple specialties. We work together with outpatient specialty departments for complicated cases. Since many of our patients are elderly individuals with cardiovascular disease, in order to carefully manage their overall medical condition, we measure oxygen saturation with a pulse oximeter, perform electrocardiography, and monitoring a blood pressure at the time of their dental treatment. We perform invasive treatments under controlled monitoring by a specialist and take extra safety measures. In addition to providing treatment, we hold consultations before treatment and carry out highly predictable safety management.

2. Outpatient dysphagia rehabilitation:

Patients in this department are mainly inpatients from hospitals affiliated with a medical school or an oral surgery department. For inpatients from oral surgery departments, we conduct the examination and training. For inpatients of our hospitals, we work together with the hospitals physical therapy department. We organize collaboration with these physical therapy and oral surgery departments, and accept about 100 to 150 cases from these departments. With the opening of the new outpatient department, we have received more and more requests from pulmonary, gastroenterology, and head and neck outpatient departments, as well as general medicine clinics and telephone consultations. For each case,

we provide continuous guidance not only to the patients but also to associated workers and family members. Furthermore, we help introduce examination and training methods upon requests from other medical institutions that wish to practice dysphagia rehabilitation.

5. Publications

Original articles

1. Shibano S, Yamawaki M, Nakane A, Uematsu H : Palatal augmentation prosthesis (PAP) influences both the pharyngeal and oral phases of swallowing. *Deglutition* 1:204-209, 2012.
2. Wakasugi Y, Tohara H, Nakane A, Murata S, Mikushi S, Susa C, Takashima M, Umeda Y, Suzuki R, Uematsu H : Usefulness of a handheld nebulizer in cough test to screen for silent aspiration. *Odontology*. 2012 Oct 6 [Epub ahead of print]
3. Yosuke A, Setsuko K, Minoru O, Saeko A, Hiroshi U, Kyoko M : Age-associated reduction of stimulatory effect of ghrelin on food intake in mice., *Archives of Gerontology and Geriatrics*, 55 : 238-243, 2012.

Review Article

Book

Laboratory Medicine

1. Staffs and Students

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

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. Takahashi Y, Ishigaki T, Okuhashi Y, Ono A, Itoh M, Nara N, Tohda S. Effect of BMP4 on the growth and clonogenicity of human leukemia and lymphoma cells. *Anticancer Res.* 2012;32: 2813-2817.
2. Ono A, Okuhashi Y, Takahashi Y, Itoh M, Nara N, Tohda S. Advantages of the quenching probe method over other PCR-based methods for detection of the JAK2 V617F mutation. *Oncol Lett.* 2012;4:205-208.
3. Kanamori E, Itoh M, Tojo N, Koyama T, Nara N, Tohda S. Flow cytometric analysis of Notch1 and Jagged1 expression in normal blood cells and leukemia cells. *Exp Ther Med.* 2012; 4:397-400.
4. Kitamura Y, Sawabe E, Ohkusu K, Tojo N, Tohda S. First report of sepsis caused by *Rhodococcus corynebacterioides* in a patient with myelodysplastic syndrome. *J Clin Microbiol.* 2012;50: 1089-1091.

Critical Care Medicine

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

Associate Professor	Chieko MITAKA
Assistant Professor	Go Haraguchi (Intensive Care Unit) (2011.4.1~) Maiko Yamauchi (Intensive Care Unit) (2011.2.1~2012.5.31) Mamoru Yamamoto (Intensive Care Medicine) (2012.6.1~) Masatoshi Jibiki (Critical Care Meedicine) (2012.4.1~) Takahiro Toyofuku (Critical Care Medicine) (2011.4.1~)
Hospital Staff	Yasuhiro Ueda (Intensive Care Unit) (2011.10.1~2012.3.31) Yutaka MIYAWAKI (Intensive Care Unit) (2009.4.1~2012.3.31) Masanori Konishi (Intensive Care Unit) (2012.4.1~2011.6.30) Naoto Fujiwara (Intensive Care Unit) (2012.4.1~) 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. 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. *Surg Today*. 2012.
2. Jibiki M, Inoue Y, Kudo T, Toyofuku T. Surgical procedures for renal artery aneurysms. *Ann Vasc Dis*. 2012;5(2):157-160.
Nohara R, Daida H, Hata M, Kaku K, Kawamori R, Kishimoto J, Kurabayashi M, Masuda I, Sakuma I, Yamazaki T, Yokoi H, Yoshida M; Justification for Atherosclerosis Regression Treatment (JART) Investigators. Effect of intensive lipid-lowering therapy with rosuvastatin on progression of carotid intima-media thickness in Japanese patients: Justification for Atherosclerosis Regression Treatment (JART) study. *Circ J*. 2012;76(1):221-9.

【Conference】

1. Tulafu M, Mitaka C, K Hnin Si May, Atrial natriuretic peptide prevents acute kidney injury in renal ischemia-reperfusion injury rat model. The 41st Critical Care Congress of Society of Critical Care Medicine, Houston, Texas, USA, February 7, 2012
2. Mitaka C, Ueda Y, Miyawaki Y, Yamauchi M, Toyofuku T, Haraguchi G, Kudo T, Polymyxin B-immobilized fiber column hemoperfusion has the ability of endotoxin removal during 24 hrs. 32nd International Symposium on Intensive care and Emergency Medicine. Brussels, March 19, 2012
3. Mitaka C, Fujiwara N, Yamamoto M, Toyofuku T, Haraguchi G, Jibiki M. Blood purification in sepsis, The 3rd Critical Care Conference in Thailand, Bangkok, Thailand, July 13, 2012
4. Mitaka C., Therapy for acute exacerbation of interstitial pneumonia. Tbilisi's Fourth International Symposium, Tbilisi, the Republic of Georgia, November 27, 2012
5. Nakamura M, Jibiki M, Inoue Y and Yamazaki S. The treatment of Raynaud's phenomenon with 5-hydroxytryptamine_{2A} receptor antagonist, sarpogrelate hydrochloride. 7th Meeting of the German-Japanese Society for Vascular Surgery 2012/9/8 (Awajishima)
6. Nishizawa M, Uchiyama H, Katsui S, Igari K, MD Koizumi S, Toyofuku T, Kudo T, Jibiki M, Inoue Y. Multidisciplinary treatment of critical limb ischemia patients with hemodialysis. ASVS2012.
7. Nishizawa M, Uchiyama H, Katsui S, Igari K, MD Koizumi S, Toyofuku T, Kudo T, Jibiki M, Inoue Y. The strategy for extracranial carotid artery aneurysms. 7th Meeting of the German-Japanese Society for Vascular Surgery 2012/9/8 (Awajishima)

【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, 2012)

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	
Research Student	Okihiko AIHARA,	Ryuhō IBARAKI,
	Natsumi NAKAMURA.	

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. Takeuchi A, Matsushima E, Kato M, Konishi M, Izumiyama H, Murata Y, Hirata Y. Characteristics of neuropsychological functions in inpatients with poorly-controlled type 2 diabetes mellitus. *J Diabetes Invest* 3(3): 325-330, 2012.
2. Terauchi M, Hiramitsu S, Akiyoshi M, Owa Y, Kato K, Obayashi S, Matsushima E, Kubota T. Associations between anxiety, depression and insomnia in peri- and post-menopausal women. *Maturitas* 72(1): 61-65, 2012.
3. Suzuki M, Takahashi S, Matsushima E, Tsunoda M, Kurachi M, Okada T, Hayashi T, Ishii Y, Morita K, Maeda H, Katayama S, Otsuka T, Hirayasu Y, Sekine M, Okubo Y, Motoshita M, Ohta K, Uchiyama M, Kojima T:

- Relationships between exploratory eye movement dysfunction and clinical symptoms in schizophrenia. *Psychiat Clin Neurosci* 66(3): 187-194, 2012.
4. Ako Terakado, Takako Watanabe: Creation of a questionnaire to measure stress among nurses engaged in palliative care on general wards. *Support Care Cancer*. 20(10). 2012
 5. ICHIKURA K, MATSUOKA S, SHIMADA M, KOBAYASHI S, SUZUKI T, NISHIMURA K, SHIGA T, SUZUKI S, HAGIWARA N, ISHIGOOKA J. Factors Associated with Depression among Japanese Patients with Implantable Cardioverter Defibrillators. *International Journal of Behavioral Medicine*. 19(1): S46.2012
 6. A. Matsuda, K. Hara, M. Miyajima et al., Distinct pre-attentive responses to non-scale notes: An auditory mismatch negativity (MMN) study. *Clin Neurophysiol*. 2013; (in press).
 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. K. Hara, K. Ohta, A. Matsuda et al., Mismatch negativity for speech sounds in temporal lobe epilepsy. *Epilepsy Behav*. 2012 ;23(3):335-41.
 9. K. Hara, T. Maehara, A. Matsuda et al., Post-operative mismatch negativity recovery in a temporal lobe epilepsy patient with cavernous angioma. *Clin Neurol Neurosurg*. 2012; (in press).
 10. Noda T, Yoshida S, Matsuda T, Okamoto N, Sakamoto K, Koseki S, Numachi Y, Matsushima E, Kunugi H, Higuchi T. Frontal and right temporal activations correlate negatively with depression severity during verbal fluency task: A multi-channel near-infrared spectroscopy study. *Journal of Psychiatric Research*, 46: 905-912, 2012.

Pharmacokinetics and Pharmacodynamics

1. Staffs and Students (April, 2012)

Professor	Masato Yasuhara	
Associate Professor	Masashi Nagata	
Graduate Student	Ryosuke Isozaki,	Seiji Karakawa

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. Arino T, Karakawa S, Ishiwata Y, Nagata M, Yasuhara M.: Effect of cimetidine on pentamidine induced hyperglycemia in rats. *Eur. J. Pharmacol.*, 693, 72-79 (2012).
2. Kawano Y, Nagata M, Kohno T, Ichimiya A, Iwakiri T, Okumura M, Arimori K: Caffeine increases the antitumor effect of cisplatin in human hepatocellular carcinoma cells. *Biol. Pharm. Bull.*, 35, 400-407 (2012).

Medical Education Research and Development

1. Staffs and Students

Professor	Yujiro TANAKA	
Junior Associate Professor	Makoto TAKAHASHI,	Shinya OOKA,
	Yuki SUMI	
Project Junior Associate Professor	Toru SUGIYAMA	
Attending Staff	Akiko KITAZUME	

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, 2009 showed 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)

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 (Takahashi, Ooka)

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. Rie Ozeki, Sei Kakinuma, Kinji Asahina, Keiko Shimizu-Saito, Shigeki Arii, Yujiro Tanaka and Hirobumi Teraoka. Hepatic stellate cells mediate differentiation of dendritic cells from monocytes. *Journal of Medical and Dental Sciences* Vol.59 No.1, March 2012, Tokyo Medical and Dental University
2. Hirai T, Kawabata S, Enomoto M, Kato T, Tomizawa S, Sakai K, Yoshii T, Sakaki K, Takahashi M, Shinomiya K, Okawa A. Presence of anterior compression of the spinal cord after laminoplasty inhibits upper extremity motor recovery in patients with cervical spondylotic myelopathy. *Spine*. 2012 Mar 1;37(5):377-384.
3. Sakai K, Okawa A, Takahashi M, Arai Y, Kawabata S, Enomoto M, Kato T, Hirai T, Shinomiya K. Five-year Follow-up Evaluation of Surgical Treatment for Cervical Myelopathy Caused by Ossification of the Posterior Longitudinal Ligament: A Prospective Comparative Study of Anterior Decompression and Fusion With Floating Method Versus Laminoplasty. *Spine*. 2012 Mar 1;37(5):367-376.
4. Sonoda S, Taniguchi M, Sato T, Yamasaki M, Enjoji M, Mae S, Irie T, Ina H, Sumi Y, Inase N, Kobayashi T: Bilateral pleural fluid caused by a pancreaticopleural fistula requiring surgical treatment. *Intern Med* 51: 2655-2661, 2012

5. Chiba S, Jinta T, Chohnabayashi N, Fujie T, Sumi Y, Inase N: Bronchiolitis obliterans organising pneumonia syndrome presenting with neutrophilia in bronchoalveolar lavage fluid after breast-conserving therapy. *BMJ Case Reports* March 20: 2012. doi:pil:bcr0920114857. 10.1136/bcr.09.2011.4857.
6. Emma Calabrese a, Francesca Zorzi, Sara Zuzzi, Shinya Ooka Sara Onali, Carmelina Petruzzello, Giovanna Jona Lasinio, Livia Biancone a, Carla Rossi, Francesco Pallone : Development of a numerical index quantitating small bowel damage as detected by ultrasonography in Crohn's disease *Journal of Crohn's and Colitis*, Volume 6, Issue 8, Pages 852-860, September 2012
7. Masato Ozaka · Yuji Matsumura · Hiroshi Ishii · Yasushi Omuro · Takao Itoi · Hisatsugu Mouri · Keiji Hanada · Yasutoshi Kimura · Iruru Maetani · Yoshinobu Okabe · Masaji Tani · Takaaki Ikeda · Susumu Hijioka · Ryouhei Watanabe · Shinya Ohoka · Yuki Hirose · Masafumi Suyama · Naoto Egawa · Atsushi Sofuni · Takaaki Ikari · Toshifusa Nakajima : Randomized phase II study of gemcitabine and S-1 combination versus gemcitabine alone in the treatment of unresectable advanced pancreatic cancer (Japan Clinical Cancer Research Organization PC-01 study). *Cancer Chemother Pharmacol*. 69:1197-1204,2012
8. Kida M, Sugiyama T (corresponding author), 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): 211-215.
9. Kato M, Inoshita N, Sugiyama T, Tani Y, Shichiri M, Sano T, Yamada S, Hirata Y. Differential expression of genes related to drug responsiveness between sparsely and densely granulated somatotroph adenomas. *Endocr J*. 2012; 59(3): 221-228.
10. Hayakawa E, Yoshimoto T, Sekizawa N, Sugiyama T, Hirata Y. Overexpression of receptor for advanced glycation end products induces monocyte chemoattractant protein-1 expression in rat vascular smooth muscle cell line. *J Atheroscler Thromb* 2012; 19(1): 13-22.
11. Kusano-Kitazume A, Sakamoto N, Okuno Y, Sekine-Osajima Y, Nakagawa M, Kakinuma S, Kiyohashi K, Nitta S, Murakawa M, Azuma S, Nishimura-Sakurai Y, Hagiwara M, Watanabe M. Identification of novel N-(morpholine-4-carbonyloxy) amidine compounds as potent inhibitors against hepatitis C virus replication. *Antimicrob Agents Chemother*. 56(3):1315-23. 2012
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*. *Hepatology*. Jan;57(1):46-58. 2013

Acute Critical Care and Disaster Medicine

1. Staffs and Students (April, 2012)

Professor	Yasuhiro OTOMO	
Junior Associate Professor	Masahito KAJI,	Junichi AIBOSHI
Assistant Professor	Tomohisa SHOUKO,	Naoki TOSAKA,
	Atsushi SHIRAISHI,	Kiyoshi MURATA,
	Syusuke MORI,	Toshiki SERA,
	Akira ENDO,	Kazuhide YOSHIKAWA,
	Kenichi HONDO,	Kyuhei MIYAKAWA,
	Marie TAKAHASHI	
Hospital Staff	Mitsuaki KOJIMA,	Hiroyuki SATO,
	Yuka MISHIMA,	Nao MIKURA,
	Sayuri INAGAKI	
Graduate Student	Koji MORISHITA,	Saori MIKAMI,
	Hiroto USHIZAWA,	Minoru UEKI,
	Hideaki ANAN	
Resident	Sinya ENOMOTO,	Wataru TAKAYAMA,
	Raira NAKAMOTO,	Asahi NEHA

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. Koji Morishita, Junichi Aiboshi, Tetsuyuki Kobayashi, Saori Mikami, Yuri Yokoyama, Kari Ogawa, Hiroyuki Yokota, Yasuhiro Otomo: Lipidomics analysis of mesenteric lymph after trauma and hemorrhagic shock. *J Trauma Acute Care Surg.* 72:1541-7, 2012.
2. Sato Y, Isotani E, Kubota Y, Otomo Y, Ohno K: Circulatory characteristics of normovolemia and normotension therapy after subarachnoid hemorrhage, focusing on pulmonary edema. *Acta Neurochirurgica*, 154:2195-202, 2012.
3. Usuki M, Matsuoka Y, Nishi D, Yonemoto N, Matsumura K, Otomo Y, Kim Y, Kanba S: Potential impact of propofol immediately after motor vehicle accident on later symptoms of posttraumatic stress disorder at 6-month follow up: a retrospective cohort study. *Critical Care* 16:R196, 2012.
4. Shoko T, Otomo Y, Shiraishi A, Ueki U: The day after the disaster: a report from a Japanese disaster medical assistance team. *Disaster Medicine and Public Health Preparedness* 6:198-9, 2012.

5. Shigeki Kushimoto, Yasuhiko Taira, Yasuhide Kitazawa, Kazuo Okuchi, Teruo Sakamoto, Hiroyasu Ishikura, Tomoyuki Endo, Satoshi Yamanouchi, Takashi Tagami, Junko Yamaguchi, Kazuhide Yoshikawa, Manabu Sugita, Yoichi Kase, Takashi Kanemura, Hiroyuki Takahashi, Yuichi Kuroki, Hiroo Izumino, Hiroshi Rinka, Ryutarou Seo, Makoto Takatori, Tadashi Kaneko, Toshiaki Nakamura, Takayuki Irahara, Nobuyuki Saito, Akihiro Watanabe: The clinical usefulness of extravascular lung water and pulmonary vascular permeability index to diagnose and characterize pulmonary edema: a prospective multicenter study on the quantitative differential diagnostic definition for acute lung injury/acute respiratory distress syndrome. *Critical Care* 16:R232, 2012.
6. Okada K, Ohde S, Otani N, Sera T, Mochizuki T, Aoki M, Ishimatsu S: Prediction protocol for neurological outcome for survivors of out-of-hospital cardiac arrest treated with targeted temperature management. *Resuscitation* 83(6):734-9, 2012.

Clinical Oncology

1. Staffs and Students (April, 2012)

Professor	Satoshi MIYAKE
Associate Professor	Yasuaki NAKAJIMA
Assistant Professor	Hiroyuki SAKASHITA

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) Osteoplastic bone metastasis in esophageal squamous cell cancer: report of a case. Nakajima Y, Ohta S, Okada T, Miyawaki Y, Hoshino A, Suzuki T, Kawada K, Nishikage T, Nagai K, Ae K, Kawachi H, Kawano T. *Surg Today*. 2012;42:376-81
- 2) A pilot trial of S-1 plus irinotecan chemotherapy for esophageal adenocarcinoma. Nakajima Y, Fujiwara N, Ryotokuji T, Ohta S, Okada T, Miyawaki Y, Hoshino A, Jirawat S, Tokairin Y, Kawada K, Nishikage T, Nagai K, Kawano T. *Hepatogastroenterology*. 2012;59:2182-5.

Dentistry for Persons with Disabilities

1. Staffs and Students(April, 2012)

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	Mariko WATANABE,	Tomo SUZUKI,
	Anna KUMAKURA,	Naoki HAYASHI
Graduate Student	Yousuke KINOSHITA	
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) General research about the dentistry for persons with disabilities
- 2) Oral bacteria and systemic illness
- 3) Oral biofilm formation and elimination (Drug Delivery system)
- 4) Gingival overgrowth of the pharmacogenic
- 5) Dental phobia

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, autism, etc.
- 2) The patients requiring systemic support are internal impediment, dental phobia, etc.

5. Publications

Original articles

1. Norihiko Kanaguchi, Naoki Narisawa, Tatsuro Ito, Yosuke Kinoshita, Yasuka Kusumoto, Osamu Shinozuka, Hidenobu Senpuku: Effects of salivary protein flow and indigenous microorganisms on initial colonization of *Candida albicans* in an *in vivo* model. BMC Oral Health, 12:36, 2012

Abstracts

1. Y. Kinoshita., N. Kanaguchi., N. Narisawa., T. Ito., A. Tominaga., Y. Kusumoto., O. Shinozuka., H. Senpuku : Effects of salivary protein flow and indigenous microorganisms on initial colonization of *Candida albicans* in an animal model. biofilms 5 Program & Abstracts.171. 2012. (Biofilms 5 International Conference. Paris, 10-12 December, 2012

General Dentistry Oral Diagnosis and General Dentistry

1. Staffs and Students (April, 2012)

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	Tomohiro ISHIDA,	Shuhei NAKAMURA,
	Ayaka INAKAZU,	Yuko MITSUMA,
	Hirono KIKUCHI,	Akina ADACHI,
	Takahumi SUZUKI	

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 of oral appliance therapy in obstructive sleep apnea
- 3) Study on new oral diagnosis for comprehensive oral health care (ex. Caries diagnosis using digital imaging)
- 4) Study on new dental treatment based on concept of minimal intervention (ex. Selective caries removal using ArF excimer laser/ chemical solvent)
- 5) 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, oral care by dental hygienists, and oral appliance therapy of obstructive sleep apnea syndrome (OSAS).

5. Publications

Original Article

- 1) Kuboki T, Ichikawa T, Baba K, Hideshima M, Sato Y, Wake H, Nagao K, Kodaira-Ueda Y, Kimura-Ono, A, Tamaki K, Tsuga K, Sakurai K, Sato H, Ishibashi K, Yatani H, Ohyama T, Akagawa Y, Hirai T, Sasaki K, Koyano K: A multi-centered epidemiological study evaluating the reliability of the treatment difficulty indices developed by the Japan Prosthodontic Society, *J of Pros Res*: 56, 71-86, 2012.
- 2) Kazunobu Sano, Ken-ichi Tonami, Shizuko Ichinose, Kouji Araki, Effects of ArF excimer laser irradiation of dentin on the tensile bonding strength to composite resin, *Photomedicine and Laser Surgery*, 30(2), 71-76, 2012.
- 3) Marwa Madi, Osama Zakaria, Kanako Noritake, Masaki Fuji, Shohei Kasugai. Ligature-induced periimplantitis surrounding thin sputtered HA-coated implants. An experimental study in dogs. *Clinical and radiographic evaluations. Journal of Bio-Integration Vol.2 No.1,111-117, 2012*
- 4) Masayuki Ueno, Satoko Ohara, Manami Inoue, Shoichiro Tsugane, Yoko Kawaguchi, Association between education level and dentition status in Japanese adults: Japan public health center-based oral health study. *Community Dentistry and Oral Epidemiology*, 40(6): 481-487, 2012.
- 5) Miyajima D, Hayata T, Suzuki T, Hemmi H, Nakamoto T, Notomi T, Amagasa T, Bottcher RT, Costell M, Fassler R, Ezura Y, Noda M. Profilin1 regulates sternum development and endochondral bone formation. *J Bio Chem*

287(40):33545-53, 2012.

- 6) 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* 2012 Jul 17, doi: 10, 1111/j, 1447-0594, 2012, 00909.

6. Review articles

- 1) Kanako Noritake, Shinji Kuroda, Shohei Kasugai. Guided bone regeneration: membrane characteristics and future perspectives. *Nano Biomedicine* 4(1), 42-46, 2012.

Psychosomatic Dentistry

1. Staffs and Students (April, 2012)

Professor	Akira Toyofuku	
Assistant Professor	Satoshi Ishida	
Hospital Staff	Miho Takenoshita,	Emi Skou,
	Tomomi Sakuma Kurasawa	
Graduate Student	Tomoko Sato,	Ayano Katagiri,
	Yojiro Umezaki,	Motoko Watanabe

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) Katagiri A, Shinoda M, Honoda K, Toyofuku A, Sessle BJ, Iwata K.; Satellite glial cell P2Y₁₂ receptor in the trigeminal ganglion is involved in lingual neuropathic pain mechanisms in rats. *Molecular Pain* 2012 Mar 30;8:23
- 2) Miyamoto M, Tsuboi Y, Honda K, Kobayashi M, Takamiya K, Haganir RL, Kondo M, Shinoda M, Sessle BJ, Katagiri A, Kita D, Suzuki I, Oi Y, Iwata K.; Involvement of AMPA receptor GluR2 and GluR3 trafficking in trigeminal spinal subnucleus caudalis and C1/C2 neurons in acute-facial inflammatory pain. *PLoS One* 2012 Aug 24;7(8):e44055
- 3) Liu MG, Matsuura S, Shinoda M, Honda K, Suzuki I, Shibuta K, Tamagawa T, Katagiri A, Kiyomoto M, Ohara K, Furukawa A, Urata K, Iwata K.; Metabotropic glutamate receptor 5 contributes to inflammatory tongue pain via extracellular signal-regulated kinase signaling in the trigeminal spinal subnucleus caudalis and upper cervical spinal cord. *Journal of Neuroinflammation* 2012 Nov 27;9:258
- 4) Yoshihiro Abiko, Hirofumi Matsuoka, Itsuo Chiba, Akira Toyofuku : Current evidence on atypical odontalgia – Diagnosis and clinical management. *International Journal of Dentistry* Volume 2012, Article ID 518548, 6 pages. doi:10.1155/2012/518548

Abstract

- 1) Ayano Katagiri, Masamichi Shinoda, Koichi Iwata.; Satellite cell-P2Y₁₂ receptor in the trigeminal ganglion is involved in mechanical and thermal hyperalgesia in rats with lingual nerve injury. The 89th Annual Meeting of the Physiological Society of Japan, Matsumoto, March 29-31 2012.
- 2) Ayano Katagiri, Masamichi Shinoda, Akira Toyofuku, Koichi Iwata.; Satellite cell-P2Y₁₂ receptor in the trigeminal ganglion is involved in mechanical and thermal hyperalgesia in rats with lingual nerve injury. International Association for the Study of Pain, Milan, Aug 27-31 2012.
- 3) Miho Takenoshita, Tomoko Sato, Ayano Katagiri, Yojiro Umezaki, Motoko Watanabe, Tatsuya Yoshikawa, Akira Toyofuku : Clinical study on patients with Atypical Odontalgia. International Association for the Study of Pain, Milan, Aug 27-31 2012.
- 4) 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 asymmetries in patients with oral somatic delusions. 2nd CNS disease world summit, San Francisco, Sep 13-14, 2012.
- 5) Ayano Katagiri, Keiichiro Okamoto, David A Bereiter.; Orexin A inhibits ocular-evoked neural activity at trigeminal subnucleus caudalis in rats. Society for Neuroscience, New Orleans, Oct 13-17, 2012.

Behavioral Dentistry

1. Staffs and Students (April, 2012)

Professor	Shiro Mataki
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) Yuki Ohara, Hirohiko Hirano, Yutaka Watanabe, Ayako Eda, Emiko Sato, Shoji Shinkai, Hiroto Yoshida and Shiro Mataki. Masseter muscle tension and chewing ability in older persons. *Geriatrics Gerontology International*, 2012 Jul 17. doi: 10.1111/j.1447-0594.2012.00909.x. [Epub ahead of print]

Abstracted Papers Presented at Scientific Meeting

- 1) Aya Toyoshima, Shinichi Sato, Yasuyuki Gondo, Taketo Furuna, Shuichiro Watanabe, Hirohiko Hirano, Kiyoshi Hirabayashi, Akira Shimanouchi, Yuki Ohara, Subjective age and well-being among the Japanese elderly. 30th International Congress of Psychology (ICP2012), 25th of July, 2012, Cape town.
- 2) Suzuki K, Konoo T, Ito T, Chiba I, Yoshida T, Ogawa T, Oishi M, Tsuruta J, Aoki S, Mataki S, Kasai K, Follow-up session for participants of a seminar of the implementation of a communication training for faculty members in dental educational institutions, 38th ADEE Meeting, Lyon, France, August 29 - September 1, 2012.
- 3) Turuta J, Minakuchi S, Knazawa M, Uzawa N, Mataki S, Morio I, Araki K, Competences for the graduates of school of dentistry, Tokyo Medical and Dental University, 38th ADEE Meeting, Lyon, France, August 29 - September 1, 2012.
- 4) Tonami K, Nitta H, Mataki S, Change in students' perception of inter-personal relationships during "Introduction to the Behavioral science" class - Seven-year survey, 38th ADEE Meeting, Lyon, France, August 29 - September 1, 2012.
- 5) Toshiko Yoshida, Kazuyoshi Suzuki, Mika Oishi, Tetsuji Ogawa, Shiro Mataki, Kazutaka Kasai, Seminar on the communication training implementation for faculties in dental educational institutions, AMEE (The Association for Medical Education in Europe) Meeting, Lyon, France, 28 August, 2012(Conference Programme, p.101)

Temporomandibular Joint and Occlusion

1. Staffs (April, 2012)

Associate Professor	Koji KINO	
Assistant Professor	Akira NISHIYAMA	
Hospital Staff	Kaori TSUKAGOSHI,	Shoko TOBE,
	Natsuko OTOMO	

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 disfunctions of temporomandibular joint and masticatory muscles. We also provide the treatments for the nocturnal bruxism and the occlusal discomfort.

Neuroanatomy and Cellular Neurobiology

1. Staffs and Students

Professor	Sumio TERADA	
Assistant Professor	Masahiko KAWAGISHI,	Mitsunobu HOSHINO(-June)
	Kenta SAITO(July-),	Keisuke SATO(July-)
Graduate Student	Toshiya TERAISHI	
Technician	Mie TAGUCHI	

2. Purpose of Education

Section 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, we offer 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
- 6) Functional image analysis on neuropsychiatric disorders

4. Publications

1. ¹³C-phenylalanine breath test detects altered phenylalanine kinetics in schizophrenia patients. Teraishi T, Ozeki Y, Hori H, Sasayama D, Chiba S, Yamamoto N, Tanaka H, Iijima Y, Matsuo J, Kawamoto Y, Kinoshita Y, Hattori K, Ota M, Kajiwara M, Terada S, Higuchi T and Kunugi H. *Translational Psychiatry* 2, e119; doi:10.1038/tp.2012.48
Published online 22 May 2012.
2. Luminescent proteins for high-speed single-cell and whole-body imaging. Saito K, Chang Y-F, Horikawa K, Hatsugai N, Higuchi Y, Hashida M, Yoshida Y, Matsuda T, Arai Y, Nagai T. *Nat Commun* 3:1262. doi: 10.1038/ncomms2248. 2012.
3. Synchronized ATP oscillations have a critical role in prechondrogenic condensation during chondrogenesis. Kwon HJ, Ohmiya Y, Honma K, Honma S, Nagai T, Saito K, and Yasuda K. *Cell Death and Disease* 3, e278, 2012.

Systems Neurophysiology

1. Staff and Students

Professor	Izumi Sugihara
Associate Professor	Yuriko Sugiuchi
Lecturer	Yoshiko Izawa
Assistant Professor	Mayu Takahashi
Graduate Student (JSPS DC1)	Hirofumi Fujita

2. Education

We participate in “Introductory Neurophysiology” (lectures, 2nd year), “Neuroscience” (systematic lectures, 2nd and 3rd years) and “Physiology Lab” (2nd and 3rd years) courses for medical students 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. We have had a “project semester” student (4th year in the medical school) and an exchange student from Imperial College London.

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. Fujita H, Sugihara I (2012) FoxP2 expression in the cerebellum and inferior olive: development of the transverse

stripe-shaped expression pattern in the mouse cerebellar cortex. *J Comp Neurol.* **520**: 656-677.

2. Aoki H, Sugihara I (2012) Morphology of single olivocerebellar axons in the denervation-reinnervation model produced by subtotal lesion of the rat inferior olive. *Brain Res.* **1449**: 24-37.
3. Fujita H, Morita N, Furuichi T, Sugihara I (2012) Clustered fine compartmentalization of the mouse embryonic cerebellar cortex and its rearrangement into the postnatal striped configuration. *J. Neurosci.* **32**: 15688-15703.
4. Brown K, Sugihara I, Shinoda Y, Ascoli G (2012) Digital morphometry of rat cerebellar climbing fibers reveals distinct branch and bouton types. *J. Neurosci.* **32**: 14670-14686.

Pharmacology and Neurobiology

1. Staffs and Students (April, 2012)

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. Molecular basis of calcium channelopathy
2. Molecular mechanism of neurodegenerative disease
3. Mechanism of modal shift of cell sensor: from touch perception to pain sensation
4. Molecular mechanism of neuropathic pain
5. Molecular mechanism of drug tolerance
6. Hormonal modulation of stem cell development

4. Publications

Meetings:

1. Tsutomu Tanabe, Hironao Saegusa and Shuqin Zong: Contribution of the enhanced expression of N-type calcium channel in microglia on neuropathic pain, 14th World Congress on Pain, Milan Italy 8.27-31, 2012.
2. Tsutomu Tanabe, Hironao Saegusa and Shuqin Zong: Effect of N-type calcium channel deficiency in microglia on neuropathic pain, the 42nd annual meeting of the Society for Neuroscience, New Orleans USA 10.13-17, 2012.

Molecular and Cognitive Neuroscience (Department of Molecular Neuroscience)

1. Staffs and Students (April, 2012)

Professor	Kohichi Tanaka	
Associate Professor	Hidenori Aizawa	
Assistant Professor	Tomomi Aida	
Project Assistant Professor	Miho Soma	
Project Assistant Professor	Yukiko Ito	
Graduate Student	Bai Ning,	Michiko Yanagisawa,
	Hayato Sugiyama,	Yuichi Hiraoka,
	Zulpiye Habibulla,	Junya Sugimoto,
	Cui Wanpeng,	Sun Weinan

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

4. Publications

Original Article

1. Aizawa H, Kobayashi M, Tanaka S, Fukai T, Okamoto H. Molecular characterization of the subnuclei in rat habenula. *J Comp Neurol*. 2012, 520:4051-4066.
2. Suzuki, K., Maekawa, F., Suzuki, S., Nakamoi, T., Sugiyama, H., Kanamatsu, T., Tanaka, K., Ohki-Hamazaki, H. Elevated expression of brain-derived neurotrophic factor facilitates visual imprinting in chicks. *J Neurochem* 123. 800-810, 2012.
3. Hayashi, H., Eguchi, Y., Fukuchi-Nakanishi, Y., Takeya, M., Nakagata, N., Tanaka, K., Vance, JE., Tanihara, H. A potential therapeutic function of apolipoprotein E-containing lipoproteins for normal tension glaucoma. *J Biol Chem* 287. 25395-25406, 2012.
4. Aida, T., Ito, Y., Takahashi, YK., Tanaka, K. Overstimulation of NMDA Receptors Impairs Early Brain Development in vivo. *PlosOne* 7:eE36853, 2012.
5. Karlsson, R-M., Adwmark, L., Molander, A., Perreau-Lenz, S., Singley, E., Solomon, M., Holmes, A., Tanaka, K., Lovinger, DM., Spanagel, R., Heiling, M. Reduced alcohol intake and reward associated with impaired endocannabinoid signaling in mice with a deletion of the glutamate transporter GLAST. *Neuropsychopharmacology* 63. 181-189, 2012.
6. Tsai, M-C., Tanaka, K., Overstreet-Wadiche, L., Wadiche, JI. Neuronal glutamate transporters regulate glial excitatory transmission. *J Neurosci* 32. 1528-1535, 2012.

Neuropathology

1. Staff and Students (April 2012)

Professor:	Hitoshi Okazawa	
Associate Professor:	Kazuhiko Tagawa	
Adjunct Lecturer:	Nobuyuki Nukina,	Masaki Sone,
	Toshiki Uchihara	
Assistant Professor:	Takuya Tamura	
Project Assistant Professor:	Hikaru Ito	
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	
Technicians:	Tayoko Tajima,	Chiharu Mizoi,
	Yuko Uyama,	Kimiko Ibagawa
Secretary:	Mari Kishimoto	
Graduate Students:	Ying Mao,	Min Xu,
	Chan Li,	Hong Zhang,
Research Trainees:	Asuka Katsuta	

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. Nakamura, Y., Tagawa, K., Oka, T., Sasabe, T., Ito, H., Shiwaku, H., La Spada, A.R. and Okazawa, H. (2012). Ataxin-7 associates with microtubules and stabilizes the cytoskeletal network. *Hum Mol Genet.* 21 (5): 1099-1110. doi: 10.1093/hmg/ddr539
2. Ress, M., Gorba, C., Gorba, C., de Chiara, C., Bui, T.T.T., Garcia-Maya, M., Drake, A.F., Okazawa, H., Pastre, A., Svergun, D. and Chen, Y.W. (2012). The solution model of the intrinsically disordered polyglutamine tract binding protein-1 (PQBP-1). *Biophys J.* 102:1608-1616. doi: 10.1016/j.bpj.2012.02.047
3. Tamura T., Sone M., Nakamura Y., Shimamura T., Imoto S., Miyano S. and Okazawa H. (2012). A restricted level of PQBP1 is needed for the best longevity of Drosophila. *Neurobiology of Aging.* 2013 Jan;34(1):356.e11-20. doi: 10.1016/j.neurobiolaging.2012.07.015

Ophthalmology and Visual Science

1. Staff and students (April, 2012)

Professor;	Manabu Mochizuki	
Associate Professor;	Kyoko Ohno-Matsui	
Assistant Professor;	Yoshiharu Sugamoto,	Hiroshi Takase
Hospital staff;	Akiko Tanaka,	Koju Kamoi,
	Masaru Miyanaga,	Manabu Ogawa.
Graduate student;	Moriyama Muka,	Murai Hideki,
	Yuko Kawazoe,	Ayano Imai,
	Naonori Ohno,	Kousei 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 retinchoroidal 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. Sugita S, Kamoi K, Ogawa M, Watanabe K, Shimizu N, Mochizuki M. Detection of *Candida* & *Aspergillus* species DNA using broad-range real-time PCR for fungal endophthalmitis. *Graefes Arch Clin Exp Ophthalmol*, 2012; 250: 391-398.
2. Kawazoe Y, Sugita S, Keino H, Yamada Y, Imai A, Horie S, Yamagami S, Mochizuki M. Retinoic acid from retinal

- pigment epithelium induces T regulatory cells. *Exp Eye Res*, 2012; 94: 32-40.
3. Shimizu M, Suzuki Y, Kiyosawa M, Wakakura M, Ishii K, Ishiwata K, Mochizuki M. Glucose hypermetabolism in the thalamus of patients with hemifacial spasm. *Mov Disord*, 2012; 27: 519-525.
 4. Akagi-Kurashige Y, Kumagai K, Yamashiro K, Nakanishi H, Nakata I, Miyake M, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yamada R, Matsuda F, Yoshimura N. Vascular endothelial growth factor gene polymorphisms and choroidal neovascularization in highly myopic eyes. *Invest Ophthalmol Vis Sci*, 2012; 53: 2349-2353.
 5. Sugita S, Kawazoe Y, Imai A, Yamada Y, Horie S, Mochizuki M. Inhibition of Th17 differentiation by anti-TNF- α therapy in uveitis patients with Behcet's disease. *Arthritis Res Ther*, 2012; 14: R19
 6. Ogawa M, Sugita S, Watanabe K, Shimizu N, Mochizuki M. Novel diagnosis of fungal endophthalmitis by broad-range real-time PCR detection of fungal 28S ribosomal DNA. *Graefes Arch Clin Exp Ophthalmol*, 2012; 250: 1877-83.
 7. Nagata K, Maruyama K, Uno K, Shinomiya K, Yoneda K, Hamuro J, Sugita S, Yoshimura T, Sonoda KH, Mochizuki M, Kinoshita S. Simultaneous Analysis of Multiple Cytokines in the Vitreous of Patients with Sarcoid Uveitis. *Invest Ophthalmol Vis Sci*, 2012; 53: 3827-33.
 8. Sugita S, Shimizu N, Watanabe K, Ogawa M, Maruyama K, Usui N, Mochizuki M. Virological Analysis in Patients with Human Herpes Virus 6 (HHV-6)-Associated Ocular Inflammatory Disorders. *Invest Ophthalmol Vis Sci*, 2012; 53: 4692-4698.
 9. Ogawa M, Sugita S, Shimizu N, Watanabe K, Nakagawa I, Mochizuki M. Broad-range real-time PCR assay for detection of bacterial DNA in ocular samples of infectious endophthalmitis. *Jpn J Ophthalmol*, 2012; 56: 529-535.
 10. Kojima K, Maruyama K, Inaba T, Nagata K, Yasuhara T, Yoneda K, Sugita S, Mochizuki M, Kinoshita S. The CD4/CD8 Ratio in Vitreous Fluid Is of High Diagnostic Value in Sarcoidosis. *Ophthalmology*, 2012; 119: 2386-92.
 11. Ohguro N, Sonoda K, Takeuchi M, Matsumura M, Mochizuki M. The 2009 prospective multi-center epidemiologic survey of uveitis in Japan. *Jpn J Ophthalmol*, 2012; 56: 432-435.
 12. Shimizu M, Suzuki Y, Kiyosawa M, Wakakura M, Ishii K, Ishiwata K, Mochizuki M. Glucose hypermetabolism in the thalamus of patients with hemifacial spasm. *Mov Disord*, 2012; 27: 519-525.
 13. Imai A, Sugita S, Kawazoe Y, Horie S, Yamada Y, Keino H, Maruyama K, Mochizuki M. Immunosuppressive properties of regulatory T cells generated by incubation of peripheral blood mononuclear cells with supernatants of human RPE cells. *Invest Ophthalmol Vis Sci*, 2012; 53: 7299-7309.
 14. Suzuki Y, Emoto H, Kiyosawa M. Hemifacial spasm-A review and update. *Neuro-ophthalmol Japan*, 2012; 29: 111-118.
 15. Suzuki Y, Nariai T, Kiyosawa M, Mochizuki M, Kimura Y, Oda K, Ishii K, Ishiwata K. Increased adenosine A1 receptor levels in hemianopia patients after cerebral injury: an application of PET using 11C-8-dicyclopropylmethyl-1-methyl-3-propylxanthine. *Clin Nucl Med*, 2012; 37: 1146-1151.
 16. Ishiwata K, Shimada J, Wang WF, Harakawa H, Ishi S, Kiyosawa M, Suzuki F, Senda M. Evaluation of iodinated and brominated [11C]styrylxanthine derivatives as in vivo radioligands mapping adenosine A2A receptor in the central nervous system *Annals of Nuclear Medicine* 2012;14:247-253.
 17. Murai H, Suzuki Y, Kiyosawa M, Tokumaru AM, Ishii K, Mochizuki M. Positive correlation between the degree of visual field defect and optic radiation damage in glaucoma patients. *Jpn J Ophthalmol*. (in press).
 18. Kawazoe Y, Sugita S, Yamada Y, Akino A, Miura K, Mochizuki M. Psoriasis Triggered by Infliximab in a Patient with Behcet's Disease. *Jpn J Ophthalmol*. 2012, in press. [Epub ahead of print]
 19. 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*, (in press)
 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*, (in press)
 21. Hayashi K, Katori N, Kasai K, Kamisasanuki T, Kokubo K, Ohno-Matsui K. Comparisons of nylon monofilament suture to polytetrafluoroethylene sheet for frontalis suspension surgery in eyes with congenital ptosis, *Am J Ophthalmol* (in press)
 22. Ishida T, Ohno-Matsui K, Mochizuki M. Polypoidal choroidal vasculopathy in a case with retinitis pigmentosa. *Int Ophthalmol*, (in press)
 23. 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. Association of paired Box 6 with high myopia in Japanese. *Mol Vis*, (in press)
 24. 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, (in press)

25. Ohno-Matsui K, Akiba M, Ishibashi T, Moriyama M. Observations of vascular structures within and posterior to sclera in eyes with pathologic myopia by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci*, 2012; 53: 7290-7298.
26. Ohno-Matsui K, Akiba M, Modegi T, PhD, Tomita M, Ishibashi T, Tokoro T, Moriyama M. Association between shape of sclera and myopic retinochoroidal lesions in patients with pathologic myopia. *Invest Ophthalmol Vis Sci*, 2012; 53: 6046-6061.
27. Wang J, Ohno-Matsui K, Morita I. Cholesterol enhances amyloid β deposition in mouse retina by modulating the activities of A β -regulating enzymes in retinal pigment epithelial cells. *Biophys Biochem Res Commun*, 2012; 424: 704-709.
28. Moriyama M, Ohno-Matsui K, Modegi T, Kondo J, Takahashi Y, Tomita M, Tokoro T, Morita I. Quantitative analyses of high-resolution 3D MR images of highly myopic eyes to determine their shapes. *Invest Ophthalmol Vis Sci*, 2012; 53: 4510-4518.
29. Wang J, Ohno-Matsui K, Morita I. Elevated amyloid β production in senescent retinal pigment epithelium, a possible mechanism of age-related subretinal accumulation of amyloid β . *Biochem Biophys Res Commun*, 2012; 423: 73-78.
30. Verhoeven VJ, Hysi PG, Saw SM, Vitart V, Mirshahi A, Guggenheim JA, Cotch MF, Yamashiro K, Baird PN, Mackey D, Wojciechowski, Ikram MK, Hewitt AW, Duggal P, Janmahasatian S, Khor CC, Fan Q, Zhou X, Young TL, Tai ES, Goh LK, Li YJ, Aung T, Vithana E, Teo YY, Tay W, Sim X, Rudan I, Hayward C, Wright AF, Polasek O, Campbell H, Wilson JF, Fleck BW, Nakata I, Yoshimura N, Yamada R, Matsuda F, Ohno-Matsui K, Nag A, McMahon G, Pourcain BS, Lu Y, Rahi JS, Cumberland PM, Bhattacharya S, Simpson CL, Atwood LD, Li X, Raffel L, Murgia F, Portas L, Despret DD, van Koolwijk LM, Wolfram C, Lackner K, Tonjes A, Magi R, Lehtimäki T, Kahonen M, Esko T, Metspalu A, Rantanen T, Parssinen O, BE, Meitinger T, Spector TD, Oostra BA, Smith AV, de Jong PT, Hofman A, Amin N, Karssen LC, Rivadeneira F, Vingerling JR, Eiriksdottir G, Gudnason V, Doring A, Bettecken T, Uitterlinden AG, Williams C, Zeller T, Castagne R, Oexle K, van Duijn CM, Iyengar SK, Mitchell P, Wang JJ, Hohn R, Pfeiffer N, Bailey-Wilson JE, Stambolian D, Wong TY, Hammond CJ, Klaver CC. Large scale international replication and meta-analysis study confirms association of the 15q14 locus with myopia. The CREAM consortium. *Human Genet*, 2012; 131: 1467-1480.
31. Fan Q, Barathi VA, Cheng CY, Zhou X, Meguro A, Nakata I, Khor CC, Goh LK, Li YJ, Lim W, Ho CEH, Hawthorne F, Zheng Y, Chua D, Inoko H, Yamashiro K, Ohno-Matsui K, Matsuo K, Matsuda F, Vithana E, Seielstad M, Mizuki N, Beuerman RW, Tai ES, Yoshimura N, Aung T, Young TL, Wong TY, Teo YY, Saw SM. Genetic variants on chromosome 1q41 influence ocular axial length and high myopia. *PLOS Genetics*, 2012; 8: e1002753.
32. Shimada N, Sugamoto Y, Ogawa M, Takase H, Ohno-Matsui K. Fovea-sparing internal limiting membrane peeling for myopic traction maculopathy. *Am J Ophthalmol*, 2012; 154: 693-701.
33. Asakuma T, Yasuda M, Ohno-Matsui K, Ishibashi T. Prevalence and risk factors for myopic retinopathy in a Japanese population: the Hisayama Study. *Ophthalmology*, 2012; 119: 1760-1765.
34. Spaide RF, Akiba M, Ohno-Matsui K. Evaluation of peripapillary intrachoroidal cavitation with swept source and enhanced depth imaging optical coherence tomography. *RETINA*, 2012; 32: 1037-1044.
35. Akagi-Kurashige Y, Kumagai K, Yamashiro K, Nakanishi H, Nakata I, Miyake M, Tsujikawa A, Moriyama M, Ohno-Matsui K, Mochizuki M, Yamada R, Matsuda F, Yoshimura N. Vascular endothelial growth factor gene polymorphisms and choroidal neovascularization in highly myopic eyes. *Invest Ophthalmol Vis Sci*, 2012; 53: 2349-2353.
36. Ohno-Matsui K, Akiba M, Moriyama M, Ishibashi T, Hirakata A, Tokoro T. Intrachoroidal cavitation in macular area of eyes with pathologic myopia. *Am J Ophthalmol*, 2012; 154: 382-393.
37. Ohno-Matsui K, Akiba M, Moriyama M, Shimada N, Ishibashi T, Tokoro T, Spaide RF. Acquired Optic Nerve and Peripapillary Pits in Pathologic Myopia. *Ophthalmology*, 2012; 119: 1685-1692.
38. Tsuchiya K, Moriyama M, Ohno-Matsui K. Development of peripapillary venous loop in eye with small optic disc. *Int Ophthalmol*, 2012; 32: 171-175.
39. Hayashi K, Shimada N, Moriyama M, Hayashi W, Tokoro T, Ohno-Matsui K. Two Year Outcomes of Intravitreal Bevacizumab for Choroidal Neovascularization in Japanese Patients with Pathological Myopia. *RETINA*, 2012; 32: 687-695.

1. Mochizuki M, Sugita S, Kamoi K. Immunological homeostasis of the eyes. *Prog Retin Eye Res*, 2012; S1350-9462(12)00072-9.
2. Ohno-Matsui K. Study finds intravitreal anti-VEGF effective for non-subfoveal myopic CNV. *Ocular Surgery News*, 2012; 23: 67-70.
3. Morgan I, Ohno-Matsui K, Saw SM. Myopia. *Lancet*, 2012; 379: 1739-1748.
4. Kamoi K, Mochizuki M. HTLV-1 uveitis. *Front Microbiol*, 2012; 3: 270.
5. Kamoi K, Mochizuki M. HTLV infection and the eye. *Curr Opin Ophthalmol*, 2012; 23:557-561.
6. Neelam K, Cheung CMG, Ohno-Matsui K, Lai TYY, Wong TY. Choroidal Neovascularization in Pathological Myopia. *Progress in Retinal and Eye Research*, 2012; 31: 495-525.
7. Takase H, Mochizuki M. The role of imaging in the diagnosis and management of ocular sarcoidosis. *Int Ophthalmol Clin*, 2012; 52: 113-20.

[Presentation]

1. Ohno-Matsui K, Masahiro Akiba, Muka Moriyama, Noriaki Shimada, Takashi Tokoro, Richard F. Spaide. Acquired pits in the optic disc and conus in the eyes with pathologic myopia. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012.5.5
2. Liu J, Copland D A, Horie S, Morgan B P, Nicholson L B, Dick A D. Local Anti-C5 Therapy Suppresses Experimental Choroidal Neovascularization Through Reduction of Macrophage Infiltrate. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012.5.6
3. Wang J, Ohno-Matsui K, Mochizuki M, Morita I. Amyloid beta enhances migration of endothelial progenitor cells via upregulation of CX3CR1. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.7
4. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.7
5. Moriyama M, Ohno-Matsui K, Ikuo Morita, Junichi Kondo, Toshio Modegi, Yoichi Takahashi. Qualitative and quantitative analyses of the eye shape of pathologic myopia obtained by high-resolution 3D MRI. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.7
6. Takahashi H, Takase H, Ishizuka A, Ohno-Matsui K, Mochizuki M. Subfoveal choroidal thickness in patients with Vogt-Koyanagi-Harada disease in the convalescent stage. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.7
7. Sugita S, Kawazoe Y, Horei S, Yamada Y, Mochizuki M. Inhibitory effect of regulatory T cells expanded in vitro by human retinal pigment epithelial (RPE) cells. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.9
8. Takahashi H, Takase H, Ishizuka K, Ohno-Matsui K, Mochizuki M. Subfoveal choroidal thickness in patients with Vogt-Koyanagi-Harada disease in the convalescent stage. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.9
9. Kamoi K, Martin-Granados C, Bobu C, Wikstrom ME, Degli-Esposti MA, Steinman RM, Forrester JV. Anti-DEC205 mediated delivery of selfantigen to dendritic cell restores tolerance in spontaneous EAU. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012.5.9
10. Kamoi K, Reid DM, Yeoh J, Forrester JV. Regulatory T Cell Expansion in Eye Draining Lymph Nodes Plays a Role in Suppressing Inflammation in Spontaneous EAU and Offers a Strategy for Cell-Based Therapy. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.10
11. Iwasaki Y, Yamamoto N, Kawaguchi T, Ozaki N, Mochizuki M, Murakami K. Association between HIV microangiopathy and systemic complications in patients with AIDS. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.10
12. Kawaguchi T, Iwasaki Y, Kanda S, Sugita S, Mochizuki M. Clinical course of patients with Behcet's uveoretinitis that discontinued infliximab therapy. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for

Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.10

13. Ohno-Matsui K. Topographical analysis of human eyes with pathologic myopia. 35th Annual Meeting of Macular Society. Jerusalem (Israel), 2012.6.11
14. Miyake M, Yamashiro K, Nakanishi H, Hayashi H, Nakata I, Akagi-Kurashige Y, Tsujikawa A, Ohno-Matsui K, Mochizuki M, Yoshimura N. Association of paired box6 gene with high myopia in Japanese. Wang J, Ohno-Matsui K, Yoshida T, Shimada N, Mochizuki M, Morita I. Amyloid β enhances migration of endothelial progenitor cells via upregulation of CX3CR1. The Association for Research in Vision and Ophthalmology Annual Meeting, Florida (U.S.A.), 2012. 5.10
15. Hayashi K, Katori N, Kasai K, Kamisanuki T, Kokubo K. Postoperative safety of frontalis suspension using polytetrafluoroethylene (Gore-tex) sheet for severe ptosis. American Society of Ophthalmic Plastic & Reconstructive Surgery 2012 Meeting, Singapore, 2012.8.27
16. Ohno-Matsui K. The Imaging of the optic nerve in eyes with pathologic myopia by using swept-source OCT. 台湾眼科学術會議 Kaoshung (Taipei), 2012.10.5
17. Ohno-Matsui K. Topographical analysis of eye shape of highly myopic patients by using 3D MRI as well as swept-source OCT. In Myopia Symposium. 台湾眼科学術會議 Kaoshung (Taipei), 2012.10.6
18. Mochizuki M. Role of regulatory T cells in uveitis. 8th International Symposium on Uveitis, Thessaloniki (Greece), 2012.10.19.
19. Ohno-Matsui K. Underlying mechanism of myopic maculopathy. Instruction course 'Cutting Edge information of Pathologic Myopia' Annual meeting of American Academy of Ophthalmology. Chicago (U.S.A.), 2012.11.11
20. Ohno-Matsui K. Types and Classification of myopic maculopathy. Instruction course 'Cutting Edge information of Pathologic Myopia' Annual meeting of American Academy of Ophthalmology. Chicago (U.S.A.), 2012.11.11
21. Hayashi K, Katori N, Kasai K, Kamisanuki T. Evaluation of different suspensory materials in frontalis suspension for congenital ptosis. Annual meeting of American Academy of Ophthalmology. Chicago (U.S.A.), 2012.11.12
22. Ohno-Matsui K. Fovea-sparing ILM peeling against myopic traction maculopathy. Symposium 'Vitreoretinal diseases in high myopia' 7th Asia-Pacific Vitreo-Retina Society (APVRS) Congress. HongKong, 2012.12.14

[Symposium, Special lecture]

1. Ohno-Matsui K. Phenotypes of myopic maculopathy. Myopia GWAS consortium. Rotterdam (Netherlands), 2012.3.15
2. Ohno-Matsui K. Symposium [Women in Ophthalmology] Balancing personal and professional life. The 27th Asia Pacific Academy of Ophthalmology Congress, Busan (Korea), 2012.4.14
3. Ohno-Matsui K. Symposium [Myopia in Asia-Pacific Region] Insights into classification, predictors and progression of pathologic myopia in the Asia-Pacific Region and Worldwide. The 27th Asia Pacific Academy of Ophthalmology Congress, Busan (Korea), 2012.4.14
4. Ohno-Matsui K. Symposium [Optic nerve and neuropathies] Peripapillary imaging in highly myopic eye. The 27th Asia Pacific Academy of Ophthalmology Congress, Busan (Korea) 2012.4.14
5. Ohno-Matsui K. Symposium [Updates on Pathologic Myopia] Topographical analysis of human eyes with pathologic myopia. The 27th Asia Pacific Academy of Ophthalmology Congress, Busan (Korea), 2012.4.16
6. Mochizuki M. Progress in the treatment of ocular inflammation in Behcet's disease. 13th Annual Meeting of the Korean Society for Behcet's Disease. Seoul(Korean). 2012.11.30.

Oto-Rhino-Laryngology

1. Staffs and Students

Professor	Ken KITAMURA	
Associate Professor	Atsunobu TSUNODA	
Junior Associate Professor	Taro SUGIMOTO,	Yoshihiro NOGUCHI,
Assistant Professor	Hisashi TOKANO,	Yasuhiro SUZUKI,
	Akemi IWASAKI,	Masatoki TAKAHASHI
Hospital Staff	Yusuke KIYOKAWA,	Yuichiro INABA
Graduate Student	Yoshimi TAMEKUCHI,	Katsura YAMAMOTO,
	Palida AIHAITI,	Ayako NISHIO,
	Keiji HONDA,	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. Kitamura K: Epidemiology of Otitis Media with Effusion (OME) in Japan. Current Opinion on Otitis Media with Effusion. Koonja publishing Inc.: 151-158, 2012.
2. Tsunoda A, Sumi T, Shirakura S, Kishimoto S, Aoyagi M, Kawano Y. Otitis media with effusion and skull base lesion. Skull Base73: 195, 2012.
3. Tsunoda K, Sasaki T, Tsunoda A, Kobayashi R, Ueha R, Shoji S. Undiagnosed submucous cleft palate interfering

with inhalation therapy and a solution. *J Allergy Clin Immunol*. Epub 2012 Sep 19.

4. Sumi T, Watanabe I, Tsunoda A, Nishio A, Komatsuzaki A, Kitamura K: Longitudinal study of 29 patients with Meniere's disease with follow-up of 10 years or more (In commemoration of Professor Emeritus Isamu Watanabe). *Acta Otolaryngol* 132: 10-15, 2012.
5. Kato T, Nishigaki Y, Noguchi Y, Fuku N, Ito T, Mikami E, Kitamura K and Tanaka M: Extended screening for major mitochondrial DNA point mutations in patients with hereditary hearing loss. *J Hum Genet* 57: 772-775, 2012.
6. Kato T, Fuku N, Noguchi Y, Murakami H, Miyachi M, Kimura Y, Tanaka M and Kitamura K: Mitochondrial DNA haplogroup associated with hereditary hearing loss in a Japanese population. *Acta Otolaryngol* 132: 1178-1182, 2012.
7. Takahashi N, Tsunoda A, Shirakura S, Kitamura K: Anatomical feature of the middle cranial fossa in fetal periods: possible etiology of superior canal dehiscence syndrome. *Acta Otolaryngol* 132: 385-390, 2012.
8. Yamada M, Tsunoda A, Hagino K, Aoyagi M, Kawano Y, Yano T, Tanaka K, Kishimoto S. Surgical management of large juvenile nasopharyngeal angiofibroma invading the infratemporal fossa with intracranial extradural parasellar involvement in an 8-year-old boy. *Auris Nasus Larynx* 39:341-344, 2012.

Conference Presentations

1. Kitamura K, Maruyama A, Suzuki Y, Tsunoda A, Ikezono T: Perilymph fistula can cause inability of walk without hearing disorder-A case report-. 27th Barany Society Meeting. Uppsala Sweden, June 2012.
2. Kitamura K: Pitfalls of bone-anchored hearing aid (BAHA) surgery from 10-year experience in Japan. 18th Combined Congress of Otorhinolaryngology Head and Neck Surgery. Gwangju Korea, October 2012.
3. Kitamura K, Nakamura Y, Noguchi Y, Takahashi M: Mastoid Obliteration Using Bone Pate in Cholesteatoma. The 9th International Conference on Cholesteatoma and Ear Surgery. Nagasaki, June 2012.
4. Tsunoda A, Sumi T, Shirakura S, Kishimoto S, Aoyagi M, Kawano Y. Otitis media with effusion and skull base lesion. 6th International Congress of the World Federation of Skull Base Society. Brighton UK, June 2012.
5. Tsunoda A, Sumi T, Kishimoto S, Kitamura K: Full Scale Three-dimensional Temporal Bone Model: an Application for Surgical Training and Simulation. The First Asian Otology Meeting & The 3rd East Asian Symposium on Otology. Nagasaki, June 2012.
6. Sugimoto T, Kishimoto S: Function preservation in pharyngeal cancers: Microscopic and endoscopic surgery for early stage hypopharyngeal cancer. The 14th Japan-Korea Joint Meeting of Otolaryngology * Head and Neck Surgery. Tokyo, April 2012.
7. Sugimoto T, Kishimoto S, Ariizumi Y, Tokumaru T, Nomura F, Kiyokawa Y: The diagnosis and management of parapharyngeal tumors: From the perspective of predictive factors of malignancy. The 14th Japan-Korea Joint Meeting of Otolaryngology * Head and Neck Surgery. Tokyo, April 2012.
8. Noguchi Y, Takahashi M, Honda K, Nishio A, Kitamura K: MicroRNA expression in the aging mouse cochlea. 35th MidWinter Meeting of Association for Research in Otolaryngology. San Diego USA, February 2012.
9. Noguchi Y, Takahashi M, Momiyama N, Maehara T, Ikezono T, Kishimoto S, Kitamura K: Two cases of giant cell reparative granuloma of the temporal bone. The 9th International Conference on Cholesteatoma and Ear Surgery. Nagasaki, June 2012.
10. Fujioka M, Tokano H, Mizutari K, Ogawa K, Okano H, Edge AS. Generating mouse models of early stages of degenerative diseases using cre/lox-mediated in vivo mosaic cell ablation. 1st Asian Otology Meeting/ 3rd East Asian Symposium on Otology. Nagasaki, June 2012.
11. Kimura Y, Kubo S, Shigemoto K, Koda H, Sawabe M, Kitamura K: Gene expression analysis of inner ear cells from formalin fixed paraffin embedded archival temporal bone section using laser microdissection. The First Asian Otology Meeting & The 3rd East Asian Symposium on Otology. Nagasaki, June 2012.
12. Kawashima Y, Geleoc G SG, Kurima K, Labay V, Lelli A, Asai Y, Makishima T, Wu D-K, Della Santina CC, Kitamura K, Holt JR, Griffith AJ: Mechanotransduction in inner ear hair cells requires transmembrane channel-like genes 1 or 2. The First Asian Otology Meeting & The 3rd East Asian Symposium on Otology. Nagasaki, June 2012.
13. Kurima K, Hertzano R, Gavrilova O, Monahan K, Shpargel K, Nadaraja G, Kawashima Y, Lee KY, Ito T, Higashi Y, Eisenman D, Strome S, Griffith A: A noncoding point mutation of zeb1 causes inner ear malformation in twirler mice. ARO 35th MidWinter Meeting. San Diego USA, February 2012.
14. Kawashima Y, Geleoc G, Kurima K, Lelli A, Labay V, Asai Y, Makishima T, Askew C, Wu D, Holt J, Griffith A: Postnatal switch in expression of transmembrane channel-like genes 1 and 2 underlies mechanotransduction in auditory hair cells. ARO 35th MidWinter Meeting. San Diego USA, February 2012.
15. Kawashima Y, Geleoc G, Kurima K, Labay V, Asai Y, Horwitz G, Makishima T, Wu D, Della Santina C, Griffith A,

- Holt J: Mechanotransduction in mouse vestibular hair cells requires transmembranechannel-like genes 1 or 2. ARO 35th MidWinter Meeting. San Diego USA, February 2012.
16. Kato T, Noguchi Y, Fuku N, Murakami H, Miyachi M, Tanaka M, Kitamura K: Mitochondrial haplogroup analysis in patients with hereditary hearing loss. The 35th Annual Midwinter Research Meeting of the Association for Research in Otolaryngology. San DiegoUSA, February 2012.
 17. Kato T, Fuku N, Kimura Y, Tanaka M, Kitamura K: Mitochondrial DNA haplogroup analysis associated with presbycusis in a Japanese population. The First Asian Otology Meeting & The 3rd East Asian Symposium on Otology. Nagasaki, June 2012.
 18. Hagino K, Tokano H, Suzuki Y, Iwasaki A, Kitamura K: Total resection of the postoperative maxillary cyst and obliteration of the maxillary sinus using beta-tricalcium phosphate (β -TCP) and autologous blood for the purpose of dental implant. 24th ERS & 31st ISIAN Congress. Toulouse France, June 2012.
 19. Takahashi M, Noguchi Y, Kitamura K: Evaluation of skin and bone condition after BAHA surgery by cone beam computed tomography. The 14th Japan-Korea Joint Meeting of Otorhinolaryngology-Head and Neck Surgery. Kyoto, April 2012.
 20. Nishio A, Noguchi Y, Kitamura K: A DFNA5 mutation in two Japanese families with autosomal dominant hereditary hearing loss. 35th MidWinter Meeting of Association for Research in Otolaryngology. San Diego USA, February 2012.
 21. Honda K, Noguchi Y, Kawashima Y, Takahashi M, Nishio A, Osawa N, Kitamura K: A morphological study of otolith organs with X-ray microtomograph. Collegium Oto-Rhino-LaryngologicumAmicitiae Sacrum. Rome Italy, August 2012.
 22. Kitamura K: Moderator. Keynote Lecture 5 SNHL associated to cholesteatoma-the role of cochlear implantation. Angel Ramos-Macias. The 9th International Conference on Cholesteatoma and Ear Surgery. Nagasaki, June 2012.
 23. Kitamura K: Moderator. Diagnosis of central and vestibular disorders. SSCDS. 27th Barany Society Meeting. Uppsala Sweden, June 2012.

Neurology and Neurological Science

1. Staffs and Students (April, 2012)

Professor, Chairman	Hidehiro Mizusawa	
Professor	Takanori Yokota	
Junior Associate Professor	Kinya Ishikawa,	Nobuo Sanjo
Assistant Professor	Satoru Ishibashi,	Takuya Ohkubo,
	Shoichiro Ishihara	
Hospital Staff	Takumi Hori,	Takahiro Nagao,
	Shunsuke Kudo,	Koutaro Yoshioka,
	Keiko Ichinose,	Eri Iwasawa
Senior Resident	Yuriko Okabe,	Fumiko Furukawa
Post-doctorial Fellow	Kazutaka Nishina,	Nozomu Sato
	Taro Ishiguro	
Graduate Students (Doctoral course)	Akira Machida,	Ayaka Yamanami,
	Kazuyuki Saito,	Yuji Hashimoto,
	Tomoko Nishina,	Kiyobumi Ota,
	Teruhiko Sekiguchi,	Saneyuki Mizutani,
	Kokoro Ozaki,	Masahiko Ichijo,
	Piao Wenying,	Temuqina

2. 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.

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) Establishment 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. Abe Y, Hashimoto K, Iinuma K, Ohtsuka Y, Ichiyama T, Kusuhara K, Nomura K, Mizuguchi M, Aiba H, Suzuki Y, Mizusawa H, Hosoya M. Survey of Subacute Sclerosing Panencephalitis in Japan. *J Child Neurol* 2012; 27: 1529-1533.
2. Aoki N, Tsuchiya K, Kobayashi Z, Arai T, Togo T, Miyazaki H, Kondo H, Ishizu H, Uchikado H, Katsuse O, Hirayasu Y, Akiyama H. Progressive nonfluent aphasia: A rare clinical subtype of FTLT-DTP in Japan. *Neuropathology* 2012; 32: 272-279.
3. Hirai T, Enomoto M, Machida A, Yamamoto M, Kuwahara H, Tajiri M, Hirai Y, Sotome S, Mizusawa H, Shinomiya K, Okawa A, Yokota T. Intrathecal shRNA-AAV9 inhibits target protein expression in the spinal cord and dorsal root ganglia of adult mice. *Hum Gene Ther Methods* 2012; 23: 119-127.
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.
5. Kanazawa T, Adachi E, Orimo S, Nakamura A, Mizusawa H, Uchihara T. Pale neurites, premature α -synuclein aggregates with centripetal extension from axon collaterals. *Brain Pathol* 2012; 1: 67-78.
6. Kanouchi T, Ohkubo T, Yokota T. Can regional spreading of amyotrophic lateral sclerosis motor symptoms be explained by prion-like propagation? *J Neurol Neurosurg Psychiatry* 2012; 83: 739-745.
7. Kobayashi Z, Arai T, Yokota O, Tsuchiya K, Hosokawa M, Oshima K, Niizato K, Akiyama H, Mizusawa H. Atypical FTLT-FUS associated with ALS-TDP: A case report. *Neuropathology* 2013; 33: 83-86.
8. Kobayashi M, Ishibashi S, Tomimitsu H, Yokota T, Mizusawa H. Proliferating immature Schwann cells contribute to nerve regeneration after ischemic peripheral nerve injury. *J Neuropathol Exp Neurol* 2012 ; 71 : 511-519.
9. Kobayashi M, Yokota T, Tomimitsu H, Ishibashi S, Sekiguchi T, Kanouchi T, Ishikawa K, Mizusawa H. Motor-dominant chronic inflammatory demyelination polyradiculoneuropathy with Uhthoff-like phenomenon is a distinct clinical entity? *Muscle Nerve* 2012; 46: 140-142.
10. 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; 15: 190-194.
11. Kuwahara H, Matsunaga S. Central pontine myelinolysis associated with pancreatic diabetes. *J Neurol* 2012; 259: 353-354.
12. Mullah SH, Inaji M, Nariai T, Ishibashi S, Maeda J, Higuchi M, Ohno K. A selective adenosine A2A receptor antagonist SCH58261 ameliorated hyperlocomotion in animal model of lateral fluid percussion brain injury. *Acta Neurochirurgica Suppl.* [in press]
13. Nakamichi K, Kishida S, Tanaka K, Sukanuma 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* 2012 Nov 9. [Epub ahead of print]
14. Nakamichi K, Mizusawa H, Yamada M, Kishida S, Miura Y, Shimokawa T, Takasaki T, Chang-Kweng Lim, Kurane I, Saijo M. Characteristics of progressive multifocal leukoencephalopathy clarified through internet-assisted laboratory surveillance in Japan. *BMC Neurology* 2012; 12: 121.
15. 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* 2012 Aug 26. [Epub ahead of print]
16. Obayashi M, Ishikawa K, Izumi Y, Takahashi M, Niimi Y, Sato N, Onodera O, Kaji R, Nishizawa M, Mizusawa H. Prevalence of inositol 1, 4, 5-triphosphate receptor type 1 gene deletion, the mutation for spinocerebellar ataxia type 15, in Japan screened by gene dosage. *J Hum Genet* 2012; 57: 202-206.
17. Ohyagi M, Ohkubo T, Taniyama T, Tomizawa S, Okawa A, Yokota T, Mizusawa H. Spinal epidural abscess caused by *Bacteroides fragilis* group after dilation and curettage for incomplete abortion. *J Glob Infect Dis* 2012; 4: 132-134.
18. Ohyagi M, Sanjo N, Yokota T, Mizusawa H. Hereditary neuropathy with liability to pressure palsy combined with suspected Schwannomas of the peroneal and radial nerves. *J Neurol* 2012; 259: 977-979.
19. 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.
20. Orimo S, Suzuki M, Inaba A, Mizusawa H. I-MIBG myocardial scintigraphy for differentiating Parkinson's disease from other parkinsonism: A systematic review and meta-analysis. *Parkinsonism Related Disord* 2012; 18: 494-500.
 21. Soga K, Irioka T, Higashi M, Mizusawa H. Stroke presenting with monoparesis in the lower limb. *Intern Med* 2012; 51: 819-820.
 22. 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* 2012 Dec 14. [Epub ahead of print]
 23. Toru S, Kobayashi T, Akaza M, Yokota T, Mizusawa H. Dropped head in polymyositis. *Rheumatol Int* 2012; 32: 1105-1107.
 24. Toru S, Ohara M, Hane Y, Ishiguro T, Kobayashi T. Successful steroid treatment for recurrent Miller Fisher syndrome. *Muscle Nerve* 2012; 45: 763-4.
 25. Yagi Y, Machida A, Toru S, Kobayashi T, Amano T, Hirokawa K, Kitagawa M. Myotonic dystrophy and lipoma: a new association. *Neurol Sci* 2012; 33: 1477-1478.
 26. Yokote H, Nagasawa M, Ichijo M, Amino T, Fujigasaki H. Autoimmune polyendocrine syndrome-3 in a patient with late-onset multiple sclerosis. *Neurologist* 2012; 18: 83-84.
 27. 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.

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	Shunsuke TAKAGI (~2012.9), Shinichiro TAMAI, Yuya TERASAWA	DaisukeIKEI, Kotaro KAWAMATA
Medical Fellow	Michio ITASAKA	
Technical Assistant	Yasuhiro OKA, Meri SASAKI, Ayano SOMEYA,	Miyuki SAITO, Yoshihumi KANEKO, Ken MATSUNAGA
Graduate Students	Kenji SASAKI, Tomoko TANAKA, Masakazu UMINO, Takuya YOSHIKE, Emiko HARAMO,	Syunsuke TAKAGI, Sayuri ISHIWATA, Kazuo TAKIGUCHI, Ayako KANIE, Momoko KOBAYASHI,
Research Student	Megumi GOTO	

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, a 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. Uezato A, Yamamoto N, Kurumaji A, Toriihara A, Umezaki Y, Toyofuku A, Nishikawa T: Improvement of asymmetrical temporal blood flow in refractory oral somatic delusion after successful electroconvulsive therapy. *J ECT* 28: 50-51, 2012.
2. Hayashi H, Naoi S, Nakagawa T, Nishikawa T, Imajoh-Ohmi S, Kondo A, Kubo K, Yabuki T, Hattori A, Hirouchi M, Sugiyama Y : Sorting nexin 27 interacts with multidrug resistance-associated protein 4 (MRP4) and mediates the internalization of MRP4. *J Biol Chem* 287: 15054-15065, 2012.
3. Ozaki A, Nishida M, Koyama K, Ishikawa K, Nishikawa T: Donepezil-induced sleep spindle in a patient with dementia with Lewy bodies. *Psychogeriatrics* 2: 255-228, 2012.

4. Kurumaji A, Nishikawa T: An anxiogenic drug, FG 7142, induced an increase in mRNA of *Btg2* and *Adamts1* in the hippocampus of adult mice. *Behavioral and Brain Functions*. 8:43, 2012.
5. Uezato A, Kimura-Sato J, Yamamoto N, Iijima Y, Kunugi H, Nishikawa T: Further evidence for a male-selective genetic association of synapse-associated protein 97 (SAP97) gene with schizophrenia. *Behav Brain Funct* 8(1):2, 2012.
6. Sasaki T, Ito H, Kimura Y, Arakawa R, Takano H, Seki C, Kodaka F, Fujie S, Takahata K, Nogami T, Suzuki M, Fujiwara H, Takahashi H, Nakao R, Fukumura T, Varrone A, Halldin C, Nishikawa T, Suhara T: Quantification of Dopamine Transporter in Human Brain Using PET with ¹⁸F-FE-PE2I. *J Nucl Med* 53(7): 1065-1073, 2012.
7. Itasaka M, Hanasawa M, Hironaka N, Miyata H, Nakayama K: Facilitation of intracranial self-stimulation behavior in rats by environmental stimuli associated with nicotine. *Physiology & Behavior* 107(3): 277-282, 2012.
8. 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. *International Journal of Neuropsychopharmacology* 1-12, 2012.

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 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. 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.* 2013;115:259-66
2. 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.* 2012 Jul 18. [Epub ahead of print]
3. Hiura M, Kinoshita N, Izumi S, Nariai T. Comparison of the kinetics of pulmonary oxygen uptake and middle cerebral artery blood flow velocity during cycling exercise. *Advances in experimental medicine and biology.* 2012;737:25-31. 2.
4. Hosoda C, Hanakawa T, Nariai T, Ohno K, Honda M. Neural mechanisms of language switch. *J Neurolinguistics.* 2012; 25:44-61.
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6. Mori C, Hakuta C, Endo K, Nariai T, Ueno M, Shinada K, Kawaguchi Y. The effects of professional oral health care on patients in the subacute stage of emergent neurosurgical disorders. *Spec Care Dentist.* 2012;32:259-64.
7. Mukawa M, Nariai T, Matsushima Y, Tanaka Y, Inaji M, Maehara T, Aoyagi M, Ohno K. Long-term follow-up of surgically treated juvenile patients with moyamoya disease. *J Neurosurg Pediatr.* 2012;10:451-6.
8. Mullah SH, Inaji M, Nariai T, Momose-Sato Y, Sato K, Ohno K. Optical analysis of developmental changes in synaptic potentiation in the neonatal rat corticostriatal projection. *Neuroscience.* 2012;201:338-48.
9. Shigeta K, Ohno K, Takasato Y, Masaoka H, Hayakawa T, Yatsushige H, Inaji M, Sumiyoshi K, Momose T, Maeda T: Analysis of DWI ASPECTS and recanalization outcome of patients with acute-phase cerebral infarction. *J Med Dent Sci* 59:57-63, 2012
10. Suzuki Y, Nariai T, Kiyosawa M, Mochizuki M, Kimura Y, Oda K, Ishii K, Ishiwata K. Increased Adenosine A1 Receptor Levels in Hemianopia Patients After Cerebral Injury: An Application of PET Using 11C-8-Dicyclopropylmethyl-1-Methyl-3-Propylxanthine. *Clinical Nuclear Medicine.* 2012;37(12):1146-51.
11. 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.* 2013;27:285-96.
12. Takeuchi S, Sugawara T, Masaoka H, Takasato Y. Fourth ventricular meningioma: a case report and literature review. *Acta Neurol Belg* 2012 Mar;112(1):97-100
13. Kaoru Tamura, Wakimoto H, Agarwal AS, Rabkin SD, Bhere D, Martuza RL, Kuroda T, Kasmieh R, Shah K: Multimchanistic tumor targeted oncolytic virus overcomes resistance in Brain tumors. *Mol Ther.* 2013 Jan;21(1):68-77
14. Yamamoto M, Kawabe T, Higuchi Y, Sato Y, Nariai T, Barfod BE, Kasuya H, Urakawa Y. Delayed complications in patients surviving at least 3 years after stereotactic radiosurgery for brain metastases. *International Journal of Radiation Oncology, Biology, Physics.* 2013;85:53-60.

Endovascular Surgery

1. Staffs and Students (December 2012)

Professor	Shigeru Nemoto	
Associate Professor	Yoshikazu Yoshino	
Assistant Professor	Toshiki Tomori	
Assistant Professor	Kazunori Miki	
Clinical Fellow	Masato Inoue	
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, Shojima M, Nemoto S: Wire-probing technique to revascularize subacute or chronic internal carotid artery occlusion. *Interv Neuroradiol.* 18(3):288-96, 2012.
2. Shinya Miyamoto, Henry Wu, Takeshi Kubo, Kenji Kawaguchi, Takafumi Ide, Nobuhiko Takemura, and Shigeru Nemoto: Single stage multiple stenting in Takayasu's arteritis -case report- *Neurologia medico-chirurgica* 52(4):219-223, 2012
3. Okada T, Teranishi K, Chen Y, Tomori T, Strasser A, Lenz FA, McCarron RM, Spatz M. Reversal of postischemic hypoperfusion by tempol: endothelial signal transduction mechanism *Neurochem Res.* 2012 Apr;37(4):680-8.
4. Ichijo M, Miki K, Ishibashi S, Tomita M, Kamata T, Fujigasaki H, Mizusawa H. Posterior cerebral artery laterality on magnetic resonance angiography predicts long-term functional outcome in middle cerebral artery occlusion. *Stroke.* Epub 2012 Nov 27.
5. Takaaki Miyagishima, Tetsuo Hara, Masato Inoue, Naruhiko Terano, Hiroyasu Ohno, Kouichiro Okamoto, Kanehiro Hasuo: Pontine venous congestion due to dural arteriovenous fistula of the cavernous sinus: Case report and review of the literature. *Surgical Neurology International* 2012, 3:53

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	Ichinohe NORITAKA
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.

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. Japan is behind Europe and USA because we do not have the system for the research resource collection of many specimens and accurate clinical information available for genetic analysis. This research group intended to organize a depository at NCNP for genetic analysis of ID.

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.

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.

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 of MSCs phenotype, expansion features, differentiation ability and therapeutic benefits *in vivo*.

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, namely, to overcome late-onset incurable neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and polyglutamine diseases, has emerged. 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 working towards understanding the molecular pathogenesis of and developing therapies for these neurodegenerative diseases by taking advantage of a variety of techniques including molecular genetics, molecular & structural biology, chemical biology, and various animal models (flies, mice, marmosets).

4. Publications**Original Articles**

1. Shimazaki H, Takiyama Y, Ishiura H, Sakai C, Matsushima Y, Hatakeyama H, Honda J, Sakoe K, Naoi T, Namekawa M, Fukuda Y, Takahashi Y, Goto J, Tsuji S, Goto Y, Nakano I and Japan Spastic Paraplegia Research Consortium (JASPAC). A homozygous mutation of C12orf65 causes spastic paraplegia with optic atrophy and neuropathy (SPG55) *J Med Genet* 49:777–784, 2012.
2. Ota M, Sato N, Ishikawa M, Hori H, Sasayama D, Hattori K, Teraishi T, Obu S, Nakata Y, Nemoto K, Moriguchi Y, Hashimoto R, Kunugi H. Discrimination of female schizophrenia patients from healthy women using multiple structural brain measures obtained with voxel-based morphometry. *Psychiatry Clin Neurosci*. 2012 Dec;66(7):611-7.
3. Takata A, Iwayama Y, Fukuo Y, Ikeda M, Okochi T, Maekawa M, Toyota T, Yamada K, Hattori E, Ohnishi T, Toyoshima M, Ujike H, Inada T, Kunugi H, Ozaki N, Nanko S, Nakamura K, Mori N, Kanba S, Iwata N, Kato T, Yoshikawa T. A Population-Specific Uncommon Variant in GRIN3A Associated with Schizophrenia. *Biol Psychiatry*. 2012 Dec 10. [Epub ahead of print]
4. 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*. 2012 Nov 22. [Epub ahead of print].
5. 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*. 2012 Nov 21. [Epub ahead of print]
6. Kishi T, Ichinose H, Yoshimura R, Fukuo Y, Kitajima T, Inada T, Kunugi H, Kato T, Yoshikawa T, Ujike H, Musso GM, Umene-Nakano W, Nakamura J, Ozaki N, Iwata N. GTP cyclohydrolase 1 gene haplotypes as predictors of SSRI response in Japanese patients with major depressive disorder. *J Affect Disord*. 2012 Dec 15;142(1-3):315-22.
7. Hori H, Teraishi T, Sasayama D, Hattori K, Ota M, Matsuo J, Kawamoto Y, Kinoshita Y, Kunugi H. Schizotypal trait in healthy women is associated with a shift away from dextrality on a spatial motor control task, but not on a force control task. *Psychiatry Res*. 2012 Dec 30;200(2-3):629-34.
8. Hori H, Matsuo J, Teraishi T, Sasayama D, Kawamoto Y, Kinoshita Y, Hattori K, Hashikura M, Higuchi T, Kunugi H. Schizotypy and genetic loading for schizophrenia impact upon neuropsychological status in bipolar II and unipolar major depressive disorders. *J Affect Disord*. 2012 Dec 15;142(1-3):225-32.
9. Okayasu H, Ozeki Y, Fujii K, Takano Y, Saeki Y, Hori H, Horie M, Higuchi T, Kunugi H, Shimoda K. Pharmacotherapeutic determinants for QTc interval prolongation in Japanese patients with mood disorder.

Pharmacopsychiatry. 2012 Nov;45(7):279-83.

10. Baba Y, Satoh S, Otsu M, Sasaki E, Okada T, Watanabe S: In vitro cell subtype-specific transduction of adeno-associated virus in mouse and marmoset retinal explant culture. *Biochimie*. Dec;94(12):2716-22, 2012.
11. Suzuki M, Nagai Y, Wada K, Koike T: Calcium leak through ryanodine receptor is involved in neuronal death induced by mutant huntingtin. *Biochem Biophys Res Commun* 429(1-2): 18-23, 2012.
12. Popiel HA, Takeuchi T, Fujita H, Yamamoto K, Ito C, Yamane H, Muramatsu S, Toda T, Wada K, Nagai Y: Hsp40 gene therapy exerts therapeutic effects on polyglutamine disease mice via a non-cell autonomous mechanism. *PLoS One* 7(11): e51069, 2012.
13. Ichinohe N, Borre E, Rockland KS. Distinct feedforward and intrinsic neurons in posterior inferotemporal cortex revealed by in vivo connection imaging. *Sci Rep*. 2012;2:934.
14. Suzuki S, Harasawa N, Ueno K, Gardner JL, Ichinohe N, Haruno M, Cheng K, Nakahara H. Learning to simulate others' decisions. *Neuron*. 2012 Jun 21;74(6):1125-1137.
15. Oga T, Aoi H, Sasaki T, Fujita I, Ichinohe N. Postnatal development of layer III pyramidal cells in the primary visual, inferior temporal, and prefrontal cortices of the marmoset. *Frontiers in Neural Circuitry*. 2013. (in press).

Immune Regulation

1. Staffs and Students

Professor	Hajime KARASUYAMA
Associate Professor	Yoshiyuki MINEGISHI (until May)
Assistant Professor	Yohei KAWANO, Shingo SATO, Soichiro YOSHIKAWA (since July)
Technical Official	Toshiyuki KOJIMA
JSPS Research Fellows	Kazushige OBATA, Masako SAITO (until Oct.)
Medical Fellow	Soichiro YOSHIKAWA (until June.)
Graduate Students	Hiromi OGAWA (until March), Hirofumi YAMAGISHI (until March), Mio FUJIMAKI (until March), Mayumi EGAWA, LI Li Hua, Kayo HORIGUCHI, Misako IKI, Hidemitsu TSUTSUI, Takuya OHTA (since April), Hayato DEKI (since April)

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 such as allergy and primary immunodeficiency, by employing advanced technology in molecular biology, biochemistry, cellular biology and developmental engineering.

3. Research Subjects

- 1) Roles of basophils in health and disease
- 2) Genetic and molecular studies on the pathogenesis of primary immunodeficiencies.
- 3) Regulation of B cell development

4. Publications

Original Articles

1. Kawano, Y., Ouchida, R., Wang, J-Y, Yoshikawa, S. Yamamoto, M., Kitamura, D., and Karasuyama, H.: A novel mechanism for the autonomous termination of pre-B cell receptor expression via induction of lysosomal-associated protein transmembrane 5. *Mol. Cell. Biol.* 32: 4462-71, 2012.
2. Jin, G., Matsushita, T., Hamaguchi, Y., Le Huu, D., Ishii, T., Hasegawa, M., Obata, K., Karasuyama, H., Takehara, K., and Fujimoto, M.: Basophils and mast cells play critical roles for leukocyte recruitment in IgE-mediated cutaneous reverse passive Arthus reaction. *J. Dermatol. Sci.* 67: 181-189, 2012.
3. Mukai, K., BenBarak, M., Tachibana, M., Nishida, K., Karasuyama, H., Taniuchi, I., Galli, SJ.: Critical role of P1-Runx1 in mouse basophil development. *Blood.* 120: 76-85, 2012.
4. Etori, M., Yonekubo, K., Sato, E., Mizukami, K., Hirahara, K., Karasuyama, H., Maeda, H., Yamashita, M.: Melanocortin Receptors 1 and 5 might mediate inhibitory effects of α -melanocyte-stimulating hormone on antigen-induced chronic allergic skin inflammation in IgE transgenic mice. *J. Invest. Dermatol.* 132(7): 1925-7, 2012.
5. Ogawa, H., Mukai, K., Kawano, Y., Minegishi, Y., and Karasuyama, H.: Th2-inducing cytokines IL-4 and IL-33 synergistically elicit the expression of transmembrane TNF- α on macrophages through the autocrine action of IL-6. *Biochem. Biophys. Res. Commun.* 420: 114-118, 2012.
6. Ma CS, Avery DT, Chan A, Batten M, Bustamante J, Boisson-Dupuis S, Arkwright PD, Kreins AY, Averbuch D, Engelhard D, Magdorf K, Kilic SS, Minegishi Y, Nonoyama S, French MA, Choo S, Smart JM, Peake J, Wong M, Gray P, Cook MC, Fulcher DA, Casanova JL, Deenick EK, Tangye SG.: Functional STAT3 deficiency compromises the generation of human T follicular helper cells. *Blood.* 119(17): 3997-4008. 2012.
7. Sawaguchi M, Tanaka S, Nakatani Y, Harada Y, Mukai K, Matsunaga Y, Ishiwata K, Oboki K, Kambayashi T, Watanabe N, Karasuyama H, Nakae S, Inoue H, Kubo M.: Role of mast cells and basophils in IgE responses and in

allergic airway Hyperresponsiveness. *J Immunol* 188: 1809-18, 2012.

Review Articles

1. Minegishi Y, Saito M. Cutaneous Manifestations of Hyper IgE Syndrome. *Allergol. Int.* 61: 191-196, 2012

Molecular Virology

1. Staffs and Students (April 2012)

Professor	Shoji YAMAOKA	
Project Professor	Eiji IDO	
Assistant Professor	Yasunori SAITOH, Hiroaki TAKEUCHI,	Ryuta SAKUMA, Shin UOTA
Laboratory Engineer	Yoshio INAGAKI	
Secretary	Kumiko THORPE-MATSUI	
Research Assitant	Reiko ONAI,	Kanako MOCHIDA
-Students-		
Ph.D. course	Yasunori HORI, Masaya UNO, Sayaka SUKEGAWA	Miho OHSAKO, Eiko OZONO,
Master course	Hideki SAITO, Yusuke HARADA, Masumi FUKAZAWA, Ayaka KAKEYA, Akiko FUKUDA	Saori SHIKAMA, Yuki HASHIDA, Masato SANNO, Ayumi WAKUTSU,

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. Especially, several projects are carried out with the emphasis on investigations 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. Ozono E, Komori H, Iwanaga R, Tanaka T, Sakae T, Kitamura H, Yamaoka S, Ohtani K. Tumor suppressor TAp73 gene specifically responds to deregulated E2F activity in human normal fibroblasts. *Genes Cells*. 8:660-72. 2012
 2. Uota S, Zahidunnabi Dewan M, Saitoh Y, Muto S, Itai A, Utsunomiya A, Watanabe T, Yamamoto N, Yamaoka S. An I κ B kinase 2 inhibitor IMD-0354 suppresses the survival of adult T-cell leukemia cells. *Cancer Sci*. 1:100-6. 2012
 3. Saitoh T, Komano J, Saitoh Y, Misawa T, Takahama M, Kozaki T, Uehata T, Iwasaki H, Omori H, Yamaoka S, Yamamoto N, Akira S. Neutrophil extracellular traps mediate a host defense response to human immunodeficiency virus-1. *Cell Host Microbe* 12:109-16 2012
 4. Adikrisna R, Tanaka S, Muramatsu S, Aihara A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Yamaoka S, Arii S. Identification of pancreatic cancer stem cells and selective toxicity of chemotherapeutic agents. *Gastroenterology*. 143:234-45 2012
 5. Sakuma R, Takeuchi H*§. SIV replication in human cells. *Frontiers in Microbiology*. 3:162. 2012.
 6. Takeuchi H*§, Ishii H, Kuwano T, Inagaki N, Akari H, Matano T. Host cell species-specific effect of cyclosporine A on simian immunodeficiency virus replication. *Retrovirology*, 9(1):3. 2012
- (* Main contribution § Corresponding author)

7. Matsunaga S, Sawasaki T, Ode H, Morishita R, Furukawa A, Sakuma R, Sugiura W, Sato H, Katahira M, Takaori-Kondo A, Yamamoto N, Ryo A. Molecular and enzymatic characterization of XMRV protease by a cell-free proteolytic analysis. *J Proteomics*. 75(15):4863-73. 2012
8. Ido E, Karhemere S, Taty-Taty R, Tada T, Yasunaga M, Iwamoto S, Umehara A, Parra HJ, Kashonguwe Z, Muyembe JJ: Molecular epidemiology of HIV in the Congo Basin-From the generation site of AIDS virus. *J International Health*, 27(3):284 2012

Immunotherapeutics

1. Staffs and Students (April, 2012)

Professor	Mari KANNAGI	
Associate Professor	Takao MASUDA	
Assistant Professor	Atsuhiko HASEGAWA	
Assistant Professor	Amane SASADA	
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	

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. 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.* In press
2. Kinpara S., Kijiyama. M, Takamori A., Hasegawa A., Sasada A., Masuda T., Tanaka Y., and Kannagi M. Interferon- α (IFN- α) suppresses human T-lymphotropic virus type-1 (HTLV-1) gene expression and cell cycling, while IFN- α combined with zidovudin induces p53 signaling and apoptosis in HTLV-1-infected cells. *Retrovirology*, in revision.
3. 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.
4. 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.
5. Takamori A, Hasegawa A, Utsunomiya A, Maeda Y, Yamano Y, Masuda M, Shimizu Y, Tamai Y, Sasada A, Zeng

N, Choi I, Uike N, Okamura J, Watanabe T, Masuda T, Kannagi M. Functional impairment of Tax-specific but not cytomegalovirus-specific CD8⁺ T lymphocytes in a minor population of asymptomatic human T-cell leukemia virus type 1-carriers. *Retrovirology*. 8:100, Dec., 2011

6. I. Choi, R. Tanosaki, N. Uike, A. Utsunomiya, M. Tomonaga, M. Harada, T.Yamanaka, M. Kannagi, J. Okamura on behalf of the ATLL allo-HSCT StudyGroup. Long-term outcomes after hematopoietic SCT for adult T-cell leukemia/lymphoma: results of prospective studies. *Bone Marrow Transplantation* 46: 116-118, 2011.

Review Article

1. 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
2. Kannagi M, Hasegawa A, Kinpara S, Shimizu Y, Takamori A, Utsunomiya A. Double control systems for human T-cell leukemia virus type 1 (HTLV-1) by innate and acquired immunity. *Cancer Sci*. 102 : 670-676, 2011.
3. Masuda, T. Non-Enzymatic Functions of Retroviral Integrase: The Next Target for Novel Anti-HIV Drug Development. *Frontiers in microbiology*. 2, 210, 2011.

International Scientific Meetings

1. Kannagi M., Kinpara S., Takamori A., Sasada A., and Hasegawa A. **Impact of innate and acquired immune responses in Adult T-cell Leukemia**. The 9th AACR-Japanese cancer association joint conference, Feb. 2013, Maui, HI, USA.
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, HI, USA.
3. Kannagi M. The roles of acquired and innate immune responses on disease development in HTLV-1 infection. 2nd International Symposium [Infection-associated Cancers] March, 2012, Sapporo.

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

1. Staffs and Students (April, 2012)

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
Project Junior Associate Professor	Yusuke Nakanishi
Project Junior Assistant Professor	Taku Sato
Project Junior Assistant Professor	Satoshi Yotsumoto
Project Junior Assistant Professor	Junpei Asano
Research Technician	Shoko Kuroda
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) Mechanism of tolerance induction and its failure in the mucosa-associated lymphoid tissues.
- 2) Differentiation and function of dendritic cells
- 3) Understanding of immunological diseases based on tissue stem cell disorder

4. Publications

[original papers]

1. Liu J, Guo YM, Hirokawa M, Iwamoto K, Ubukawa K, Michishita Y, Fujishima N, Tagawa H, Takahashi N, Xiao W, Yamashita J, Ohteki T, and Sawada K. A synthetic double-stranded RNA, poly I:C, induces a rapid apoptosis of human CD34+ cells. **Exp Hematol.** Apr 40(4), 330-341,2012.
2. Ichikawa A, Kuba K, Morita M, Chiba S, Tezuka H, Hara H, Sasaki T, Ohteki T, Ranieri V.M, dos Santos C C, Kawaoka Y, Akira S, Luster A D, Lu B, Penninger J M, Uhlig S, Slutsky A S, and Imai Y. CXCL10-CXCR3 enhances the development of neutrophil-mediated fulminant lung injury of viral and non-viral origin. **Am J Respir Crit Care Med.** November 9, 2012. (Epub ahead of print)

5. Presentation at international meetings

1. Ohteki T. Role for plasmacytoid dendritic cells in gut IgA induction. The 4th Symposium for the Mext Priority Research on Immunological Self. Kyoto 2012.1.28
2. Sato T, Ikeda M, Yotsumoto S and Ohteki T. Combination effects of type-I IFNs and imatinib against Leukemia-initiating cells I mouse CML model. 10th Stem Cell Research Symposium Awaji 2012.5.31
3. Tezuka H, Abe Y, and Ohteki T. Prominent role for plasmacytoid dendritic cells in mucosal T cell-independent IgA induction. The 20th International Symposium on Molecular Cell Biology of Macrophages 2012. (MMCB2012) Tokyo 2012.6.15
4. Onai N. Monocyte derived dendritic cells perform hemophagocytosis to fine-tune excessive immune responses. The 20th International Symposium on Molecular Cell Biology of Macrophages 2012. (MMCB2012) Tokyo 2012.6.15
5. Ohteki T. Monocyte-derived dendritic cells perform hemophagocytosis to fine-tune excessive immune responses. The 11h Awaji International Forum on Infection and Immunity Awaji 2012.9.14
6. Ohteki T. Role for monocyte-derived cells in fine-tuning excessive immune responses. The 12th International Symposium on Dendritic Cells Daegu, Korea 2012.10.9
7. Onai N, Oyagi H. Sato T, Yotsumoto S, Kurabayashi, Hosoi-Amaike M, Sawada K, and Ohteki T. Monocyte-derived dendritic cells perform hemophagocytosis to control excessive immune response. The 12th International Symposium on Dendritic Cells Daegu, Korea 2012.10.9

8. Tezuka H, and Ohteki T. Prominent role for plasmacytoid dendritic cells in mucosal T cell-independent IGA Induction. The 12th International Symposium on Dendritic Cells Daegu, Korea 2012.10.11
9. Sato T, Yotsumoto S, and Ohteki T. Combination effects of type-I IFNs and imatinib against Leukemia-initiating cells in mouse CML model. 2012 Annual Meeting of the Japanese Society for Immunology Kobe 2012.12.6
10. Onai N, Ohyagi H, Sato T, Yotsumoto S, Kurabayashi K, Sawada K, and Ohteki T. Monocyte derived dendritic cells perform hemophagocytosis to fine-tune excessive immune responses during chronic virus infection. 2012 Annual Meeting of the Japanese Society for Immunology Kobe 2012.12.7

Pathological Cell Biology

1. Staffs and Students (April, 2012)

Professor	Shigeomi SHIMIZU	
Associate Professor	Norio SHIMIZU	
Junior Associate Professor	Akimitsu KONISHI	
Tokunin Junior Associate Professor	Tatsushi YOSHIDA	
Assistant Professor	Satoko ARAKAWA	
Tokunin Assistant Professor	Michiko MUROHASHI,	Shinya HONDA,
	Hirofumi YAMAGUCHI	
Secretary	Sachiko OTSUKA	
Graduate Student	Yuichiro WATANABE,	Yuna SUGIMOTO,
	Dai MIYAZAKI,	Kanako TAKEDA,
	Meruna NAGATA	

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

5. Publications

Original Article

1. Yoshioka Y, **Shimizu S**, Ito T, Taniguchi M, Nomura M, Nishida T, Sawa Y. p53 Inhibits Vascular Endothelial Growth Factor Expression in Solid Tumor. *J Surg Res.* 174 : 291-297, 2012
2. Konishi A, Arakawa S, Yue Z, **Shimizu S**. Involvement of Beclin 1 in the engulfment of apoptotic cells. *J. Biol. Chem.* 287: 13919-29, 2012
3. Fukamatsu M, Ogawa M, Arakawa S, Ashida H, Suzuki M, Furuse M, Nakayama K, **Shimizu S**, Kin M, Mimuro H, Sasakawa C. Shigella targets epithelial tricellular junctions to spread between cells via a noncanonical clathrin-dependent endocytic pathway. *Cell Host Microbe.* 11: 325-336, 2012
4. Miyaoka Y, Ebato K, Kato H, Arakawa S, **Shimizu S**, Miyajima A. Hypertrophy and unconventional cell division of hepatocytes underlie liver regeneration. *Curr. Biol.* 22: 1166-75, 2012
5. Nakase I, Okumura S, Katayama S, Hirose H, Pujals S, Yamaguchi H, Arakawa S, **Shimizu S**, Futaki S. Transformation of an antimicrobial peptide into a plasma membrane-permeable, mitochondria-targeted peptide via the substitution of lysine with arginine *Chemical Commun.* 48: 11097-99, 2012
6. Ramakrishnan R, Donahue H, Garcia D, Tan J, **Shimizu N**, Rice AP, Ling PD. Epstein-Barr virus BART9 miRNA modulates LMP1 levels and affects growth rate of nasal NK T cell lymphomas. *PLoS One.* 2011:e27271.
7. Ogawa M, Sugita S, **Shimizu N**, Watanabe K, Nakagawa I, Mochizuki M. Broad-range real-time PCR assay for detection of bacterial DNA in ocular samples from infectious endophthalmitis. *Jpn J Ophthalmol.* 56(6):529-535, 2012.
8. Sugita S, **Shimizu N**, Watanabe K, Ogawa M, Maruyama K, Usui N, Mochizuki M. Virological analysis in patients with human herpes virus 6-associated ocular inflammatory disorders. *Invest Ophthalmol Vis Sci.* 2012 Jul 12;53(8):4692-8. Print 2012 Jul.
9. Ogawa M, Sugita S, Watanabe K, **Shimizu N**, Mochizuki M. Novel diagnosis of fungal endophthalmitis by broad-

range real-time PCR detection of fungal 28S ribosomal DNA. *Graefes Arch Clin Exp Ophthalmol.* 250(12):1877-1883, 2012.

10. Sugita S, Kamoi K, Ogawa M, Watanabe K, Shimizu N, Mochizuki M. Detection of Candida & Aspergillus species DNA using broad-range real-time PCR for fungal endophthalmitis. *Graefes Arch Clin Exp Ophthalmol.* 250:391-398, 2012.

Immunology

1. Staffs and Students

Professor	Takeshi TSUBATA, M.D., Ph.D.	
Associate Professor	Takahiro ADACHI, Ph.D.	
Assistant Professor	Kozo WATANABE, Ph.D.	
Assistant Professor	Yusuke KISHI,	Naoko MATSUBARA
Technician	Yukie KURUSU	
Secretary	Hiroko TAKAHASHI	
Graduate Student	XU Miduo,	TANG Miao,
	Toshitaro TAKATA,	Satoya OMORI,
	Shirly PHOON,	Ayse Ucar KONUSKAN,
	Sumiyo EZAKI,	JIAO Xuyang

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 good research 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 immune system distinguishes pathogens from non-microbial antigens and self-antigens is already clarified for protein antigens. However, little is know 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.

5. Publications

[Original Article]

1. Klionsky, D.J., Abdalla, F. C. Tsubata, T. et al. (2012): Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy* 8: 1-100.
2. Kishi, Y., Higuchi, T., Phoon, S., Kamiya, K., Riemekasten, G., Akiyoshi, K., Weigert, M. and Tsubata, T. (2012): Apoptotic marginal zone deletion of anti-Sm/ribonucleoprotein B cells. *Proc. Natl. Acad. Sci. USA* 109: 7811-7816.
3. Tsubata, T. (2012): Role of inhibitory BCR co-receptors in immunity. *Infect Disord Drug Targets* 12:181-190.
4. Maeno, E., Tsubata, T. and Okada, Y (2012): Apoptotic volume decrease (AVD) is independent of mitochondrial dysfunction and initiator caspase activation. *Cells* 1: 1156-1167.
5. Hitomi, Y., Adachi, T., Tsuchiya, N., Honda, Z.-I., Tokunaga, K and Tsubata, T. (2012): Human CD72 splicing isoform responsible for resistance to systemic lupus erythematosus regulates serum immunoglobulin level and is localized in endoplasmic resticulum. *BMC Immunol.* 13: 72.
6. Shimoda, M., Bolduc, A., Takezaki, M., Amtani, Y., Huang, L., Nutt S. L., Kamanaka, M., Flavell, R. A., Mellor A. L, Tsubata, T., Koni, P. (2013): Constitutively CD40-activated B cells regulate CD8 T cell inflammatory response by IL-10 induction. *J. Immunol.* (in press).

7. Adachi T, Harumiya S, Takematsu H, Kozutsumi Y, Wabl M, Fujimoto M, Tedder TF. (2012): CD22 serves as a receptor for soluble IgM. *Eur J Immunol.* 2012 42:241-7.

Pediatrics and Developmental Biology

1. Staffs and Students (April, 2012)

Professor	Shuki Mizutani	
Associate Professor	Tomohiro Morio	
Junior Associate Professor	Masatoshi Takagi,	Mitunori Nisiyama
Assistant Professor	Yaeko Motoyoshi, Daisuke Tomizawa, Taku Ishii,	Yuuji Sugawara, Kenichi Kashimada,
	(Apr~) Takeshi Isoda, Manabu Sugie,	Atsuko Taki, Tomohiro Udagawa,
	(Mar~) Keisuke Enomoto	
Graduate Student	Norimasa Ihara, Yuuko Ohnishi, Yuki Aoki, Susumu hosokawa, Kei Takasawa, Takahiro Kamiya, Keisuke Nakajima, Yohei Matsubara,	Kaori Nakatani, Eriko Tanaka, Fumihiko Takizawa, Setuko kaneko, Noriko Mituiki, Tetsuro Nagasawa, Eriko Kikuchi ,
	(~Mar) Takeshi Isoda,	Yuuko Komatu,
	(Apr~) Akifumi Endo, RinaNishii, Miko Shigeno	Chikako Morioka, Rie Kumaki,
Special Study Student	Sayaka Osada,	
	(Apr~) 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) Atsuko Taki,
	(Apr~) ShigeruTakishima

Department of Research for Regional Pediatrics

Professor	Masayuki Nagasawa
Assistant Professor	(Apr~) Kengo Moriyama, Teppei Ookawa
	(~Mar) Akifumi Endo, Tomohiro Udagawa

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), Istitute 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 Insitute, 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 DNA damage repair response and the analysis of molecules that play important roles in human immune responses. The main projects include the following.

- # Development of in vitro and in vivo leukemogenesis model that stemmed from defective tumor surveillance system.
- # Involvement of ATM in T-cell differentiation and adipocyte differentiation.
- # Molecular pathogenesis of T-cell malignancy in ATM deficiency
- # Identification of stem cells of infantile leukemia using leukemic-cell transplanted NOG-SCID mice.
- # Lymphoproliferation and leukemia in Ras associated ALPS like disorder (RALD)
- # Responsible gene hunting for CVID and for radiosensitive hyperIgM syndrome using next generation sequencing system
- # Negative regulation of activation and apoptosis of granulocytes by Btk
- # Application of protein transduction strategy for congenital gene defect
- # Development of adoptive immunotherapy for immune reconstitution after SCT
- # Develepment 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

We have achieved two great discoveries in this year. Most remarkable achievement in this year is identification of novel roles of BTK for regulation of reactive oxygen species (ROS) and neutrophil survival done by F Honda and T Morio. Btk is responsible genes for a gamma globulinemia. Only, function in B cell has been explored. This finding opens a window for new filed of neutrophil research. The report was published in Nature Immunology. Second is explication of T cell developmental failure in Ataxia Telangiectasia done by T Isoda, M Takagi and S Mizutani. In this research, we found how ATM deficiency causes T cell developmental failure, and increased susceptibility of chromosomal translocation which leads to tumor development during double negative phase of T cell development.. The report was published in Blood.

●Cardiology Group

We performed both the basic and clinical studies.

The basic studies were related to the vascular remodeling in pulmonary hypertension (PH), whose mechanisms are still unknown but thought to be inflammation as one factor. Dipeptidyl peptidase-4(DPP-4) inhibitors (Alogliptin) are new drugs for type 2 diabetes mellitus and have an important role for cardiovascular protection by its anti-inflammation effect. Therefore we investigated the role of DPP-4 in PH. In vivo study, Alogliptin markedly improved the survival and pulmonary artery pressure of monocrotaline (MCT)-induced PH rats by improving medial hypertrophy. In 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 effect of EPA in PH as well. 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 (PSMCs) proliferation stimulated with TGF-beta or FGF2. EPA also suppressed nuclear factor-kappa B p65 translocation into the nucleus in PSMCs. 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 77th Annual Scientific Meeting of Japanese Circulation Society.

Secondly, 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”, “Randomized controlled trial to assess immunoglobulin plus steroid efficacy for Kawasaki disease (RAISE study)”, “Efficacy of school-based heart examination in early detection of idiopathic pulmonary arterial hypertension” and “Gene mutations in idiopathic pulmonary arterial hypertension”. The result of RAISE study were published in The LANCET and the result of gene mutations in IPAH was published in American Journal of Cardiology.

●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 diseases of endocrine organs, especially adrenal glands and gonads. We are looking at developing the radical treatment systems for the congenital endocrine diseases by using regenerative medicine as a final target.

Our ongoing projects are bellows

#1: Molecular mechanisms of sexual determination, collaborating with P. Koopman’s lab (IMB, The university of Queensland, Brisbane, Australia) A. Sinclair’s Lab. (Royal Children’s Hospital, Melbourne, Australia) and V. Harely’s Lab (Prince Henry’s Institute, Melbourne, Australia)

#2: Molecular pathological mechanisms in congenital adrenal hyperplasia

Current ongoing projects will be integrated systematically, and be developed further in order to accomplish our final target.

●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.

●Nephrology Group

- 1) Analyses of the mechanism of pathogenesis for IgA nephropathy in Wiskott-Aldrich syndrome patients
- 2) Analyses of glomerular epithelial cells (podocytes) unknown function
- 3) Analyses of the mechanism of tubulointerstitial injury in nephrotic syndrome patients

We work on these researches in cooperation with The National Institute of Advanced Industrial Science and Technology(1), Juntendo University (2), and Division of Nephrology and Hypertension, Miller School of Medicine, University of Miami (2).

●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 patients 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 and/or hematology 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 and professional training with other professional facilities such as St. Luke's International Hospital and Juntendo University Hospital.

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/or novel therapies for childhood cancers and other non-malignant diseases.
2. Participation in industry-based clinical trials for drug approval: In 2012, 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 2012, we performed HSCT for 9 cases; related bone marrow transplantation (BMT) (n=2), unrelated BMT (n=2), unrelated cord blood transplantation (n=4), and related peripheral blood stem cell transplantation (n=1). Our experience of HSCT exceeds 140 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/or 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), two general pediatric cardiologists (Watanabe T, Sazuka M) and one senior resident in The University Hospital who were mainly engaged in the diagnosis and treatment for every kind 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) and three part-time doctors (Tashiro R, Matsumura Y, Sakurai M) were also joined to back up the procedures.

In-patients were 109 and chiefly introduced from the affiliated hospitals and out-patients field in The University Hospital. The diseases we dealt with were 46 congenital heart diseases, acquired heart diseases such as 30 Kawasaki diseases, 15 pulmonary hypertensions and 4 cardiomyopathies, and 14 cardiac arrhythmia. We performed invasive examination of cardiac catheterization, cardiovascular angiogram and myocardial biopsy as well as non-invasive examinations such as nuclear medicine, CT and MRI for differential diagnosis, decision of medication strategy and evaluation of treatments. In 65 cardiac catheterizations per year, catheter intervention included 1 coil embolization for PDA and 3 catheter ablation for arrhythmias. Twenty five cases were radically or palliatively operated at The Sakakibara Heart Institute. 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. Three KD patients were treated by infliximab and one was treated by cyclosporine. 15 patients with pulmonary hypertension (PH) 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 tree 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. 14 patients with cardiac arrhythmia was admitted. Among them, six patients was prolonged QT elongation (PQT) and one was Brugada syndrome. They were examined to be diagnosed, on drug provocation test,

exercise-tolerated ECG, face drop in cold water examination or gene mutation evaluation. Moreover, three patients were performed catheter ablation therapy, one was ventricular fibrillation with arrhythmogenic right ventricular cardiomyopathy (ARVC) and two were AVRT with WPW syndrome.

Out-patients for pediatric cardiology were up to 1,500 patients with the 1400 examinations of echocardiogram. Moreover, Holter 24-hours ECG monitoring examination was performed on about 100 patients, and Treadmill exercise tolerance examination were also performed on the same number patients. We have participated in the school heart screening program of Tokyo Metropolitan Institute for Preventive Medicine and Tokyo Medical Association, and checked more than 10,000 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, and more than 80 children with endocrine disorders hospitalized yearly our university.

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

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

Type1 DM is another disease into which 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.

●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.

●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 perform special examination such as kidney biopsy, renogram, MRU, etc. We also participate positively in urinary analysis screening performed at schools.

We operate clinical trial to examine the efficacy and safety of eculizumab for treatment of atypical hemolytic uremic syndrome patient.

We participate in multi-institutional joint research of refractory nephrotic syndrome operated by Japanese Study Group of Kidney Disease in Children.

We hold conference together with neighboring institutions regularly to discuss about better treatment for serious kidney diseases and to improve our knowledge. Some members study treatment for serious kidney diseases, kidney transplantation and renal replacement therapy for children at National Research Institute for Child Health and Development.

●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. 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.* 2012; S0091-6749(12)01839-8.
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International congress

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3. Mitsuiki N, Oshim K, Imai K, Ohara O, Morio T, Mizutani S. Genetic Analysis For 207 Cases With Primary Immunodeficiency (PID) Consulted to A Single Center Through PID Network in JAPAN (PIDJ) in 5 Years (2007-2011). 15th Biennial Meeting of the European Society of Immunodeficiencies (ESID2012). Florence, Italy. Oct. 2012.
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 28. Nakajima K, Miyata R, Tanuma N, Hayashi M. Glial markers in the cerebrospinal fluid in cases of acute encephalopathy with biphasic seizures and late reduced diffusion (AESD). Joint Congress of ICNA and AOCNA, Brisbane, May, 2012.
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 31. Ono M, Alankarage D, Ludbrook L, Bagheri-Fam S, Svingen T, Sinclair A, Koopman P, Harley V. Screening for novel SOX9 target genes in mammalian gonadal development and sex determination, 6th International Symposium on the Biology of Vertebrate Sex Determination, Kona, Hawaii, USA, Apr 23-27, 2012
 32. K. Kashimada, T. Svingen, C. Feng, E. Pelosi, S. Bagheri-Fam, VR. Harley, D. Schlessinger, J. Bowles, P. Koopman. Antagonistic regulation of Cyp26b1 by transcription factors SOX9/SF1 and FOXL2 during gonadal development in mice. 6th International Symposium on the Biology of Vertebrate Sex Determination, Kona, Hawaii, USA, Apr 23-27, 2012
 33. Motoyoshi Y, Udagawa T, Chiga M, Yoshida Y, Fujimura Y, Nagasawa M, Morio T, Mizutani S, Nagata M. A case of atypical hemolytic uremic syndrome successfully treated with anti-C5 antibody. Continuous Professional Development program of International Pediatric Nephrology Association. Japan-Korea The 10th Pediatric Nephrology Seminar 2012. Tokyo, Japan. May 2012.
 34. Tanaka E, Asanuma K, Nonaka K, Seki T, Asao R, Hosoe Y, Takagi M, Oliva A, Mizutani S, Yagita H, Tomino Y. Notch2 pathway reactivation ameliorates urinary protein and glomerular sclerosis in adriamycin nephropathy mice. 9th International Podocyte Conference 2012, Miami, Florida, USA. Apr. 2012.
 35. Tanaka E, Asanuma K, Nonaka K, Oliva trejo J, Seki T, Asao R, Hosoe Y, Kim E, Takagi M, Yagita H, Tomino Y. Notch2 Pathway Reactivation Ameliorates Urinary Protein and Glomerular Sclerosis in Adriamycin Nephropathy Mice. American Society of Nephrology Kidney Week 2012, San Diego, California, USA. Nov. 2012.

Medicine and Rheumatology

1. Staffs and Students (April, 2012)

Professor	Nobuyuki MIYASAKA Masayoshi HARIGAI(1)	
Associate Professor	Hitoshi KOHSAKA Tetsuo KUBOTA(2), Kazuki TAKADA(4),	Ryuji KOIKE(3), Toshihiro NANKI(1),
Junior Associate Professor	Hideyuki IWAI	
Assistant Professor	Fumitaka MIZOGUCHI, Kaori WATANABE(1),	Akito TAKAMURA, Ryoko SAKAI(1)
Visiting Lecturer	Rieko TSUBATA, Yoshiki NONOMURA, Kenji NAGASAKA, Fumihito SUZUKI, Peter Y. Shane,	Hiroyuki HAGIYAMA, Yukiko KOMANO, Jun OGAWA, Kayoko KANEKO, Toru KINO
Graduate Student	Yoshishige MIYABE*, Tadashi HOSOYA*, Akiko SUZUKI*, Yoko NAKAZATO*, Waka YOKOYAMA*, Kenchi TAKENAKA*, Mari KIHARA, Syoko KASAI (*GCOE QAISS)	Hisanori HASEGAWA*, Naoki KIMURA*, Hayato YAMAZAKI, Shin FUKUDA*, Tetsuya SAITO*, Natsuka UMEZAWA*, Fumio HIRANO,
Research Student	Chie MIYABE,	
Resident Physician	Mineto OTA, Yoji KOMIYA,	Hiroyoshi MORI, Mari NAKAJIMA
Research Worker	Yusuke TAGATA	
Office Administrator	Rie FUJIME, Tomoko TAKAHASHI(1), Marie YAJIMA(1)	Kaori KONNO, Momoko MITSUISHI,
Technical Staff	Eri YOSHIMOTO,	Sayaka ONO

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

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 27,957 clinic visits and 274 hospital admissions in 2012. 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. Sakai R, Komano Y, Tanaka M, Nanki T, Koike R, Nagasawa H, Amano K, Nakajima A, Atsumi T, Koike T, Ihata A, Ishigatsubo Y, Saito K, Tanaka Y, Ito S, Sumida T, Tohma S, Tamura N, Fujii T, Sugihara T, Kawakami A, Hagino N, Ueki Y, Hashiramoto A, Nagasaka K, Miyasaka N, Harigai M. Time-dependent increased risk for serious infection from continuous use of tumor necrosis factor antagonists over three years in patients with rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2012, 64(8): 1125-1134.
2. Okada Y, Shimane K, Kochi Y, Tahira T, Suzuki A, Higasa K, Takahashi A, Horita T, Atsumi T, Ishii T, Okamoto A, Fujio K, Hirakata M, Amano H, Kondo Y, Ito S, Takada K, Mimori A, Saito K, Kamachi M, Kawaguchi Y, Ikari K, Mohammed OW, Matsuda K, Terao C, Ohmura K, Myouzen K, Hosono N, Tsunoda T, Nishimoto N, Mimori T, Matsuda F, Tanaka Y, Sumida T, Yamanaka H, Takasaki Y, Koike T, Horiuchi T, Hayashi K, Kubo M, Kamatani N, Yamada R, Nakamura Y, Yamamoto K. A Genome-Wide Association Study Identified AFF1 as a Susceptibility Locus for Systemic Lupus Erythematosus in Japanese *PLoS Genet.* 2012 Jan;8(1)
3. Enosawa S, Yamazaki T, Kohsaka H, Tokiwa T. Repopulation of human origin hepatocyte progenitor-like cell line, THLE-5b, in the SCID mouse liver under p21-mediated cell growth-arresting conditions. *Cell Transplant* 2012, 21(2-3): 447-452.
4. Murakami Y, Mizoguchi F, Saito T, Miyasaka N, Kohsaka H. p16(INK4a) exerts an anti-inflammatory effect through accelerated IRAK1 degradation in macrophages. *J Immunol* 2012, 189(10): 5066-5072.
5. Nishimura K, Omori M, Sato E, Katsumata Y, Gono T, Kawaguchi Y, Harigai M, Yamanaka H, Ishigooka J. Risperidone in the treatment of corticosteroid-induced mood disorders, manic/mixed episodes, in systemic lupus erythematosus: a case series. *Psychosomatics* 2012, 53(3): 289-293.
6. Izu Y, Ezura Y, Mizoguchi F, Kawamata A, Nakamoto T, Nakashima K, Hayata T, Hemmi H, Bonaldo P, Noda M. Type VI collagen deficiency induces osteopenia with distortion of osteoblastic cell morphology. *Tissue Cell* 2012, 44(1): 1-6.
7. Sugihara T, Okiyama N, Watanabe N, Miyasaka N, Kohsaka H. Interleukin-1 and tumor necrosis factor alpha blockade treatment of experimental polymyositis in mice. *Arthritis Rheum* 2012, 64(8): 2655-2662.
8. Okiyama N, Sugihara T, Oida T, Ohata J, Yokozeki H, Miyasaka N, Kohsaka H. T lymphocytes and muscle condition act like seeds and soil in a murine polymyositis model. *Arthritis Rheum* 2012, 64(11): 3741-3749.
9. Komano Y, Yagi N, Onoue I, Kaneko K, Miyasaka N, Nanki T. Arthritic joint-targeting small interfering RNA-encapsulated liposome: implication for treatment strategy for rheumatoid arthritis. *J Pharmacol Exp Ther* 2012, 340(1): 109-113.
10. Suzuki F, Kubota T, Miyazaki Y, Ishikawa K, Ebisawa M, Hirohata S, Ogura T, Mizusawa H, Imai T, Miyasaka N, Nanki T. Serum level of soluble CX3CL1/fractalkine is elevated in patients with polymyositis and dermatomyositis, which is correlated with disease activity. *Arthritis Res Ther* 2012, 14(2): R48.
11. Takeuchi T, Harigai M, Tanaka Y, Yamanaka H, Ishiguro N, Yamamoto K, Miyasaka N, Koike T, Kanazawa M, Oba T, Yoshinari T, Baker D. 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* 2012.
12. Tanaka Y, Harigai M, Takeuchi T, Yamanaka H, Ishiguro N, Yamamoto K, Miyasaka N, Koike T, Kanazawa M, Oba T, Yoshinari T, Baker D. Golimumab in combination with methotrexate in Japanese patients with active rheumatoid arthritis: results of the GO-FORTH study. *Ann Rheum Dis* 2012, 71(6): 817-824.
13. Takeuchi T, Miyasaka N, Tatsuki Y, Yano T, Yoshinari T, Abe T, Koike T. Inhibition of plasma IL-6 in addition to maintenance of an efficacious trough level of infliximab associated with clinical remission in patients with rheumatoid arthritis: analysis of the RISING Study. *Ann Rheum Dis* 2012, 71(9): 1583-1585.
14. Sakai R, Tanaka M, Nanki T, Watanabe K, Yamazaki H, Koike R, Nagasawa H, Amano K, Saito K, Tanaka Y, Ito S, Sumida T, Ihata A, Ishigatsubo Y, Atsumi T, Koike T, Nakajima A, Tamura N, Fujii T, Dobashi H, Tohma S, Sugihara T, Ueki Y, Hashiramoto A, Kawakami A, Hagino N, Miyasaka N, Harigai M. Drug retention rates and relevant risk factors for drug discontinuation due to adverse events in rheumatoid arthritis patients receiving

- anticytokine therapy with different target molecules. *Ann Rheum Dis* 2012, 71(11): 1820-1826.
15. 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* 2012.
 16. Harigai M, Mochida S, Mimura T, Koike T, Miyasaka N. A proposal for management of rheumatic disease patients with hepatitis B virus infection receiving immunosuppressive therapy. *Mod Rheumatol* 2012.
 17. 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* 2012.
 18. Matsubara T, Yamana S, Tohma S, Takeuchi T, Kondo H, Kohsaka H, Ozaki S, Hashimoto H, Miyasaka N, Yamamoto A, Hiraoka M, Abe T. Tolerability and efficacy of abatacept in Japanese patients with rheumatoid arthritis: a phase I study. *Mod Rheumatol* 2012.
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 20. Takeuchi T, Matsubara T, Nitobe T, Suematsu E, Ohta S, Honjo S, Abe T, Yamamoto A, Miyasaka N. Phase II dose-response study of abatacept in Japanese patients with active rheumatoid arthritis with an inadequate response to methotrexate. *Mod Rheumatol* 2012.
 21. Takeuchi T, Miyasaka N, Zang C, Alvarez D, Fletcher T, Wajdula J, Yuasa H, Vlahos B. 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* 2012.
 22. 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* 2012.
 23. Umezawa N, Kohsaka H, Nanki T, Watanabe K, Tanaka M, Shane PY, Miyasaka N. Successful treatment of eosinophilic granulomatosis with polyangiitis (EGPA; formerly Churg-Strauss syndrome) with rituximab in a case refractory to glucocorticoids, cyclophosphamide, and IVIG. *Mod Rheumatol* 2012.
 24. 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* 2012.
 25. Miyasaka N, Hara M, Koike T, Saito E, Yamada M, Tanaka Y. Effects of intravenous immunoglobulin therapy in Japanese patients with polymyositis and dermatomyositis resistant to corticosteroids: a randomized double-blind placebo-controlled trial. *Mod Rheumatol* 2012, 22(3): 382-393.
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 27. Koike T, Harigai M, Ishiguro N, Inokuma S, Takei S, Takeuchi T, Yamanaka H, Tanaka Y. Safety and effectiveness of adalimumab in Japanese rheumatoid arthritis patients: postmarketing surveillance report of the first 3,000 patients. *Mod Rheumatol* 2012, 22(4): 498-508.
 28. Harigai M, Takeuchi T, Tanaka Y, Matsubara T, Yamanaka H, Miyasaka N. Discontinuation of adalimumab treatment in rheumatoid arthritis patients after achieving low disease activity. *Mod Rheumatol* 2012, 22(6): 814-822.
 29. Tanaka M, Sakai R, Koike R, Komano Y, Nanki T, Sakai F, Sugiyama H, Matsushima H, Kojima T, Ohta S, Ishibe Y, Sawabe T, Ota Y, Ohishi K, Miyazato H, Nonomura Y, Saito K, Tanaka Y, Nagasawa H, Takeuchi T, Nakajima A, Ohtsubo H, Onishi M, Goto Y, Dobashi H, Miyasaka N, Harigai M. *Pneumocystis jirovecii* pneumonia associated with etanercept treatment in patients with rheumatoid arthritis: a retrospective review of 15 cases and analysis of risk factors. *Mod Rheumatol* 2012, 22(6): 849-858.
 30. Koike T, Harigai M, Inokuma S, Ishiguro N, Ryu J, Takeuchi T, Tanaka Y, Yamanaka H, Fujii K, Yoshinaga T, Freundlich B, Suzukawa M. Safety and effectiveness of switching from infliximab to etanercept in patients with

- rheumatoid arthritis: results from a large Japanese postmarketing surveillance study. *Rheumatol Int* 2012, 32(6): 1617-1624.
31. Koike T, Harigai M, Inokuma S, Ishiguro N, Ryu J, Takeuchi T, Tanaka Y, Yamanaka H, Fujii K, Yoshinaga T, Freundlich B, Suzukawa M. Safety and effectiveness responses to etanercept for rheumatoid arthritis in Japan: a sub-analysis of a post-marketing surveillance study focusing on the duration of rheumatoid arthritis. *Rheumatol Int* 2012, 32(6): 1511-1519.
 32. Arai A, Imadome K, Wang L, Wu N, Kurosu T, Wake A, Yamamoto H, Ota Y, Harigai M, Fujiwara S, Miura O. Recurrence of chronic active Epstein-Barr virus infection from donor cells after achieving complete response through allogeneic bone marrow transplantation. *Intern Med* 2012, 51(7): 777-782.
 33. Harigai M, Tanaka Y, Maisawa S. Safety and efficacy of various dosages of orelizumab in Japanese patients with rheumatoid arthritis with an inadequate response to methotrexate therapy: a placebo-controlled double-blind parallel-group study. *J Rheumatol* 2012, 39(3): 486-495.
 34. Yamazaki H, Nanki T, Harigai M, Miyasaka N. Successful treatment of refractory Takayasu arteritis with tacrolimus. *J Rheumatol* 2012, 39(7): 1487-1488.
 35. Hasegawa H, Kohsaka H, Takada K, Miyasaka N. Renal involvement in antimyeloperoxidase antineutrophil cytoplasmic antibody-positive granulomatosis with polyangiitis with chronic hypertrophic pachymeningitis. *J Rheumatol* 2012, 39(10): 2053-2055.

Dermatology

1. Staffs and Students (April 2012)

Professor	Hiroo YOKOZEKI	
Junior Associate Professor	Kaoru TAKAYAMA, Ken IGAWA	Aya NISHIZAWA,
Assistant Professor	Kunitaro FUKUYAMA, Akiko FUJIWARA,	Takichi MUNETSUGU, Hitomi Satoh
Hospital Staff	Tsukasa UGAJIN, Ai AKINO, Sayaka SHIBAMA, Takahiro ISHIKAWA, Hana TERAKI, Natsumi NOGUCHI	Aiko HIRAI, Risa WATANABE, Ayako MORISHITA, Marina SAEKI, Yoshimi NISHIHARA,
Secretary	Yukako KIKUCHI, Mina ARAI	Masae SAKATA,
Graduate students	Makiko UENO, Kazumi SAEKI, Risako INOUE, Rie YU, Minako INAZAWA,	Yasumasa KANAI, Yuki TAKEHARA, Takashi HASHIMOTO, Chen YUE, Aiko HIRAI

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. Okiyama N, Sugihara T, Oida T, Ohata J, Yokozeki H, Miyasaka N, Kohsaka H : T lymphocytes and muscle condition act like seeds and soil in a murine polymyositis model., *Arthritis Rheum*, 64:3741-3749, 2012
2. Nishizawa A, Satoh T, Yokozeki H : Erythrodermic psoriasis improved by panitumumab, but not bevacizumab.,

Acta Derm Venereol, 92:360-361, 2012

3. Sekine R, Satoh T, Takaoka A, Saeki K, Yokozeki H : Anti pruritic effects of topical crotamiton, capsaicin, and a corticosteroid on pruritogen-induced scratching behavior., *Exp Dermatol*, 21:201-204, 2012
4. Kanai Y, Satoh T, Igawa K, Yokozeki H : Impaired expression of Tim-3 on Th17 and Th1 cells in psoriasis., *Acta Derm Venereol*, 92:367-361, 2012
5. Oka K, Ohtaki N, Kasai S, Takayama K, Yokozeki H : Two cases of eruptive pseudoangiomatosis induced by mosquito bites., *J Dermatol*, 39:301-305, 2012
6. Tanaka T, Satoh T, Tanaka A, Yokozeki H : Congenital insensitivity to pain with anhidrosis: a case with preserved itch sensation to histamine and partial pain sensation., *Br J Dermatol*, 166:888-891, 2012
7. Yu R, Satoh T, Wakabayashi T, Ueda N, Yokozeki H : Disseminated BCG infection in severe combined immunodeficiency., *Acta Derm Venereol*, 92:158-159, 2012
8. Sugihara T, Okiyama N, Suzuki M, Kohyama K, Matsumoto Y, Miyasaka N, Kohsaka H : Interleukin-1 and tumor necrosis factor α blockade treatment of experimental polymyositis in mice., *Arthritis and Rheumatism*, 64:2655-2662, 2012
9. 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*, 2012 Oct 18.

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	Yuan BAE,	Naoki AKAZAWA,
	Tadatsune IIDA,	Akira TAKEMOTO,
	Shohei TOMII,	Atsuko KONTA,
	Katsumi OISHI,	Yoshimi SUZUKI,
	Nilufar LOKMAN,	Teruko NAKAMURA,
	Kana MINEGISHI,	Pariko YOROZU,
	Hiroki AIKAWA,	Mami HANAO,
	Yurika UENO,	Kousuke TAKEMURA,
	Kentaro BABA,	Chisato ITO,
	Sayoko CHIBA,	Ayaka MATSUKAZE,
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. Amodini Rajakaruna G, Umeda M, Uchida K, Furukawa A, Yuan B, Suzuki Y, Noriko E, Izumi Y, Eishi Y. Possible translocation of periodontal pathogens into the lymph nodes draining the oral cavity. *J Microbiol* 50(5):827-36,2012
2. Furusawa H, Suzuki Y, Miyazaki Y, Inase N, Eishi Y. Th1 and Th17 immune responses to viable *Propionibacterium acnes* in patients with sarcoidosis. *Respir Investig* 50(3):104-9,2012
3. Negi M, Takemura T, Guzman J, Uchida K, Furukawa A, Suzuki Y, Iida T, Ishige I, Minami J, Yamada T, Kawachi H, Costabel U, Eishi Y. Localization of *propionibacterium acnes* in granulomas supports a possible etiologic link between sarcoidosis and the bacterium. *Mod Pathol* 25(9):1284-97,2012
4. Miyawaki Y, Kawachi H, Ooi A, Eishi Y, Kawano T, Inazawa J, Imoto I. Genomic copy-number alterations of MYC and FHIT genes are associated with survival in esophageal squamous-cell carcinoma. *Cancer Sci* 103(8):1558-66,2012
5. Aikawa C, Furukawa N, Watanabe T, Minegishi K, Furukawa A, Eishi Y, Oshima K, Kurokawa K, Hattori M, Nakano K, Maruyama F, Nakagawa I, Ooshima T. Complete genome sequence of the serotype k *Streptococcus mutans* strain LJ23. *J Bacteriol* 194(10):2754-5,2012
6. Takahashi M, Ishikawa K, Sato N, Obayashi M, Niimi Y, Ishiguro T, Yamada M, Toyoshima Y, Takahashi H, Kato T, Takao M, Murayama S, Mori O, Eishi Y, Mizusawa H. Reduced brain-derived neurotrophic factor (BDNF) mRNA expression and presence of BDNF-immunoreactive granules in the spinocerebellar ataxia type 6 (SCA6)cerebellum.

Neuropathology 32(6):595-603,2012

7. Amano T, Eishi Y, Yamada T, Uchida K, Minegishi K, Tamura T, Kobayashi D, Hiroshi K, Suzuki T, Board PG. Widespread expression of γ -glutamyl cyclotransferase suggests it is not a general tumor marker. *J Histochem Cytochem* 60(1):76-86,2012
8. Toriihara A, Taniguchi Y, Negi M, Kubota K, Makino T, Shibuya H. FDG PET/CT of a benign ovarian Brenner tumor. *Clin Imaging*. 36(5):650-3,2012
9. Fujita K, Naganuma M, Saito E, Suzuki S, Araki A, Negi M, Kawachi H, Watanabe M. Histologically confirmed IgG4-related small intestinal lesions diagnosed via double balloon enteroscopy. *Dig Dis Sci*. 57(12):3303-6,2012
10. Oda G, Sato T, Ishikawa T, Kawachi H, Nakagawa T, Kuwayama T, Ishiguro M, Iida S, Uetake H, Sugihara K. Significance of stromal decorin expression during the progression of breast cancer. *Oncol Rep*. 28(6):2003-2008,2012
11. Takashima M, Kawachi H, Yamaguchi T, Nakajima Y, Kitagaki K, Sekine M, Iida T, Takemura K, Kawano T, Eishi Y. Reduced expression of cytokeratin 4 and 13 is a valuable marker for histologic grading of esophageal squamous intraepithelial neoplasia. *J Med Dent Sci*. 59:17-28,2012
12. Ueno H, Mochizuki H, Akagi Y, Kusumi T, Yamada K, Ikegami M, Kawachi H, Kameoka S, Ohkura Y, Masaki T, Kushima R, Takahashi K, Ajioka Y, Hase K, Ochiai A, Wada R, Iwaya K, Shimazaki H, Nakamura T, Sugihara K. Optimal Colorectal Cancer Staging Criteria in TNM Classification. *J Clin Oncol*. 30(13):1519-1526,2012
13. Nakajima Y, Ohta S, Okada T, Miyawaki Y, Hoshino A, Suzuki T, Kawada K, Nishikage T, Nagai K, Ae K, Kawachi H, Kawano T. Osteoplastic bone metastasis in esophageal squamous cell cancer: report of a case. *Surg Today*. 42(4):376-381,2012
14. Sekine M, Kobayashi D, Ito T, Uchida K, Sekiya T, Eishi Y. Immunohistochemical detection of *Helicobacter pylori* with a novel monoclonal antibody: Its clinicopathological significance and validity in the routine pathological diagnosis. *Rinsho Byori* 60(4):287-93,2012 Japanese.

Physiology and Cell Biology

1. Staffs and Students

Professor	Noboru MIZUSHIMA (~September)	
Adjunct Professor	Noboru MIZUSHIMA (October~)	
Assistant Professor	Akiko KUMA,	Taki NISHIMURA,
	Atsushi TANAKA	
Adjunct Lecturer	Ikuko HONDA (August~)	
Tokunin Assistant Professor	Chieko KISHI (April~July),	Eisuke ITAKURA (April~July.)
Medical Fellow	Chieko KISHI (~March),	Ikuko HONDA (June~July)
Postdoctoral Fellow	Eisuke ITAKURA (~March),	Ikuko HONDA (~May)
Graduate Students	Anoop Kumar Gopi VELIKKAKATH (~March),	
	Kay KITAMURA (~March),	Mayurbhai Himatbhai SAHANI,
	Hideaki MORISHITA,	Quy PHAM NGUYEN,
	Takako NAITO,	Takeshi KAIZUKA,
	Peidu JIANG,	Saori YOSHII (April~),
	Norito TAMURA (April~)	

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 autophagy, a dynamic degradation system within cells
- 2) Physiological and pathophysiological roles of autophagy
- 3) Development of new methods for monitoring autophagy

4. Publications

Original Article

1. Itakura, E., Kishi-Itakura, C., Mizushima, N. The hairpin-type tail-anchored SNARE syntaxin 17 targets to autophagosomes for fusion with endosomes/lysosomes. *Cell* 151: 1256-1269 (2012)
2. Quy, P.N., Kuma, A., Pierre, P., Mizushima, N. Proteasome-dependent activation of mammalian target of rapamycin complex 1 (mTORC1) is essential for autophagy suppression and muscle remodeling following denervation. *J. Biol. Chem.* Epub 2012 Dec 3
3. Onoue, K., Jofuku, A., Ban-Ishihara, R., Ishihara, T., Maeda, M., Koshihara, T., Itoh, T., Fukuda, M., Otera, H., Oka, T., Takano, H., Mizushima, N., Mihara, K., Ishihara, N. Fis1 acts as mitochondrial recruitment factor for TBC1D15 that involved in regulation of mitochondrial morphology. *J. Cell Sci.* 2012 Oct 17. [Epub ahead of print]
4. Imaizumi Y, Okada Y, Akamatsu W, Koike M, Kuzumaki N, Hayakawa H, Nihira T, Kobayashi T, Ohshima M, Sato S, Takanashi M, Funayama M, Hirayama A, Soga T, Hishiki T, Suematsu M, Yagi T, Ito D, Kosakai A, Hayashi K, Shouji M, Nakanishi A, Suzuki N, Mizuno Y, Mizushima N, Amagai M, Uchiyama Y, Mochizuki H, Hattori N, Okano H. Mitochondrial dysfunction associated with increased oxidative stress and alpha-synuclein accumulation in PARK2 iPSC-derived neurons and postmortem brain tissue. *Mol. Brain.* 2012 Oct 6;5(1):35. [Epub ahead of print]
5. Lin, T.C., Chen, Y.R., Kensicki, E., Li, A.Y., Kong, M., Li, Y., Mohney, R.P., Shen, H.M., Stiles, B., Mizushima, N., Lin, L.I., Ann, D.K. Autophagy: Resetting glutamine-dependent metabolism and oxygen consumption. *Autophagy* 8: 1477-1493 (2012)
6. Kitamura, K., Kishi-Itakura, C., Tsuboi, T., Sato, S., Kita, K., Ohta, N., Mizushima, N. Autophagy-Related Atg8 Localizes to the Apicoplast of the Human Malaria Parasite Plasmodium falciparum. *PLoS One* 7:e42977 (2012)
7. Liu, S., Hartleben, B., Kretz, O., Wiech, T., Igarashi, P., Mizushima, N., Walz, G., Huber, T.B. Autophagy plays a critical role in kidney tubule maintenance, aging and ischemia-reperfusion injury. *Autophagy* 8: 826-837 (2012).
8. Itakura, E., Kishi-Itakura, C., Koyama-Honda, I., Mizushima, N. Structures containing Atg9A and the ULK1 complex independently target depolarized mitochondria at initial stages of Parkin-mediated mitophagy. *J. Cell Sci.* 125: 1488-

1499 (2012).

9. Velikkakath, A.K.G, Nishimura, T., Oita, E., Ishihara, N., Mizushima, N. Mammalian Atg2 proteins are essential for autophagosome formation and important for regulation of size and distribution of lipid droplets. *Mol. Biol. Cell* 23: 896-909 (2012).

Review Article

1. Klionsky, D.J., Mizushima, N., ····, et al. Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy* 8:445-544 (2012).
2. Shpilka, T., Mizushima, N., Elazar, Z. Ubiquitin-like proteins and autophagy at a glance. *J. Cell Sci.* 125:2343-2348 (2012).

Molecular Cellular Cardiology Bio-informational Pharmacology

1. Staffs and Students (April, 2012)

Professor Tetsushi Furukawa, MD, PhD
Assistant professor Yusuke Ebana, MD, PhD

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)

Atrial fibrillation (AF) is the most frequent arrhythmias, reaching more than 3.5 million patients in Japan. Associated cerebral infarction due to cardiogenic thrombosis (250,000 patients /year in Japan) causes reduced QOL and is one of the main causes of bedridden old people. We have taken following approaches to establish protection and treatment of atrial AF.

a. GWAS (genome-wide association study) in AF

We carry out most extensive GWAS (genome-wide association study) in Japan to determine gene polymorphisms associated with AF. Since 2011, we have participated in the international Meta-analysis called as CHARGE study. We found 10 SNPs associated with AF: among them, 6 SNPs were associated with both European/American and Japanese, and 4 with European/American but not with Japanese.

b. Inflammatory and immunological mechanisms in atrial fibrillation

AF is a multifactorial disease, and inflammatory response is believed to play a role in linking between these risks and AF. In vitro Boyden chamber experiments and in vivo TAC experiments, we showed that stretch-induced ATP release via a gap-junction channel, pannexin-2, induces recruitment of macrophages, acting as an initial factor to provoke atrial inflammation. This paper was selected as the Best Basic Paper on AF 2012 in Boston AF symposium 2013.

2. Pathogenesis of ventricular tachyarrhythmias and sudden cardiac death

Despite extensive effort by many researchers for years, ventricular tachycardia and fibrillation remain the main cause of sudden death, and the biggest challenge in arrhythmia research. Our laboratory approaches this issue using genetically engineered mice. In this year, we found that the mice with genetic deletion of the His-Purkinje system-specific transcription factor were susceptible to exercise-related atrio-ventricular block and ventricular tachyarrhythmias. In human, genetic mutations in the His-Purkinje system-specific transcription factor are associated with idiopathic ventricular fibrillation related to exercise.

3. Use of iPS cells for arrhythmia research

Traditional arrhythmia researches have been performed in cardiomyocytes of species other than human, or in cultured cells, in which human ion channel genes have been heterologously expressed. The milieu different from human cardiac myocytes (especially the lack of excitation-contraction coupling machinery) is the serious limitation for arrhythmia research. Cardiomyocytes differentiated from human iPS cells could overcome this critical limitation, and would bring marked advance in arrhythmias researches. We take following 2 approaches.

a. Establishment and functional analysis of human iPS-derived cardiomyocytes (hiPS-CM) from familiar sudden death patients (LQT, Brugada syndrome)

We established and characterized iPS cell-derived cardiomyocytes from human fibroblasts obtained from familiar sudden death patients (LQT, Brugada syndrome). We have able to establish iPS cells from LQT1, LQT2, LQT3, and Brugada syndrome. Our data showed that hiPS-CM from LQT patients maintain some of electrophysiological phenotype found in LQT patients' hearts.

b. 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

To analyze cardiac contractility, one has to perform echocardiography or catheter measurement of intra-cardiac pressure/intra-cardiac volume in vivo. Thus, to examine possible cardiac toxicity of new drugs, one must wait until in vivo assay. Motion vector technology created by Sony Co. can non-invasively estimate contraction and relaxation speed of cardiac myocytes in vitro. We verified using well-defined drugs that motion vector technology can assess drug's effects on contraction and relaxation of cardiac myocytes. We also confirmed that motion vector can be monitored simultaneously with electrical activity of cardiomyocytes (MEA), and also that this technology can be applied to the hiPS-CMs.

b. Basic research for generation of 3-D simulator of cardiac electrical activity

4. Publications List

Original Article

1. Ellinor PT, Lunetta KL, Albert CM, Glazer NL, Ritchie MD, Smith AV, Arking DE, Muller-Nurasyid M, Krijthe BP, Lubitz SA, Bis JC, Chung MK, Dorr M, Ozaki K, Roberts JD, Smith JG, Pfeufer A, Sinner MF, Lohman K, Ding J, Smith NL, Smith JD, Rienstra M, Rice KM, Van Wagener DR, Magnani JW, Wakili R, Clauss S, Rotter JI, Steinbeck G, Launer LJ, Davies RW, Borkovich M, Harris TB, Lin H, Volker U, Volzke H, Milan DJ, Hofman A, Boerwinjle E, Chen LY, Soliman EZ, Voight BF, Li G, Chakravarti A, Kubo M, Tedrow UB, Rose LM, Ridker PM, Conen D, Tsunoda T, Furukawa T, Sotoodehnia N, Xu S, Kamatani N, Levy D, Nakamura Y, Parvez B, Mahida S, Furie KL, Rosand J, Muhammad R, Psaty BM, Meitinger T, Perz S, Wichmann HE, Witteman JC, Kao WH, Kathiresan S, Roden DM, Uitterlinden AG, Rivadeneira F, McKnight B, Sjogren M, Newman AB, Liu Y, Gollob MH, Melander O, Tanaka T, Stricker BH, Felix SB, Alonso A, Darbar D, Barnard J, Chasman DI, Heckbert SR, Benjamin EJ, Gudnason V, Kaab S. Meta-analysis identifies six new susceptibility loci for atrial fibrillation. *Nat. Genet.*, 2012;44:670-675.
2. Oishi S, Sasano T, Tateishi Y, Tamura N, Isobe M, Furukawa T. Stretch of atrial myocytes stimulates recruitment of macrophages via ATP released through gap-junction channels. *J. Pharmacol. Sci.* 2012;120:296-304.
3. Egashira T, Yuasa S, Suzuki T, Aizawa Y, Yamakawa H, Matsuhashi T, Ohno Y, Tohyama S, Okata S, Seki T, Kuroda Y, Yae K, Hashimoto H, Tanaka T, Hattori F, Sato T, Miyoshi S, Takatsuki S, Murata M, Kurokawa J, Furukawa T, Makita N, Aiba T, Shimizu W, Horie M, Kamiya K, Kodama I, Ogawa S, Fukuda K. Disease characterization using LQTS-specific induced pluripotent stem cells. *Cardiovasc. Res.* 2012;95:419-429.
5. Takamura C, Ohhigashi H, Ebana Y, Isobe M. New human leukocyte antigen risk allele in Japanese patients with Takayasu arthritis. *Circ. J.* 2012;76:1697-1702.

Molecular Medicine and Metabolism

1. Staffs and Students (April, 2012)

Associate Professor Takayoshi SUGANAMI

2. Purpose of Education

The concept of the metabolic syndrome has come before the footlight because it is a precursory state of atherosclerotic diseases. It has been defined as a constellation of abdominal obesity, insulin resistance, hyperlipidemia, and hypertension, and is a multi-factorial pathologic condition that arises from complex interactions between genetic and environmental factors. In our laboratory, all the staffs and students have been provided the unique opportunities to investigate the pathophysiologic role of chronic inflammation and therapeutic implication of adipocytokines toward the better understanding of the molecular mechanism of the metabolic syndrome.

3. Research Subjects

- 1) Role of adipose tissue inflammation in the metabolic syndrome
- 2) Molecular mechanisms of saturated fatty acid-induced chronic inflammation

4. Publications

Original Articles

1. Watanabe Y, Nakamura T, Ishikawa S, Fujisaka S, Usui I, Tsuneyama K, Ichihara Y, Wada T, Hirata Y, Suganami T, Izaki H, Akira S, Miyake K, Kanayama HO, Shimabukuro M, Sata M, Sasaoka T, Ogawa Y, Tobe K, Takatsu K, Nagai Y. The Radioprotective 105/MD-1 complex contributes to diet-induced obesity and adipose tissue inflammation. **Diabetes** 61: 1199-1209, 2012
2. Ehara T, Kamei Y, Takahashi M, Yuan X, Kanai S, Tamura E, Tanaka M, Yamazaki T, Miura S, Ezaki O, Suganami T, Okano M, Ogawa Y. Role of DNA methylation in the regulation of lipogenic glycerol-3-phosphate acyltransferase 1 gene expression in the mouse neonatal liver. **Diabetes** 61: 2442-2450, 2012
3. Satoh-Asahara N, Shimatsu A, Sasaki Y, Nakaoka H, Himeno A, Tochiya M, Kono S, Takaya T, Ono K, Wada H, Suganami T, Hasegawa K, Ogawa Y. Highly purified eicosapentaenoic acid increases interleukin-10 levels of peripheral blood monocytes in obese patients with dyslipidemia. **Diabetes Care** 35: 2631-2639, 2012
4. Yamakawa N, Ohto U, Akashi-Takamura S, Takahashi K, Saitoh SI, 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.** 2012 Sep 7. [Epub ahead of print].

Review Articles

1. Suganami T, Tanaka M, Ogawa Y. Adipose tissue inflammation and ectopic lipid accumulation. **Endocr. J.** 59: 849-857, 2012

Stem Cell Regulation

1. Staffs and Students

Professor	Tetsuya TAGA
Associate Professor	Tetsushi KAGAWA
Associate Professor	Ikuo NOBUHISA
Project Assistant Professor	Kouichi TABU (April 2012-)
Administrative Assistant	Mako FUSHIMI
Technical Assistant	Yuko ONISHI (-March 2012)
Technical Assistant	Hiroko SUZUKI (-March 2012)
Technical Assistant	Kazuko INOUE (April 2012-)
Graduate Student	Norihisa BIZEN
Graduate Student	Maha ANANI
Graduate Student	Genki SUDO (April 2012-)
Graduate Student	Yasuhiro KOKUBU (-March 2012, October 2012-)
Graduate Student	Suguru KINOSHITA (-March 2012)
Graduate Student	Yuuki TAKAZAWA (-March 2012)
Graduate Student	Reiko NOMURA (-March 2012)
Graduate Student	Nozomi MURAMATSU
Graduate Student	Kaho HARADA (April 2012-)
Graduate Student	Mayumi AMANO (April 2012-)
Graduate Student	Sachiko KANEKO (April 2012-)
Graduate Student	Yoshitaka MUROTA (April 2012-)
Research Student	Kazuo TERASHIMA (April 2012-)
Research Student	Wenqian WANG (October 2012-)

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. Nobuhisa I, Yamasaki S, Ramadan A and Taga T: CD45^{low} c-Kit high cells have hematopoietic properties in the mouse aorta-gonad-mesonephros region. *Exp. Cell Res.*, 318:705-715, 2012.
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, in press.

Review Article

1. Tabu K, Taga T, and Tanaka S. Tumor stem cells: CD133 gene regulation and tumor stemness. In *Stem Cells and Cancer Stem Cells*, Volume 2, Part 2, (Springer.) 145-153, 2012.
2. 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.*, in press.

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.	
GCOE International Coordinator:	Tetsuya Nakamoto, M.D., Ph.D.	
GCOE Research Instructor:	Takuya Notomi, Ph.D.	
Secretary:	Naoko Ogawa	
GCOE Secretary:	Yuko Oshie,	Kumiko Tomita
Graduate Students:	Smriti Aryal A.C.,	Chiho Watanabe,
	Makiri Kawasaki,	Junpei Shirakawa,
	Shuichi Moriya,	Takayuki Yamada
Undergraduate Student:	Arina Hatta	

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. Hanyu R, Wehbi VL, Hayata T, Moriya S, Feinstein TN, Ezura Y, Nagao M, Saita Y, Hemmi H, Notomi T, Nakamoto T, Schipani E, Takeda S, Kaneko K, Kurosawa H, Karsenty G, Kronenberg HM, Vilaridaga JP, Noda M. Anabolic action of parathyroid hormone regulated by the β 2-adrenergic receptor. *Proc Natl Acad Sci U S A* 109:7433-8, 2012.
2. Hemmi H, Zaidi N, Wang B, Matos I, Fiorese C, Lubkin A, Zbytniuk L, Suda K, Zhang K, Noda M, Kaisho T, Steinman RM, Idoyaga J. Trem14, an Ig superfamily member, mediates presentation of several antigens to T cells in vivo, including protective immunity to HER2 protein. *J Immunol* 188:1147-55, 2012.
3. Notomi T, Ezura Y, Noda M. Identification of two-pore channel 2 as a novel regulator of osteoclastogenesis. *J Biol Chem* 287:35057-64, 2012.
4. Miyajima D, Hayata T, Suzuki T, Hemmi H, Nakamoto T, Notomi T, Amagasa T, Böttcher RT, Costell M, Fässler R, Ezura Y, Noda M. Profilin1 regulates sternum development and endochondral bone formation. *J Biol Chem* 287:33545-53, 2012.
5. 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* (in press).
6. Aryal AC S, Miyai K, Ezura Y, Hayata T, Notomi T, Nakamoto T, Pawson T, Noda M. Nck1 deficiency accelerates unloading-induced bone loss. *J Cell Physiol* (in press).
7. Sakuma T, Nakamoto T, Hemmi H, Kitazawa S, Kitazawa R, Notomi T, Hayata T, Ezura Y, Amagasa T, Noda M. CIZ/NMP4 is expressed in B16 melanoma and forms a positive feedback loop with RANKL to promote migration of the melanoma cells. *J Cell Physiol* 227:2807-12, 2012.
8. Izu Y, Ezura Y, Mizoguchi F, Kawamata A, Nakamoto T, Nakashima K, Hayata T, Hemmi H, Bonaldo P, Noda M. Type VI collagen deficiency induces osteopenia with distortion of osteoblastic cell morphology. *Tissue Cell* 44:1-6,

2012.

9. Ono N, Nakashima K, Schipani E, Hayata T, Ezura Y, Soma K, Kronenberg HM, Noda M. Constitutively active pth/pthrp receptor specifically expressed in osteoblasts enhances bone formation induced by bone marrow ablation. *J Cell Physiol* 227:408-15, 2012.

Chronobiology

1. Staffs (April. 2012)

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. Shoji Hata, Jun Hirayama, Hiroaki Kajihio, Kentaro Nakagawa, Yutaka Hata, Toshiaki Katada, Makoto Furutani-Seiki and Hiroshi Nishina (2012) A novel acetylation cycle of the transcription co-activator Yes-associated protein that is downstream of the Hippo pathway is triggered in response to SN2 alkylating agents. *J. Biol. Chem.* 287, 22089-22098.
2. Yoshimi Uchida, Tomomi Osaki, Tokiwa Yamasaki, Tadanori Shimomura, Shoji Hata, Kazumasa Horikawa, Shigenobu Shibata, Takeshi Todo, Jun Hirayama and Hiroshi Nishina (2012) Involvement of the Stress Kinase Mitogen-activated Protein Kinase Kinase 7 in the Regulation of the Mammalian Circadian Clock. *J. Biol. Chem.* 287, 8318-8326.
3. Yoshimi Uchida, Tadanori Shimomura, Jun Hirayama and Hiroshi Nishina (2012) Light, reactive oxygen species, and magnetic fields activate ERK/MAPK signaling pathway in cultured zebrafish cells. *Appl. Magn. Reson.* 42, 69-77.
4. Miki Nishio, Koichi Hamada, Kohichi Kawahara, Masato Sasaki, Fumihito Noguchi, Shuhei Chiba, Kensaku Mizuno, Satoshi O. Suzuki, Youyi Dong, Masaaki Tokuda, Takumi Morikawa, Hiroki Hikasa, Jonathan Eggenschwiler, Norikazu Yabuta, Hiroshi Nojima, Kentaro Nakagawa, Yutaka Hata, Hiroshi Nishina, Koshi Mimori, Masaki Mori, Takehiko Sasaki, Tak W. Mak, Toru Nakano, Satoshi Itami, and Akira Suzuki (2012) Cancer Susceptibility and embryonic lethality in Mob1A/1B double mutant mice. *J. Clin. Invest.* 122(12):4505-4518.
5. Tadashi Yokoi, Yuko Seko, Tae Yokoi, Hatsune Makino, Shin Hatou, Masakazu Yamada, Tohru Kiyono, Akihiro Umezawa, Hiroshi Nishina, Noriyuki Azuma (2012) Establishment of Functioning Human Corneal Endothelial Cell Line with High Growth Potential. *PLoS ONE* 7(1):e29677
6. Ken Okada, Akihide Kamiya, Keiichi Ito, Ayaka Yanagida, Hidenori Ito, Hiroki Kondou, Hiroshi Nishina and Hiromitsu Nakauchi (2012) Prospective isolation and characterization of bipotent progenitor cells in early mouse liver development. *Stem Cells and Development* 21, 1124-1133.
7. Takuya Iwamoto, Shuji Terai, Yuko Mizunaga, Naoki Yamamoto, Kaoru Omori, Koichi Uchida, Takahiro Yamasaki, Yasuhiko Fujii, Hiroshi Nishina, and Isao Sakaida (2012) Splenectomy enhances the anti-fibrotic effect of bone marrow cell infusion and improves liver function in cirrhotic mice and patients *J. Gastroenterol.* 47, 300-312.
8. Toshiyuki Oishi, Shuji Terai, Shinya Kuwashiro, Koichi Fujisawa, Toshihiko Matsumoto, Hiroshi Nishina and Isao Sakaida (2012) Ezetimibe reduces fatty acid quantity in liver and decreased inflammatory cell infiltration and improved NASH in medaka model. *Biochem. Biophys. Res. Commun.* 422, 22-27.
9. Shoji Hata and Hiroshi Nishina (2012) [Letters to the Editor] Reply to Sun et al.: Targeting YAP acetylation in cancer. *J. Biol. Chem.* 287, 35443.

10. Tokiwa Yamasaki, Hiroshi Kawasaki and Hiroshi Nishina (2012) [review] Diverse roles of JNK and MKK pathways in the brain. *J. Signal Trans.* 2012: 459265.
11. Hiroshi Nishina (2012) [commentary] hDlk-1: A cell surface marker common to normal hepatic stem/progenitor cells and carcinomas. *J. Biochem.* 152, 121-123.

Stem cell Biology

1. Staffs and Students (April 2012)

Professor	Emi NISHIMURA	
Assistant Professor	Takahiro AOTO,	Hiroyuki MATSUMURA
Research Associate	Yasuaki MOHRI,	Jun SUNAYAMA
Graduate Student	Makiko UENO,	Ryoko TAGUCHI,
	Hikaru KOBAYASHI	
Research Student	Nguyen Thanh BINH	
Technical Staff	Koki ONISHI	
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 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. Mohammad S, Matsumura H, Okubo-Suzuki R, Ohkawa N, Inokuchi K. Neuronal stimulation induces autophagy in hippocampal neurons that is involved in AMPA Receptor degradation after chemical long-term depression. *J Neurosci.* 32(30): 10413-10422. 2012
2. Mohri Y, Oyama K, Sone M, Akamatsu A, Nishimori K. LGR4 is required for the cell survival of the peripheral mesenchyme at the embryonic stages of nephrogenesis. *Biosci Biotechnol Biochem.* 76(5): 888-91. 2012

Integrated Pulmonology

1. Staffs and Students (December, 2012)

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

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. Okamoto T, Miyazaki Y, Shirahama R, Tamaoka M, Inase N: Proteome analysis of bronchoalveolar lavage fluid in chronic hypersensitivity pneumonitis. *Allergol Int* 61: 83-92, 2012
2. Sonoda S, Taniguchi M, Sato T, Yamasaki M, Enjoji M, Mae S, Irie T, Ina H, Sumi Y, Inase N, Kobayashi T: Bilateral pleural fluid caused by a pancreaticopleural fistula requiring surgical treatment. *Intern Med* 51: 2655-2661, 2012
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5. Honda T, Kobayashi H, Saiki M, Sogami Y, Miyashita Y, Inase N.: Gastroesophageal variceal hemorrhage induced by metastatic liver tumor of lung cancer. *Case Rep Oncol* 5: 644-650, 2012

Gastroenterology and Hepatology

1. Staffs and Students (April, 2012)

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)	
Junior Associate Professor	Akihiro ARAKI Shinya OOKA (Department of Professional Development), Sei KAKINUMA (Department for Hepatitis Control), Kiichiro TSUCHIYA (Department of Advanced Therapeutics in Gastrointestinal Diseases)	
Assistant Professor	Masakazu NAGAHORI, Takashi NAGAISHI, Yasuhiro NEMOTO, Eriko OKADA (Department of Endoscopic Diagnosis and Therapeutics), Shigeru OOSHIMA (Department of Advanced Therapeutics in Gastrointestinal Diseases)	Cheng-Hsin AZUMA, Mina NAKAGAWA,
Tokunin Assistant Professor	Megumi TASAKA	
Hospital Staff	Yuki SAKURAI, Eiko SAITO, Yoshihito KANO(April~), Fumio GOTO(April~), Sayuri NITTA(April~)	Toshimitsu FUJII, Akiko KITAZUME, Syun KANEKO(April~), Yoichi NIBE(April~),
Medical Fellow	Shiro YUI,	Tomohiro MIZUTANI,(April~)
Graduate Student	Masahiro SUZUKI, Michihiro SHIMIZU, Tatsuro MURANO, Kouhei YOSHINO, Nobukatsu HORITA, Kengo NOZAKI, Yuki YAMAUCHI, Hukiko KAWAI Hideto YAMANAKA, Keita FUKUSHIMA, Satoru FUJII,	Xiu ZHENG, Miyako MURAKAWA, Masayoshi FUKUDA, Go ITOH, Yu MATSUZAWA, Masahiro TAKAHARA, Junnko FUJIKI, Miki TANIGUCHI, Kenji OOTANI, Masanori KOBAYASHI, Hideji HIBIYA

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.

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. Araki A, Suzuki S, Tsuchiya K, Oshima S, Okada E, Watanabe M: Modified single-operator method for double-balloon endoscopy. **Digestive Endoscopy**. 24(6):470-474, 2012
2. Araki A, Tsuchiya K, Oshima S, Okada E, Suzuki S, Morio-Akiyama J, Fujii T, Okamoto R, Watanabe M: Endoscopic ultrasound with double-balloon endoscopy for the diagnosis of inverted Meckel's diverticulum: a case report. **Journal of Medical Case Reports**. 6(1):328, 2012
3. Asahina Y, Tsuchiya K, Muraoka M, Tanaka K, Suzuki Y, Tamaki N, Hoshioka Y, Yasui Y, Katoh T, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nitta S, Sakamoto N, Izumi N: Association of gene expression involving innate immunity and genetic variation in interleukin 28B with antiviral response. **Hepatology**. 55: 20- 29, 2012
4. Calabrese E, Zorzi F, Zuzzi S, Ooka S, Onali S, Petruzzello C, Lasinio GJ, Biancone L, Rossi C, Pallone F: Development of a numerical index quantitating small bowel damage as detected by ultrasonography in Crohn's disease. **Journal of Crohn's and Colitis**. 6: 852- 860, 2012
5. Fujita K, Naganuma M, Saito E, Suzuki S, Araki A, Negi M, Kawachi H, Watanabe M: Histologically confirmed IgG4-related small intestinal lesions diagnosed via double balloon enteroscopy. **Dig Dis Sci**. 57(12):3303-3308, 2012
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7. Izumi N, Asahina Y, Kurosaki M, Yamada G, Kawai T, Kajiwarra 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**. (Epub ahead of print) , 2012
8. 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. **Biochem Biophys Res Commun**. (Epub ahead of print), 2013.
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17. 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.** (Epub ahead of print), 2012
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 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, 2012
 32. Watanabe M, Hanai H, Nishino H, Yokoyama T, Terada T, Suzuki Y: Comparison of QD and TID oral mesalazine for maintainance of remission in quiescent ulcerative colitis: a double-blind, double-dummy, randomized multicenter study. **Inflammatory Bowel Dis**. (in press), 2012
 33. Watanabe T, Sasaki I, Sugita A, Fukushima K, Futami K, Hibi T, Watanabe M: Interval of less than 5 years between the first and second operation is a risk factor for a third operation for Crohn's disease. **Inflamm Bowel Dis**. 18: 17- 24, 2012
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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, Takatoshi MATSUYAMA, Kazuo MOTOYAMA, Makoto NAGAHARA, Satoshi OKAZAKI
Professor:	Kazuyuki KOJIMA (Minimally invasive surgery center)
Associate Professor:	Hiroyuki UETAKE (Translational oncology)
Associate Professor:	Hiroto KOBAYASHI (Minimally invasive surgery center)
Assistant Professor:	Megumi ISHIGURO (Translational oncology)
Graduate Student:	Yasushi TAKATSUNO, Ken HINOUE, Hirofumi SUGITA, Goshi ODA, Akifumi KIKUCHI, 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

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. Kotake K, Honjyo S, Sugihara K, Hashiguchi Y, Kato T, Kodaira S, Muto T, Koyama Y. Number of lymph nodes retrieved is an important determinant of survival of patients with stage II and stage III colorectal cancer. *Jpn J Clin Oncol* 2012;42(1):29-35
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 10. Khamas A, Ishikawa T, Mogushi K, Iida S, Ishiguro M, Tanaka H, Uetake H, Sugihara K. Genome-wide screening for methylation-silenced genes in colorectal cancer. *Int J Oncol* 2012;41(2):490-496
 11. Sugihara K, Ohtsu A, Shimada Y, Mizunuma N, Lee PH, de Gramont A, Goldberg RM, Rothenberg ML, Andre T, Brienza S, Gomi K. Safty analysis of FOLFOX4 treatment in colorectal cancer patients: A comparison between two Asian studies and four Western Studies. *Clin Colorectal Cancer* 2012;11(2):127-136
 12. Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, Hamaguchi T, Hyodo I, Igarashi M, Ishida H, Ishiguro M, Kanemitsu Y, Kokudo N, Muro K, Ochiai A, Ohkura Y, Saito Y, Sakai Y, Ueno H, Yoshino T, Fujimori T, Koinuma N, Morita T, Nishimura G, Sakata Y, Takahashi K, Takiuchi H, Tsuruta O, Yamaguchi T, Yoshida M, Yamaguchi N, Kotake K, Sugihara K, JSCCR. Japanese society for cancer of the colon and recum (JSCCR) guidelines 2010 for the treatment of colorectal cancer. *Int J Clin Oncol* 2012;17(1):1-29
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 23. Kudo A, Ban D, Akashi T, Kumagai J, Aihara A, Inokuchi M, Kojima K, Kawano T, Tanaka S, Arii S. Prognoses of

- GEP-Nets with Undetermined Malignant Potentials of their Primary Sites. *Hepatogastroenterology*. 2012;59(118):1682-1686
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 31. Fujita S, Akasu T, Mizusawa J, Saito N, Kinugasa Y, Ohue M, Fujii S, Shiozawa M, Yamaguchi T, Moriya Y. Postoperative morbidity and mortality after mesorectal excision with and without lateral lymph node dissection for clinical stage II or stage III lower rectal cancer(JCOG0212): results from a multicentre, randomized controlled, non-inferiority trial. *Lancet Oncol* 2012;13:616-621
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 35. Azzoli C, Drilon A, Sugita H, Sima C, Huang E, Danenberg P, Kris M, Rusch V. Prospective study of tumor suppressor gene(TSG) methylation as a prognostic biomarker in surgically resected non-small cell lung cancer(NSCLC). *J Clin Oncol* 2012;30 in print

Review Articles

1. Sugihara K, Uetake H. The therapeutic strategies for hepatic metastasis of colorectal cancer: overview. *J Hepatobiliary Pancreat Sci* 2012;19(5):523-527

Books

1. Kinugasa Y, Moriya Y. Surgical anatomy in intersphincteric resection. *Intersphincteric Resection for Low Rectal Tumors*. Rudolf Schiessel, Peter Metzgered. Austria: Springer Wien New York 2012:57-63
2. Kobayashi K, Sugihara K. Surveillance and Characteristics of Recurrence After Curative Resection for Colorectal Cancer. *Contemporary Issues in Colorectal Surgical Practice*. Yik-Hong Ho ed. INTECH 2012:89-112
3. Kojima K, Sugihara K, Sohn TS, Lee JH. Dissection of lymph nodes around the common hepatic artery (Nos.7,8a,9 lymph nodes). *Laparoscopic Gastrectomy for Cancer* Kitano S Yang HK ed. INTECH 2012 : 79 – 80

Cardiovascular Medicine

1. Staffs and Students (April, 2012)

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), Daisuke Tezuka	Ryoko Azuma, Ken Kurihara, Shingo Maeda,
Graduate Student	Chisato Takamura, Yu Hatano, Kentaro Takahashi, Tatsuya Hayashi, Tetsuo Kamiishi, Susumu Tao, Hiroshi Kawata, Tomoyo Sugiyama, Tomofumi Nakamura, Kei Takayama, Toru Miyazaki, Yuji Konishi, Masa-- Takigawa, Tatsuya Fujinami, Masahito, Suzuki, Rena Nakamura	Koji Higuchi, Kiyoshi Ohtomo, Masahiko Setoguchi, Tomoko Manno, Daisuke Ueshima, Kensuke Ihara, Koji Sugiyama, Ryota Iwatsuka, Yoko Kato, Yoichi Otaki, Atsuhiko Yagishita, Osamu Inaba, Naoyuki Miwa,

2. Education

We are dealing with pathophysiology of circulatory system especially cardiovascular diseases. Cardiovascular diseases are principal cause of death in our country. These diseases are categorized into several fields. They include ischemic heart disease, myocardial disease, valvular disease, atherosclerosis, arrhythmia, and infectious disease. The common final figure of these diseases is heart failure leading to patients' death. Based on recent progresses in molecular biology and bioengineering our knowledge on the pathophysiology of these diseases has been expanded rapidly. There are variety of new diagnostic technologies including imaging tests, hematological tests and electrophysiological tests. In addition, development in the treatment of cardiovascular disease is overwhelming. They include intravascular catheter intervention, catheter ablation and operation. Medical treatment has also been progressed rapidly. Further, gene therapy for cardiovascular diseases has started. All of these fields are our focus for education. In this course, students learn about modern knowledge and technologies in cardiovascular diseases, especially in the field of pathophysiology, diagnosis, treatment and prevention.

3. Research Subjects

The purposes of our investigation are to reveal the etiology and pathophysiology of cardiovascular diseases, and to develop new technologies for diagnosis and treatment. For that purpose we investigate clinical cases and model animals. Currently our investigations are focusd on arteriosclerosis, atherosclerosis, cardiomyopathy, myocarditis, arrhythmias, cardiac rejection and heart failure. The relationship between gene mutation and cardiovascular disease, electrophysiology, myocardial cell transplantation and myocardial regeneration are also our major subjects of research.

- 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, Suzuki)
- 8) Regulation of arteriosclerosis by targeting transcription factors (Isobe)
- 9) Gene therapy of vascular disease (Isobe)
- 10) Diagnostic imaging of aortitis (Isobe)
- 11) Molecular mechanism and treatment of aortitis (Isobe)
- 12) Assessment of vascular endothelial dysfunction in vasculitis, heart failure and arrhythmia(Isobe)
- 13) Application in gene therapy for heart failure and cardiomyopathy(Isobe)
- 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 Cardioendoscope(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)

We conduct collaborative researches with not only Medical Research Institute and other facilities in our university but also domestic and foreign institutes according to research projects. Since clinical cases in our hospital are diverse and abundant, clinical investigations are also our major target. Therefore, we can provide many research projects depending on students' need. We encourage and help students to pursue their own original way of investigation.

4. Clinical Services

Students are also encouraged to learn about clinical cardiology. They can participate in any clinical activities underwent in our hospital including cardiac catheterization, electrophysiological study, catheter ablation, various imaging tests, cardiac pathology, and patients care.

5. Publications

Review

1. Adachi S, Isobe M: Plakophilin-2 gene could be a causative factor in arrhythmogenic right ventricular cardiomyopathy. *Circ J* 76(1): 51-52, 2012

Original Article

1. Maeda S, Yamauchi Y, Obayashi T, Hirao K, Isobe M: Atrial fibrillation arising from the left brachiocephalic vein. *J Am Coll Cardiol* 59: 773, 2012
2. Ozaki, S; Ando, M; Isobe, M; Kobayashi, S; Matsunaga, N ; Miyata, T; Nakabayashi, K; Nakajima, Y; Nose, M; Ohta, T; Shigematsu, H; Sueishi, K; Tanemoto, K ; Yoshida, A; Yoshida, M; Yutani, C ; Arimura, Y; Fukaya, S ; Hamaguchi, S ; Hashimoto, H; Hiromura, K ; Ishizu, A; Iwai, T; Kaneko, K; Kataoka, H; Kawana, S; Kida, I ; Kobayashi, Y; Komori, K; Masaki, H; Matsumoto, T; Nagaoka, T; Nagasawa, K; Nojima, Y; Okada, M; Okazaki, T; Sakamoto, I; Shigematsu, K; Shiiya, N; Takahashi, A; Takizawa, H ; Yamada, H; Yoshida, S; Fukui, T; Horie, M; Koike, T; Kumagai, S; Sasajima, T: Guideline for Management of Vasculitis Syndrome (JCS 2008) Digest Version. *Circ J* 75(2): 474-503, Feb 2012
3. Maeda S, Yamauchi Y, Obayashi T, Hirao K, Isobe M: Atrial fibrillation arising from the left brachiocephalic vein. *J Am Coll Cardiol* 59(8): 773, Feb 2012
4. Miyazaki S, Kuwahara T, Kobori A, Takahashi Y, Takei A, Sato A, Isobe M, Takahashi A: Impact of the Adenosine Provoked Acute Dormant Pulmonary Vein Conduction on Recurrence of Atrial Fibrillation. *J Cardiovasc Electrophysiol* 23: 256-260, Mar 2012.
5. Watanabe R, Ogawa M, Suzuki J (corresponding author), Hirata Y, Nagai R, Isobe M. A comparison between imidapril and ramipril on attenuation of ventricular remodeling after myocardial infarction. *J Cardiovasc Pharmacol*. 59(4): 323-330, 2012

6. Hamaya R, Ogawa M, Kobayashi N, Suzuki J, Hirata Y, Nagai R, Isobe M: A Novel IKK Inhibitor Prevents Progression of Restenosis after Arterial Injury in Mice. *Int Heart J* 53(2): 133-138, 2012
7. Ohigashi H, Haraguchi G, Konishi M, Tezuka D, Kamiishi T, Ishihara T, Isobe M: Improved Prognosis of Takayasu Arteritis in the Last Decade: Comprehensive Analysis of 106 Patients. *Circ J* 76(4): 1004-1011, 2012
8. Kawata H, Noda T, Yamada Y, Okamura H, Satomi K, Aiba T, Takaki H, Aihara N, Isobe M, Kamakura S, Shimizu W: Effect of sodium-channel blockade on early repolarization in inferior/lateral leads in patients with idiopathic ventricular fibrillation and Brugada syndrome. *Heart Rhythm* 9: 77-83, 2012
9. Tezuka D, Haraguchi G, Ishihara T, Ohigashi H, Inagaki H, Suzuki J, Hirao K, Isobe M: Role of FDG-PET/CT and Utility of Maximum Standard Uptake Value in Takayasu Arteritis: Sensitive Detection of Recurrence. *J Am Coll Cardiol Imaging* 5(4): 422-429, 2012
10. Kamimura M, Moroi M, Isobe M, Hiroe M: Role of coronary CT angiography in asymptomatic patients with type 2 diabetes mellitus. *Int Heart J* 53(1): 23-28, 2012
11. Suzuki J, Ogawa M, Sakai Y, Hirata Y, Isobe M, Nagai R: A prostacycline analog prevents chronic myocardial remodeling in murine cardiac allografts. *Int Heart J* 53(1): 64-67, 2012
12. Matsumoto R, Suzuki J, Watanabe R, Ogawa M, Isobe M: Inhibition of I κ B phosphorylation by a novel IKK inhibitor IMD-1041 attenuates myocardial dysfunction after infarction. *Immunol Endocr Metab Agents Med Chem*. 12: 137-42, 2012
13. Yamada R, Suzuki J, Isobe M: Clarithromycin Attenuates Left Ventricular Remodeling and Dysfunction after Pressure Overload in Mice. *Immunol Endocr Metab Agents Med Chem*, 12: 147-151, 2012
14. Shima N, Suzuki J, Isobe M: Clarithromycin Attenuates Left Ventricular Remodeling and Dysfunction after Pressure Overload in Mice Via Matrix Metalloproteinase Suppression. *Immunol Endocr Metab Agents Med Chem*, 12: 143-6, 2012
15. Takamura C, Ohigashi H, Ebana Y, Isobe M: A New HLA Risk Allele in Japanese Patients with Takayasu Arteritis. *Circ J* 76(7): 1697-1702, 2012
16. Suzuki J, Tezuka D, Morishita R, Isobe M. Eight-year follow-up of an initial case with NF-kB decoy oligodeoxynucleotide transfection after coronary stent implantation. *Immun Endoc Metab Agents in Med Chem*. 12: 40-2, 2012
17. Otsuka H, Arimura T, Abe T, Kawai H, Aizawa Y, Kubo T, Kitaoka H, Nakamura H, Nakamura K, Okamoto H, Ichida F, Ayusawa M, Nunoda S, Isobe M, Matsuzaki M, Doi YL, Fukuda K, Sasaoka T, Izumi T, Ashizawa N, Kimura A: Prevalence and Distribution of Sarcomeric Gene Mutations in Japanese Patients With Familial Hypertrophic Cardiomyopathy. *Circ J* 76(2): 453-461, 2012
18. Hikita, H ; Kuroda, S ; Kawaguchi, N ; Nakashima, E ; Fujinami, T ; Sugiyama, T ; Kamiishi, T ; Takahashi, Y ; Nozato, T ; Kuwahara, T ; Satoh, A ; Takahashi, A ; Isobe, M. Differential Characteristics of Inflammatory Responses to Stent Implantation Between De Novo and Intrastent Restenosis Lesion in Patients With Stable Angina. *ANGIOLOGY* 63(Feb): 92-95, 2012
19. Kohro, T ; Iwata, H ; Fujiu, K ; Manabe, I ; Fujita, H ; Haraguchi, G ; Morino, Y ; Oguri, A ; Ikenouchi, H ; Kurabayashi, M ; Ikari, Y ; Isobe, M ; Ohe, K ; Nagai, R: Development and Implementation of an Advanced Coronary Angiography and Intervention Database System. *Int Heart J* 53(1): 35-42, 2012
20. Hanatani T, Aoyama N, Suzuki J, Izumi Y, Isobe M: A Periodontal Pathogen *Aggregatibacter actinomycetemcomitans* Deteriorates Ventricular Remodeling after Myocardial Infarction in Mice. *Int Heart J* 53(4): 253-256, 2012
21. Konishi M, Haraguchi G, Ohigashi H, Sasaoka T, Yoshikawa S, Inagaki H, Ashikaga T, Isobe M: Progression of Hyponatremia is Associated with Increased Cardiac Mortality in Patients Hospitalized for Acute Decompensated Heart Failure. *J Cardiac Failure* 18(8):620-5, 2012
22. Sekinishi A, Suzuki J, Aoyama N, Ogawa M, Watanabe R, Kobayashi N, Hanatani T, Ashigaki N, Hirata Y, Nagai R, Izumi Y, Isobe M: A Periodontal Pathogen *Aggregatibacter actinomycetemcomitans* Deteriorates Pressure Overload-Induced Myocardial Hypertrophy in Mice. *Int Heart J* 53(5): 324-330, 2012
23. Oishi S, Sasano T, Tateishi Y, Tamura N, Isobe M, Furukawa T: Stretch of atrial myocytes stimulates recruitment of macrophages via ATP released through gap-junction channels. *J Pharmacol Sci* 120: 296-304, 2012
24. Kameda T, Usami Y, Shimada S, Haraguchi G, Matsuda K, Sugano M, Kurihara Y, Isobe M, Tozuka M: Determination of myeloperoxidase-induced apoAI-apoAII heterodimers in high-density lipoprotein. *Ann Clin Lab Sci* 42(4): 384-391, 2012
25. Tanaka T, Suzuki J, Ogawa M, Itai A, Hirata Y, Nagai R, Isobe M. Inhibition of I kappaB phosphorylation prevents

load-induced cardiac dysfunction in mice. *Am J Physiol Heart Circ Physiol.* 303: H1435-45, 2012

26. Ashikaga T, Inagaki H, Satoh Y, Isobe M: Proximal balloon deflation technique: a novel method to retrieve retained or entrapped equipment from the coronary system. *Cardiovasc Revasc Med.* 13(4):253-255, 2012

Anesthesiology

1. Staffs and Students (April, 2012)

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. Ishikawa S, Griesdale DEG, Lohser J. Acute kidney injury after lung resection surgery: incidence and perioperative risk factors. *Anesth Analg* 2012; 114: 1256-62.
2. Ishikawa S. Alveolar recruitment maneuver as an important part of protective one-lung ventilation. *J Anesth* 2012; 26: 794-5.
3. Kopman AF, Kurata J. Can't intubate, can't ventilate: is "rescue reversal" a pipe-dream? (Editorial) *Anesth Analg* 2012; 114: 924-6
4. Kopman AF, Kurata J: Rescue reversal: an addendum. *Anesth Analg* 2012; 114:1254-5
5. Nakazawa K, Yokoyama K, Makita K. Cardiac arrest due to pulmonary thromboembolism following administration of spinal anesthesia – a case with femoral neck fracture who was successfully resuscitated with thrombolytic treatment. *Anesthesia & Resuscitation* 2012;48:71-2,
6. Otsubo Y, Satoh Y, Kodama M, Araki Y, Satomoto M, Sakamoto E, Pagès G, Pouysségur J, Endo S, Kazama T. Mechanical allodynia but not thermal hyperalgesia is impaired in mice deficient for ERK2 in the central nervous system. *Pain*. 2012;153:2241-52.
7. Yamauchi-Satomoto M, Adachi YU, Kurita T, Morita K, Sato S. Cross-clamping of the descending thoracic aorta leads to the asymmetrical distribution of propofol during cardiopulmonary bypass surgery. *Korean J Anesthesiol*.

2012;62:327-31.

8. Yanagawa Y, Hirano Y, Takemoto M, Takei T, Ito T, Iba T. Characteristics of Severe Alcoholic Ketoacidosis with a Reversible Visual Disturbance. *J Clin Toxicol* 2012;S7:001.

Cardiovascular Surgery

1. Staffs and Students (April. 2012)

Professor	Hirokuni ARAI	
Associate Professor	Tomohiro MIZUNO	
Junior Associate Professor		
Assistant Professor	Masafumi YASHIMA, Susumu MANABE, Akane MIHARA,	Satoru KAWAGUCHI, Tsuyoshi HACHIMARU, Shuhei FUJITA
Graduate Student	Hidehito KUROKI, Tatsuki FUJIWARA	Taiju WATANABE,
Hospital Staff	3	

Department of Cardiovascular Surgery, Research and Innovation for Advanced Surgery

Associate Professor Katsuhiko OHUCHI

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. Christopher G.A. McGregor, Davide Ricci, Naoto Miyagi, Paul G. Stalboerger, Zeji Du, Elise A. Oehler, Henry D. Tazelaar, Guerard W. Byrne. Human CD55 Expression Blocks Hyperacute Rejection and Restricts Complement Activation in Gal Knockout Cardiac Xenografts. Accepted for publication. *Transplantation*. 2012 Apr; 93(7): 686-92
2. Hosoda H, Izumi H, Tukada Y, Takagiwa J, Ghiaki T, Yano M, Arai H. Plasma Hepatocyte Growth Factor Elevation May be Associated with Early Metastatic Disease in Primary Lung Cancer Patients. *Ann Thorac Cardiovasc Surg* 2012; 18: 1-7
3. Tamura K, Arai H, Yoshizaki T. Long-Term Outcome of Active Infective Endocarditis with Renal Insufficiency in Cardiac Surgery. *Ann Thorac Cardiovasc Surg* 2012; 18: 216-221
4. Miyagi N, Arai H. What Is Optimal Revascularization for Hemodialysis Patients? *Circulation Journal* 2012; 76(5): 1085-1086

Presentation in international conference

1. Hirokuni Arai Coronary Surgery in PCI Era: Changes and Challenges. Special Guest Lecture, The 1st Heart Care

- Heart International Symposium, Hua Hin, Thailand 2012, March 2
2. Hirokuni Arai A novel approach for optimum exposure in OPCAB: A key for success. Special Guest Lecture, The 1st Heart Care Heart International Symposium, Hua Hin, Thailand 2012, March 2
 3. Hirokuni Arai Beating Heart MV surgery: The beauty of beating. Special Guest Lecture, The 1st Heart Care Heart International Symposium, Hua Hin, Thailand 2012, March 3
 4. Hirokuni Arai MV Complex remodeling: A novel approach for FMR. Special Guest Lecture, The 1st Heart Care Heart International Symposium, Hua Hin, Thailand 2012, March 3
 5. Hirokuni Arai Impact of intra-operative direct coronary scanning and epi-aortic echo using VeriQ C: its effectiveness and economical benefits. Medistim Lunch Symposium, EACTS, Barcelona, Spain 2012, November 24
 6. Naoto Miyagi, Hirokuni Arai, Kiyoshi Tamura, Satoru Kawaguchi, Satoru Makita, Taiju Watanabe, Tatsuki Fujiwara, Shogo Sakurai, Kenji Yokoyama, Shuhei Fujita Surgical strategy for severe ischemic cardiomyopathy and outcome. The 14th Annual Meeting of Asian Society for Cardiovascular Surgery Bali, Indonesia, 2012, March 8-11
 7. Kiyoshi Tamura, Hirokuni Arai, Satoru Kawaguchi, Satoru Makita, Naoto Miyagi, Taiju Watanabe, Tatsuki Fujiwara, Shuhei Fujita. Long-term results of modified Bentall procedure using flanged composite aortic prosthesis. The 14th Annual Meeting of Asian Society for Cardiovascular Surgery Bali, Indonesia, 2012, March 8-11
 8. Shuhei Fujita, Hirokuni Arai, Kiyoshi Tamura, Satoru Kawaguchi, Satoru Makita, Taiju Watanabe, Tatsuki Fujiwara, Naoto Miyagi The most suitable annuloplasty ring size in TAP for functional TR. The 14th Annual Meeting of Asian Society for Cardiovascular Surgery Bali, Indonesia, 2012, March 8-11
 9. Tatsuki Fujiwara, Eiki Nagaoka, Taiju Watanabe, Takashi Kitao, Daisuke Sakota, Tadahiko Shinshi, Hirokuni Arai, and Setsuo Takatani. A New ECMO System with a Single-use Magnetically Levitated Centrifugal Blood Pump MedTech Mag-Lev intended for Bridge-to-Heart-and-Lung-Transplantation. ISRBP 20th Congress of the International Society for Rotary Blood Pumps, Istanbul, Turkey, 20-22, September, 2012
 10. Hirokuni Arai, Tomohito Mizuno, Taiju Watanabe, Tatsuki Fujiwara, Akane Mihara, Tsuyoshi Hachimaru, Satoru Kawaguchi, Kiyoshi Tamura. Which Direction is Optimal for The Papillary Muscle Relocation Procedure in Functional Mitral Regurgitation? Session II Ischemic Mitral Valve Disease 2012, September 15 Karuizawa, Japan
 11. Shuhei Fujita, Hirokuni Arai, Tomohiro Mizuno, Kiyoshi Tamura, Satoru Kawaguchi, Tsuyoshi Hachimaru, Naoto Miyagi Proposal of a novel index for selection of optimal annuloplasty ring size for tricuspid annuloplication. 2012 AATS Mitral Conclave Session IV Tricuspid Valve Repair/Atrial Fibrillation Surgery Karuizawa, Japan 2012 September 15-16

Nephrology

1. Staffs and Students (April, 2012)

Professor	Sei SASAKI	
Associate Professor	Shinichi UCHIDA,	Tatemitsu RAI (Dept. of Blood Purification)
	Yumi NODA (Dept. of Chronic Kidney Disease)	
Junior Associate Professor	Tomokazu OKADO	
Assistant Professor	Naofumi YUI,	Eisei SOHARA (Dept. of Blood Purification)
	Katsuyuki OI (Dept. of Blood Purification)	
Project Assistant Professor	Soichiro IIMORI	
Hospital Staff	Miyuki SAZUKA,	Yoshihito TSUZAKI
	Fumiaki ANDO (2012.7~),	Yuki YOSHIZAKI (Dept. of Blood Purification, 2012.7~)
	Keita KUSAKA (Dept. of Blood Purification, 2012.6~)	
Technician	Motoko CHIGA	
Secretary	Asa MURANO,	Miki SAKIYAMA,
	Yukiko ITO	
Graduate Student	Mai WAKABAYASHI,	Hidenori NISHIDA
	Muhammad Zakir Hossain Khan,	
	Koichiro SUSA,	Kiyoshi ISOBE,
	Takayasu MORI,	Yuichi INOUE,
	Daiei TAKAHASHI,	Moko ZENIYA,
	Eriko KIKUCHI,	Yuya ARAKI,
	Yutaro MORI	

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). 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. Aoki T, Suzuki T, Hagiwara H, Kuwahara M, Sasaki S, Takata K, Matsuzaki T. Close association of aquaporin-2 internalization with caveolin-1. *Acta. Histochem. Cytochem.* 45:139-46, 2012.
2. Chang JM, Hwang SJ, Tsukamoto Y, Chen HC. Chronic kidney disease prevention - a challenge for Asian countries:

- report of the Third Asian Forum of Chronic Kidney Disease Initiatives. *Clin. Exp. Nephrol.* 16:187-94, 2012.
3. Hara-Chikuma M, Sugiyama Y, Kabashima K, Sohara E, Uchida S, Sasaki S, Inoue S, Miyachi Y. Involvement of aquaporin-7 in the cutaneous primary immune response through modulation of antigen uptake and migration in dendritic cells. *FASEB J.* 26:211-8, 2012.
 4. Hossain Khan MZ, Sohara E, Ohta A, Chiga M, Inoue Y, Isobe K, Wakabayashi M, Oi K, Rai T, Sasaki S, Uchida S. Phosphorylation of Na-Cl cotransporter by OSR1 and SPAK kinases regulates its ubiquitination. *Biochem. Biophys. Res. Commun.* 425:456-61, 2012.
 5. Iimori S, Mori Y, Akita W, Takada S, Kuyama T, Ohnishi T, Shikuma S, Ishigami J, Tajima M, Asai T, Okado T, Kuwahara M, Sasaki S, Tsukamoto Y. Effects of sevelamer hydrochloride on mortality, lipid abnormality and arterial stiffness in hemodialyzed patients: a propensity-matched observational study. *Clin. Exp. Nephrol.* 16:930-7, 2012.
 6. Iimori S, Mori Y, Akita W, Kuyama T, Takada S, Asai T, Kuwahara M, Sasaki S, Tsukamoto Y. Diagnostic usefulness of bone mineral density and biochemical markers of bone turnover in predicting fracture in CKD stage 5D patients - a single-center cohort study. *Nephrol. Dial. Transplant.* 27:345-351, 2012.
 7. Irie T, Ito K, Ozasa H, Noda Y, Ikeda S, Tanaka S, Arii S, Horikawa S. Splenic artery ligation: A protection against hepatic ischemia/reperfusion injury in partially hepatectomized rats. *Hepatol. Res.* 42:819-827, 2012.
 8. Kanda E, Yoshida M, Sasaki S. Applicability of fibroblast growth factor 23 for evaluation of risk of vertebral fracture and chronic kidney disease-mineral bone disease in elderly chronic kidney disease patients. *BMC Nephrol.* 13:122, 2012.
 9. Koiwa F, Komukai D, Hirose M, Yoshimura A, Ando R, Sakaguchi T, Komatsu Y, Shinoda T, Inaguma D, Joki N, Nishida H, Ikeda M, Shigematsu T. Influence of renin-angiotensin system on serum parathyroid hormone levels in uremic patients. *Clin. Exp. Nephrol.* 16:130-135, 2012.
 10. Louchami K, Best L, Brown P, Virreira M, Hupkens E, Perret J, Devuyt O, Uchida S, Delporte C, Malaisse WJ, Beauwens R, Sener A. A new role for aquaporin 7 in insulin secretion. *Cell Physiol. Biochem.* 29:65-74, 2012.
 11. Magdeldin S, Yoshida Y, Li H, Maeda Y, Yokoyama M, Enany S, Zhang Y, Xu B, Fujinaka H, Yaoita E, Sasaki S, Yamamoto T. Murine colon proteome and characterization of the protein pathways. *BioData Min.* 5:11, 2012.
 12. Mandai S, Arai Y, Hirasawa S, Hirai T, Aki S, Inaba N, Aoyagi M, Tanaka H, Tamura T, Sasaki S. Anti-centromere antibody-positive subjects presenting with hypertensive emergency and renal dysfunction in the absence of skin manifestations: a variant of systemic sclerosis or a novel entity? *Intern. Med.* 51:1567-72, 2012.
 13. Morishita Y, Watanabe M, Hanawa S, Iimura O, Tsunematsu S, Ishibashi K, Kusano E. Long-term effects of aliskiren on blood pressure and the renin-angiotensin-aldosterone system in hypertensive hemodialysis patients. *Int. J. Nephrol. Renovasc. Dis.* 5:45-51, 2012.
 14. Morishita Y, Yasui T, Numata A, Onishi A, Ishibashi K, Kusano E. Aliskiren suppresses the renin-angiotensin-aldosterone system and reduces blood pressure and albuminuria in elderly chronic kidney disease patients with hypertension. *Int. J. Nephrol. Renovasc. Dis.* 5:125-132, 2012.
 15. Naguro I, Umeda T, Kobayashi Y, Maruyama J, Hattori K, Shimizu Y, Kataoka K, Kim-Mitsuyama S, Uchida S, Vandewalle A, Noguchi T, Nishitoh H, Matsuzawa A, Takeda K, Ichijo H. ASK3 responds to osmotic stress and regulates blood pressure by suppressing WNK1-SPAK/OSR1 signaling in the kidney. *Nat. Commun.* 3:1285, 2012.
 16. Nishida H, Sohara E, Nomura N, Chiga M, Alessi DR, Rai T, Sasaki S, Uchida S. Phosphatidylinositol 3-kinase/Akt signaling pathway activates the WNK-OSR1/SPAK-NCC phosphorylation cascade in hyperinsulinemic db/db mice. *Hypertension.* 60:981-90, 2012.
 17. Ohta E, Akazawa M, Noda Y, Mandai S, Naito S, Ohta A, Sohara E, Okado T, Rai T, Uchida S, Sasaki S. Severe hyperparathyroidism in a pre-dialysis chronic kidney disease patient treated with a very low protein diet. *J. Bone Miner. Metab.* 30:238-42, 2012.
 18. Ohtaki H, Ohara K, Song D, Miyamoto K, Tsumuraya T, Yofu S, Dohi K, Tanabe S, Sasaki S, Uchida S, Matsunaga M, Shioda S. Accumulation of autofluorescent storage material in brain is accelerated by ischemia in chloride channel 3 gene-deficient mice. *J. Neurosci. Res.* 90:2163-72, 2012.
 19. Oi K, Sohara E, Rai T, Misawa M, Chiga M, Alessi DR, Sasaki S, Uchida S. A minor role of WNK3 in regulating phosphorylation of renal NKCC2 and NCC co-transporters in vivo. *Biol. Open.* 1:120-7, 2012.
 20. Sasaki S, Ohmoto Y, Mori T, Iwata F, Muraguchi M. Daily variance of urinary excretion of AQP2 determined by sandwich ELISA method. *Clin. Exp. Nephrol.* 16:406-10, 2012.
 21. Shehata SN, Hunter RW, Ohta E, Pegg MW, Lou HJ, Sicheri F, Zeqiraj E, Turk BE, Sakamoto K. Analysis of substrate specificity and cyclin Y binding of PCTAIRE-1 kinase. *Cell Signal.* 24:2085-94, 2012.

22. Susa K, Kita S, Iwamoto T, Yang SS, Lin SH, Ohta A, Sohara E, Rai T, Sasaki S, Alessi DR, Uchida S. Effect of heterozygous deletion of WNK1 on the WNK-OSR1/ SPAK-NCC/NKCC1/NKCC2 signal cascade in the kidney and blood vessels. *Clin. Exp. Nephrol.* 16:530-8, 2012.
23. Susa K, Sohara E, Isobe K, Chiga M, Rai T, Sasaki S, Uchida S. WNK-OSR1/SPAK-NCC signal cascade has circadian rhythm dependent on aldosterone. *Biochem. Biophys. Res. Commun.* 427:743-7, 2012.
24. Takahashi D, Nagahama K, Tsuura Y, Tanaka H, Tamura T. Sunitinib-induced nephrotic syndrome and irreversible renal dysfunction. *Clin. Exp. Nephrol.* 16:310-5, 2012.
25. Tanaka Y, Joki N, Hase H, Iwasaki M, Ikeda M, Ando R, Shinoda T, Inaguma D, Sakaguchi T, Komatsu Y, Koiwa F, Yamaka T, Shigematsu T. Effect of erythropoietin-stimulating agent on uremic inflammation. *J. Inflamm. (Lond).* 9:17, 2012.
26. Uchida S, Chiga M, Sohara E, Rai T, Sasaki S. Does a β 2-adrenergic receptor-WNK4-Na-Cl co-transporter signal cascade exist in the in vivo kidney? *Nat. Med.* 18:1324-5, 2012.
27. Yahata M, Takahashi S, Nakaya I, Sakuma T, Sato H, and Soma J. Possible IgG4-related kidney disease requiring a differential diagnosis of membranous lupus nephritis. *Intern. Med.* 51:1731-6, 2012.

Review Articles

1. Sasaki S. Aquaporin 2: from its discovery to molecular structure and medical implications. *Mol. Aspects Med.* 33:535-46, 2012.

Books

1. Noda Y, Sasaki S. Chapter 4. Regulation of Water Balance: Urine Concentration and Dilution. *Diseases of the Kidney & Urinary Tract, Ninth Edition*, pp.132-158, eds Coffman TM, Falk RJ, Molitoris BA, Neilson EG, Schrier RW. Lippincott Williams & Wilkins, 2012.

Comprehensive Reproductive Medicine (Maternal and Women's Clinic)

1. Staffs and Students (2012)

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,	Yuki Iwahara,
	Masato Yamanaka,	Asami Hirata,
	Rie Oi,	Makiko Egawa
Hospital Staff :	Takeru Ichimura,	Shunsuke Ishiyama
Graduate Student :	Masaya Uno,	Shiro Hiramitsu,
	Yoshinori Okura,	Reiko Tajirika,
	Atsushi Yamamoto,	Makoto Iizuka,
	Kiyotaka Takagi,	Izumi Honda,
	Aiko Motoshita,	Asuka Kajiyama,
	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 stuffs, 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. Jung Su Lee, Hayashi K, Gita Mishra, Yasui T, Kubota T, Mizunuma H. Independent association between age at natural menopause and hypercholesterolemia, hypertension, and diabetes mellitus. *Japan Nurses' Health Study J Atheroscler Thromb* Published online : Oct 19, 2012
2. Yasui T, Hayashi K, Mizunuma H, Kubota T, Aso T, Matsumura Y, Jung-Su Lee, Suzuki S. Factors associated with premature ovarian failure, early menopause and earlier onset of menopause in Japanese women. *Maturitas* 72:249-255, 2012
3. Hosokawa M, Imazeki S, Mizunuma H, Kubota T, Hayashi K. Secular trends in age at menarche and time to establish regular menstrual cycling in Japanese women born between 1930 and 1985. *BMC Womens Health* 16:12-19, 2012
4. Yoshiki N, Okawa T, Kubota T. Hybrid transvaginal and transumbilical laparoendoscopic adnexal surgery. *Journal of Laparoendoscopic & Advanced Surgical Techniques* 22(10):992-995,2012
5. Terauchi M, Hiramitsu S, Obayashi S, Akiyoshi M, Owa Y, Kato K, Matsushima E, Kubota T. Associations between anxiety, depression and insomnia in peri- and post-menopausal women. *Maturitas* 72(1): 61-65, 2012
6. Terauchi M, Honjo H, Mizunuma H, Aso T. Effects of oral estradiol and levonorgestrel on cardiovascular risk markers in postmenopausal women. *Arch Gynecol Obstet* 285(6):1647-1656, 2012
7. Iwahara Y, Nagai A, Yoshiki N, Igarashi K, Yamashita K, Kubota T. Expression of hemoxygenase in the eutopic and ectopic endometrium in patients with adenomyosis. *Gynecol Endocrinol* 28(11):892-896, 2012
8. Tajima M, Harada T, Ishikawa T, Iwahara Y, Kubota T. Augmentation of arginase II expression in the human endometrial epithelium in the secretory phase. *Journal of Medical and Dental Sciences* 59(4): 75-82, 2012

International Presentation

1. Oshima-Sudo N, Hoshino Y, Komaki M, Nakahama K, Kubota T, Abe M, Morita I. Optimized method for culturing outgrowth endothelial progenitor cells from human umbilical cord blood and adult peripheral blood. 17th International Vascular Biology Meeting, Wiesbaden/Germany, Jun 5, 2012
2. Egawa M, Hayashi S, Yang L, Sakamoto N, Sago H. Chorioamniotic membrane separation after fetoscopic laser surgery for twin-twin transfusion syndrome. The 16th International Conference on Prenatal Diagnosis and Therapy, Miami, Jun 5, 2012
3. Oi R, Matsuoka K, Sagou H. Evaluation of perinatal course of congenital lower urinary tract obstruction in 34 cases. 22nd World Congress on Ultrasound in Obstetrics and Gynecology, Copenhagen, Denmark, Sep, 2012
4. Egawa M, Hayashi S, Matsuoka K, Motomura K, Sugibayashi R, Ogawa K, Sumie M, Sago H. Residual vascular communications after fetoscopic laser surgery in twin-twin transfusion syndrome: Frequency and Outcome. IFPA Meeting 2012, Japan Placenta Association(JPA), Hiroshima, Sep 19, 2012
5. 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. 23rd North American Menopause Society Annual Meeting, Orlando, FL, Oct 4, 2012

Urology

1. Staffs and Students (December, 2012)

Professor and Chairman	Kazunori Kihara	
Associate Professor	Hitoshi Masuda (~June),	Yasuhisa Fujii (July~),
Lecturer	Fumitaka Koga,	Kazutaka Saito
Assistant Professor	Yoh Matsuoka,	Junichirou Ishioka,
	Minato Yokoyama,	Manabu Tatokoro (~May),
	Soichiro Yoshida (June~)	
Hospital Staff	Shuichiro Kobayashi,	Toshiki Kijima,
	Yasukazu Nakanishi,	Hideki Takeshita,
	Masaya Ito,	Takayuki Nakayama,
	Saori Higuchi,	Yuma Waseda,
	Makoto Kagawa,	Akitetsu Miyakawa,
	Hiroshi Fukushima	
Graduate Student	Naoko Kawamura,	Shuichiro Kobayashi,
	Toshiki Kijima,	Naotaka Fukui,
	Sachi Kitayama,	Yasukazu Nakanishi,
	Toshihiro Kanda,	Hideki Takeshita,
	Masaya Ito,	Masaharu Inoue,
	Hajime Tanaka,	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

1. Fukui N, Kohno Y, Ishioka JI, Fukuda H, Kageyama Y, Higashi Y. Treatment outcome of patients with extragonadal nonseminomatous germ cell tumors: the Saitama Cancer Center experience. *Int J Clin Oncol*. 2012 Jul 5. [Epub ahead of print].
2. Fukushima H, Tatokoro M, Saito K, Fujii Y, Sakura M, Numao N, Koga F, Masuda H, Yamada H, Kihara K. Diagnostic contribution of C-reactive protein kinetics for gastric metastasis from renal cell carcinoma. *Int Cancer Conf J* . 1:93-95, 2012.
3. Fukushima H, Masuda H, Kawakami S, Ito M, Sakura M, Numao N, Koga F, Saito K, Fujii Y, Yamamoto S, Yonese J, Fukui I, Kihara K. Effect of diabetes mellitus on high-grade prostate cancer detection among Japanese obese patients with prostate-specific antigen less than 10 ng/mL. *Urology* . 79: 1329-34, 2012.
4. Fukushima H, Masuda H. Reply. *Urology*. 79: 1335, 2012.
5. Ishioka J, Saito K, Sakura M, Yokoyama M, Matsuoka Y, Numao N, Koga F, Masuda H, Fujii Y, Kawakami S, Kihara K.. Development of a nomogram incorporating serum C-reactive protein level to predict overall survival of patients with advanced urothelial carcinoma and its evaluation by decision curve analysis. *Br J Cancer*. 107:1031-6, 2012.
6. Kihara K, Fujii Y, Masuda H, Saito K, Koga F, Matsuoka Y, Numao N, Kojima K. New three-dimensional head-mounted display system, TMDU-S-3D system, for minimally invasive surgery application: procedures for gasless single-port radical nephrectomy. *Int J Urol*. 19:886-9, author reply 890, 2012.
7. Kihara K. Application of gasless laparoendoscopic single port surgery, GasLESS, to partial nephrectomy for renal cell carcinoma: GasLESS-clampless partial nephrectomy as a multiply satisfactory method. *Int J Urol*. 19:3-4, 2012.
8. Kijima T, Masuda H, Yoshida S, Tatokoro M, Yokoyama M, Numao N, Saito K, Koga F, Fujii Y, Kihara K. Antimicrobial prophylaxis is not necessary in clean category minimally invasive surgery for renal and adrenal tumors: a prospective study of 373 consecutive patients. *Urology*. 80:570-5, 2012.
9. Koga F, Fujii Y, Masuda H, Numao N, Yokoyama M, Ishioka J, Saito K, Kawakami S, Kihara K. Pathology-based risk stratification of muscle-invasive bladder cancer patients undergoing cystectomy for persistent disease after induction chemoradiotherapy in bladder-sparing approaches. *BJU Int*. 110: E203-E208, 2012.
10. Koga F, Kihara K, Yoshida S, Yokoyama M, Saito K, Masuda H, Fujii Y, Kawakami S. Selective bladder-sparing protocol consisting of induction low-dose chemoradiotherapy plus partial cystectomy with pelvic lymph node dissection against muscle-invasive bladder cancer: Oncological outcomes of the initial 46 cases. *BJU Int* . 109: 860-866, 2012.
11. Komai Y, Kawakami S, Numao N, Fujii Y, Saito K, Kubo Y, Koga F, Kumagai J, Yamamoto S, Yonese J, Ishikawa Y, Fukui I, Kihara K. Extended biopsy based criteria incorporating cumulative cancer length for predicting clinically insignificant prostate cancer. *BJU Int*. 2012 Jul 3. doi: 10.1111/j.1464-410X.2012.11272.x.
12. Inamura K, Fujiwara M, Togashi Y, Nomura K, Mukai H, Fujii Y, Yamamoto S, Yonese J, Fukui I, Ishikawa Y. Diverse Fusion Patterns and Heterogeneous Clinicopathologic Features of Renal Cell Carcinoma With t(6;11) Translocation. *Am J Surg Pathol*. 36: 35-42, 2012.
13. Iwai A, Bourbouli D, Mollapour M, Jensen-Taubman S, Lee S, Donnelly AC, Yoshida S, Miyajima N, Tsutsumi S, Smith AK, Sun D, Wu X, Blagg BS, Trepel JB, Stetler-Stevenson WG, Neckers L. Combined inhibition of Wee1 and Hsp90 activates intrinsic apoptosis in cancer cells. *Cell Cycle*. 11: 3649-55, 2012.
14. Masuda H, Kawakami S, Sakura M, Fujii Y, Koga F, Saito K, Numao N, Yonese J, Fukui I, Kihara K. Performance of prostate-specific antigen mass in estimation of prostate volume in Japanese men with benign prostate hyperplasia. *Int J Urol*. 19:929-35, 2012.
15. Matsuoka Y, Numao N, Saito K, Tanaka H, Kumagai J, Yoshida S, Koga F, Masuda H, Kawakami S, Fujii Y, Kihara K. Combination of diffusion-weighted magnetic resonance imaging and extended prostate biopsy predicts lobes

- without significant cancer: application in patient selection for hemiablativ focal therapy. *Eur Urol*, 2012 Oct 16. pii: S0302-2838(12)01229-8. doi: 10.1016/j.eururo.2012.10.010. [Epub ahead of print]
16. Nakanishi Y, Masuda H, Kawakami S, Sakura M, Fujii Y, Saito K, Koga F, Ito M, Yonese J, Fukui I, Kihara K. A novel equation and nomogram including body weight for estimating prostate volumes in men with biopsy-proven benign prostatic hyperplasia. *Asian Journal of Andrology* . 14: 703-7, 2012.
 17. Numao N, Kawakami S, Sakura M, Yoshida S, Koga F, Saito K, Masuda H, Fujii Y, Yamamoto S, Yonese J, Ishikawa Y, Fukui I, Kihara K. Characteristics and clinical significance of prostate cancers missed by initial transrectal 12-core biopsy. *BJU Int*. 109(5):665-71, 2012.
 18. Saito K, Urakami S, Komai Y, Yasuda Y, Kubo Y, Kitsukawa S, Okubo Y, Yamamoto S, Yonese J, Fukui I. Impact of C-reactive protein kinetics on survival of patients with advanced urothelial carcinoma treated by second-line chemotherapy with gemcitabine, etoposide and cisplatin. *BJU Int*. 2012 Nov;110(10):1478-84. doi: 10.1111/j.1464-410X.2012.11153.x. Epub 2012 Apr 23.
 19. Sugawara E, Togashi Y, Kuroda N, Sakata S, Hatano S, Asaka R, Yuasa T, Yonese J, Kitagawa M, Mano H, Ishikawa Y, Takeuchi K. Identification of anaplastic lymphoma kinase fusions in renal cancer: large-scale immunohistochemical screening by the intercalated antibody-enhanced polymer method. *Cancer*. 15;118:4427-36. 2012.
 20. Takazawa R, Kitayama S, Tsujii T. Successful outcome of flexible ureteroscopy with holmium laser lithotripsy for renal stones 2 cm or greater. *Int. J. Urol*. 19: 264-267, 2012.
 21. Takazawa R, Kitayama S, Tsujii T. Single-session ureteroscopy with holmium laser lithotripsy for multiple stones. *Int. J. Urol*. 19: 1118-1121, 2012.
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 23. Takeshita H, Yokoyama M, Fujii Y, Chiba K, Ishioka J, Noro A, Kihara K. Impact of renal function on cardiovascular events in patients undergoing radical nephrectomy for renal cancer. *Int J Urol*. 19:722-8, 2012.
 24. Tatokoro M, Koga F, Yoshida S, Kawakami S, Fujii Y, Neckers L, Kihara K. Potential role of Hsp90 inhibitors in overcoming cisplatin resistance of bladder cancer-initiating cells. *Int J Cancer* .131: 987-996, 2012.
 25. Tsutsumi S, Mollapour M, Prodromou C, Lee CT, Panaretou B, Yoshida S, Mayer MP, Neckers LM. Charged linker sequence modulates eukaryotic heat shock protein 90 (Hsp90) chaperone activity. *Proc Natl Acad Sci U S A*. 109: 2937-42, 2012.
 26. Yamamoto S, Kawakami S, Yonese J, Fujii Y, Urakami S, Masuda H, Numao N, Ishikawa Y, Kohno A, Fukui I. Long-term Oncological Outcome and Risk Stratification in Men with High-risk Prostate Cancer Treated with Radical Prostatectomy. *Jpn J Clin Oncol* . 42: 541-547, 2012.
 27. 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*. 2012 Aug 11. [Epub ahead of print]
 28. 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*. 2012 Sep 11. [Epub ahead of print]
 29. Yasuda Y, Yuasa T, Yamamoto S, Urakami S, Ito M, Sukegawa G, Kitsukawa S, Yonese J, Fukui I. Evaluation of the RENAL Nephrometry Scoring System in Adopting Nephron-Sparing Surgery for cT1 Renal Cancer. *Urol Int*. 2012 Nov 7. [Epub ahead of print]
 30. Yoshida S, Koga F (co-first author), Kobayashi S, Ishii C, Tanaka H, Tanaka H, Komai Y, Saito K, Masuda H, Fujii Y, Kawakami S, Kihara K. Role of diffusion-weighted magnetic resonance imaging in predicting sensitivity to chemoradiotherapy in muscle-invasive bladder cancer. *Int J Radiat Oncol Biol Phys* 83: e21-e27, 2012.
 31. Waseda Y, Komai Y, Yano A, Fujii Y, Noguchi N, Kihara K. Pathological complete response and two-year disease-free survival in a primary gastric choriocarcinoma patient with advanced liver metastases treated with germ cell tumor-based chemotherapy: a case report. *Jpn J Clin Oncol*. 42:1197-201, 2012.
 32. Waseda Y, Tanaka H, Nakagomi K, Goto S, Ido A. A case of hereditary persistence of α -fetoprotein: diagnostic usefulness of the subfraction profile. *Jpn J Clin Oncol*. 42:767-9, 2012.

Review Article

1. Jibiki M, Inoue Y, Kudo T, Toyofuku T, Saito K, Kihara K, Kudo A, Ban D, Arii S. Combined resection of a tumor and the inferior vena cava: report of two cases. *Surg Today*. 2012.

2. Koga F, Kihara K. Selective bladder preservation with curative intent for muscle-invasive bladder cancer: a contemporary review. *Int J Urol.* 19:388-401, 2012.
3. Kihara K. IJU this issue. *Int J Urol.* 19(9):795, 2012.
4. Kihara K, Fujii Y, Masuda H, Saito K, Koga F, Matsuoka Y, Numao N, Kojima K. New three-dimensional head-mounted display system, TMDU-S-3D system, for minimally invasive surgery application: procedures for gasless single-port radical nephrectomy. *Int J Urol.* 19(9):886-9, 2012.
5. Kihara K. IJU this issue. *Int J Urol.* 19(2):95, 2012.
6. Kihara K. Application of gasless laparoendoscopic single port surgery, GasLESS, to partial nephrectomy for renal cell carcinoma: GasLESS-clampless partial nephrectomy as a multiply satisfactory method. *Int J Urol.* 19(1):3-4, 2012.
7. Saito K, Kihara K. C-reactive protein as a biomarker for urological cancers. *Nat Rev Urol.* 8:659-66, 2012.
8. Yuasa T, Fujii Y, Takahashi S, Fukui I, Yonese J. Molecular Targeted Therapies for Patients with Metastatic Renal Cell Cancer. *Translational Medic S2: (web journal) 2012.*
9. Yuasa T, Yamamoto S, Urakami S, Fukui I, Yonese J. Denosumab: a new option in the treatment of bone metastases from urological cancers. *Onco Targets Ther.* 5:221-9. 2012.

Award

1. Kihara K, Koga F (presenting author), Masuda H, Saito K, Tatokoro M, Yokoyama M, Matsuoka Y, Numao N, Kawakami S, Fujii Y. Feasibility of gasless single-port clampless partial nephrectomy for peripheral renal tumor: An experience of 118 consecutive cases. "Best Poster Presentation" The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/27.
2. Matsuoka Y, Numao N, Saito K, Tanaka H, Kijima T, Kobayashi S, Tatokoro M, Sakura M, Yokoyama M, Ishioka J, Koga F, Masuda H, Kihara K. Candidate selection for hemiablativ focal therapy of prostate cancer through a combination of extended 14-core biopsy and MRI. "Best Poster Presentation" The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
3. Numao N. International Journal of Urology Reviewer of the Year 2011. Awarded by Japanese Urological Association, 2012.
4. Tatokoro M, Masuda H, Kijima T, Yoshida S, Sakura M, Yokoyama M, Saito K, Koga F, Fujii Y, Kawakami S, Kihara K. Successful reduction of hospital-acquired methicillin-resistant *Staphylococcus Aureus* (MRSA) in a urology ward possibly due to avoidance of antimicrobial prophylaxis in minimally invasive surgery: Our 11-year trial. "Best Poster Presentation" The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.

Presentations at International Meetings

1. Kagawa M, Masuda H, Kawakami S, Ito M, Takeshita H, Sakura M, Numao N, Koga F, Saito K, Fujii Y, Yamamoto S, Fukui I, Kihara K. Better performance of plasma volume than body mass index for high-grade prostate cancer detection at extended biopsy in Japanese men. The 106th annual meeting of the American Urological Association, Atlanta, GA, USA, 2012/5/19.
2. Fukushima H, Masuda H, Kawakami S, Ito M, Sakura M, Numao N, Koga F, Saito K, Fujii Y, Yonose J, Fukui I, Kihara K. Positive association between diabetes mellitus and high grade prostate cancer detection via extended prostate biopsy in obese Japanese men with PSA less than 10 ng/ml. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
3. Kihara K, Koga F, Masuda H, Saito K, Tatokoro M, Yokoyama M, Matsuoka Y, Numao N, Kawakami S, Fujii Y. Feasibility of gasless single - port clampless partial nephrectomy for peripheral renal tumor: An experience of 118 consecutive cases. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
4. Kihara K, Koga F, Masuda H, Saito K, Tatokoro M, Yokoyama M, Matsuoka Y, Numao N, Kawakami S, Fujii Y. Gasless single-port clampless partial nephrectomy for peripheral renal tumor: Surgical, short-term oncological, and functional outcomes. AUA 2012 annual meeting, Atlanta, USA, 2012/5/21
5. Kobayashi S, Fujii Y, Koga F, Yokoyama M, Sakura M, Ishioka J, Matsuoka Y, Numao N, Saito K, Masuda H, Kihara K. Impact of bladder neck involvement on progression in patients with non-muscle invasive bladder cancer: a validation study. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/27.
6. Koga F, Yoshida S, Kobayashi S, Ishii C, Tanaka H, Fujii Y, Tanaka H, Masuda H, Saito K, Komai Y, Kawakami S, Kihara K. Diffusion - weighted MRI predicts sensitivity to chemoradiation in muscle - invasive bladder cancer. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/27.
7. Ishioka J, Saito K, Sakura M, Yokoyama M, Matsuoka Y, Numao N, Koga F, Masuda H, Kihara K. A contribution of

- C-reactive protein to predict overall survival in patients with advanced urothelial carcinoma: Development of a nomogram and evaluation by decision curve analysis. The 2012 Genitourinary Cancer Symposium, San Francisco, CA, 2012/2/2.
8. 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 T1c biopsy-referred Japanese men with prostate-specific antigen < 10 ng/ml. SIU, 2012//.
 9. Masuda H, Nakanishi Y, Kawakami S, Saito K, Koga F, Numao N, Matsuoka Y, Ishioka J, Yokoyama M, Fujii Y, Yonese J, Fukui I, Kihara K. Performance of free PSA mass for estimation of prostate volume in Japanese men with benign prostate hyperplasia. AUA, Atlanta, 2012/5/19-23.
 10. Matsuoka Y, Numao N, Saito K, Tanaka H, Kijima T, Kobayashi S, Tatokoro M, Sakura M, Yokoyama M, Ishioka J, Koga F, Masuda H, Kihara K. Candidate selection for hemiablativ focal therapy of prostate cancer through a combination of extended 14-core biopsy and MRI. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
 11. Matsuoka Y, Numao N, Saito K, Tanaka H, Kijima T, Kobayashi S, Tatokoro M, Sakura M, Yokoyama M, Ishioka J, Koga F, Masuda H, Kihara K. Combination of 14-core biopsy and magnetic resonance imaging can identify appropriate candidates for hemiablativ focal therapy of prostate cancer. The 106th annual meeting of the American Urological Association, Atlanta, USA, 2012/5/20.
 12. Numao N, Yoshida S, Komai Y, Ishii C, Kagawa M, Takeshita H, Nakanishi Y, Kijima T, Tatokoro M, Sakura M, Yokoyama M, Ishioka J, Matsuoka Y, Koga F, Saito K, Masuda H, Kawakami S, Kihara K. Prebiopsy multi-parametric magnetic resonance imaging has an ability to substantially reduce unnecessary prostate biopsy in men with PSA less than 10 ng/mL and a normal DRE. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
 13. Numao N, Yoshida S, Komai Y, Ishii C, Kagawa M, Matsuoka Y, Koga F, Saito K, Masuda H, Kawakami S, Kihara K. Prebiopsy multi-parametric MRI potentially reduces unnecessary prostate biopsy in men with PSA less than 10 ng/mL and a normal digital rectal examination. The 106th annual meeting of the American Urological Association, Atlanta, GA, USA, 2012/05/21.
 14. Saito K, Ishioka J, Koga F, Masuda H, Fujii Y, Arisawa C, Kamata S, Yonese J, Morimoto S, Tsujii T, Kitahara S, Goto S, Higashi Y, Kihara K. Prognostic impact of C-reactive protein in pre- and postoperative multivariate models to predict cancer-specific mortality for patients with upper urinary tract urothelial carcinoma in a multicenter database. The 107th annual meeting of the American Urological Association, Atlanta, USA, 2012/5/20.
 15. Saito K, Kijima T, Tatokoro M, Ishioka J, Matsuoka Y, Numao N, Masuda H, Koga F, Hayashi K, Shibuya H, Kihara K. Focal therapy for prostate cancer using I125 seed implantation: Hemiablativ brachytherapy for patients selected by extended biopsy and MRI findings. 32nd Congress of the Societe Internationale d'Urologie, Fukuoka, Japan, 2012/10/3.
 16. Takazawa R, Kitayama S, Tsujii T. Efficacy of a single-session ureteroscopy with holmium laser lithotripsy for multiple stones. The 11th Asian Congress of Urology of the Urological Association of Asia, Pattaya, Thailand, 2012/8/25.
 17. Takazawa R, Kitayama S, Tsujii T. Efficacy of a single-session ureteroscopy with holmium laser lithotripsy for multiple stones. 32nd Congress of the Societe Internationale d'Urologie, Fukuoka, Japan, 2012/10/1.
 18. Takeshita H, Yokoyama M, Fujii Y, Chiba K, Ishioka J, Saito K, Koga F, Masuda H, Noro A, Kihara K. Impact of renal function immediately after radical nephrectomy on cardiovascular events in patients with kidney cancer. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/25.
 19. Takeshita H, Numao N, Kawakami S, Sakura M, Yokoyama M, Ishioka J, Matusoka Y, Koga F, Saito K, Masuda H, Yamamoto S, Yonese J, Ishikawa Y, Fukui I, Kihara K. Characteristics of prostate cancers missed by initial transperineal extended biopsy. The 106th annual meeting of the American Urological Association, Atlanta, GA, USA, 2012/05/23.
 20. Tatokoro M, Masuda H, Kijima T, Yoshida S, Sakura M, Yokoyama M, Saito K, Koga F, Fujii Y, Kawakami S, Kihara K. Successful reduction of hospital-acquired methicillin-resistant Staphylococcus Aureus (MRSA) in a urology ward possibly due to avoidance of antimicrobial prophylaxis in minimally invasive surgery: Our 11-year trial. EAU, Paris, 2012/2/25.
 21. Tatokoro M, Koga F, Yoshida S, Fukushima H, Kawakami S, Fujii Y, Neckers L, Kihara K. Potential role of Hsp90 Inhibitors in overcoming cisplatin resistance of bladder cancer stem cells. EAU, Paris, 2012/2/26.
 22. Tatokoro M, Masuda H, Kijima T, Yoshida S, Sakura M, Yokoyama M, Saito K, Koga F, Kawakami S, Fujii Y,

- Kihara K. Successful control of Methicillin-resistant *Staphylococcus aureus* in a urology ward possibly due to avoidance of antimicrobial prophylaxis in minimally invasive surgery: our 11 years trial. The 106th annual meeting of the American Urological Association, Atlanta, GA, USA, 2012/05/21.
23. Yasuda Y, Saito K, Sukegawa G, Tanaka H, Ito M, Kitsukawa S, Yuasa T, Urakami S, Yamamoto S, Fujii Y, Takahashi S, Fukui I, Yonese J. IMPACT OF PRETREATMENT C-REACTIVE PROTEIN ON OVERALL SURVIVAL FOR PATIENTS WITH METASTATIC RENAL CELL CARCINOMA TREATED WITH SUNITINIB. The 2012 Genitourinary Cancer Symposium, San Francisco, CA, 2012/2/2.
 24. Yokoyama M, Fujii F, Takeshita H, Sakura M, Ishioka J, Iimura Y, Saito K, Koga F, Masuda H, Noro A, Kihara K. Novel nomogram and formula to predict renal function after radical nephrectomy. The 27th Annual Congress of the European Association of Urology, Paris, France, 2012/2/27.
 25. Yokoyama M, Fujii Y, Takeshita H, Sakura M, Ishioka J, Iimura Y, Saito S, Koga F, Masuda H, Noro A, Kihara K. Development and validation of predictive models for renal function after radical nephrectomy. American Urological Association 2012 Annual Meeting, Atlanta, USA, 2012/5/12.
 26. Yokoyama M, Fujii Y, Takeshita H, Iimura Y, Saito K, Koga F, Masuda H, Noro A, Kihara K. Longitudinal recovery of renal function after radical nephrectomy. American Urological Association 2012 Annual Meeting, Atlanta, USA, 2012/5/12.
 27. Yoshida S, Tsutsumi S, Neckers L. Suppression of mitochondrial respiratory activity by TRAP1. The 6th International Conference on the Hsp90 Chaperone Machine, Les Diablerets, Switzerland, 2012/9/21

Invited Lecture and International Symposium

1. Kihara K. Minimum incision endoscopic urological surgery: Ship-in-a-bottle endoscopic urological surgery. The 8th triennial of the German-Japanese confederation of urology, Shizuoka, 2012/4/30.

Esophageal and General Surgery

1. Staffs and Students

Professor	Tatsuyuki KAWANO	
Associate Professor	Yoichi KUMAGAI	
Project Associate Professor	Yasuaki NAKAJIMA	
Junior Associate Professor	Yoshinori INOUE,	Tetsuro NISHIKAGE
Assistant Professor	Kagami NAGAI,	Toshifumi KUDO,
	Kenro KAWADA,	Yutaka TOKAIRIN,
	Koji TANAKA,	Masatoshi JIBIKI,
	Takahiro TOYOFUKU	
Project Assistant Professor	Yutaka MIYAWAKI	
Graduate Student	Tomoyoshi SUZUKI,	Akihiro HOSHINO,
	Takuya OKADA,	Hidetoshi UCHIYAMA,
	Shinya KOIZUMI,	Koji YONEKURA,
	Kimihiko IGARI,	Shunsuke OHTA,
	Tairo RYOTOKUJI,	Naoto FUJIWARA,
	Masato NISHIZAWA,	Katsumasa SAITO,
	Hisashi FUJIWARA,	Sotaro KATSUI
	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. Nakajima Y, Fujiwara N, Ryotokuji T, Ohta S, Okada T, Miyawaki Y, Hoshino A, Jirawat S, Tokairin Y, Kawada K, Nishikage T, Nagai K, Kawano T. A pilot trial of S-1 plus irinotecan chemotherapy for esophageal adenocarcinoma. *Hepato-Gastroenterology* 2012; 119: 2182-2185.
2. Nakajima Y, Ohta S, Okada T, Miyawaki Y, Hoshino A, Suzuki T, Kawada K, Nishikage T, Nagai K, Ae K, Kawachi H, Kawano T. Osteoplastic bone metastasis in esophageal squamous cell cancer; report of a case. *Surg Today*, 2012; 42: 376-381.
3. Kumagai Y, Kawada K, Yamazaki S, Iida M, Odajima H, Ochiai T, Kawano T., Takubo K. Current status and limitations of the newly developed endocytoscope GIF-Y0002 with reference to its diagnostic performance for common esophageal lesions. *J Dig Diseases*, 2012; 13: 393-400.
4. Kumagai Y, Yagi M, Aida J, Ishida H, Suzuki S, Hashimoto T, Amanuma Y, Kusano M, Mukai S, Yamazaki S, Iida M, Ochiai T, Matsuura M, Iwakiri K, Kawano T, Hoshihara Y, Takubo K. Detailed features of palisade vessels as a marker of the esophageal mucosa revealed by magnifying endoscopy with narrow band imaging. *Dis Esophagus*,

2012; 25: 484-490.

5. Kumagai Y, Miura K, Nishida T, Igari K, Ochiai T, Iida M, Yamazaki S, Odajima H, Kawano T, Takubo K. Simultaneous resection of metastatic melanoma in the esophagus and primary cutaneous melanoma showing partial regression: report of a case. *Surg Today*, 2012; 42: 884-890.
6. Miyawaki Y, Kawachi H, Ooi A, Eishi Y, Kawano T, Inazawa J, Imoto I. Genomic copy-number alterations of MYC and FHIT genes are associated with survival in esophageal squamous-cell carcinoma. *Cancer Sci* 2012; 103(8): 1558-1566.
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* 2012, doi: 10.1093/jjco/hys184”
8. Igari K, Kudo T, Onishi I, Toyofuku T, Jibiki M, Inoue Y. Angiolymphoid Hyperplasia with Eosinophilia Presenting as an Ulnar Artery Pseudoaneurysm. *EJVES Extra* 2012;23:e9-e10.
9. Igari K, Kudo T, Toyofuku T, Jibiki M, Inoue Y. Multidisciplinary Approach to a Peripheral Arteriovenous Malformation. *EJVES Extra* 2012;23:e11-e13.
10. Jibiki M, Inoue Y, Kudo T. Conservative treatment for isolated superior mesenteric artery dissection. *Surg Today*. 2012 Aug 26. [Epub ahead of print]
11. Jibiki M, Inoue Y, Kudo T, Toyohuku T. Combined resection of a tumor and the inferior vena cava: report of two cases. *Surg Today*. 2012 Sep 22. [Epub ahead of print]
12. Jibiki M, Inoue Y, Kudo T, Toyofuku T. Surgical procedures for renal artery aneurysms. *Ann Vasc Dis*. 2012;5(2):157-160.

Thoracic Surgery

1. Staffs and Students

Professor:	Kenichi OKUBO	
Junior Associate Professor:	Hironori ISHIBASHI	
Assistant Professor:	Ryo MAEDA,	Naoyuki FUJIWARA
Hospital Staff:	Sachiko KUMAZAWA,	Ken TAKAHASHI

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. Chen F, Okubo K, Sonobe M, Shibuya K, Matsuo Y, Kim YH, Yanagihara K, Bando T, Date H. Hyperfractionated irradiation with 3 cycles of induction chemotherapy in stage IIIA-N2 lung cancer. *World J Surg* 2012 ;36:2858-64.
2. Maeda R, Ishii G, Ito M, Yoshida J, Hishida T, Nishimura M, Haga H, Nagai K, Ochiai A. Number of Circulating Endothelial Progenitor Cells and Intratumoral Microvessel Density in Non-small Cell Lung Cancer Patients; Differences in Angiogenic Status between Adenocarcinoma Histologic Subtypes. *J Thorac Oncol* 2012; 7: 503-11.
3. Maeda R, Yoshida J, Ishii G, Hishida T, Nishimura M, Nagai K. Influence of cigarette smoking on survival and tumor invasiveness in clinical stage IA lung adenocarcinoma. *Ann Thorac Surg* 2012;93: 1626-32.

6. International conference

1. Lateral internal thoracic artery - forgotten in recent famous textbooks - described more than 130 years ago Hironori Ishibashi, S. Ohta, M. Hirose, N. Tanio, N. Nakajima 20th European Conference on General Thoracic Surgery, Messe Essen, Essen, Germany, 10 - 13 June 2012 (Oral)
2. Benefit of 3-dimensional computed tomography for traumatic rib fractures Hironori Ishibashi, S. Ohta, M. Hirose, N. Tanio, N. Nakajima 20th European Conference on General Thoracic Surgery, Messe Essen, Essen, Germany, 10 - 13 June 2012 (poster)

7. Invited lecture

1. Okubo K. Multimodality treatment for malignant pleural mesothelioma - an institutional review in Japan Penn Mesothelioma and Pleural Program Conference 2012.9.10. University of Pennsylvania

Igakuken Disease-oriented Molecular Biology

1. Staffs and Students

Visiting Professor	Takahiko Hara (November ~)
Visiting Professor	Masanari Itokawa (November ~)
Visiting Professor	Masato Hasegawa (November ~)
Visiting Professor	Haruo Okado (November ~)

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 knock-out 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. Tsuji H, Arai T, Kametani F, Nonaka T, Yamashita M, Suzukake M, Hosokawa M, Yoshida M, Hatsuta H, Takao M, Saito Y, Murayama S, Akiyama H, Hasegawa M, Mann DM, Tamaoka A: Molecular analysis and biochemical classification of TDP-43 proteinopathy. *Brain* 135: 3380-3391, 2012.
2. Hosokawa M, Arai T, Masuda-Suzukake M, Nonaka T, Yamashita M, Akiyama H, Hasegawa M: Methylene blue reduced abnormal tau accumulation in P301L tau transgenic mice. *PLoS One* 7: e52389, 2012.
3. Nishizawa D, Fukuda K, Kasai S, Hasegawa J, Aoki Y, Nishi A, Saita N, Koukita Y, Nagashima M, Katoh R, Satoh Y, Tagami M, Higuchi S, Ujike H, Ozaki N, Inada T, Iwata N, Sora I, Iyo M, Kondo N, Won MJ, Naruse N, Uehara-Aoyama K, Itokawa M, Koga M, Arinami T, Kaneko Y, Hayashida M, Ikeda K. Genome-wide association study identifies a potent locus associated with human opioid sensitivity. *Mol Psychiatry* (in press).

Review Articles

1. Doi N, Hoshi Y, Itokawa M, Yoshikawa T, Ichikawa T. Impact of Epidemiology on Molecular Genetics of Schizophrenia. *Epidemiology Insights* p113-138, 2012.
2. Nonaka T, Hasegawa M. Intracellular seeded aggregation of TDP-43. *Rinsho Shinkeigaku* 52: 1056-1058, 2012.

Clinical Anatomy

1. Staffs and Students

Professor	Keiichi AKITA	
Junior Associate Professor	Kumiko YAMAGUCHI (Center for Interprofessional Education)	
Assistant Professor	Akimoto NIMURA,	Masayo HARADA
Graduate Student	Yasuo NAKAJIMA,	Hisayo NASU,
	Kazuhiro SAKAMOTO,	Atsushi TASAKI,
	Kazuhito SEKIZAWA,	Masataka NAKAZAWA,
	Hitomi FUJISHIRO,	Keiko OKUMURA(April~),
	Tatsuya TAMAKI(April~),	Sachiyuki TUKADA(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.* 2012 Sep 29. [Epub ahead of print]
2. Sato K, Nimura A, Yamaguchi K, Akita K: Anatomical study of the proximal origin of hamstring muscles. *J Orthop Sci.* 2012 Sep;17(5):614-8.
3. Nasu H, Yamaguchi K, Nimura A, Akita K: An anatomic study of structure and innervation of the serratus anterior muscle. *Surg Radiol Anat.* 34: 921-928.
4. Tsukada S, Ikeda H, Seki Y, Shimaya M, Hoshino A, Niga S: Intramedullary screw fixation with bone autografting to treat proximal fifth metatarsal metaphyseal-diaphyseal fracture in athletes: a case series. *Sports Med Arthrosc Rehabil Ther Technol* 2012;4:25
5. J. Imatani, K Akita, K. Yamaguchi, H Shimizu, T Ozaki: An anatomical study of the watershed line on the volar, distal aspect of the radius: Implications for plate placement and avoidance of tendon ruptures. *J Hand Surg Am*, 37 (8), 1550-1554,2012.1 Sep;51(3):102-9

Systems BioMedicine

1. Staffs and Students

Professor	Hiroshi ASAHARA	
Lecturer	Masahiro SHINOHARA(Oct.-)	
Assistant Professor	Toshihiro ARAMAKI(Apr.-), Yoshiaki ITO(Apr.-)	
Project Assistant Professor	Yoko TANAKA-Watanabe(Apr.-), Takahide MATSUSHIMA(Apr.-)	
Adjunct Professor	Syuji TAKADA,	Masafumi INUI(Oct.-)
Research Associate	Tomoki CHIBA(Apr.-),	Atsushi KUBO(Apr.-)
Graduate Students	Tempei SATO(Mar.),	Kohei MIYATA,
	Akiko KUGAI,	Takeshi SAITO,
	Daiki FUKUCHI,	Akira TAKAHASHI(Apr.-),
	Kentaro ABE(Apr.-),	Yohei MATSUBARA(Apr.-),
	Ryo NAKAMICHI(Apr.-),	Tomohiro KAYAMA(Apr.-),
	Masashi NAITO(June-),	Yusuke MOCHIZUKI(Oct.-),
	Naoki KODA(Oct.-)	

2. Purpose of Education

Undergraduate:

Conducting “Molecular Genetics”, which is 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 at system level.

3. Research Subjects

- The function of non-coding RNA in development and diseases will be examined.
- Development and regeneration using ES and other stem cells will be analyzed.
- Genome dynamics during embryogenesis will be monitored by new technique.
- Novel systems approaches will be established and applied for developmental biology and medicine.

4. Publications

Original Articles

1. Uchibe K, Shimizu H, Yokoyama S, Kuboki T, Asahara H. Identification of novel transcription-regulating genes expressed during murine molar development. *Dev Dyn*. 241(7):1217-26. (2012)
2. Yamashita S, Miyaki S, Kato Y, Yokoyama S, Sato T, Barrionuevo F, Akiyama H, Scherer G, Takada S, Asahara H. L-Sox5 and Sox6 proteins enhance chondrogenic miR-140 microRNA expression by strengthening dimeric Sox9 activity. *J Biol Chem*. 287(26):22206-15. (2012)
3. Fukami M, Tsuchiya T, Takada S, Kanbara A, Asahara H, Igarashi A, Kamiyama Y, Nishimura G, Ogata T. Complex genomic rearrangement in the SOX9 5' region in a patient with Pierre Robin sequence and hypoplastic left scapula. *Am J Med Genet A*. 158A(7):1529-34. (2012)
4. Al-Bari A, Shinohara M, Nagai Y, Takayanagi H. Inhibitory effect of chloroquine on bone resorption reveals the essential role of lysosomes in osteoclast differentiation and function, *Inflamma Regener*. 32(5): 222-231.(2012)
5. Shinohara M, Nakamura M, Masuda H, Kadono Y, Iwasawa M, Nagase Y, Ueki K, Kadowaki T, Sasaki T, Kato S, Nakamura H, Nakamura K, Tanaka S, Takayanagi H, Class IA Phosphatidylinositol 3-kinases regulates osteoclastic bone resorption through Akt-mediated vesicle transport in mice, *J Bone Miner Res*. 27(12):2464-2475.(2012)
6. Otero K#, Shinohara M#, Zhao H#, Cella M, Gilfillan S, Colucci A, Faccio R, Ross FP, Teitelbaum SL, Takayanagi H, Colonna M. TREM2 and β -Catenin Regulate Bone Homeostasis by Controlling the Rate of Osteoclastogenesis. *J*

Immunol. 188(6):2612-2621.(2012) (#equal contributors)

Review Articles

1. Ito Y, Kayama T, Asahara H. A systems approach and skeletal myogenesis. *Comp Funct Genomics*. 2012;759407. (2012)
2. Yamashita S, Asahara H. miRNA functions in arthritis. *Curr Rheumatol Rev*. 8: 98-102. (2012)
3. Miyaki S, Asahara H. Macro view of microRNA function in osteoarthritis. *Nat Rev Rheumatol*. 8(9):543-52. (2012)
4. Chan EF, Harjanto R, Asahara H, Inoue N, Masuda K, Bugbee WD, Firestein GS, Hosalkar HS, Lotz MK, Sah RL. Structural and functional maturation of distal femoral cartilage and bone during postnatal development and growth in humans and mice. *Orthop Clin North Am*. 43(2):173-85, v. (2012)
5. Takada S, Asahara H. Current strategies for microRNA research. *Mod Rheumatol*. 22(5):645-53. (2012)

Comprehensive Pathology

1. Staffs and Students

Professor	Masanobu KITAGAWA	
Assistant Professor	Morito KURATA, Shiho ABE-Suzuki,	Shinya ABE, Kouhei YAMAMOTO (on administrative leave)
Laboratory Technician	Miori INOUE	
Technical Assistant	Sachiko ISHIBASHI	
Graduate Students	Yukako MIWA, Ruri DAGET, Toshiya NAGIRI, Kenichi MIYAMOTO, Kazuhito SUZUKI, Kenichiro KATO	Ichiro ONISHI, Na LI, Tatsuro HIDAKA, Keiko YAGI, Masafumi INOUE,

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. Abe S, Kurata M, Suzuki S, Yamamoto K, Aisaki K, Kanno J, Kitagawa M. Minichromosome Maintenance 2 Bound with Retroviral Gp70 Is Localized to Cytoplasm and Enhances DNA-Damage-Induced Apoptosis. *PLoS One*. 2012;7(6):e40129
2. Umeda S, Yamamoto K, Murayama T, Hidaka M, Kurata M, Ohshima T, Suzuki S, Sugawara E, Kawano F, Kitagawa M. Prognostic significance of HOXB4 in de novo acute myeloid leukemia. *Hematology*. 2012 May; 17(3):125-31.
3. Taira N, Mimoto R, Kurata M, Yamaguchi T, Kitagawa M, Miki Y, Yoshida K. DYRK2 priming phosphorylation of c-Jun and c-Myc modulates cell cycle progression in human cancer cells. *J Clin Invest*. 2012 Mar 1; 122(3):859-72.
4. Suzuki S, Kurata M, Abe S, Miyazawa R, Murayama T, Hidaka M, Yamamoto K, Kitagawa M. Overexpression of MCM2 in myelodysplastic syndromes: association with bone marrow cell apoptosis and peripheral cytopenia. *Exp Mol Pathol*. 2012 Feb; 92(1):160-6.
5. Sugawara E, Yamamoto K, Umeda S, Suzuki S, Kurata M, Endo Y, Uchibori K, Akashi T, Inase N, Kitagawa M. Giant cell carcinoma causing rapidly progressive respiratory failure as the presenting feature of AIDS. *Int J STD AIDS*. 2012 Jul;23(7):e7-8.
6. Uchida E, Honma R, Igarashi A, Kurata M, Imadome K, Omoto E, Miura O, Arai A. [Sequential monitoring of plasma EBV-DNA level in a patient with EBV-positive Hodgkin lymphoma]. *Rinsho Ketsueki*. 2012 Jan;53(1):87-91.
7. Arai A, Nogami A, Imadome K, Kurata M, Murakami N, Fujiwara S, Miura O. Sequential monitoring of serum IL-6, TNF- α , and IFN- γ levels in a CAEBV patient treated by plasma exchange and immunochemotherapy. *Int J Hematol*. 2012 Nov;96(5):669-73.
8. Sugawara E, Togashi Y, Kuroda N, Sakata S, Hatano S, Asaka R, Yuasa T, Yonese J, Kitagawa M, Mano H, Ishikawa Y, Takeuchi K. Identification of ALK Fusions in Renal Cancer: a Large Scale Immunohistochemical

Screening by intercalated Antibody-enhanced Polymer Method. *Cancer* 118(18):4427-4436, 2012.

9. Yagi Y, Machida A, Toru S, Kobayashi T, Amano T, Hirokawa K, Kitagawa M. Myotonic dystrophy and lipoma: A new association. *Neurol Sci*, 2012, Epub ahead of print.
10. 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*, 2012, Epub ahead of print.

National meeting

Morito Kurata, Yohei Kanno, Tomoko Takahara, Yukari Yamazaki, Daisuke Kitamura, Takuro Nakamura *The role of C/EBP β and Blnk cooperation in the pre-B ALL*. Ninth international workshop on molecular aspects of myeloid stem cell development and leukemia. 2012 Cincinnati, USA.

Molecular Oncology

1. Staffs and Students

Professor	Yasuhito YUASA	
Lecturer	Yoshimitsu AKIYAMA,	Hiroshi FUKAMACHI
Assistant Professor	Shu SHIMADA	
Secretary	Yoshiko Abe	
JSPS Research Fellow	Yutaka HASHIMOTO,	Rika TSUCHIDA
Graduate Student	Shogo KOJIMA,	Ayuna SAKAMOTO,
	Taketo NISHIKAWAJI,	Kanako BABA
Visiting Professor	Masabumi SHIBUYA	

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, food poisoning, anoxia and heat-related diseases.

• 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 bi weekly seminars, the students present their own research data and introduce important papers from newly-arrived journals. Once the students get new findings, they are encouraged to present them at the domestic or international meeting and write manuscripts.

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. Yuasa Y, Nagasaki H, Oze I, Akiyama Y, Yoshida S, Shitara K, Ito S, Hosono S, Watanabe M, Ito H, Tanaka H, Kang DH, Pan K-F, You W-C, Matsuo K. IGF2 hypomethylation of blood leukocyte DNA is associated with gastric cancer risk. *Int. J. Cancer* 2012;131:2596-2603.
2. Shimada S, Mimata A, Sekine M, Mogushi K, Akiyama Y, Fukamachi H, Jonkers J, Tanaka H, Eishi Y, Yuasa Y. Synergistic tumour suppressor activity of E-cadherin and p53 in a conditional mouse model for metastatic diffuse-type gastric cancer. *Gut* 2012;61:344-353.
3. Song M-Y, Pan K-F, Su H-J, Zhang L, Ma J-L, Li J-Y, Yuasa Y, KangDH, Kim YS, You W-C. Identification of serum microRNAs as novel non-invasive biomarkers for early detection of gastric cancer. *PLoS One* 2012;7:e33608.
4. Li L, Choi JY, Lee KM, Sung H, Park SK, Oze I, Pan KF, You WC, Chen YX, Fang JY, Matsuo K, Kim WH, Yuasa Y, Kang D. DNA methylation in peripheral blood: a potential biomarker for cancer molecular epidemiology. *J. Epidemiol.* 2012;22:384-394.
5. Voon D. C., Wang, H., Koo, J. K., Nguyen, T. A., Hor, Y. T., Chu, Y. S., Ito, K., Fukamachi, H., Chan, S. L., Thiery, J. P., Ito, Y. (2012) Runx3 protects gastric epithelial cells against epithelial-mesenchymal transition-induced cellular

plasticity and tumorigenicity. *Stem Cells* 2012;30:2088-2099.

6. Tsuchiya, Y., Saito, Y., Taniuchi, S., Sakuma, A., Maekawa, T., Fukamachi, H., Takeuchi, S., Takahashi, S. (2012) Runx3 expression and its roles in mouse endometrial cells. *J. Reprod. Develop.* 2012;58:592-598.
7. Jin J, Sison K, Li C, Tian R, Wnuk M, Sung HK, Jeansson M, Zhang C, Tucholska M, Jones N, Kerjaschki D, Shibuya M, Fantus IG, Nagy A, Gerber HP, Ferrara N, Pawson T, Quaggin SE. Soluble FLT1 Binds Lipid Microdomains in Podocytes to Control Cell Morphology and Glomerular Barrier Function. *Cell.* 151:384-399, 2012.

Surgical Pathology

1. Staff and Students

Professor	Yoshinobu EISHI	
Associate Professor	Takumi AKASHI	
Assistant Professor	Eisaku ITO,	Tomonari AMANO,
	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. Amodini Rajakaruna G, Umeda M, Uchida K, Furukawa A, Yuan B, Suzuki Y, Noriko E, Izumi Y, Eishi Y. Possible translocation of periodontal pathogens into the lymph nodes draining the oral cavity. *J Microbiol* 50(5):827-36,2012
2. Furusawa H, Suzuki Y, Miyazaki Y, Inase N, Eishi Y. Th1 and Th17 immune responses to viable *Propionibacterium acnes* in patients with sarcoidosis. *Respir Investig* 50(3):104-9,2012
3. Negi M, Takemura T, Guzman J, Uchida K, Furukawa A, Suzuki Y, Iida T, Ishige I, Minami J, Yamada T, Kawachi H, Costabel U, Eishi Y. Localization of *propionibacterium acnes* in granulomas supports a possible etiologic link between sarcoidosis and the bacterium. *Mod Pathol* 25(9):1284-97,2012
4. Miyawaki Y, Kawachi H, Ooi A, Eishi Y, Kawano T, Inazawa J, Imoto I. Genomic copy-number alterations of MYC and FHIT genes are associated with survival in esophageal squamous-cell carcinoma. *Cancer Sci* 103(8):1558-66,2012
5. Aikawa C, Furukawa N, Watanabe T, Minegishi K, Furukawa A, Eishi Y, Oshima K, Kurokawa K, Hattori M, Nakano K, Maruyama F, Nakagawa I, Ooshima T. Complete genome sequence of the serotype k *Streptococcus mutans* strain LJ23. *J Bacteriol* 194(10):2754-5,2012
6. Takahashi M, Ishikawa K, Sato N, Obayashi M, Niimi Y, Ishiguro T, Yamada M, Toyoshima Y, Takahashi H, Kato T, Takao M, Murayama S, Mori O, Eishi Y, Mizusawa H. Reduced brain-derived neurotrophic factor (BDNF) mRNA expression and presence of BDNF-immunoreactive granules in the spinocerebellar ataxia type 6 (SCA6)cerebellum. *Neuropathology* 32(6):595-603,2012
7. Amano T, Eishi Y, Yamada T, Uchida K, Minegishi K, Tamura T, Kobayashi D, Hiroshi K, Suzuki T, Board PG. Widespread expression of γ -glutamyl cyclotransferase suggests it is not a general tumor marker. *J Histochem Cytochem* 60(1):76-86,2012
8. Toriihara A, Taniguchi Y, Negi M, Kubota K, Makino T, Shibuya H. FDG PET/CT of a benign ovarian Brenner tumor. *Clin Imaging*. 36(5):650-3,2012
9. Fujita K, Naganuma M, Saito E, Suzuki S, Araki A, Negi M, Kawachi H, Watanabe M. Histologically confirmed IgG4-related small intestinal lesions diagnosed via double balloon enteroscopy. *Dig Dis Sci*. 57(12):3303-6,2012

10. Oda G, Sato T, Ishikawa T, Kawachi H, Nakagawa T, Kuwayama T, Ishiguro M, Iida S, Uetake H, Sugihara K. Significance of stromal decorin expression during the progression of breast cancer. *Oncol Rep.* 28(6):2003-2008,2012
11. Takashima M, Kawachi H, Yamaguchi T, Nakajima Y, Kitagaki K, Sekine M, Iida T, Takemura K, Kawano T, Eishi Y. Reduced expression of cytokeratin 4 and 13 is a valuable marker for histologic grading of esophageal squamous intraepithelial neoplasia. *J Med Dent Sci.* 59:17-28,2012
12. Ueno H, Mochizuki H, Akagi Y, Kusumi T, Yamada K, Ikegami M, Kawachi H, Kameoka S, Ohkura Y, Masaki T, Kushima R, Takahashi K, Ajioka Y, Hase K, Ochiai A, Wada R, Iwaya K, Shimazaki H, Nakamura T, Sugihara K. Optimal Colorectal Cancer Staging Criteria in TNM Classification. *J Clin Oncol.* 30(13):1519-1526,2012
13. Ueno H, Mochizuki H, Shirouzu K, Kusumi T, Yamada K, Ikegami M, Kawachi H, Kameoka S, Ohkura Y, Masaki T, Kushima R, Takahashi K, Ajioka Y, Hase K, Ochiai A, Wada R, Iwaya K, Nakamura T, Sugihara K. Multicenter Study for Optimal Categorization of Extramural Tumor Deposits for Colorectal Cancer Staging. *Annals of surgery.* 255(4):739-746,2012
14. Nakajima Y, Ohta S, Okada T, Miyawaki Y, Hoshino A, Suzuki T, Kawada K, Nishikage T, Nagai K, Ae K, Kawachi H, Kawano T. Osteoplastic bone metastasis in esophageal squamous cell cancer: report of a case. *Surg Today.* 42(4):376-381,2012
15. Takemura T, Akashi T, Kamiya H, Ikushima S, Ando T, Oritsu M, Sawahata M, Ogura T. Pathological differentiation of chronic hypersensitivity pneumonitis from idiopathic pulmonary fibrosis/usual interstitial pneumonia. *Histopathology* 61:1026-1035,2012
16. Kudo A, Akashi T, Kumagai J, Ban D, Inokuchi M, Kojima K, Kawano T, Tanaka S, Arie S. The importance of clinical information in patients with gastroenteropancreatic neuroendocrine tumor. *Hepato-gastroenterology* 59:2450-2453,2012
17. Kudo A, Ban D, Akashi T, Kumagai J, Aihara A, Inokuchi M, Kojima K, Kawano T, Tanaka S, Arie S. Prognoses of GEP-NETS with undetermined malignant potentials of their primary sites. *Hepato-gastroenterology* 59:1682-1686,2012
18. Sugawara E, Yamamoto K, Umeda S, Suzuki S, Kurata M, Endo Y, Uchibori K, Akashi T, Inase N, Kitagawa M. Giant cell carcinoma causing rapidly progressive respiratory failure as the presenting feature of AIDS. *International journal of STD & AIDS* 23:e7-8,2012
19. Sugawara E, Togashi Y, Kuroda N, Mano H, Ishikawa Y, Takeuchi K et al. Identification of anaplastic lymphoma kinase fusions in renal cancer: large-scale immunohistochemical screening by the intercalated antibody-enhanced polymer method. *Cancer* 118(18):4427-36,2012
20. Togashi Y, Soda M, Sakata S, Sugawara E, Mano H, Takeuchi K et al. KLC1-ALK: a novel fusion in lung cancer identified using a formalin-fixed paraffin-embedded tissue only. *PLoS One* 7(2):e31323,2012
21. Umeda S, Yamamoto K, Murayama T, Sugawara E, Kawano F, Kitagawa M et al. Prognostic significance of HOXB4 in de novo acute myeloid leukemia. *Hematology* 17(3):125-31,2012
22. Abe S, Kurata M, Suzuki S, Yamamoto K, Aisaki K, Kanno J, Kitagawa M. Minichromosome Maintenance 2 Bound with Retroviral Gp70 Is Localized to Cytoplasm and Enhances DNA-Damage-Induced Apoptosis. *PLoS One* 7(6):e40129,2012
23. Taira N, Mimoto R, Kurata M, Yamaguchi T, Kitagawa M, Miki Y, Yoshida K. DYRK2 priming phosphorylation of c-Jun and c-Myc modulates cell cycle progression in human cancer cells. *J Clin Invest* 1; 122(3):859-72,2012
24. Suzuki S, Kurata M, Abe S, Miyazawa R, Murayama T, Hidaka M, Yamamoto K, Kitagawa M. Overexpression of MCM2 in myelodysplastic syndromes: association with bone marrow cell apoptosis and peripheral cytopenia. *Exp Mol Pathol* 92(1):160-6,2012.
25. Uchida E, Honma R, Igarashi A, Kurata M, Imadome K, Omoto E, Miura O, Arai A. [Sequential monitoring of plasma EBV-DNA level in a patient with EBV-positive Hodgkin lymphoma]. *Rinsho Ketsueki* 53(1):87-91,2012
26. Arai A, Nogami A, Imadome K, Kurata M, Murakami N, Fujiwara S, Miura O. Sequential monitoring of serum IL-6, TNF- α , and IFN- γ levels in a CAEBV patient treated by plasma exchange and immunochemotherapy. *Int J Hematol* 96(5):669-73,2012
27. Sekine M, Kobayashi D, Ito T, Uchida K, Sekiya T, Eishi Y. Immunohistochemical detection of *Helicobacter pylori* with a novel monoclonal antibody: Its clinicopathological significance and validity in the routine pathological diagnosis. *Rinsho Byori* 60(4):287-93,2012 Japanese.

Experimental Animal Model for Human Disease

1. Staffs (April, 2012)

Professor Masami Kanai-Azuma
 Assistant Professor Shu Endo, Miyuri Kawasumi,
 Hitomi Suzuki (Aug.~)

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) Mechanism of primordial follicle activation in mammalian ovary

3. Publications

Original Articles

1. **Dynamics of GFR α 1-positive Spermatogonia at the Early Stages of Colonization in the Recipient Testes of W/W (vv) Male Mice.**
 Nagai R, Shinomura M, Kishi K, Aiyama Y, Harikae K, Sato T, Kanai-Azuma M, Kurohmaru M, Tsunekawa N, Kanai Y, Dev Dyn. 2012 Aug; 241(8):1374-1384. Epub 2012 Jul 9.
2. **Gut endoderm is involved in the transfer of left-right asymmetry from the node to the lateral plate mesoderm in the mouse embryo.**
 Saund RS, Kanai-Azuma M, Kanai Y, Kim I, Lucero MT, Saijoh Y., Development. 2012 Jul; 139(13):2426-35. Epub 2012 May 23.
3. **Expression of matrix metalloproteinases 2 and 9 and tissue inhibitors of matrix metalloproteinases 2 and 1 in the glomeruli of human glomerular diseases: the results of studies using immunofluorescence, in situ hybridization, and immunoelectron microscopy.**
 Sekiuchi M, Kudo A, Nakabayashi K, Kanai-Azuma M, Akimoto Y, Kawakami H, Yamada A., Clin Exp Nephrol. 2012 Dec;16(6):863-874. Epub 2012 May 22.

Conference Paper Index

1. Masami Kanai-Azuma¹, Yoshiakira Kanai² (¹ Cent. For Exp. Anim., Tokyo Med. and Dent., ² Univ. Dept. of Vet. Anat., Univ. of Tokyo): Haploinsufficiency of Sox17 causes biliary atresia and perinatal hepatitis in C57BL/6 mice, Hong Kong Society for Development Biology Symposium., Nov. 26-27, 2012, Hong Kong.
2. Masami Kanai-Azuma¹, Yoshimi Aiyama², Miyuri Kawasumi¹, Yoshiakira Kanai² (¹ Cent. For Exp. Anim., Tokyo Med. and Dent., ² Univ. Dept. of Vet. Anat., Univ. of Tokyo): Influence of Luminal Fluid Flow on Dynamics of Spermatogenic Stem Cells in Mouse Testes, The 6th International Symposium of Vertebrate Sex Determination., Apr. 23-27, 2012, Hawaii(U.S.A.).
3. Hitomi Suzuki¹, Krishna Jagarlamudi² and Aleksandar Rajkovic¹ (1. University of Pittsburgh Dept. OBGYN-RS, Pittsburgh, PA, 15213. 2.Baylor College of Medicine, Dept. Pathology and Immunology, Houston, TX. 77030): LIM-homeobox protein 8 inhibits primordial oocyte activation that is independent of the KIT signaling pathways. 2012 Germ Cell meeting at Cold Spring Harbor Laboratory (Talk). Oct 2-6 2012, USA.

Human Gene Sciences Center (Signal Gene Regulation)

1. Staff and Student

Professor	Masataka NAKAMURA (Director)
Junior Associate Professor	Noriko FUNATO
Assistant Professor	Mariko MIZUGUCHI (April~)
Foreign Reseacher	Hussein Abdelaziz Abdalla (~March)
Postdoctral Fellow	Mariko MIZUGUCHI (~March), Mamami YOSHITA (April~)
Graduate Student	Terumi MIZUKOSHI (~March), Tomoaki KUMAGAI (April~), Yating WANG (~September), Lindsay Preston

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. Funato N, Nakamura M, Richardson JA, Srivastava D, Yanagisawa H: Tbx1 regulates oral epithelial adhesion and palatal development. *Hum Mol Genet.* 21: 2524-2437, 2012.
2. Suzuki H, Suda N, Shiga M, Kobayashi Y, Nakamura M, Iseki S, Moriyama K: Apert syndrome mutant FGFR2 and its soluble form reciprocally alter osteogenesis of primary calvarial osteoblasts. *J Cell Physiol.* 227: 3267-3277, 2012.
3. Ishii M, Asano K, Namkoong H, Tasaka S, Mizoguchi K, Asami T, Kamata H, Kimizuka Y, Fujiwara H, Funatsu Y, Kagawa S, Miyata J, Ishii K, Nakamura M, Hirai H, Nagata K, Kunkel SL, Hasegawa N, Betsuyaku T: CRTH2 is a critical regulator of neutrophil migration and resistance to polymicrobial sepsis. *J Immunol.* 188: 5655-5664, 2012.
4. Ito H, Yan X, Nagata N, Aritake K, Katsumata Y, Matsuhashi T, Nakamura M, Hirai H, Urade Y, Asano K, Kubo M, Utsunomiya Y, Hosoya Y, Fukuda K, Sano M: PGD2-CRTH-2 pathway promotes tubulointestinal fibrosis. *J Am Soc Nephrol.* 23: 1797-1809, 2012.
5. Yoshita M, Higuchi M, Takahashi M, Oie M, Tanaka Y, Fujii M: Activation of mTOR by human T-cell leukemia virus type 1 Tax is important for the transformation of mouse T cells to interleukin-2-independent growth. *Cancer Sci.* 103: 369-374, 2012.

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. Gao P, Hirano T, Chen Z, Yasuhara T, Nakata Y, Sugimoto A: Isolation and identification of C-19 fatty acids with anti-tumor activity from the spores of *Ganoderma lucidum* (reishi mushroom). *Fitoterapia*. 83: 490–499, 2012.
2. Kanai M, Hirano T, Azumaya I, Okamoto I, Kagechika H, Tanatani A: Solvent-dependent conformational and fluorescence change of an *N*-phenylbenzohydroxamic acid derivative bearing two pyrene moieties. *Tetrahedron* 68: 2778-2783, 2012.
3. Taniguchi K, Takizawa S, Hirano T, Murata S, Kagechika H, Kishida A, Ohsaki A: Amarastelline A: A Fluorescent Alkaloid from *Quassia amara* and Its Properties in Living Cells. *ChemPlusChem* 77: 427 – 431, 2012.
4. Hirano T, Kubo H, Shiraishi T, Hiromoto K, Fujiwara T, Kagechika H: Fluorescent properties of coumarins with dual functions constructed by two sequential reactions. *Tetrahedron Lett.* 53: 5916–5919, 2012.

Medicinal-Chemical Biology (Medicinal Chemistry)

1. Staffs and Students (April, 2012)

Professor	Hirokazu TAMAMURA	
Junior Associate Professor	Wataru NOMURA	
Assistant Professor	Tetsuo NARUMI,	Haruo AIKAWA
Research Staff	Kyoko ITOTANI	
Technical Staff	Nami OHASHI	
Secretary	Rika NARUMI	
Graduate Student	Yosuke NONAKA,	Chie HASHIMOTO,
	Akemi MASUDA,	Takaharu SUZUKI,
	Mamiko KANEKO,	Makoto KONNO,
	Natsuki MINATO,	Atsushi ITO,
	Taisuke KOSEKI,	Takuya KOBAYAKAWA,
	Hikaru TAKANO,	Yuki HIROTA,
	Daichi MATSUMOTO	

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-genome 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) Narumi T, Kobayakawa T, Aikawa H, Seike S, Tamamura H. Stereoselective Formation of Trisubstituted (Z)-Chloroalkenes Adjacent to a Tertiary Carbon Stereogenic Center by Organocuprate-Mediated Reduction/Alkylation. *Org Lett* 14: 4490-4493, 2012.
- 2) Narumi T, Tanaka T, Hashimoto C, Nomura W, Aikawa H, Sohma A, Itotani K, Kawamata M, Murakami T, Yamamoto N, Tamamura H. Pharmacophore-Based Small Molecule CXCR4 Ligands. *Bioorg Med Chem Lett* 22: 4169-4172, 2012.
- 3) Hashimoto C, Nomura W, Ohya A, Urano E, Miyauchi K, Narumi T, Aikawa H, Komano JA, Yamamoto N, Tamamura H. Evaluation of a Synthetic C34 Trimer of HIV-1 gp41 as AIDS Vaccines. *Bioorg Med Chem* 20: 3287-3291, 2012.
- 4) Nomura W, Masuda A, Ohba K, Urabe A, Ito N, Ryo A, Yamamoto N, Tamamura H. Effects of DNA Binding of Zinc Finger and Linkers for Domain Fusion. on Catalytic Activity of Sequence-Specific Chimeric Recombinases Determined by a Facile Fluorescent System. *Biochemistry* 51: 1510-1517, 2012.
- 5) Nomura W, Hashimoto C, Ohya A, Miyauchi K, Urano E, Tanaka T, Narumi T, Nakahara T, Komano J, Yamamoto N, Tamamura H. Synthetic C34 Trimer of HIV-1 gp41 Shows Significant Increase of Inhibition Potency. *ChemMedChem* 7: 205-208, 2012.
- 6) Narumi T, Komoriya M, Hashimoto C, Wu H, Nomura W, Suzuki S, Tanaka T, Chiba J, Yamamoto N, Murakami T, Tamamura H. Conjugation of Cell-penetrating Peptides Leads to Identification of Anti-HIV Peptides from Matrix Proteins. *Bioorg Med Chem* 20: 1468-1474, 2012.

Books

- 1) Nomura W, Tanaka T, Aoki T, Soma A, Aikawa H, Narumi T, Tamamura H. Development of Designed Bivalent Ligands for CXCR4 and their Function on Receptor Binding. *Peptide Science 2011* Sakaguchi K (Ed), The Japanese Peptide Society, Sapporo: 79-80, 2012.

- 2) Nomura W, Hashimoto C, Nakahara T, Ohya A, Miyauchi K, Ohba K, Narumi T, Aikawa H, Komano J, Yamamoto N, Tamamura H. Designed Antigens Based on the Dynamic Structural Changes of GP41 for Development of Effective HIV-1 Vaccines. Peptide Science 2011 Sakaguchi K (Ed), The Japanese Peptide Society, Sapporo: 295-296, 2012.
- 3) Nomura W, Tsutsumi H, Abe S, Mori A, Narumi T, Aikawa H, Tamamura H. Intense Blue Fluorescence of Tag-probe Systems Based on a Leucine Zipper Assembly. Peptide Science 2011 Sakaguchi K (Ed), The Japanese Peptide Society, Sapporo: 317-318, 2012.
- 4) Nomura W, Tanaka T, Aikawa H, Narumi T, Tamamura H. Bivalent Ligands for the Chemokine Receptor CXCR4 Dimer and Their Function. Proceedings of the Thirty-Second European Peptide Symposium, George Kokotos, Violetta Constantinou-Kokotou, John Matsoukas (Eds.), European Peptide Society, Athens, Greece, 98-99, 2012.

Medical Instrument (Biomedical Information)

1. Staffs and Students (April, 2012)

Associate Professor Tomoyuki KANEKO

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. Kaneko T, Nomura F, Hattori A, Yasuda K. Improvement of Electrical Stimulation Protocol for Simultaneous Measurement of Extracellular Potential with On-Chip Multi-Electrode Array System. *Jpn J Appl Phys*, 51, 06FK02, 2012.
2. Nomura F, Kaneko T, Hamada T, Hattori A, Yasuda K. Quantitative Evaluation of Closed-Loop-Shaped Cardiomyocyte Network by Using Ring-Shaped Electrode. *Jpn J Appl Phys*, 51, 06FK06, 2012.
3. Hamada T, Nomura F, Kaneko T, Yasuda K. Importance of Thickness in Human Cardiomyocyte Network for Effective Electrophysiological Stimulation Using On-Chip Extracellular Microelectrodes. *Jpn J Appl Phys*, 51, 06FK03, 2012.
4. Terazono H, Kim H, Hayashi M, Hattori A, Nomura F, Kaneko T, Yasuda K. A Non-Destructive Culturing and Cell Sorting Method for Cardiomyocytes and Neurons Using a Double Alginate Layer. *PLoS ONE*, 7(8), e42485, 2012.
5. 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 Constructive On-Chip Cellomics. *Microfluidics and Nanofluidics*, DOI:10.1007/s10404-012-1112-6, 2012.

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*, 2771-Pos, San Diego, USA, Feb. 2012.
2. Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada, Tomoyuki Kaneko, Hideo Takamori, Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho. Toward quasi-in vivo from in vitro assay (I). On-chip cardiomyocyte network screening assay for predictive cardiotoxicity. *Safety Pharmacology Society 12th Annual Meeting*, 088, Phoenix, USA, Oct. 2012.
3. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda, . Toward Quasi-in vivo from in vitro assay (II). Development of on-chip predictive cardiotoxicity assay for cardiac contraction fluctuation measurement using dual recording of electrical field potential and optical image analysis. *Safety Pharmacology Society 12th Annual Meeting*, 089, Phoenix, USA, Oct. 2012.
4. Tomoyo Hamada, Fumimasa Nomura, Tomoyuki Kaneko, Hideo Takamori, Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro assay (III). Evaluation of Temporal Field Potential Duration Fluctuation and Spatial Conduction Velocity Fluctuation of Cardiomyocyte Network for In Vitro Predictive Cardiotoxicity Measurement. *Safety Pharmacology Society 12th Annual Meeting*, 090, Phoenix, USA, Oct. 2012.
5. Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (IV). Quasi-electrocardiogram measurement for direct prediction of TdP occurrence using ring-shaped

- cardiomyocyte network with ring electrode array. Safety Pharmacology Society 12th Annual Meeting, 091, Phoenix, USA, Oct. 2012.
6. Hideyuki Terazono, Hyonchol Kim, Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Kenji Yasuda. Toward quasi-in vivo from in vitro assay (V). Non-invasive precise purification of ventricular cells from mixture of differentiated human stem cell derived cardiomyocytes using spot digestion of double alginate layers on a multi-electrode array chip. Safety Pharmacology Society 12th Annual Meeting, 092, Phoenix, USA, Oct. 2012.
 7. Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho, Fumimasa Nomura, Tomoyo Hamada, Tomoyuki Kaneko, Kenji Yasuda. Evaluation of ion channel trafficking of human stem cell derived cardiomyocytes for cardiotoxicity screening. Safety Pharmacology Society 12th Annual Meeting, 022, Phoenix, USA, Oct. 2012.
 8. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Development of On-Chip Dual Measurement System for Cardiac Contraction Flu Ctuation Assay using Simultaneous Recording of Extracellular Field Potential and Optical Image. 25th International Microprocesses and Nanotechnology Conference(MNC2012), 1P-7-93, Kobe, Japan, Nov. 1 2012.
 9. Fumimasa Nomura, Tomoyuki Kaneko, Akihiro Hattori, Kenji Yasuda. Quantitative Evaluation of Quasi-electrocardiogram Measurement for Direct Prediction of Lethal Arrhythmic Beating Occurrence using Ring-shaped Cardiomyocyte Network with Ring Electrode Array. 25th International Microprocesses and Nanotechnology Conference(MNC2012), 1P-7-95, Kobe, Japan, Nov. 2012.
 10. Tomoyo Hamada, Fumimasa Nomura, Tomoyuki Kaneko, Kenji Yasuda. Tempospatial External Field Potential Fluctuation Measurement in Constructive Cardiomyocyte Network for in Vitro Predictive Cardiotoxicity. 25th International Microprocesses and Nanotechnology Conference(MNC2012), 1B-4-2, Kobe, Japan, Nov. 2012.
 11. Hideyuki Terazono, Masahito Hayashi, Hiroyuki Takei, Akihiro Hattori, Tomoyuki Kaneko, Kenji Yasuda. Ultra High-speed Microdroplet Polymerase Chain Reaction System for Three-step Reverse Transcription of Single Cells using On-chip Three-channel Switching High-speed Liquid Circulating Module. 25th International Microprocesses and Nanotechnology Conference(MNC2012), 1P-7-84, Kobe, Japan, Nov. 2012.
 12. Akihiro Hattori, Tomoyuki Kaneko, Fumimasa Nomura, Kenji Yasuda. Surface Roughness of Cells as Index of Label-free Cell Identification and Separation in On-chip Imaging Cell Sorting System. 25th International Microprocesses and Nanotechnology Conference(MNC2012), 1P-7-85, Kobe, Japan, Nov. 2012.
 13. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Long-term simultaneous dual measurement of electrophysiological properties and mechanical responses of cardiomyocytes using on-chip extracellular field potential recording and real-time optical image analysis. The American Society for Cell Biology 2012 Annual Meeting, 1719, San Francisco, USA, Dec. 2012.
 14. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Fumimasa Nomura, Tomoyuki Kaneko, Kenji Yasuda. Non-invasive/destructive single cell purification method for re-cultivation of functionally identified specific cells using spot digestion of double alginate sol layers on a multielectrode array chip.. The American Society for Cell Biology 2012 Annual Meeting, 926, San Francisco, USA, Dec. 2012.

Genetic Regulation

1. Staffs and Students (in 2012)

Professor	Akinori KIMURA	
Associate Professor	Takuro ARIMURA	
Assistant Professor	Daisuke SAKURAI	
Research Associate	Taeko NARUSE	
Graduate Student	Taisuke ISHIKAWA,	Junji IIZULA
Graduate Student (Biomedical Science PhD program)	Jianbo AN,	Chika KADOTA,
	Kei KATSURAGI	
Visiting Graduate Student	Shinya KOIZUMI	
Visiting Student (Tokyo University of Science)	Tomoko KATO	

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. Ishii H, Kawada M, Tsukamoto T, Yamamoto H, Matsuoka S, Shiino T, Takeda A, Inoue M, Iida A, Hara H, Shu T, Hasegawa M, Naruse TK, Kimura A, Takiguchi M, Matano T. Impact of vaccination on cytotoxic T lymphocyte immunodominance and cooperation against simian immunodeficiency virus replication in rhesus macaques. *J Virol*. 2012; 86(2): 738-745.
2. Takaki A, Yamazaki A, Maekawa T, Shibata H, Hirayama K, Kimura A, Hirai H, Yasunami M. Positive selection of Toll-like receptor 2 polymorphisms in two closely related old world monkey species, rhesus and Japanese macaques. *Immunogenetics*. 2012; 64(1): 15-29.
3. Saito Y, Naruse TK, Akari H, Matano T, Kimura A. Diversity of MHC class I haplotypes in cynomolgus macaques. *Immunogenetics*. 2012; 64(2): 131-141.
4. Otsuka H, Arimura T, Abe T, Kawai H, Aizawa Y, Kubo T, Kitaoka H, Nakamura H, Nakamura K, Okamoto H, Ichida F, Ayusawa M, Nunoda S, Isobe M, Matsuzaki M, Doi YL, Fukuda K, Sasaoka T, Izumi T, Ashizawa N, Kimura A. Prevalence and distribution of sarcomeric gene mutations in Japanese patients with familial hypertrophic cardiomyopathy. *Circ J*. 2012; 76(2): 453-461.
5. Purevjav E, Arimura T, Augustin S, Huby A-C, Takagi K, Nunoda S, Kearney DL, Taylor MD, Terasaki F, Bos JM, Ommen SR, Shibata H, Takahashi M, Itoh-Satoh M, McKenna W, Murphy RT, Labeit S, Yamanaka Y, Machida N, Park JE, Alexander PMA, Weintraub RG, Kitaura Y, Ackerman MJ, Kimura A, Towbin JA. Molecular basis for clinical heterogeneity in inherited cardiomyopathies due to myopalladin mutations. *Hum Mol Genet*. 2012; 21(9): 2039-2053.
6. Watanabe H, Nogami A, Ohkubo K, Kawata H, Hayashi Y, Ishikawa T, Nagao S, Yagihara N, Takehara N, Kawamura Y, Sato A, Okamura K, Sato M, Hosaka Y, Fukae S, Chinushi M, Oda H, Okabe H, Kimura A, Maemura K, Watanabe I, Kamakura S, Aizawa Y, Shimizu W, Makita N. Similarities and differences in genetic and clinical

- characteristics between early repolarization syndrome and Brugada syndrome. *Circ Arrhythm Electrophysiol.* 2012; 5(2): e60-e61.
7. Nomura T, Terahara K, Yamamoto H, Shiino T, Takahashi N, Nakane T, Iwamoto N, Ishii H, Tsukamoto T, Kawada M, Matsuoka S, Takeda A, Terahara K, Tsunetsugu-Yokota Y, Iwata-Yoshikawa N, Hasegawa H, Sata T, Naruse TK, Kimura A, Matano T. Association of major histocompatibility complex class I haplotypes with disease progression after simian immunodeficiency virus challenge in Burmese rhesus macaques. *J Virol.* 2012; 86(12): 6481-6490.
 8. Tabara Y, Kohara K, Miki T; Millennium Genome Project for Hypertension (Fujioka A, Hanada H, Hata A, Hirawa N, Hiura Y, Imai Y, Inoko H, Itoh N, Iwai N, Kulski JK, Kamide K, Kato N, Osaka TK, Kawamoto R, Kawano Y, Kimura A, Kita Y, Kohara K, Kokubo Y, Mano H, Mano S, Miki T, Miyata T, Mizuki N, Morisaki T, Nakamura Y, Nakao K, Nakayama T, Nakura J, Ogawa M, Ogihara T, Ohkubo T, Ohno S, Oka A, Okamura T, Saruta T, Sekine A, Shiwa T, Soma M, Sugano S, Tabara Y, Tajima A, Takahashi N, Takashima N, Takeuchi F, Tokunaga K, Tomoike H, Umemura S, Yamane T, Yanai K, Yasunami M, Yatsu K, Yoshida T, Tabara Y). Hunting for genes for hypertension: the Millennium Genome Project for Hypertension. *Hypertension Res.* 2012; 35(6): 567-573.
 9. Ohtani H, Naruse TK, Iwasaki Y, Ishida T, Akari H, Matano T, Kimura A. Lineage-specific evolution of T-cell immunoglobulin and mucin domain 1 gene in the primates. *Immunogenetics.* 2012; 64(9): 669-678
 10. Watanabe H, Nogami A, Ohkubo K, Kawata H, Hayashi Y, Ishikawa T, Makiyama T, Nagao S, Yagihara N, Takehara N, Kawamura Y, Sato A, Okamura K, Hosaka Y, Sato M, Fukae S, Chinushi M, Oda H, Okabe M, Kimura A, Maemura K, Watanabe I, Kamakura S, Horie M, Aizawa Y, Shimizu W, Makita N. Clinical characteristics and risk of arrhythmia recurrences in patients with idiopathic ventricular fibrillation associated with early repolarization. *Int J Cardiol.* 2012; 159(3): 238-240.
 11. Xi Y, Ai T, De Lange E, Li Z, Wu G, Brunelli L, Kyle WB, Cheng J, Ackerman MJ, Kimura A, Weiss JN, Qu Z, Kim JJ, Faulkner G, Vatta M. Loss-of-function of hNav1.5 by ZASPI-D117N associated with intraventricular conduction disturbances in left ventricular noncompaction. *Circ Arrhythm Electrophysiol.* 2012; 5(5): 1017-1026
 12. Sato A, Sakamoto N, Ando K, Kaneshiro T, Uekita H, Sugimoto K, Yamaki T, Kunii H, Nakazato K, Suzuki H, Saitoh S, Sato M, Tamagawa K, Arimura T, Kimura A, Takeishi Y. Dilated phase of hypertrophic cardiomyopathy caused by two different sarcomere mutations, treated with surgical left ventricular reconstruction and cardiac resynchronization therapy with a defibrillator. *Intern Med.* 2012; 51(18): 2559-2564.
 13. Ishikawa T, Sato A, Marcou CA, Tester DJ, Ackerman MJ, Crotti L, Schwartz PJ, On YK, Park JE, Nakamura K, Hiraoka M, Nakazawa K, Sakurada H, Arimura T, Makita N, Kimura A. A novel disease gene for Brugada syndrome: sarcolemmal membrane-associated protein gene mutations impair intracellular trafficking of hNav1.5. *Circ Arrhythm Electrophysiol.* 2012; 5(6): 1098-1107.
 14. Minami T, Kuwahara K, Nakagawa Y, Takaoka M, Kinoshita H, Nakao K, Kuwabara Y, Yamada Y, Yamada C, Shibata J, Usami S, Yasuno S, Nishikimi T, Ueshima K, Sata M, Nakano H, Seno T, Kawahito Y, Sobue K, Kimura A, Nagai R, Nakao K. Reciprocal expression of MRTF-A and myocardin is crucial for pathological vascular remodeling in mice. *EMBO J.* 2012; 31(23):4428-4440.

Applied Genetics (Molecular Genetics)

1. Staffs and Students (April, 2012)

Professor	Yoshio MIKI	
Project Associate Professor	Akira NAKANISHI	
Assistant professor	Katsuya TAKENAKA	
Project Assistant Professor	Ken Miyaguchi	
Graduate Student	Miho TAKAOKA,	Nadila WALI,
	Nurmaa DASHZEVEG,	Yuya KAGAMI,
	Hitomi KIMURA,	Ryoko TAKIZAWA,
	Kazuya NAKAZAWA,	Takenori YAMAMOTO,
	Shota WADA,	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 BRCA1/2-deficient breast cancers
 - ② Identification of novel BRCA2-associated proteins functioning in DNA damage repair.
 - ③ Identification of novel BRCA2-associated proteins and analyses of functions of their association in numerical integrity of centrosomes.
- 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.
- 3) Identification of UVSSA gene as the responsible gene for UV-sensitive syndrome.

4. Publication

Original Article

1. Kawazu, M., Ueno, T., Kontani, K., Ogita, Y., Ando, M., Fukumura, K., Yamato, A., Soda, M., Takeuchi, K., Miki, Y., Yamaguchi, H., Yasuda, T., Naoe, T., Yamashita, Y., Katada, T., Choi, Y.L. and Mano, H. (2013) Transforming mutations of RAC guanosine triphosphatases in human cancers. *Proc Natl Acad Sci U S A*.
2. Wang, L., Tsutsumi, S., Kawaguchi, T., Nagasaki, K., Tatsuno, K., Yamamoto, S., Sang, F., Sonoda, K., Sugawara, M., Saiura, A., Hirono, S., Yamaue, H., Miki, Y., Isomura, M., Totoki, Y., Nagae, G., Isagawa, T., Ueda, H., Murayama-Hosokawa, S., Shibata, T., Sakamoto, H., Kanai, Y., Kaneda, A., Noda, T. and Aburatani, H. (2012) Whole-exome sequencing of human pancreatic cancers and characterization of genomic instability caused by MLH1 haploinsufficiency and complete deficiency. *Genome Res*, **22**, 208-19.
3. Taira, N., Mimoto, R., Kurata, M., Yamaguchi, T., Kitagawa, M., Miki, Y. and Yoshida, K. (2012) DYRK2 priming phosphorylation of c-Jun and c-Myc modulates cell cycle progression in human cancer cells. *J Clin Invest*, **122**, 859-72.
4. Suzuki, K., Dashzeveg, N., Lu, Z.G., Taira, N., Miki, Y. and Yoshida, K. (2012) Programmed cell death 6, a novel p53-responsive gene, targets to the nucleus in the apoptotic response to DNA damage. *Cancer Sci*, **103**, 1788-94.
5. Satoh, Y., Sugai, S., Uehara, H., Mun, M., Sakao, Y., Okumura, S., Nakagawa, K., Ishikawa, Y., Miki, Y. and Miyata, S. (2012) Clinical impact of intraoperative detection of carcinoembryonic antigen mRNA in pleural lavage specimens from nonsmall cell lung cancer patients. *Thorac Cardiovasc Surg*, **60**, 533-40.
6. Sakamoto, K., Fujii, T., Kawachi, H., Miki, Y., Omura, K., Morita, K., Kayamori, K., Katsube, K. and Yamaguchi, A. (2012) Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lab Invest*, **92**, 688-702.
7. Khanom, R., Sakamoto, K., Pal, S.K., Shimada, Y., Morita, K., Omura, K., Miki, Y. and Yamaguchi, A. (2012) Expression of basal cell keratin 15 and keratin 19 in oral squamous neoplasms represents diverse pathophysiologies.

Histol Histopathol, **27**, 949-59.

8. Iyevleva, A.G., Kuligina, E., Mitiushkina, N.V., Togo, A.V., Miki, Y. and Imyanitov, E.N. (2012) High level of miR-21, miR-10b, and miR-31 expression in bilateral vs. unilateral breast carcinomas. *Breast Cancer Res Treat*, **131**, 1049-59.
9. Elgazzar, S., Zembutsu, H., Takahashi, A., Kubo, M., Aki, F., Hirata, K., Takatsuka, Y., Okazaki, M., Ohsumi, S., Yamakawa, T., Sasa, M., Katagiri, T., Miki, Y. and Nakamura, Y. (2012) A genome-wide association study identifies a genetic variant in the SIAH2 locus associated with hormonal receptor-positive breast cancer in Japanese. *J Hum Genet*, **57**, 766-71.
10. Nakazawa Y, Sasaki K, Mitsutake N, Matsuse M, Shimada M, Nardo T, Takahashi Y, Ohyama K, Ito K, Mishima H, Nomura M, Kinoshita A, Ono S, Takenaka K, Masuyama R, Kudo T, Slor H, Utani A, Tateishi S, Yamashita S, Stefanini M, Lehmann AR, Yoshiura K, Ogi T. (2012) Mutations in UVSSA cause UV-sensitive syndrome and impair RNA polymerase IIo processing in transcription-coupled nucleotide-excision repair. *Nature Genetics* **44**, 586-592.

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	Kosuke Tanimoto Ph.D.	
Tokunin Lecturer	Shin Hayashi M.D., Ph.D.	
Doctoral course students (DC2)	Mayuko Furuta,	Tomoki Muramatsu
Global COE program Advanced I	super student (AISS)	
	Nuylan Michelle Loyola,	Daniela Tiaki Uehara
Graduate Student	Mitsuyo Naganawa,	Sujata Sakha
Research Student	Hiroaki Nagata,	Reiko Iwadate

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. Endo H, Muramatsu T, Furuta M, Uzawa N, Pimkhaokham A, Amagasa T, Inazawa J, Kozaki K: Potential of tumor-suppressive miR-596 targeting LGALS3BP as a therapeutic agent in oral cancer. *Carcinogenesis*, 34: 560-569, 2013.
2. 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* 43: 69-73, 2013.
3. Takanashi J, Okamoto N, Yamamoto Y, Hayashi S, Arai H, Takahashi Y, Maruyama K, Mizuno S, Shimakawa S, Ono H, Oyanagi R, Kubo S, Barkovich AJ, Inazawa J: Clinical and radiological features of Japanese patients with a severe phenotype due to CASK mutations. *Am J Med Genet A* 158A: 3112-3118, 2012.
4. Gaffney CJ, Oka T, Mazack V, Hilman D, Gat U, Muramatsu T, Inazawa J, Golden A, Carey DJ, Farooq A, Tromp G, Sudol M: Identification, basic characterization and evolutionary analysis of differentially spliced mRNA isoforms of human YAP1 gene. *Gene* 509: 215-222, 2012.
5. Dobashi Y, Kimura M, Matsubara H, Endo S, Inazawa J, Ooi A: Molecular alterations in AKT and its protein

- activation in human lung carcinomas. *Hum Pathol* 43: 2229-2240, 2012.
6. Miyawaki Y, Kawachi H, Ooi A, Eishi Y, Kawano T, Inazawa J, Imoto I: Genomic copy-number alterations of MYC and FHIT genes are associated with survival in esophageal squamous-cell carcinoma. *Cancer Sci* 103: 1558-1566, 2012.
 7. Matsumura S, Imoto I, Kozaki K, Matsui T, Muramatsu T, Furuta M, Tanaka S, Sakamoto M, Ariei S, Inazawa J: Integrative array-based approach identifies MZB1 as a frequently methylated putative tumor-suppressor in hepatocellular carcinoma. *Clin Cancer Res* 18: 3541-3551, 2012.
 8. Honda S, Hayashi S, Nakane T, Imoto I, Kurosawa K, Mizuno S, Okamoto N, Kato M, Yoshihashi H, Kubota T, Nakagawa E, Goto Y, Inazawa J: The incidence of hypoplasia corpus callosum in patients with dup (X) (q28) involving MECP2 is associated with the location of distal breakpoints. *Am J Med Genet A* 158A: 1292-1303, 2012.
 9. Akamatsu S, Takata R, Haiman CA, Takahashi A, Inoue T, Kubo M, Furihata M, Kamatani N, Inazawa J, Chen GK, Le Marchand L, Kolonel LN, Katoh T, Yamano Y, Yamakado M, Takahashi H, Yamada H, Egawa S, Fujioka T, Henderson BE, Habuchi T, Ogawa O, Nakamura Y, Nakagawa H: Common variants at 11q12, 10q26 and 3p11.2 are associated with prostate cancer susceptibility in Japanese. *Nat Genet* 44: 426-429, 2012.
 10. Yamamoto S, Tsuda H, Honda K, Takano M, Tamai S, Imoto I, Inazawa J, Yamada T, Matsubara O: ACTN4 gene amplification and actinin-4 protein overexpression drive tumour development and histological progression in a high-grade subset of ovarian clear-cell adenocarcinomas. *Histopathology* 60: 1073-1083, 2012.
 11. Ono H, Imoto I, Kozaki K, Tsuda H, Matsui T, Kurasawa Y, Muramatsu T, Sugihara K, Inazawa J: SIX1 promotes epithelial-mesenchymal transition in colorectal cancer through ZEB1 activation. *Oncogene* 31: 4923-4934, 2012.
 12. Maeda M, Mitsui J, Soong B, Takahashi Y, Ishiura H, Hayashi S, Shirota Y, Ichikawa Y, Matsumoto H, Arai M, Okamoto T, Miyama S, Shimizu J, Inazawa J, Goto J, Tsuji S: Increased gene dosage of myelin protein zero causes Charcot-Marie-Tooth disease. *Ann Neurol* 71: 84-92, 2012.
 13. Okamoto N, Hayashi S, Masui A, Kosaki R, Oguri I, Hasegawa T, Imoto I, Makita Y, Hata A, Moriyama K, Inazawa J: Deletion at chromosome 10p11.23-p12.1 defines characteristic phenotypes with marked midface retrusion. *J Hum Genet* 57: 191-196, 2012.
 14. Bai H, Inoue J, Kawano T, Inazawa J: A transcriptional variant of the LC3A gene is involved in autophagy and frequently inactivated in human cancers. *Oncogene* 31: 4397-4408, 2012.
 15. Ooi A, Inokuchi M, Harada S, Inazawa J, Tajiri R, Sawada-Kitamura S, Ikeda H, Kawashima H, Dobashi Y: Gene amplification of ESR1 in breast cancers - Fact or fiction? A fluorescence in situ hybridization and multiplex ligation-dependent probe amplification study. *J Pathol* 227: 8-16, 2012.
 16. Honda S, Satomura S, Hayashi S, Imoto I, Nakagawa E, Goto Y, Inazawa J: Concomitant microduplications of MECP2 and ATRX in male patients with severe mental retardation. *J Hum Genet* 57: 73-77, 2012.
 17. Kurasawa Y, Kozaki K, Pimkhaokham A, Muramatsu T, Ono H, Ishihara T, Uzawa N, Imoto I, Amagasa T, Inazawa J: Stabilization of phenotypic plasticity through mesenchymal-specific DNA hypermethylation in cancer cells. *Oncogene* 31: 1963-1974, 2012.
 18. Hayashi S, Okamoto N, Chinen Y, Takanashi J, Makita Y, Hata A, Imoto I, Inazawa J: Novel intragenic duplications and mutations of CASK in patients with mental retardation and microcephaly with pontine and cerebellar hypoplasia (MICPCH). *Hum Genet* 131: 99-110, 2012.

Review Article

1. Kozaki K and Inazawa J: Tumor-suppressive microRNA silenced by tumor-specific DNA hypermethylation in cancer cells. *Cancer Sci* 103: 837-845, 2012.

Biochemical Genetics and Genome Structure and Regulation

1. Staffs and Students (April, 2012)

Professor	Shigetaka Kitajima MD, PhD	
Associate Professor	Yujiro Tanaka MD, PhD	
Assistant Professor	Junya Kawauchi MD, PhD	
Secretary	Kuniko Takayanagi	
Graduate Student	Makoto Inoue,	Hiroto Goshima ,
	Makoto Edagawa	
Research Student	Satoshi Fukumoto,	Yohei Uchida,
	Takuya Takahashi	
Foreign Scholar	Liu Jia, MD	

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. Yasukawa T, Bhatt S, Takeuchi T, Kawauchi J, Takahashi H, Tsutsui A, Muraoka T, Inoue M, Tsuda M, Kitajima S, Conaway RC, Conaway JW, Trainor PA, Aso T. Transcriptional Elongation Factor Elongin A Regulates Retinoic Acid-Induced Gene Expression during Neuronal Differentiation. *Cell Reports* 10.1016/j.celrep.2012.09.031
2. Kawauchi J, Kitajima S. "Mechanism of Transcriptional Termination" in *Encyclopedia of Systems Biology* chapter 1408 (W. Dubitzky, O. Wolkenhauer, K. Cho & H. Yokota (eds.), DOI 10.1007/978-1-4419-9863-7, Springer Science+Business Media LLC, 2012
3. Cabianca DS, Casa V, Bodega B, Carvalho C, Ginelli E, Tanaka Y, Carmo-Fonseca M, Gabellini D. A ncRNA regulating a Polycomb/Trithorax epigenetic switch in muscular dystrophy. *Cell* in press, 2012
4. Taketani K, Kawauchi J, Tanaka-Okamoto M, Ishizaki H, Tanaka Y, Sakai T, Miyoshi J, Maehara Y, Kitajima S. Key role of ATF3 in p53-dependent DR5 induction upon DNA damage of human colon cancer cells. *Oncogene*. 2012 Apr 26;31(17):2210-21

Hematology

1. Staffs and Students

Professor	Osamu MIURA	
Junior Associate Professor	Ayako ARAI	
Assistant Professor	Tetsuya FUKUDA, Masahide YAMAMOTO,	Tetsuya KUROSU, Toshikage NAGAO
Hospital Staff	Hiroki AKIYAMA, Megumi AKIYAMA,	Dsisuke WATANABE, Keigo OKADA
Hospital Staff/Graduate Student	Shihoko SUWA	
Graduate Student	Minako JINTA, Ayako ICHIKAWA, Nan WU,	Ken WATANABE, Ayako NOGAMI, Lu Dan Wang

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. Arai A, Imadome K, Wang L, Wu N, Kurosu T, Wake A, Yamamoto H, Ota Y, Harigai M, Fujiwara S, Miura O: Recurrence of chronic active Epstein-Barr virus infection from donor cells after achieving complete response through allogeneic bone marrow transplantation. *Int Medicine* 51:777-782, 2012.
2. Arai A, Nogami A, Imadome K, Kurata M, Murakami N, Fujiwara S, Miura O: Sequential monitoring of serum IL-6, TNF- α , and IFN- γ levels in a CAEBV patient treated by plasma exchange and immunochemotherapy. *Int J Hematol* 96:669-673, 2012.
3. Keiko Yagi, Kouhei Yamamoto, Shigeaki Umeda, Shinya Abe, Shiho Suzuki, Iichiroh Onishi, Susumu Kirimura, Masashi Fukayama, Ayako Arai, Toshihiko Murayama, Michihiro Hidaka, Masanobu Kitagawa, Morito Kurata: Expression of multidrug resistance 1 gene in B-cell lymphomas: association with follicular dendritic cells. *Histopathology* 62:414-420, 2012.

Molecular Endocrinology and Metabolism

1. Staffs and Students (2012)

Professor	Yoshihiro Ogawa	
Junior Associate Professor	Takanobu Yoshimoto,	Hajime Izumiyama
Assistant Professor	Masatomo Mihara,	Isao Minami,
	Masako Kato	
Project Junior Associate Professor	Toru Sugiyama	
Project Junior Assistant Professor	Misa Saijo,	Michiya Kida
Resident	Eri Hayakawa,	Yuichiro Nishio,
	Kazutaka Tsujimoto,	Noriaki Okiba,
	Tamaki Ando	
Graduate Students	Michiya Kida,	Takako Watanabe,
	Fumihiko Takizawa,	Tatuya Ebara,
	Naoto Tsuda,	Yorihiro Iwasaki,
	Chikako Aoyama,	Toshiyuki Sakurai,
	Kuniha Konuma,	Takuya Ohashi,
	Yasutaka Chiba,	Chikara Komiya,
	Kenji Ikeda,	Hideaki Kato,
	Masanobu Kano,	Kazumi Kasahara,
	Erina Tamura	
Medical Fellow	Miyako Tanaka	
JSPS RPD Fellow	Rumi Hachiya	
Student	Yukino Hatazawa	
Department of Organ Network and Metabolism		
Project Professor	Yasutomi Kamei	
Project Assistant Professor	Michiko Ito,	Xunmei Yuan,
	Mayumi Takahashi,	Ibuki Shirakawa
Department of Molecular Medicine and Metabolism		
Associate Professor	Takayoshi Suganami	
GCOE Project Junior Associate Professor	Naoki Sawada	

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. Watanabe Y, Nakamura T, Ishikawa S, Fujisaka S, Usui I, Tsuneyama K, Ichihara Y, Wada T, Hirata Y, Suganami T, Izaki H, Akira S, Miyake K, Kanayama HO, Shimabukuro M, Sata M, Sasaoka T, Ogawa Y, Tobe K, Takatsu K, Nagai Y. The Radioprotective 105/MD-1 complex contributes to diet-induced obesity and adipose tissue inflammation. **Diabetes** 61:1199-1209, 2012.
2. Ehara T, Kamei Y, Takahashi M, Yuan X, Kanai S, Tamura E, Tanaka M, Yamazaki T, Miura S, Ezaki O, Suganami T, Okano M, Ogawa Y. Role of DNA methylation in the regulation of lipogenic glycerol-3-phosphate acyltransferase 1 gene expression in the mouse neonatal liver. **Diabetes** 61:2442-2450, 2012.
3. Satoh-Asahara N, Shimatsu A, Sasaki Y, Nakaoka H, Himeno A, Tochiya M, Kono S, Takaya T, Ono K, Wada H, Suganami T, Hasegawa K, Ogawa Y. Highly purified eicosapentaenoic acid increases interleukin-10 levels of peripheral blood monocytes in obese patients with dyslipidemia. **Diabetes Care** 35:2631-2639, 2012.
4. Sakurai A, Yamazaki M, Suzuki S, Fukushima T, Imai T, Kikumori T, Okamoto T, Horiuchi K, Uchino S, Kosugi S, Yamada M, Komoto I, Hanazaki K, Itoh M, Kondo T, Mihara M, Imamura M : Clinical features of insulinoma in patients with multiple endocrine neoplasia type 1: analysis of the database of the MEN Consortium of Japan. **Endocr J** 59:859-866, 2012.
5. Tateishi Y, Kouyama R, Mihara M, Doi M, Yoshimoto T, Hirata Y : Evaluation of salivary cortisol measurements for the diagnosis of subclinical Cushing's syndrome. **Endocr J** 59:283-289, 2012.
6. Kato M, Inoshita N, Sugiyama T, Tani Y, Shichiri M, Sano T, Yamada S, Hirata Y. Differential expression of genes related to drug responsiveness between sparsely and densely granulated somatotroph adenomas. **Endocr J** 59:221-228, 2012.
7. Suganami T, Tanaka M, Ogawa Y. Adipose tissue inflammation and ectopic lipid accumulation. **Endocr J** 59: 849-857, 2012.
8. Hayakawa E, Yoshimoto T, Sekizawa N, Sugiyama T, Hirata Y. Overexpression of α receptor for advanced glycation end products induces monocyte chemoattractant protein-1 expression in rat vascular smooth muscle cell line. **J Atheroscler Thromb.** 19:13-22, 2012.

2) International Meeting

1. Ogawa Y: Chronic Inflammation and Ectopic Fat Accumulation in the Metabolic Syndrome: **The 2012 Spring Conference of the Korean Association of Immunologists.** Seoul, Korea (2012.4)
2. Ogawa Y, Suganami T: Chronic inflammation and ectopic fat accumulation in the metabolic syndrome. **20th International Symposium on Molecular Cell Biology of Macrophages 2012.** Tokyo (2012.6)
3. Ogawa Y: Adipose tissue remodeling as homeostatic inflammation. **The 12th Biennial International Endotoxin & Innate Immunity Society (IEIIS) meeting, The Homeostatic Inflammation International Symposium.** Tokyo (2012.10)
4. Ogawa Y: Chronic Inflammation, A Molecular Basis Underlying the Metabolic Syndrome : **2012 Shanghai Symposium on Obesity & Diabetes.** Shanghai, China (2012.4)
5. Suganami T, Ogawa Y: Adipose tissue inflammation and ectopic fat accumulation. **2nd International Symposium for the Study of Obesity.** Kyoto (2012.10)
6. Sawada N: Rac1 GTPase is a critical mediator of endothelium-derived neurotrophic activity. **Neuro-Vascular Wiring Symposium.** Nara (2012.11)
7. Suganami T, Itoh M, Tanaka M, Kamei Y, Terai S, Sakaida I, Ogawa Y: Melanocortin-4 receptor-deficient mice as a novel mouse model of non-alcoholic steatohepatitis. **2012 Keystone Symposia.** Boston, US (2012.3)
8. Tanaka M, Suganami T, Ogawa Y: Role of central leptin signaling in the starvation-induced alteration of B-cell development. **2012 Keystone Symposia.** Boston, USA (2012.3)
9. Kamei Y, Ehara T, Takahashi M, Yuan X, Kanai S, Tamura E, Tanaka M, Yamazaki T, Ezaki O, Suganami T, Okano M, Ogawa Y: Role of DNA methylation in the regulation of lipogenic gene expression in the mouse neonatal liver. **Experimental Biology.** San Diego, USA (2012.4)

Hepato-Biliary-Pancreatic Surgery

1. Staffs and Students

Professor	Shigeki Arie (~March, 2012)	
Associate Professor	Shinji Tanaka	
Assistant Professor	Noriaki Nakamura,	Atsushi Kudo,
	Takumi Irie,	Takenori Ochiai,
	Daisuke Ban,	Arihiro Aihara (~March, 2012),
	Satoshi Matsumura (April, 2012~)	
Tokunin Assistant Professor	Yasen Mahmut (~November,2012)	
Graduate Student	Rama Adikrisna (~September,2012),	
	Syunsuke Muramatsu (~March, 2012),	
	Chisato Okajima,	Kouta Sato,
	Kousuke Ogawa,	Yuichiro Watanabe,
	Tomoya Miura,	Hiroko Matsunaga,
	Eriko Katsuta,	Takaki Furuyama,
	Hiromitsu Ito,	Keisuke Nakao,
	Keiichi Akahoshi (April, 2012~),	
	Xirali Mamat,	Maynur Abdurahman

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, their interest in surgery is nurtured through medical education.

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 extended indication of the hepatic resection for hepato-biliary malignancies.
- 4) Research in the transporter for bile metabolism
- 5) Research in the improvement of liver preservation
- 6) Research in the microcirculation of the liver
- 7) Research in immunological tolerance for organ transplantation
- 8) Research in technical improvement of laparoscopic surgery

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 135 on 2012, which was ranked among high volume centers of our country.

5. Publications

Original Article

1. Adikrisna R, Tanaka S, Muramatsu S, Aihara A, Ban D, Ochiai T, Irie T, Kudo A, Nakamura N, Yamaoka S, Arii S. Identification of pancreatic cancer stem cells and selective toxicity of chemotherapeutic agents. *Gastroenterology*.143(1)234-245, 2012
2. Matsumura S, Imoto I, Kozaki K, Matsui T, Muramatsu T, Furuta M, Tanaka S, Sakamoto M, Arii S, Inazawa J. Integrative array-based approach identifies MZB1 as a frequently methylated putative tumor suppressor in hepatocellular carcinoma. *Clin Cancer Res*. 18(13):3541-51, 2012
3. 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 signification. *Hepatology*, in press
4. 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*, in press
5. Kudo A, Ban D, Aihara A, Irie T, Ochiai T, Nakamura N, Tanaka S and Arii S. Decreased Mrp2 transports in severe macrovesicular fatty liver grafts. *J Surg Res*. 2012;178(2):915-21.
6. Kudo A, Ban D, Akashi T, Kumagai J, Aihara A, Inokuchi M, Kojima K, Kawano T, Tanaka S, Arii S. Prognoses of GEP-Nets with undetermined malignant potentials of their primary sites. *Hepatogastroenterology*. 2012;59(118):1682-6.
7. Kudo A, Akashi T, Kumagai J, Ban D, Inokuchi M, Kojima K, Kawano T, Tanaka S, Arii S. The Importance of Clinical Information in Patients with Gastroenteropancreatic Neuroendocrine Tumor. *Hepatogastroenterology*. 2012;59(120):2450-3
8. Kudo A, Igari T, Kumagai J, Tanaka S, Ban D, Noguchi N, Irie T, Nakamura N, and Arii S. A simple index to predict liver functional reserve after hepatectomy. *Hepatogastroenterology*, in press
9. Irie T, Ito K, Ozasa H, Noda Y, Ikeda S, Tanaka S, Arii S, Horikawa S. Splenic artery ligation: A protection against hepatic ischemia/reperfusion injury in partially hepatectomized rats. *Hepatology Research*, 42(8):819-827, 2012
10. Ochiai T, Ohta K, Iida M, Kumagai Y, Mitsunori M, Aihara A, Noguchi N, Tanaka S, Arii S, Yamazaki S. High resectability of colorectal liver metastases with aggressive chemotherapy in the era of molecular target-based agents. *Hepatogastroenterology*, in press
11. Xieraili M, Yasen M, Mogushi K, Obulhasim G, Maynuer A, Aihara A, Tanaka S, Mizushima H, Tanaka H, Arii S. Villin 1 is a predictive factor for the recurrence of high serum alpha-fetoprotein-associated hepatocellular carcinoma after hepatectomy. *Cancer Sci* 2012;103(8)1493-1501
12. Yasen M, Obulhasim G, Kajino K, Mogushi K, Mizushima H, Tanaka S, Tanaka H, Hino O, Ari S. DNA binding protein A expression and methylation status in hepatocellular carcinoma and the adjacent tissue. *International Journal of Oncology*, 2012;40(3):789-97.
13. 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
14. Sakai S, Inamoto K, Liu Y, Tanaka S, Arii S, Taya M. Multicellular tumor spheroid formation in duplex microcapsules for analysis of chemosensitivity. *Cancer Sci* 2012;103(3):549-54.
15. Yamamoto Y, Sakamoto Y, Ban D, Shimada K, Esaki M, Nara S, Kosuge T. Is celiac axis resection justified for T4 pancreatic body cancer? *Surgery*. 2012;151(1):61-9.
16. Yamada Y, Boskovic S, Aoyama A, Murakami T, Putheti P, Smith RN, Ochiai T, Nadazdin O, Koyama I, Boenisch O, Najafian N, Bhasin MK, Colvin RB, Madsen JC, Strom TB, Sachs DH, Benichou G, Cosimi AB, Kawai T. Overcoming memory T-cell responses for induction of delayed tolerance in nonhuman primates. *Am J Transplant*. 2012; 12(2):330-40.
17. Kumagai Y, Kawada K, Yamazaki S, Iida M, Odajima H, Ochiai T, Kawano T, Takubo K. Current status and limitations of the newly developed endocytoscope GIF-Y0002 with reference to its diagnostic performance for common esophageal lesions. *J Dig Dis*. 2012;13(8):393-400.
18. Kumagai Y, Yagi M, Aida J, Ishida H, Suzuki S, Hashimoto T, Amanuma Y, Kusano M, Mukai S, Yamazaki S, Iida M, Ochiai T, Matsuura M, Iwakiri K, Kawano T, Hoshihara Y, Takubo K. Detailed features of palisade vessels as a marker of the esophageal mucosa revealed by magnifying endoscopy with narrow band imaging. *Dis Esophagus*. 2012;25(6):484-90.
19. Ban D, Shimada K, Konishi M, Saiura A, Hashimoto M, Uesaka K. Stapler and nonstapler closure of the pancreatic remnant after distal pancreatectomy: multicenter retrospective analysis of 388 patients. *World J Surg*.

Review Article, Case Report , etc.

1. Tanaka S, Arii S. Molecular Targeted Therapies in Hepatocellular Carcinoma. *Seminars in Oncology*. 2012; 39(4):486-492
2. Ochiai T, Masuda T, Yagi M, Kasai R, Furuyama T, Tsukamoto K, Ito H, Igari K, Aihara A, Kumagai Y, Iida M, Odajima H, Tanaka S, Arii S, Yamazaki S. Successful combination therapy of radical liver resection with 5-fluorouracil/leucovorin, oxaliplatin, plus bevacizumab for ascending colon cancer with pulmonary and 43 liver metastases: report of a case. *Int Surg*. 2012;97(1):6-13
3. Jibiki M, Inoue Y, Kudo T, Toyofuku T, Saito K, Kihara K, Kudo A, Ban D, Arii S. Combined resection of a tumor and the inferior vena cava: report of two cases. *Surg Today*. in press
4. Kumagai Y, Miura K, Nishida T, Igari K, Ochiai T, Iida M, Yamazaki S, Odajima H, Kawano T, Takubo K. Simultaneous resection of metastatic melanoma in the esophagus and primary cutaneous melanoma showing partial regression: report of a case. *Surg Today*. 2012; 42(9):884-90.
5. Uetake H, Tanaka S, Ishikawa T, Sugihara K, Arii S. Fate of metastatic foci after chemotherapy and usefulness of contrast-enhanced intraoperative ultrasonography to detect minute hepatic lesions. *J Hepatobiliary Pancreat Sci*. 2012;19(5):509-14

International Presentation

1. Nakamura N. Result of surgical treatment for peritoneal dissemination of hepatocellular carcinoma. 10th World Congress of the International Hepato-Pancreato-Biliary Association, Paris, 2012.7.1-5.
2. Ochiai T, Ohta K, Kumagai Y, Iida M, Yamazaki S, Tanaka S, Arii S. Aggressive resection of colorectal liver metastases after approval of molecular target-based drugs. 7th Academic Surgical Congress, Las Vegas, 2012.02.14.
3. Ochiai T, Kumagai Y, Iida M, Yamazaki S, Arii S. Efficacy of adjuvant chemotherapy for colorectal cancer with liver metastases since approval of molecular targeted agents. UICC World Cancer Congress 2012, Montoreal, 2012.8.27-30
4. Ochiai T, Yamazaki S, Kawachi H, Tanaka S, Arii S. Expression of sonic hedgehog in ampullary neoplasm. UICC World Cancer Congress 2012, Montoreal, 2012.8.27-30.
5. Ochiai T, Sato K, Matsumura S, Ban D, Irie T, Kudo A, Nakamura N, Tanaka S. Comparison of two classifications, TNM staging and Japanese classification of biliary tract carcinoma, for ampullary carcinoma: analysis of consecutive 24 resected cases. 22nd IASGO 2012, Bangkok, 2012.12.6
6. Ochiai T, Igari K, Nishizawa M, Yagi M, Kumagai Y, Iida M, Tanaka S, Arii S, Yamazaki S. A case report of pancreatic adenosquamous carcinoma presenting as recurrence of remnant pancreas after pylorus preserving pancreatoduodenectomy for pancreatic ductal adenocarcinoma. 22nd IASGO 2012, Bangkok, 2012.12.6
7. Ochiai T, Kumagai Y, Iida M, Tanaka S, Arii S, Yamazaki S. Surgical results of pancreatic ductal carcinoma: consecutive 81 cases from single institute in Japan. 22nd IASGO 2012, Bangkok, 2012.12.6
8. Sato T, Ochiai T, Ban D, Matsumura S, Irie T, Kudo A, Nakamura N, Tanaka S. A Case Report of Required Total Pancreatectomy for Ampullary Carcinoma: Due to Invasion to The Main Pancreatic Duct. 22nd IASGO 2012, Bangkok, 2012.12.6
9. Takamatsu S, Nagano H, Ootsukasa S, Kawachi Y, Maruyama H. A case report of the liver metastasis of colon cancer with the tumor thrombus in the intrahepatic bile duct. 10th World Congress of the International Hepato-Pancreato-Biliary Association, Paris, 2012.7.1-5.
10. Baba H, Sanada T, Goseki N, Ishida H. Can postoperative pancreatic fistula be predicted by simple clinical measure? 10th World Congress of Hepato-Pancreato-Biliary-Association. July 2, 2012, Paris, France
11. Baba H, Sanada T, Goseki N, Ishida H. Cystic duct cancer presenting hemobilia. 10th World Congress of Hepato-Pancreato-Biliary-Association. July 2, 2012, Paris, France

Orthopaedic and spinal surgery

1. Staffs and Students (April, 2012)

Professor	Atsushi OKAWA	
Junior Associate Professor	Tetsuya JINNO, Shigenori KAWABATA	Yoshiaki WAKABAYASHI,
Assistant Professor	Tsuyoshi KATO, Toshitaka YOSHII, Hiroyuki INOSE	Daisuke KOGA, Chigusa SAWAMURA,
Graduate Student	Hiroataka KOYANAGI, Dai UKEGAWA, Takashi TANIYAMA, Madoka UKEGAWA, Sei JO, Chengshan MA, Hidetoshi KABURAGI, Hidetsugu SUZUKI,	Masato YUASA, Tsuyoshi YAMADA, Yoto OH, Yuki FUNAUCHI, Ren XU, Gaku KOYANO, Satoshi SUMIYA, Masanori SAITO
Department of Orthopaedics Research and Development		
Associate Professor	Shinichi Sotome,	Yoshinori Asou

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. Yamada T, Yoshii T, Sotome S, Yuasa M, Kato T, Arai Y, Kawabata S, Tomizawa S, Sakaki K, Hirai T, Shinomiya K, Okawa A. : Hybrid grafting using bone marrow aspirate combined with porous β -tricalcium phosphate and trephine bone for lumbar posterolateral spinal fusion: a prospective, comparative study versus local bone grafting. *Spine (Phila Pa 1976)*. Feb 1;37(3):E174-9, 2012.
2. Yamada T, Yoshii T, Yoshimura H, Suzuki K, Okawa A : Upper limb amputation due to a brachial arterial embolism associated with a superior mesenteric arterial embolism: a case report. *BMC Res Notes*. Jul 24;5:372, 2012.
3. Nimura A, Kato A, Yamaguchi K, Mochizuki T, Okawa A, Sugaya H, Akita K: The superior capsule of the shoulder joint complements the insertion of the rotator cuff. *J Shoulder Elbow Surg*. 21(7):867-72, 2012.
4. Fujita K, Iwasaki M, Ochi H, Fukuda T, Ma C, Miyamoto T, Takitani K, Negishi-Koga T, Sunamura S, Kodama T, Takayanagi H, Tamai H, Kato S, Arai H, Shinomiya K, Itoh H, Okawa A, Takeda S: Vitamin E decreases bone mass by stimulating osteoclast fusion. *Nature Medicine* 18(4):589-594, 2012.
5. Sakaki K, Kawabata S, Ukegawa D, Hirai T, Ishii S, Tomori M, Inose H, Yoshii T, Tomizawa S, Kato T, Shinomiya K, Okawa A: Warning thresholds on the basis of origin of amplitude changes in transcranial electrical motor-evoked potential monitoring for cervical compression myelopathy. *Spine*. Jul 1; 37(15): E913-21, 2012.
6. Iwasaki M, Piao J, Kimura A, Sato S, Inose H, Ochi H, Asou Y, Shinomiya K, Okawa A, Takeda S: Runx2 haploinsufficiency ameliorates the development of Ossification of the Posterior Longitudinal Ligament. *PLoS ONE*. 7(8): e43372, 2012.
7. Kuroiwa T, Yoshii T, Sakaki K, Inose H, Tomizawa S, Kato T, Kawabata S, Shinomiya K, Okawa A: Vertebral locking lesion following cervical spine fracture in ankylosing spondylitis. *Orthopedics*. 35(6):1005-1008, 2012.
8. Wei J, Shi Y, Zheng L, Zhou B, Inose H, Wang J, Guo XE, Grosschedl R, Karsenty G : Mir-34s inhibit osteoblast proliferation and differentiation in the mouse by targeting SATB2. *J Cell Biol* 197(4):509-521, 2012.
9. Ishii S, Kawabata S, Tomizawa S, Tomori M, Sakaki K, Shinomiya K, Sekihara K, Sato T, Adachi Y, Okawa A: Conductive neuromagnetic fields in the lumbar spinal canal. *Clin Neurophysiol*. Aug;123(8):1656-61, 2012.
10. Yoshii T, Dumas JE, Okawa A, Spengler DM, Guelcher SA: Synthesis, characterization of calcium phosphates/polyurethane composites for weight-bearing implants. *J Biomed Mater Res B Appl Biomater*. Jan;100(1):32-40, 2012.
11. Yoshii T, Hafeman AE, Esparza JM, Okawa A, Gutierrez G, Guelcher SA: Local injection of lovastatin in biodegradable polyurethane scaffolds enhances bone regeneration in A critical-sized segmental defect in rat femora. *J Tissue Eng Regen Med*. Jun 20, 2012.
12. Yoshii T, Nakai O, Hirai T, Sotome S, Shinomiya K, Okawa A, Myositis Ossificans Traumatica Secondary to Fracture of the Odontoid in a Five- Month-Old Infant. A Case Report. *JBJS Case Connector*, Feb 22;2(1):e7 1-4, 2012.
13. 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)*. Dec 3, 2012. [Epub ahead of print]
14. Itoh H, Hara Y, Tagawa M, Kato T, Ochi H, Koga D, Okawa A, Asou Y: Evaluation of the association between runt-related transcription factor 2 expression and intervertebral disk aging in dogs. *Am J Vet Res*. Oct;73(10):1553-9, 2012.
15. Aini H, Ochi H, Iwata M, Okawa A, Koga D, Okazaki M, Sano A, Asou Y: Procyanidin B3 prevents articular

- cartilage degeneration and heterotopic cartilage formation in a mouse surgical osteoarthritis model. *PLoS One*. 2012;7(5):e37728, 2012.
16. Koyanagi H, Matsumoto S, Shimoji T, Tanizawa T, Ae K, Shinomiya K, Okawa A, Kawaguchi N: Long-term results from use of pasteurized bone. *J Orthop Sci*. Sep;17(5):605-13, 2012.
 17. Sawamura C, Matsumoto S, Shimoji T, Ae K, Tanizawa T, Gokita T, Koyanagi H, Okawa A: Indications for and surgical complications of rotationplasty. *J Orthop Sci*. 2012 Nov;17(6):775-81, 2012.
 18. Sawamura C, Matsumoto S, Shimoji T, Tanizawa T, Ae K: What are risk factors for local recurrence of deep high-grade soft-tissue sarcomas? *Clin Orthop Relat Res*. 2012 Mar;470(3):700-5, 2012.
 19. Li W, Enomoto M, Ukegawa M, Hirai T, Sotome S, Wakabayashi Y, Shinomiya K, Okawa A: Subcutaneous injections of platelet-rich plasma into skin flaps modulate proangiogenic gene expression and improve survival rates. *Plast Reconstr Surg*. Apr;129(4):858-66, 2012.
 20. Enomoto M, Ukegawa D, Sakaki K, Tomizawa S, Arai Y, Kawabata S, Kato T, Yoshii T, Shinomiya K, Okawa A: Increase in paravertebral muscle activity in lumbar kyphosis patients by surface electromyography compared with lumbar spinal canal stenosis patients and healthy volunteers. *J Spinal Disord Tech*. Aug;25(6):E167-73, 2012.
 21. Hirai T, Enomoto M, Machida A, Yamamoto M, Kuwahara H, Tajiri M, Hirai Y, Sotome S, Mizusawa H, Shinomiya K, Okawa A, Yokota T: Intrathecal shRNA-AAV9 inhibits target protein expression in the spinal cord and dorsal root ganglia of adult mice. *Hum Gene Ther Methods*. Apr;23(2):119-27, 2012.

Biomedical Devices and Instrumentation

1. Staffs and Students (April 2012)

Professor	Kohji MITSUBAYASHI	
Associate Professor	Hiroyuki KUDO	
Assistant Professor	Takahiro ARAKAWA	
Lecturer (part-time)	Kazuyoshi YANO	
Research Staff	Mika HAYASHI	
Graduate Student	Elito KAZAWA,	Tomoko GESSEI,
	Munkhjargal MUNKHBAYAR,	Kumiko MIYAJIMA,
	Ming YE,	Koji MIZUKOSHI,
	Rei SATO,	Sota YAMASHITA

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

1. Kudo H, Wang X, Suzuki Y, Ye M, Yamashita T, Gessei T, Miyajima K, Arakawa T, Mitsubayashi K, Fiber-optic biochemical gas sensor (bio-sniffer) for sub-ppb monitoring of formaldehyde vapor, *Sensors and Actuators B-Chemical*, 161(1), 486-492, 2012.
2. Arakawa T, Eri Ando, Xin Wang, Miyajima Kumiko, Hiroyuki Kudo, Hirokazu Saito, Tomoyo Mitani, Mitsuo Takahashi, Kohji Mitsubayashi, A highly sensitive and temporal visualization system for gaseous ethanol with chemiluminescence enhancer, *Luminescence*, 27, 328-333, 2012.
3. Nishi Y, Uyama M, Kawazu H, Takei H, Iwata K, Kudo H, Mitsubayashi K, Effects of Electron Beam Irradiation on Adhesive Force of Laminated Sheet of High Strength Polytetrafluoroethylene (PTFE) and Bio-Adaptable Polydimethylsiloxane (PDMS), *Materials Transactions*, 53(9), 1657-1664, 2012.

Biomedical Information

1. Staffs and Students (April, 2012)

Professor	Kenji YASUDA
Associate Professor	Tomoyuki KANEKO
Assistant Professor	Fumimasa NOMURA
Project Assistant Professor	Tomoyo HAYASHI (HAMADA) Fernando LOPEZ-REDONDO
Graduate Student	Tetsuo KITAMURA

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. Hattori A, Yasuda K: Evaluation of a Centrifuged Double Y-Shape Microfluidic Platform for Simple Continuous Cell Environment Exchange. *International Journal of Molecular Sciences* 13: 1, 2012.
2. Yasuda K: On-Chip Cellomics Assay Enabling Algebraic and Geometric Understanding of Epigenetic Information in Cellular Networks of Living Systems. 1. Temporal Aspects of Epigenetic Information in Bacteria. *Sensors* 12: 7169-7206, 2012.
3. Kaneko T, Nomura F, Hattori A, Yasuda K: Improvement of Electrical Stimulation Protocol for Simultaneous Measurement of Extracellular Potential with On-Chip Multi-Electrode Array System. *Jpn J Appl Phys* 51: 06FK02, 2012.
4. Nomura F, Kaneko T, Hamada T, Hattori A, Yasuda K: Quantitative Evaluation of Closed-Loop-Shaped Cardiomyocyte Network by Using Ring-Shaped Electrode. *Jpn J Appl Phys* 51: 06FK06, 2012.
5. Hamada T, Nomura F, Kaneko T, Yasuda K: Importance of Thickness in Human Cardiomyocyte Network for Effective Electrophysiological Stimulation Using On-Chip Extracellular Microelectrodes. *Jpn J Appl Phys* 51: 06FK03, 2012.
6. Kim H, Terazono H, Hayashi M, Takei H, Yasuda K: Highly Sensitive Detection of Target Biomolecules on Cell Surface Using Gold Nanoparticle Conjugated with Aptamer Probe. *Jpn J Appl Phys* 51: 06FH01, 2012.
7. Terazono H, Hayashi M, Kim H, Hattori A, Yasuda K: Cell-Sorting System with On-Chip Imaging for Label-Free Shape-Based Selection of Cells. *Jpn J Appl Phys* 51: 06FK08, 2012.
8. Hattori A, Yasuda K: Extended Depth of Field Optics for Precise Image Analysis in Microfluidic Flow Cytometry. *Jpn J Appl Phys* 51: 06FK05, 2012.
9. Kim H, Takei H, Negishi T, Kudo M, Terazono H, Yasuda K: Contribution of Metal Layer Thickness for Quantitative Backscattered Electron Imaging of Field Emission Scanning Electron Microscopy. *e-J Surf Sci Nanotech (e-JSSNT)* 10: 301-304, 2012.
10. Terazono H, Kim H, Hayashi M, Hattori A, Nomura F, Kaneko T, Yasuda K: A Non-Destructive Culturing and Cell Sorting Method for Cardiomyocytes and Neurons Using a Double Alginate Layer. *PLoS ONE* 7: e42485, 2012.
11. Yasuda K: On-Chip Cellomics: Constructive Understanding of Multicellular Network Using On-Chip Cellomics Technology. *Jpn J Appl Phys* 51: 08KA03, 2012.

Invited Talks

1. Kenji Yasuda. On-chip cellomics: constructive cell network assay of cardiomyocytes, and neurons for quasi in-vivo drug discovery technology. University of Helsinki Viikki, Life Science Campus Seminar, Helsinki, Finland, June 2012.

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. Kenji Yasuda, Fumimasa Nomura, Tomoyo Hamada, Tomoyuki Kaneko, Hideo Takamori, Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho. Toward Quasi-In Vivo from In Vitro Assay (I). On-Chip Cardiomyocyte Network Screening Assay for Predictive Cardiotoxicity. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
3. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Toward Quasi-in vivo from In Vitro Assay (II). Development of On-chip Predictive Cardiotoxicity Assay for Cardiac Contraction Fluctuation Measurement Using Dual Recording of Electrical Field Potential and Optical Image Analysis. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
4. Tomoyo Hamada, Fumimasa Nomura, Tomoyuki Kaneko, Hideo Takamori, Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (III). Evaluation of Temporal Field Potential Duration Fluctuation and Spatial Conduction Velocity Fluctuation of Cardiomyocyte Network for In Vitro Predictive Cardiotoxicity Measurement. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
5. Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (IV). Quasi-Electrocardiogram Measurement for Direct Prediction of TdP Occurrence Using Ring-Shaped Cardiomyocyte Network with Ring Electrode Array. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
6. Hideyuki Terazono, Hyonchol Kim, Fumimasa Nomura, Tomoyuki Kaneko, Tomoyo Hamada, Kenji Yasuda. Toward Quasi-In Vivo from In Vitro Assay (V). Non-Invasive Precise Purification of Ventricular Cells from Mixture of Differentiated Human Stem Cell Derived Cardiomyocytes Using Spot Digestion of Double Alginate Layers on a Multi-Electrode Array Chip. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
7. Yasuyuki Abe, Tomoko Sakakura, Kiyoshi Takasuna, Atsushi Sanbuissho, Fumimasa Nomura, Tomoyo Hamada, Tomoyuki Kaneko, Kenji Yasuda. Evaluation of Ion Channel Trafficking of Human Stem Cell Derived Cardiomyocytes for Cardiotoxicity Screening. Safety Pharmacology Society 12th Annual Meeting, Phoenix, USA, Oct. 2012.
8. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Development of On-Chip Dual Measurement System for Cardiac Contraction Fluctuation Assay using Simultaneous Recording of Extracellular Field Potential and Optical Image. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.
9. Fumimasa Nomura, Tomoyuki Kaneko, Akihiro Hattori, Kenji Yasuda. Quantitative Evaluation of Quasi-electrocardiogram Measurement for Direct Prediction of Lethal Arrhythmic Beating Occurrence using Ring-shaped Cardiomyocyte Network with Ring Electrode Array. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.
10. Tomoyo Hamada, Fumimasa Nomura, Tomoyuki Kaneko, Kenji Yasuda. Temporal External Field Potential Fluctuation Measurement in Constructive Cardiomyocyte Network for In Vitro Predictive Cardiotoxicity. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.
11. Hyonchol Kim, Hideyuki Terazono, Hiroyuki Takei, Kenji Yasuda. Fabrication of Superparamagnetic Nano-Particles Having Various Diameters by Strict Controlling of Magnetic Material Thickness. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.
12. Hideyuki Terazono, Masahito Hayashi, Hiroyuki Takei, Akihiro Hattori, Tomoyuki Kaneko, Kenji Yasuda. Ultra High-speed Microdroplet Polymerase Chain Reaction System for Three-step Reverse Transcription of Single Cells using On-chip Three-channel Switching High-speed Liquid Circulating Module. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.
13. Akihiro Hattori, Tomoyuki Kaneko, Fumimasa Nomura, Kenji Yasuda. Surface Roughness of Cells as Index of Label-free Cell Identification and Separation in On-chip Imaging Cell Sorting System. 25th International Microprocesses and Nanotechnology Conference (MNC2012), Kobe, Japan, Nov. 2012.

14. Tomoyuki Kaneko, Fumimasa Nomura, Tomoyo Hamada, Akihiro Hattori, Kenji Yasuda. Long-Term Simultaneous Dual Measurement of Electrophysiological Properties and Mechanical Responses of Cardiomyocytes Using On-Chip Extracellular Field Potential Recording and Real-Time Optical Image Analysis. The American Society for Cell Biology 2012 Annual Meeting, San Francisco, USA, Dec. 2012.
15. Hideyuki Terazono, Hyonchol Kim, Akihiro Hattori, Fumimasa Nomura, Tomoyuki Kaneko, Kenji Yasuda. Non-Invasive/Destructive Single Cell Purification Method for Re-Cultivation of Functionally Identified Specific Cells Using Spot Digestion of Double Alginate Sol Layers on a Multielectrode Array Chip. The American Society for Cell Biology 2012 Annual Meeting, San Francisco, USA, Dec. 2012.

Bioelectronics (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
Project Assistant Professor	Daniel SCHAFFHAUSER
Graduate Student	Eriko YAMADA

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. Tatsuro Goda and Yuji Miyahara, "A hairpin DNA aptamer coupled with groove binders as a smart switch for a field-effect transistor biosensor", *Biosens. Bioelectron.*, **2012**, 32, 244-249. DOI: 10.1016/j.bios.2011.12.022

2. Yasuhiro Maeda, Akira Matsumoto, Yoshiko Miura and Yuji Miyahara, "Preparation of alpha-Mannoside hydrogel and electrical detection of saccharide-protein interactions using the smart gel-modified gate field effect transistor", *Nanoscale Res. Lett.*, **2012**, 7, 108. DOI: 10.1186/1556-276X-7-108
3. Daniel Felix Schaffhauser, Monica Patti, Tatsuro Goda, Yuji Miyahara, Ian Cameron Forster and Petra Stephanie Dittrich, "An integrated field-effect microdevice for monitoring membrane transport in *Xenopus laevis* oocytes via lateral proton diffusion", *PLoS ONE*, **2012**, 7(7), e39238. DOI: 10.1371/journal.pone.0039238
4. Mitsuru Naito, Takehiko Ishii, Akira Matsumoto, Kanjiro Miyata, Yuji Miyahara, Kazunori Kataoka, "A phenylboronate-functionalized polyion complex micelle for ATP-triggered release of siRNA", *Angew. Chem. Int. Ed.*, **2012**, 51(43), 10751-10755. DOI: 10.1002/anie.201203360
5. Tatsuro Goda, Yasuhiro Maeda, Yuji Miyahara, "Simultaneous monitoring of protein adsorption kinetics using a quartz crystal microbalance and field-effect transistor integrated device", *Anal. Chem.*, **2012**, 84(17), 7308-7314. DOI: 10.1021/ac3015092.
6. Tatsuro Goda, Yuji Miyahara, "Interpretation of protein adsorption through its intrinsic electric charges: a comparative study using a field-effect transistor, surface plasmon resonance, and quartz crystal microbalance", *Langmuir*, **2012**, 28(41), 14730-14738. DOI: 10.1021/la302977s.
7. Tatsuro Goda, Kozue Masuno, Junko Nishida, Nobuyoshi Kosaka, Takahiro Ochiya, Akira Matsumoto, Yuji Miyahara, "A Label-free Electrical Detection of Exosomal microRNAs using Microelectrode Array", *Chem. Commun.*, **2012**, 48(98), 11942-11944. DOI: 10.1039/c2cc36111f.

Books

1. Matsumoto, A., Miyahara, Y., Kataoka, K. "4. Intelligent Surfaces for Field-Effect Transistor-Based Nanobiosensing" In: *Intelligent Surfaces in Biotechnology: Scientific and Engineering Concepts, Enabling Technologies, and Translation to Bio-Oriented Applications* (ed.: H. Michelle Grandin, Marcus Textor), John Wiley & Sons, Inc., USA, 123-140 (2012), DOI: 10.1002/9781118181249.ch4
2. Goda, T., Miyahara, Y. "Chapter 12 Sensing of Biomolecular Charges at Designer Nanointerfaces" In: *Manipulation of Nanoscale Materials: An Introduction to Nanoarchitectonics* (ed.: K. Ariga), The Royal Society of Chemistry, UK, 302-317 (2012), DOI: 10.1039/9781849735124-00302

Functional Materials (Applied Functional Molecules)

1. Staffs and Students

Professor	Akio KISHIDA	
Assistant Professor	Tsuyoshi KIMURA,	Kwangwoo NAM
Secretary	Naomi HIWATARI	
Graduate Student	Jun NEGISHI,	Kwang-il KIM,
	Naoko NAKAMURA,	PingLi WU,
	Mitsuki UEKI,	Rie MATSUSHIMA,
	Satoshi Honda,	Ayumi TANZAWA
Research Student	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) Control of cell functions by physical stimuli.

Using physical stimuli such as nano-vibration or pressure, the technology for the control of cell functions such as the proliferation and differentiation is being developed.

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) Jun Negishi, Seiichi Funamoto, Tsuyoshi Kimura, Kwangwoo Nam, Tetsuya Higami, Akio Kishida, Porcine radial artery decellularization by high hydrostatic pressure, *J. Tissue Eng. Regen. Med.* 2012; DOI: 10.1002/term. 1662
- 2) Kwangwoo Nam, Yuuki Sakai, Yoshihide Hashimoto, Tsuyoshi Kimura, Akio Kishida, Fabrication of a heterostructural fibrillated collagen matrix for the regeneration of soft tissue function, *Soft Matter* 2012; 8; 472-480.
- 3) Kaori Taniguchi, Shinya Takizawa, Tomoya Hirano, Shigeru Murata, Hiroyuki Kagechika, Akio Kishida, Ayumi Ohsaki, Amarastelline A:A Fluorescent Alkaloid from *Quassia amara* and Its Properties in Living Cells, *Chem Plus Chem* 2012; 77(6):427-431.
- 4) Ayumi Ohsaki, Masaaki Ozawa, Kanki Komiyama, Akio Kishida, Takahiko Isobe, The cytotoxic activity of diterpenoids from *Isodon* species, *Nat. Prod. Commun.* 2012; 7(8); 977-978.
- 5) Toshiyuki Aodai, Toru Masuzawa, Kazuhide Ozeki, Akio Kishida, Tetsuya Higami, Effect of metal surface characteristics on the adhesion performance of the integrated low-level energies method of adhesion, *J. Artif Organs* 2012; 15(4); 386-394.

Organic and Medicinal Chemistry

1. Staffs and Students (April 2010)

Professor	Hiroyuki KAGECHIKA	
Assistant Professor	Shinya FUJII	
Assistant Professor	Syuichi MORI	
Assistant Professor	Mari YUASA	
Graduate Student	Ayumi YAMADA,	Takashi FUJIWARA,
	Minoru IMAI,	Takuya SHIRAIISHI,
	Akitaka SHIMIZU,	Asuka TAKAGUCHI,
	Yuki TAKEUCHI,	Seika NOJO,
	Tomoaki HIGUCHI,	Noriko FUJIWARA,
	Yuko WATANABE,	Yosiaki MUSYA,
	Kanako OSHIRO,	Kasumi OHIRA,
	Toshiki SAITO,	Haruka TSUKADA,
	Kenji, HATTA,	Yohei WATANABE

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 and 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

1. Wongmayura, A.; Fujii, S.; Ito, S.; Kano, A.; Taoda, Y.; Kawachi, E.; Kagechika, H.; Tanatani, A. Novel vitamin D receptor ligands bearing a spherical hydrophobic core structure—Comparison of bicyclic hydrocarbon derivatives with boron cluster derivatives. *Bioorg. Med Chem. Lett.* 22, 1756-1760, 2012.
2. Ishizawa, M.; Kagechika, H.; Makishima, M. NR4A nuclear receptors mediate carnitine palmitoyltransferase 1A gene expression by the rexinoid HX600. *Biochem. Biophys. Res. Commun.* 418: 780–785, 2012.
3. Nakatsuka, A.; Wada, J.; Hida, K.; Hida, A.; Eguchi, J.; Teshigawara, S.; Murakami, K.; Kanzaki, M.; Inoue, K.; Terami, T.; Katayama, A.; Ogawa, D.; Kagechika, H.; Makino, H. RXR antagonism induces G0/G1 cell cycle arrest and

- ameliorates obesity by up-regulating the p53/p21/Cip1 pathway in adipocytes *J. Pathology* 226: 784-795, 2012.
4. Kanai, M.; Hirano, T.; Azumaya, I.; Okamoto, I.; Kagechika, H.; Tanatani, A. Solvent-dependent conformational and fluorescence change of an N-phenylbenzohydroxamic acid derivative bearing two pyrene moieties. *Tetrahedron*, 68: 2778-2783, 2012.
 5. Fujimoto, N.; Matsumura, M.; Azumaya, I.; Nishiyama, S.; Masu, H.; Kagechika, H.; Tanatani, A. Molecular Chirality and Chiral Capsule-type Dimer Formation of Cyclic Triamides via Hydrogen-Bonding Interactions. *Chem. Commun.* 48: 4809-4811, 2012.
 6. Kudo, M.; Katagiri, K.; Azumaya, I.; Kagechika, H.; Tanatani, A. Synthesis and helical properties of aromatic multilayered oligoureas. *Tetrahedron* 68: 4455-4463, 2012.
 7. Ayaori, M.; Yakushiji, E.; Ogura, M.; Nakaya, K.; Hisada, T.; Uto-Kondo, H.; Takiguchi, S.; Terao, Y.; Sasaki, M.; Komatsu, T.; Iizuka, M.; Yogo, M.; Uehara, Y.; Kagechika, H.; Nakanishi, T.; Ikewaki, K. Retinoic acid receptor agonists regulate expression of ATP-binding cassette transporter G1 in macrophages. *Biochim. Biophys. Acta- Mol Cell Biol. Lipids* 1821: 561-572, 2012.
 8. Fujii, S.; Ohta, K.; Goto, T.; Oda, A.; Masuno, H.; Endo, Y.; Kagechika, H. Development of androgen receptor ligands by application of ten-vertex para-carborane as a novel hydrophobic core structure. *Med. Chem. Commun.*, 3: 680-684, 2012.
 9. Okamoto, I.; Takahashi, Y.; Sawamura, M.; Matsumura, M.; Masu, H.; Katagiri, K.; Azumaya, I.; Nishino, M.; Kohama, Y.; Morita, N.; Tamura, O.; Kagechika, H.; Tanatani, A. Redox-responsive conformational alteration of aromatic amides bearing N-quinonyl system. *Tetrahedron* 68: 5346-5355, 2012.
 10. Taniguchi, K.; Takizawa, S.; Hirano, T.; Murata, S.; Kagechika, H.; Kishida, A.; Ohsaki, A. Amarastelline A: A Fluorescent Alkaloid from *Quassia amara* and Its Properties in Living Cells. *ChemPlusChem*, 77: 427-431, 2012.
 11. Hirano, T.; Kubo, H.; Shiraishi, T.; Hiromoto, K.; Fujiwara, T.; Kagechika, H. Fluorescent properties of coumarins with dual functions constructed by two sequential reactions. *Tetrahedron Lett.* 53: 5916-5919, 2012.
 12. Hurst, R. J. M.; Bell, L. V.; de Caul, A.; Kagechika, H.; Else, K. J. The retinoic acid receptor agonist Am80 increases mucosal inflammation during an intestinal helminth infection of mice. *Immunology*, 137: 125-126, 2012.

Chemical Bioscience

1. Staffs and Students

Professor	Takamitsu HOSOYA	
Assistant Professor	Suguru YOSHIDA	
Assistant Professor	Yuto SUMIDA	
Technical Assistant	Tomoe KATO, Yoshihiro MISAWA	Takako NONAKA
Clerical Assistant	Naomi SAITA	
Graduate Students	Ryu HARADA,	Takamoto MORITA
Collaborator	Kimiyuki KANNO, Junko TANAKA	Keisuke UCHIDA,

2. Purpose of Education

Developing new synthetic methods, new chemical methodologies, and new chemical tools, those are useful for biological researches and drug discovery.

3. Research Subjects

- 1) Development of new azide chemistry for chemical biology researches.
- 2) Development of new methodology, photoreactive functional groups, and molecular probes for radioisotope-free (non-RI) photoaffinity labeling to identify target proteins of bioactive small compounds.
- 3) Design and synthesis of efficient substrates for bioluminescence reactions and fluorescent probes for bioimaging and diagnosis of diseases.
- 4) Drug seeds development based on new synthetic methodologies.
- 5) Design and synthesis of new PET (positron emission tomography) probe candidates for in vivo imaging to promote drug discovery.

4. Publications

Original Articles

1. Sumida Y, Kato T, Yoshida S, Hosoya T. Palladium-Catalyzed Regio- and Stereoselective Hydrosilylation of Electron-Deficient Alkynes. *Org Lett*, 14(6): 1552-1555, 2012.
2. Yoshimura SH, Khan S, Ohno S, Yokogawa T, Nishikawa K, Hosoya T, Maruyama H, Nakayama Y, Takeyasu K. *Bioconjugate Chem*, 23(7): 1488-1493, 2012.
3. Yoshida S, Igawa K, Tomooka K. Nucleophilic substitution reaction at the nitrogen of arylsulfonamides with phosphide anion. *J Am Chem Soc*, 134(47): 19358-19361, 2012.

Metallic Biomaterials

1. Staffs and Students

Associate Professor	Naoyuki NOMURA	
Professor	Takao HANAWA	
Assistant Professor	Hisashi DOI,	Yusuke TSUTSUMII
Research Assistant	Osamu FUKUSHIMA	
Project Assistant Professor	SUYALATU,	Satoshi MIGITA
Secretary	Toshie NAKANISHI,	Yasuko SEKI
Graduate Student	Ryota KONDO,	Takahiro SAKAI

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

- Jamleh A, Sadr A, Nomura N, Yahata Y, Ebihara A, Hanawa T, Tagami J, Suda H. Nano-indentation testing of new and fractured NiTi Endodontic Instruments. *International Endodontic Journal* 45:462-468, 2012.
- Tsutsumi Y, Niinomi M, Nakai M, Tsutsumi H, Doi H, Nomura N, Hanawa T. Micro-arc oxidation treatment to improve the hard-tissue compatibility of Ti-29Nb-13Ta-4.6Zr alloy. *Applied Surface Science* 262:34-38, 2012.
- Ma C, Nagai A, Yamazaki Y, Toyama T, Tsutsumi Y, Hanawa T, Wang W, Yamashita K. Electrically polarized micro-arc oxidized TiO₂ coatings with enhanced surface hydrophilicity. *Acta Biomaterialia* 8:860-865, 2012.
- Hieda J, Niinomi M, Nakai M, Kamura H, Tsutsumi H, Hanawa T. Effect of terminal functional groups of silane layers on adhesive strength between biomedical Ti-29Nb-13Ta-4.6Zr alloy and segment polyurethanes. *Surface and Coatings Technology* 206(13):3137-3141, 2012.
- Yoda K, Suyalatu, Takaichi A, Nomura N, Tsutsumi Y, Doi H, Kurosu S, Chiba A, Igarashi Y, Hanawa T. Effects of chromium and nitrogen content on the microstructures and mechanical properties of as-cast Co-Cr-Mo alloys for dental applications. *Acta Biomaterialia* 8(7):2856-2862, 2012.
- Nagai A, Tsutsumi Y, Suzuki Y, Katayama K, Hanawa T, Yamashita K. Characterization of air-formed surface oxide film on a Co-Ni-Cr-Mo alloy (MP35N) and its change in Hanks f solution. *Applied Surface Science* 258(14):5490-5498, 2012.

7. Tsutsumi Y, Bartakova S, Prachar P, Suyalatu, Migita S, Doi H, Nomura N, Hanawa T. Long-term corrosion behavior of biocompatible β -type Ti alloy in simulated body fluid. *Journal of the Electrochemical Society* 159(10):C435-C440, 2012.
8. Hastuty S, Tsutsumi Y, Nishikata A, Tsuru T. Pitting corrosion of type 430 stainless steel in the process of drying of chloride solution layer. *ISIJ International* 52(5):863-867, 2012.
9. Murata M, Akazawa T, Yuasa T, Okayama M, Tazaki J, Hanawa T, Arisue M, Mizoguchi I. Quantitative analysis on orientation of human bone integrated with midpalatal implant by micro X-ray diffractometer. *Applied Surface Science* 262: 222-226, 2012.
10. (Supplement) Nam K, Tsutsumi Y, Yoshikawa C, Tanaka Y, Fukaya R, Kimura T, Hanawa T, Kishida A. Preparation of novel polymer-metal oxide nanocomposites with nanophase separated hierarchical structure. *Bulletin of Material Science* 34(7):1289-1296, 2011.

Organic Biomaterials

1. Staffs and Students (April, 2012)

Professor	Nobuhiko YUI	
Associate Professor	Yoshihiro SASAKI	
Assistant Professor	Ji-Hun SEO	
Research Assistant Professor	Atsushi TAMURA	
Secretary	Nanae NISHI	
Graduate Student	Junichi YASUOKA,	Yuji TSUCHIDO,
	Nanako Yokoyama,	Hajime TANAKA

2. Purpose of Education

Courses: Biomaterials, Advanced Medical Materials, Advanced Organic Materials

3. Research Subjects

- 1) Design of Dynamic Biomaterials Surfaces
- 2) Modulation of Cellular Functions by Dynamic Ligand-Polymers
- 3) Design of Intracellularly Functionalizing Biomaterials
- 4) Design of Liposomal Device and Hybrid Nanomaterials

4. Clinical Services

5. Publications

Original Articles

1. Inoue Y, Lin Ye, Ishihara K, Yui N. Preparation and surface properties of polyrotaxane-containing tri-block copolymers as a design for dynamic biomaterials surfaces. *Colloids Surf. B* 89(1): 223-227, 2012.
2. Yamada Y, Nomura T, Harashima H, Yamashita A, Yui N. Post-nuclear gene delivery events for transgene expression by biocleavable polyrotaxanes. *Biomaterials* 33(15): 3952-3958, 2012.
3. Yamada Y, Hashida M, Nomura T, Harashima H, Yamasaki Y, Kataoka K, Yamashita A, Katoono R, Yui N. Different mechanisms for nanoparticle formation between pDNA and siRNA using polyrotaxane as the polycation. *ChemPhysChem* 13(5): 1161-1165, 2012.
4. Yamada K, Katoono R, Yui N. Controlled loop and graft formations of water-soluble polymers on SAM for the design of biomaterials surfaces. *Polym J* 44: 286-293, 2012.
5. Seo J-H, Kakinoki S, Inoue Y, Yamaoka T, Ishihara K, Yui N. Designing dynamic surfaces for regulation of biological responses. *Soft Matter* 8: 5477-5485, 2012.
6. Jang S, Lee S, Kim H, Ham J, Seo J-H, Mok Y, Noh M, Lee Y. Preparation of pH-sensitive CaP nanoparticles coated with a phosphate-based block copolymer for efficient gene delivery. *Polymer* 53: 4678-4685, 2012.
7. Jin GW, Kim H, Seo J-H, Ham J, Park JS, Lee Y. Formation of polyion complex micelles with tunable isoelectric points based on zwitterionic block copolymers. *Macromol. Res.*, 20(12): 1249-1256, 2012.
8. Noh M, Mok Y, Lee S, Kim H, Lee SH, Jin GW, Seo J-H, Koo H, Park TH, Lee Y. Novel lower critical solution temperature phase transition materials effectively control osmosis by mild temperature change. *Chem. Comm.* 48: 3845-3847, 2012.
9. Tamura A, Kobayashi J, Yamato M, Okano T. Thermally responsive microcarriers with optimal poly(N-isopropylacrylamide) grafted density for facilitating cell adhesion/detachment in suspension culture. *Acta Biomater* 8: 3904-3913, 2012.
10. Tamura A, Nishi M, Kobayashi J, Nagase K, Yajima H, Yamato M, Okano T. Simultaneous enhancement of cell proliferation and thermally-induced harvest efficiency based on temperature-responsive cationic copolymer-grafted. *Biomacromolecules* 13: 1765-1773, 2012.
11. Tamura A, Kobayashi J, Yamato M, Okano T. Temperature-responsive poly(N-isopropylacrylamide)-grafted microcarriers for large-scale noninvasive harvest of anchorage-dependent cells. *Biomaterials* 33: 3803-3812, 2012.
12. Tamura G, Shinohara Y, Tamura A, Sanada Y, Oishi M, Akiba I, Nagasaki Y, Sakurai K, Amemiya Y. Dependence of Swelling Behavior of pH-responsive PEGylated Nanogel on Cross-link Density. *Polymer Journal*, 44(3):240-244, 2012.

13. Sekine Y, Moritani Y, Ikeda-Fukazawa T, Sasaki Y, Akiyoshi K. A Hybrid Hydrogel Biomaterial by Nanogel Engineering: Bottom-Up Design with Nanogel and Liposome Building Blocks to Develop a Multidrug Delivery System. *Adv Healthcare Mater* 1:722-728, 2012.
14. Sekine Y, Abe K, Shimizu A, Sasaki Y, Sawada S, Akiyoshi K. Shear Flow-Induced Nanotubulation of Surface-Immobilized Liposomes. *Rsc Advances* 2:2682-2684, 2012.
15. Sasaki Y, Yamane Y, Kurosu K, Sawada S, Akiyoshi K. Templated Formation of Hydroxyapatite Nanoparticles from Self-Assembled Nanogels Containing Tricarboxylate Groups. *Polymers* 4:1056-1064, 2012.
16. Mukai M, Sasaki Y, Kikuchi J. Fusion-Triggered Switching of Enzymatic Activity on an Artificial Cell Membrane. *Sensors* 12:5966-5977, 2012.
17. Mukai M, Maruo K, Sasaki Y, Kikuchi J. Intermolecular Communication on a Liposomal Membrane: Enzymatic Amplification of a Photonic Signal with a Gemini Peptide Lipid as a Membrane-Bound Artificial Receptor. *Chem-Eur J* 18:3258-3263, 2012.

Molecular Cell Biology

1. Staffs and Students

Professor	Hiroshi Shibuya	
Associate Professor	Toshiyasu Goto	
Assistant Professor	Atsushi Sato	
Graduate Students	Masahiro Shimizu,	Yu-ichi Okuma

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) WNK protein kinases, the causative genes of pseudohypoaldosteronism type II (PHAII) disease
- 2) Roles of IQGAP1 on 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** in press.
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.** in press.

Developmental and Regenerative Biology

1. Staffs and Students (April, 2012)

Professor	Hiroshi NISHINA	
Associate Professor	Jun HIRAYAMA	
Assistant Professor	Yoichi ASAOKA	
Project Assistant Professor	Tokiwa YAMASAKI,	Shoji HATA,
	Mamiko IWATSUKI	
Graduate Students	Makoto YAMAMOTO,	Eiichiro NODA,

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. Shoji Hata, Jun Hirayama, Hiroaki Kajiho, Kentaro Nakagawa, Yutaka Hata, Toshiaki Katada, Makoto Furutani-Seiki and Hiroshi Nishina (2012) A novel acetylation cycle of the transcription co-activator Yes-associated protein that is downstream of the Hippo pathway is triggered in response to SN2 alkylating agents. *J. Biol. Chem.* 287, 22089-22098.
2. Yoshimi Uchida, Tomomi Osaki, Tokiwa Yamasaki, Tadanori Shimomura, Shoji Hata, Kazumasa Horikawa, Shigenobu Shibata, Takeshi Todo, Jun Hirayama and Hiroshi Nishina (2012) Involvement of the Stress Kinase Mitogen-activated Protein Kinase Kinase 7 in the Regulation of the Mammalian Circadian Clock. *J. Biol. Chem.* 287, 8318-8326.
3. Yoshimi Uchida, Tadanori Shimomura, Jun Hirayama and Hiroshi Nishina (2012) Light, reactive oxygen species, and magnetic fields activate ERK/MAPK signaling pathway in cultured zebrafish cells. *Appl. Magn. Reson.* 42, 69-77.
4. Miki Nishio, Koichi Hamada, Kohichi Kawahara, Masato Sasaki, Fumihito Noguchi, Shuhei Chiba, Kensaku Mizuno, Satoshi O. Suzuki, Youyi Dong, Masaaki Tokuda, Takumi Morikawa, Hiroki Hikasa, Jonathan Eggenschwiler, Norikazu Yabuta, Hiroshi Nojima, Kentaro Nakagawa, Yutaka Hata, Hiroshi Nishina, Koshi Mimori, Masaki Mori, Takehiko Sasaki, Tak W. Mak, Toru Nakano, Satoshi Itami, and Akira Suzuki (2012) Cancer Susceptibility and embryonic lethality in Mob1A/1B double mutant mice. *J. Clin. Invest.* 122(12),4505-4518.
5. Tadashi Yokoi, Yuko Seko, Tae Yokoi, Hatsune Makino, Shin Hatou, Masakazu Yamada, Tohru Kiyono, Akihiro Umezawa, Hiroshi Nishina, Noriyuki Azuma (2012) Establishment of Functioning Human Corneal Endothelial Cell Line with High Growth Potential. *PLoS ONE* 7(1):e29677
6. Ken Okada, Akihide Kamiya, Keiichi Ito, Ayaka Yanagida, Hidenori Ito, Hiroki Kondou, Hiroshi Nishina and Hiromitsu Nakauchi (2012) Prospective isolation and characterization of bipotent progenitor cells in early mouse liver development. *Stem Cells and Development* 21, 1124-1133.
7. Takuya Iwamoto, Shuji Terai, Yuko Mizunaga, Naoki Yamamoto, Kaoru Omori, Koichi Uchida, Takahiro Yamasaki, Yasuhiko Fujii, Hiroshi Nishina, and Isao Sakaida (2012) Splenectomy enhances the anti-fibrotic effect of bone marrow cell infusion and improves liver function in cirrhotic mice and patients *J. Gastroenterol.* 47, 300-312.
8. Toshiyuki Oishi, Shuji Terai, Shinya Kuwashiro, Koichi Fujisawa, Toshihiko Matsumoto, Hiroshi Nishina and Isao

Sakaida (2012) Ezetimibe reduces fatty acid quantity in liver and decreased inflammatory cell infiltration and improved NASH in medaka model. *Biochem. Biophys. Res. Commun.* 422, 22-27.

9. Shoji Hata and Hiroshi Nishina (2012) [Letters to the Editor] Reply to Sun et al.: Targeting YAP acetylation in cancer. *J. Biol. Chem.* 287, 35443.
10. Tokiwa Yamasaki, Hiroshi Kawasaki and Hiroshi Nishina (2012) [review] Diverse roles of JNK and MKK pathways in the brain. *J. Signal Trans.* 2012: 459265.
11. Hiroshi Nishina (2012) [commentary] hDlk-1: A cell surface marker common to normal hepatic stem/progenitor cells and carcinomas. *J. Biochem.* 152, 121-123.

Immunology

1. Staffs and Students

Professor	Takeshi TSUBATA, M.D., Ph.D.	
Associate Professor	Takahiro ADACHI, Ph.D.	
Assistant Professor	Kozo WATANABE, Ph.D.	
Assistant Professor	Yusuke KISHI, Naoko MATSUBARA	
Technician	Yukie KURUSU	
Secretary	Hiroko TAKAHASHI	
Graduate Student	XU Miduo,	TANG Miao,
	Toshitaro TAKATA,	Satoya OMORI,
	Shirly PHOON,	Ayşe Ucar KONUSKAN,
	Sumiyo EZAKI,	JIAO Xuyang

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 good research 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 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. Klionsky, D.J., Abdalla, F. C. Tsubata, T. et al. (2012): Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy* 8: 1-100.
2. Kishi, Y., Higuchi, T., Phoon, S., Kamiya, K., Riemekasten, G., Akiyoshi, K., Weigert, M. and Tsubata, T. (2012): Apoptotic marginal zone deletion of anti-Sm/ribonucleoprotein B cells. *Proc. Natl. Acad. Sci. USA* 109: 7811-7816.
3. Tsubata, T. (2012): Role of inhibitory BCR co-receptors in immunity. *Infect Disord Drug Targets* 12:181-190.
4. Maeno, E., Tsubata, T. and Okada, Y (2012): Apoptotic volume decrease (AVD) is independent of mitochondrial dysfunction and initiator caspase activation. *Cells* 1: 1156-1167.
5. Hitomi, Y., Adachi, T., Tsuchiya, N., Honda, Z.-I., Tokunaga, K and Tsubata, T. (2012): Human CD72 splicing isoform responsible for resistance to systemic lupus erythematosus regulates serum immunoglobulin level and is localized in endoplasmic reticulum. *BMC Immunol.* 13: 72.
6. Shimoda, M., Bolduc, A., Takezaki, M., Amtani, Y., Huang, L., Nutt S. L., Kamanaka, M., Flavell, R. A., Mellor A. L, Tsubata, T., Koni, P. (2013): Constitutively CD40-activated B cells regulate CD8 T cell inflammatory response by IL-10 induction. *J. Immunol.* (in press).

7. Adachi T, Harumiya S, Takematsu H, Kozutsumi Y, Wabl M, Fujimoto M, Tedder TF. (2012): CD22 serves as a receptor for soluble IgM. *Eur J Immunol.* 2012 42:241-7.

Epigenetics

1. Staffs and Students

Professor	Fumitoshi ISHINO	
Associate Professor	Takashi KOHDA	
GCOE Lecturer	Jiyoung LEE	
Adjunct Lecturer	Shin KOBAYASHI,	
Assistant Professor	Ryuichi ONO,	
Tokunin Assistant Professor	Mie NARUSE	
Secretary	Ikuko MAEDA	
Technical assistant	Masayuki ISHII	
Graduate students	Yuki YAMAGUCHI,	Mami OIKAWA,
	Saori TAKAHASHI,	Miki SOMA,
	Kiyotaka TAKAGI,	Moe KITAZAWA,
	Narutoshi KAWASHIRI	

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. Kohda, T., Kishigami, S., Kaneko-Ishino, T., Wakayama T. and Ishino F. Gene expression profile normalization in cloned mice by trichostatin A treatment. *Cellular Reprogramming* 14(1), 45-55 (2012).
2. Kaneko-Ishino, T. and Ishino, F. The role of genes domesticated from LTR retrotransposons and retroviruses in mammals. *Frontiers Microbiol* 3, Article 262 (1-10) (2012).
3. Kaneko-Ishino, T. and Ishino, F. Evolution of viviparity and genomic imprinting in mammals by retrotransposons. *In Evolutionary Biology: Mechanisms and Trends* (ed. Pontarotti, P.), Springer-Verlag Berlin Heidelberg, pp.265-282 (2012).
4. Ishino, F., Shinkai, Y. and Whitelaw, E. Mammalian epigenetics in biology and medicine. *In Mammalian Epigenetics in Biology and Medicine* (eds. Ishino, F., Shinkai, Y. and Whitelaw, E.), Royal Society Publishing, *Philos Trans R Soc Lond B Biol Sci*, 368(1609): 20120386 (2012).
5. Kohda, T. and Ishino, F. Embryo manipulation via assisted reproductive technology and epigenetic asymmetry in mammalian early development. *In Mammalian Epigenetics in Biology and Medicine* (eds. Ishino, F., Shinkai, Y. and Whitelaw, E.), Royal Society Publishing, *Philos Trans R Soc Lond B Biol Sci*, 368(1609): 20120353 (2012).

Department of Systems Biology, School of Biomedical Sciences Department of Bioinformatics, Medical Research Institute

1. Staffs and Students

Professor:	Hiroshi Tanaka	
Associate Professor:	Yoshihito Niimura	
Assistant Professor:	Soichi Ogishima (~April),	Kaoru Mogushi (June~)
Project Associate Professor:	Fengrong Ren, Jun Nakaya (~March)	Takako Takai (~April),
Project Lecturer:	Kanae Oda (~March)	
Project Assistant Professor:	Takeshi Hase, Naoki Hasegawa (~March),	Kaoru Mogushi (~May), Kumiko Iijima
Technical Staff:	Ken Miyaguchi (~March)	
Graduate Students:	Hironobu Yamaguchi, Ryosuke Ishiwata, Satoru Suzuki, Tadashi Urashima, Masataka Kikuchi, Hajime Sawai, Taro Kishimoto, Syed Ali Zaidi, Hiroaki Hasegawa, Noriaki Koizumi, Norihiro Inoue, Ko Watanabe, Asiya Hapaer, Tadashi Miyamoto, Jun-ya Hagiwara, Kasumi Otsubo	Yoshiyuki Kaneko, Arihito Endo, Eiichi Ueno, Sakiko Ohta, Yasuha Tanaka, Asami Suzuki, Chikako Shimizu, Shoko Nukaya, Aw Wanping, Akihiko Hoshi, Tomohisa Maruyama, Sophia Subat, Kota Koide, Teruaki Tsuji, Toshihiro Takahashi,

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 supervises 31 students in total (18 PhD and one Master course students in Graduate School of Medical and Dental Sciences and six PhD and six Master course students in Biomedical Science PhD Program).

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) 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 analysis or machine learning methods is one of the most crucial tasks for bioinformatics research. We have been performing collaborative research with our university hospital and other institutes mainly based on transcriptome analysis using DNA microarray, including the

following topics: 1) identification of diagnosis marker for prognosis prediction in hepatocellular carcinoma patients, 2) development of predictive marker for metastatic relapse in colorectal cancer, and 3) analysis of spinocerebellar ataxia and hepatocellular carcinoma using next generation sequencing technologies.

2) *Systems pathology analyses on disease progression of cancer, metastasis, and Alzheimer's disease*

Our mission is systems pathology studies on cancer, metastasis (epithelial-mesenchymal transition: EMT), and neurodegenerative disease (Alzheimer's disease) using large-scale molecular biology data, so-called omics data. We inferred transcriptional, gene regulatory and protein interaction networks of disease progression, and then explored master regulator, that is key molecule in their networks. We then estimated an attractor for each cellular state based on gene regulatory network for disease progression, cellular transformation (EMT), and cellular differentiation (iPSC/ESC) processes, showing transition of attractors along with these processes. For omics data analyses, data integration is necessary. We worked on integration of incurable diseases data using Linked Data technology.

3) *i2b2: A novel technology of clinical databases as an infrastructure of translational informatics*

Translational informatics is an emerging research field of computational technology for facilitating translation of genome information into the clinical application. It targets collection and computation of clinical and genomic information on the basis of mathematical models for diseases. It is a part of promoted researches after the completion of human genome sequencing, which includes industry and academia partnership in drug development and patient-centered translational research. Among the ongoing projects, the i2b2 provides an ontology-based object-oriented database system for integration of clinical information dispersed in different laboratories and different hospitals. Due to its highly flexible data-schema, the i2b2 enables persons without expert knowledge of database to collect clinical information into a database. We constructed i2b2 database with 392 clinical patients' data collected in the university hospital of Tokyo Medical and Dental University. The patients' data includes biomedical and clinicopathological information extracted from carcinoma and non-carcinoma specimens of cancer patients recorded in 'Integrated Clinical Omics Database' (iCOD). We transferred 8,580 English and 54,579 Japanese descriptions into i2b2. We employed Japanese NLP technologies in order to extract clinical terms from doctors' comments in Japanese free texts. We built a pipeline for extraction of clinical terms and translation of the extracted terms into English computationally.

4) *Analyses of the human protein-protein interaction networks and their applications to drug discovery*

Since proteins exert their functions through interaction to other proteins, networks of protein-protein interactions are inevitable to discover novel drug-target genes. To discover novel targets, it is of use to understand topological and statistical characteristics of protein-protein interaction networks (PINs), and how the target-genes are distributed over the PINs. To uncover the topological features of PINs, we developed a novel method to decompose a very large complex network into simple sub-networks. Our method decomposed the genome-wide human PIN into several small simple sub-networks and mapped target-genes on to the sub-networks. Among the sub-networks, a sub-network contains almost 60% of target-genes of small molecule drugs (e.g., kinase inhibitors) for cancerous diseases. Further, pathway enrichment analyses revealed that genes in the sub-network are involved in cancer-related signaling pathways (e.g., vascular endothelial growth factor signaling pathway). These results indicate that the listing of genes and interactions in the sub-network may help drug companies to search more efficiently for mechanisms of drug action and novel target genes for cancerous diseases.

5) *Diversity of olfactory receptor gene repertoires among mammals*

Olfaction, the sense of smell, is essential for the survival of animals. Odor molecules in the environment are detected by olfactory receptors (ORs) encoded by a large multigene family. To investigate the diversity of OR gene repertoires among mammals, I extensively identified the OR genes from the draft genome sequences of 38 diverse mammals. The results demonstrated that the estimated numbers of functional OR genes are extremely variable, ranging from only ~10 in dolphins to ~2,000 in elephants. However, the number of functional OR genes is not correlated with the fractions of pseudogenes. Identification of orthologous gene sets among 13 eutherian mammals with the genome of deep coverage (>6x) revealed that hundreds of gene gains and losses have occurred during eutherian evolution, suggesting dynamic changes of OR gene repertoires depending on each species' living environment. I also examined OR genes from two turtle species with the whole genome sequences, showing drastic class I OR gene expansion, which is characteristic to turtles among amniotes.

6) *Omics Research about mechanism of liver cancer progression*

The complete sequencing of the human genome has ushered in a new era of systems biology referred to as Omics. The "Omics" refers to the comprehensive analysis of biological systems. Likewise, the field of bioinformatics has grown in parallel and with the help of rapid data analysis and information exchange is now possible. We have been collecting clinical and Omics (Genomics, Transcriptomics, Proteomics, Epigenomics, etc.) data. This includes both comprehensive molecular

Omics information and comprehensive clinical information from almost 400 patients who has liver cancer at TMD-Hospital. In case of liver cancer, it is very difficult to find the related gene for subtypes of liver cancer, but could find possible relation using data cleaning and integrated analysis, along with molecular biological analysis. Omics will not only have an impact on our understanding of biological processes, but the prospect of more accurately diagnosing and treating disease will soon become a reality.

7) Inferring evolutionary dynamics of SIV/HIV-1 Vpu and its co-evolution with Nef and Tetherin

Many studies on the function changes of SIV/HIV-1 Vpu after cross-species transmission have been reported in recent years, but little is known about the evolutionary history of this accessory gene. To elucidate possible evolutionary mechanisms responsible for the functional change, we conducted a computational analysis to investigate the evolutionary dynamics of Vpu and also its co-evolution with SIV/HIV Nef and primate Tetherin. Eighty-seven Vpu genes, 108 Nef genes and 35 primate Tetherin genes were retrieved from public databases. The reconstructed phylogenetic tree of Vpu was consistent with those reported in previous studies. The positive selection detection revealed that both Vpu and Tetherin had experienced adaptive evolution. Importantly, the tRMCA of SIVcpz Nef was estimated to be more ancient than that of SIVcpz Vpu, suggesting that the recombination event might be an evolutionary force driving the function loss of Vpu in SIVcpz. Notably, two SIVcpz sub-clades, SIVcpzPtt and SIVcpzPts, showed very different features at both molecular and structural levels. These results provided important information on the Vpu evolution and its co-evolution with Nef and Tetherin, which would give a new insight into the studies of SIV/HIV Vpu in future.

4. Publications

Original Article

1. Boeck M, Ogishima S, Tanaka H, Kramer S, Kaderali L: Hub-centered gene network reconstruction using automatic relevance determination. *PLoS ONE*, 7(5):e35077, 2012
2. 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. *ONCOLOGY LETTERS*, 4:817-23, 2012
3. Khamas A, Ishikawa T, Mogushi K, Iida S, Ishiguro M, Tanaka H, Uetake H, Sugihara K: Genome-wide screening for methylation-silenced genes in colorectal cancer. *International Journal of Oncology*, 41:490-6, 2012
4. Khamas A, Ishikawa T, Shimokawa K, Mogushi K, Iida S, Ishiguro M, Mizushima H, Tanaka H, Uetake H, Sugihara K: Screening for epigenetically masked genes in colorectal cancer using 5-Aza-2'-deoxycytidine, microarray and gene expression profile. *Cancer Genomics & Proteomics*, 9:67-75, 2012
5. Kikuchi A, Ishikawa T, Mogushi K, Ishiguro M, Iida S, Mizushima H, Uetake H, Tanaka H, Sugihara K: Identification of NUCKS1 as a colorectal cancer prognostic marker through integrated expression and copy number analysis. *International Journal of Cancer*, Doi:10.1002/ijc.27911, 2012
6. 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*, DOI 10.1245/s10434-012-2395-2, 2012
7. Miyaguchi K, Uzawa N, Mogushi K, Takahashi K.I, Michikawa C, Nakata Y, Sumino J, Okada N, Mizushima H, Fukuoka Y, Tanaka H: Loss of NKX3-1 as potential marker for an increased risk of occult lymph node metastasis and poor prognosis in oral squamous cell carcinoma. *International Journal of Oncology*, 40:1907-14, 2012
8. Mizuno S, Iijima R, Ogishima S, Kikuchi M, Matsuoka Y, Ghosh S, Miyamoto T, Miyashita A, Kuwano R, Tanaka H: AlzPathway: a comprehensive map of signaling pathways of Alzheimer's disease. *BMC Syst Biol*, 6:52, 2012
9. Nomura F, Sogawa K, Noda K, Seimiya M, Matsushita K, Miura T, Tomonaga T, Yoshitomi H, Imazeki F, Takizawa H, Mogushi K, Miyazaki M, Yokosuka O: Serum anti-Ku86 is a potential biomarker for early detection of hepatitis C virus-related hepatocellular carcinoma. *Biochem Biophys Res Commun*, 421:837-43, 2012
10. Nukaya S, Shino T, Kurihara Y, Watanabe K, Tanaka H: Noninvasive Bed Sensing of Human Biosignals via Piezoceramic Devices Sandwiched Between the Floor and Bed. *IEEE SENSORS JOURNAL*, 12:431-438, 2012
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*, Doi: 10.1007/s12072-012-9357-4, 2012
12. Okazaki S, Ishikawa T, Iida S, Ishiguro M, Kobayashi H, Higuchi T, Enomoto M, Mogushi K, Mizushima H, Tanaka H, Uetake H, Sugihara K: Clinical significance of UNC5B expression in colorectal cancer. *International Journal of Oncology*, 40:209-16, 2012

13. Shimada S, Mimata A, Sekine M, Mogushi K, Akiyama Y, Fukamachi H, Jonkers J, Tanaka H, Eishi Y, Yuasa Y: Synergistic tumour suppressor activity of E-cadherin and p53 in a conditional mouse model for metastatic diffuse-type gastric cancer, *Gut*, 61:344-53, 2012
14. Sekiya I, Ojima M, Suzuki S, Yamaga M, Horie M, Koga H, Tsuji K, Miyaguchi K, Ogishima S, Tanaka H, Muneta T: Human mesenchymal stem cells in synovial fluid increase in the knee with degenerated cartilage and osteoarthritis, *Journal of Orthopaedic Research*, 30:943-9, 2012
15. Suzuki S, Takai-Igarashi T, Fukuoka Y, Wall D.P, Tanaka H, Tonellato P.J: Systems analysis of inflammatory bowel disease based on comprehensive gene information. *BMC Medical Genetics*, Apr 5; 13:25, 2012
16. Xieraili M, Yasen M, Mogushi K, Obulhasim G, Mayinuer A, Aihara A, Tanaka S, Mizushima H, Tanaka H, Arii S: Villin 1 is a predictive factor for the recurrence of high serum alpha-fetoprotein-associated hepatocellular carcinoma after hepatectomy, *Cancer Science*, 103:1493-501, 2012
17. Yae T, Tsuchihashi K, Ishimoto T, Motohara T, Yoshikawa M, Yoshida GJ, Wada T, Masuko T, Mogushi K, Tanaka H, Osawa T, Kanki Y, Minami T, Aburatani H, Ohmura M, Kubo A, Suematsu M, Takahashi K, Saya H, Nagano O: Alternative splicing of CD44 mRNA by ESRP1 enhances lung colonization of metastatic cancer cell, *Nature Communications*, 6:883, 2012
18. Yasen M, Obulhasim G., Kajino K, Mogushi K, Mizushima H, Tanaka S, Tanaka H, Hino O, Arii S: DNA binding protein A expression and methylation status in hepatocellular carcinoma and the adjacent tissue, *International Journal of Oncology*, 40:789-97, 2012

Reviews

1. Niimura Y: Olfactory receptor multigene family in vertebrates: from the viewpoint of evolutionary genomics. *Current Genomics* 13, 103-111, 2012

Book chapters

1. Niimura Y: Evolution of chemosensory receptor genes in primates and other mammals. *Post-Genome Biology of Primates, Primatology Monographs* (eds. Hirai H, Imai H, Go Y), Springer, 2012
2. Hase T, Niimura Y: Protein-protein interaction networks: Structures, evolution, and application to drug design. *Protein Interaction / Book 2* (ed. Weibo Cai), InTech, 2012

Structural Biology

1. Staffs and Students

Professor	Nobutoshi ITO	
Associate Professor	Teikichi IKURA	
Assistant Professor	Nobutaka NUMOTO	
Project Assistant Professor	Minako ABE	
Technical Assistant	Michiko HATTORI	
Graduate Students	Kenrou Shinagawa,	Michika MIYASHITA

2. Purpose of Education

The students learn theoretical basis of structure determination, mainly X-ray crystallography, of proteins and other biomacromolecules. 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 structure.

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. Tamashiro T, Tanabe Y, Ikura T, Ito N, Oda M: Critical roles of Asp270 and Trp273 in the α -repeat of the carbohydrate-binding module of endo-1,3- β -glucanase for laminarin-binding avidity. *Glycoconj J* 29: 77-85, 2012.
2. Iwaya N, Akiyama K, Goda N, Tenno T, Fujiwara Y, Hamada D, Ikura T, Shirakawa M, Hiroaki H: Effect of Ca(2+) on the microtubule-severing enzyme p60-katanin: Insight into the substrate-dependent activation mechanism. *FEBS J* 279: 1339-1352, 2012.

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.
2. Egashira T, Yuasa S, Suzuki T, Aizawa Y, Yamakawa H, Matsuhashi Tomohiro, Ohno Y, Tohyama S, Okata S, Seki T, Kuroda Y, Yae K, Hashimoto H, Tanaka T, Hattori F, Sato T, Miyoshi S, Takatsuki S, Murata M, Kurokawa J, Furukawa T, Makita N, Aiba T, Shimizu W, Horie M, Kamiya K, Kodama I, Ogawa S, Fukuda K. Disease characterization using LQTS-specific induced pluripotent stem cells. *Cardiovascular Research*, 2012;95:419-29.

Review articles

1. Kurokawa J, Furukawa T. (2013) Non-genomic action of sex steroid hormones and cardiac repolarization. *Biol. Pharmacol. Bull*, 36, 8-12.
2. Kurokawa J, Furukawa T. (2012) Region- and condition-dependence of the membrane and Ca²⁺ clocks in the sinus node. *Circ J*, 76, 293-294. Editorial Comments.

Books

1. Sasano T, Kurokawa J (2012) Remodeling of potassium channels in cardiac hypertrophy In: *Molecular Mechanisms of Cardiac Remodeling*. Jugdutt BI, Dhalla NS (Eds): Springer, New York, in press.
2. Kurokawa J, Kodama M, Furukawa T, Clancy CE (2012) Sex and gender aspects in anti-arrhythmic therapy. In: *Sex and Gender Difference in Pharmacology*. Handbook of Experimental Pharmacology 214, Rigitz-Zagosek V (Ed): Springer-Verlag, Germany. Pp237-263. DOI 10.1007/978-3-642-30726-3_12

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. Endo H, Muramatsu T, Furuta M, Uzawa N, Pimkhaokham A, Amagasa T, Inazawa J, Kozaki K: Potential of tumor-suppressive miR-596 targeting LGALS3BP as a therapeutic agent in oral cancer. *Carcinogenesis* 34: 560-569, 2013.
2. Matsumura S, Imoto I, Kozaki K, Matsui T, Muramatsu T, Furuta M, Tanaka S, Sakamoto M, Arii S, Inazawa J: Integrative array-based approach identifies MZB1 as a frequently methylated putative tumor-suppressor in hepatocellular carcinoma. *Clin Cancer Res* 18: 3541-3551, 2012.
3. Ono H, Imoto I, Kozaki K, Tsuda H, Matsui T, Kurasawa Y, Muramatsu T, Sugihara K, Inazawa J: SIX1 promotes epithelial-mesenchymal transition in colorectal cancer through ZEB1 activation. *Oncogene* 31: 4923-4934, 2012.
4. Kurasawa Y, Kozaki K, Pimkhaokham A, Muramatsu T, Ono H, Ishihara T, Uzawa N, Imoto I, Amagasa T, Inazawa J: Stabilization of phenotypic plasticity through mesenchymal-specific DNA hypermethylation in cancer cells. *Oncogene* 31: 1963-1974, 2012.
5. Bai H, Inoue J, Kawano T, Inazawa J: A transcriptional variant of the LC3A gene is involved in autophagy and frequently inactivated in human cancers. *Oncogene* 31: 4397-408, 2012.

Review Article

1. Kozaki K and Inazawa J: Tumor-suppressive microRNA silenced by tumor-specific DNA hypermethylation in cancer cells. *Cancer Sci* 103: 837-845, 2012.

Molecular Genetics

1. Staffs and Students (April, 2012)

Professor	Yoshio MIKI	
Associate Professor	Kiyotsugu YOSHIDA	
Project Associate Professor	Akira NAKANISHI	
Assistant Professor	Katsuya TAKENAKA	
Project Assistant Professor	Ken MIYAGUCHI	
Graduate Student	Miho TAKAOKA,	Nadila WALI,
	Nurmaa DASHZEVEG,	Yuya KAGAMI,
	Hitomi KIMURA,	Ryoko TAKIZAWA,
	Kazuya NAKAZAWA,	Takenori YAMAMOTO,
	Shota WADA,	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 BRCA1/2-deficient breast cancers
 - ② Identification of novel BRCA2-associated proteins functioning in DNA damage repair.
 - ③ Identification of novel BRCA2-associated proteins and analyses of functions of their association in numerical integrity of centrosomes.
- 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. Kawazu, M., Ueno, T., Kontani, K., Ogita, Y., Ando, M., Fukumura, K., Yamato, A., Soda, M., Takeuchi, K., Miki, Y., Yamaguchi, H., Yasuda, T., Naoe, T., Yamashita, Y., Katada, T., Choi, Y.L. and Mano, H. (2013) Transforming mutations of RAC guanosine triphosphatases in human cancers. *Proc Natl Acad Sci U S A*.
2. Wang, L., Tsutsumi, S., Kawaguchi, T., Nagasaki, K., Tatsuno, K., Yamamoto, S., Sang, F., Sonoda, K., Sugawara, M., Saiura, A., Hirono, S., Yamaue, H., Miki, Y., Isomura, M., Totoki, Y., Nagae, G., Isagawa, T., Ueda, H., Murayama-Hosokawa, S., Shibata, T., Sakamoto, H., Kanai, Y., Kaneda, A., Noda, T. and Aburatani, H. (2012) Whole-exome sequencing of human pancreatic cancers and characterization of genomic instability caused by MLH1 haploinsufficiency and complete deficiency. *Genome Res*, **22**, 208-19.
3. Taira, N., Mimoto, R., Kurata, M., Yamaguchi, T., Kitagawa, M., Miki, Y. and Yoshida, K. (2012) DYRK2 priming phosphorylation of c-Jun and c-Myc modulates cell cycle progression in human cancer cells. *J Clin Invest*, **122**, 859-72.
4. Suzuki, K., Dashzeveg, N., Lu, Z.G., Taira, N., Miki, Y. and Yoshida, K. (2012) Programmed cell death 6, a novel p53-responsive gene, targets to the nucleus in the apoptotic response to DNA damage. *Cancer Sci*, **103**, 1788-94.
5. Satoh, Y., Sugai, S., Uehara, H., Mun, M., Sakao, Y., Okumura, S., Nakagawa, K., Ishikawa, Y., Miki, Y. and Miyata, S. (2012) Clinical impact of intraoperative detection of carcinoembryonic antigen mRNA in pleural lavage specimens from nonsmall cell lung cancer patients. *Thorac Cardiovasc Surg*, **60**, 533-40.
6. Sakamoto, K., Fujii, T., Kawachi, H., Miki, Y., Omura, K., Morita, K., Kayamori, K., Katsube, K. and Yamaguchi, A. (2012) Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lab Invest*, **92**, 688-702.
7. Khanom, R., Sakamoto, K., Pal, S.K., Shimada, Y., Morita, K., Omura, K., Miki, Y. and Yamaguchi, A. (2012) Expression of basal cell keratin 15 and keratin 19 in oral squamous neoplasms represents diverse pathophysiologies. *Histol Histopathol*, **27**, 949-59.

8. Iyevleva, A.G., Kuligina, E., Mitiushkina, N.V., Togo, A.V., Miki, Y. and Imyanitov, E.N. (2012) High level of miR-21, miR-10b, and miR-31 expression in bilateral vs. unilateral breast carcinomas. *Breast Cancer Res Treat*, **131**, 1049-59.
9. Elgazzar, S., Zembutsu, H., Takahashi, A., Kubo, M., Aki, F., Hirata, K., Takatsuka, Y., Okazaki, M., Ohsumi, S., Yamakawa, T., Sasa, M., Katagiri, T., Miki, Y. and Nakamura, Y. (2012) A genome-wide association study identifies a genetic variant in the SIAH2 locus associated with hormonal receptor-positive breast cancer in Japanese. *J Hum Genet*, **57**, 766-71.

Epigenetic Epidemiology

1. Staffs and Students

Professor	Masaaki MURAMATSU	
Associate Professor	Noriko SATO	
Assistant Professor	Shinobu IKEDA	
Adjunct Instructor	Katsuko SUDO	
Graduate Student	Miki Yamada, Nay Chi Htun, Atsuko Hiraishi, Zhao Chen-xi, Mia Sawabe,	Kyi Chan Ko, Cuneyd Palrayan, Sae Masuda, Sariya Dechamethakun, Kaung Si Thu,
Research Students	Khin Thet Thet Zaw,	Azusa Sengoku

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. We also study the role of epigenetic changes in common diseases. A new project has been started to build methods for educating genome-based health literacy from information generated by personal genome sequence.

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. Severe cutaneous adverse response (Stevens-Johnson's Syndrome) and HLA genotypes.
4. The role of epigenetic regulation and fetal programming in common diseases.
5. Annotation of personal genome sequence produced by next generation sequencer.

4. Publications

1. Ikeda S, Tanaka N, Arai T, Chida K, Muramatsu M, Sawabe M. Polymorphisms of LTA, LGALS2, and PSMA6 genes and coronary atherosclerosis: a pathological study of 1503 consecutive autopsy cases. *Atherosclerosis*. 221:458-60 (2012)
2. Ko MK, Ikeda S, Mieno-Naka M, Arai T, Zaidi SA, Sato N, Muramatsu M, Sawabe M. J *Atheroscler Thromb. Association of COMT gene polymorphisms with systemic atherosclerosis in elderly Japanese*.19:552-8 (2012)
3. Xi C, Miyaki K, Ikeda S, Song Y, Sinbo T, Muramatsu M. Association of GLUT4 gene variants with HbA1c level in Japanese men. *Endocr J*.59:677-84 (2012)
4. Ishii T, Hagiwara K, Kamio K, Ikeda S, Arai T, Mieno MN, Kumasaka T, Muramatsu M, Sawabe M, Gemma A, Kida K. Involvement of surfactant protein D in emphysema revealed by genetic association study. *Eur J Hum Genet*.20:230-5 (2012)
5. Ishii T, Hagiwara K, Ikeda S, Arai T, Mieno MN, Kumasaka T, Muramatsu M, Sawabe M, Gemma A, Kida K. Association between genetic variations in surfactant protein d and emphysema, interstitial pneumonia, and lung cancer in a Japanese population. *COPD* 9:409-16 (2012)
6. 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. *Epub* 2012 Jul 3.
7. 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*.Epub 2012 Sep 5

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	
Graduate Students	D3 Marie Kato	
	D2 Kenji Hayamizu	
	D1 Rajan Shrestha	
	M2 Motonari Sakai,	Eri Nishizawa
	M1 Kumiko Ugata,	Asami Shibuya,
	Rin Tokunaga,	Yuka Yamamoto,

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 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. Tsuchiya A, Hirai G, Koyama Y, Oonuma K, Otani Y, Osada H, Sodeoka M: Dual-specificity Protein Phosphatase CDC25A/B Inhibitor Identified from a Focused Library with Non-electrophilic Enamine Core Structure. *ACS Med. Chem. Lett.* 3: 294-298, 2012.
2. Subedi GP, Satoh T, Hanashima S, Ikeda A, Nakada H, Sato R, Mizuno M, Yuasa N, Fujita-Yamaguchi Y, Yamaguchi Y: Overproduction of anti-Tn antibody MLS128 single-chain Fv fragment in *Escherichia coli* cytoplasm using a novel pCold-PDI vector. *Protein Expr Purif.* 82:197-204, 2012.
3. Kuo T-F, Tatsukawa H, Matsuura T, Nagatsuma K, Hirose S, Kojima S: Free fatty acids induce transglutaminase 2-dependent apoptosis in hepatocytes via ER stress-stimulated PERK pathways. *J. Cell. Physiol.* 227(3):1130-1137, 2012.
4. Yokosuka T, Takamatsu M, Kobayashi-Imanishi W, Hashimoto-Tane A, Azuma M, Saito T.: Programmed cell death-

1 forms negative costimulatory microclusters that directly inhibit T cell receptor signals by recruitment of phosphatase SHP2. *J. Exp. Med.* 209:1201-1217, 2012.

Review Articles

1. Nagae M, Yamaguchi Y: Function and 3D structure of the N-glycans on glycoproteins. *Int J Mol Sci.* 13: 8398-8429, 2012.

Books

1. Saito T: Mechanisms of T-lymphocyte signaling and activation. *In* *Fundamental Immunology*, 7th ed. (Paul W (ed)), Lippincott Williams & Wilkins, Philadelphia, 2012, pp. 306-324.

Meetings & Conferences

1. Kojima S, Lee E, Suzuki Y, Sato Y, An essential role of transglutaminase 2 in tumor angiogenesis by suppression of VASH1 expression. 2012 Cell Symposia : Angiogenesis, Metabolic Regulation, and Cancer Biology in association with VIB, Leuven Belgium, July, 2012.

Miscellaneous

<Invited Lectures>

1. Kojima S. "Acyclic retinoid induces tumor-selective cell death in hepatocarcinoma tumor stem cells and inhibits angiogenesis via suppressing phosphorylation" 2012 FASB Summer Conference on Retinoids, Snowmass, CO, USA, June 2012.
2. Kojima S. "Essential role of transglutaminase 2 in tumor angiogenesis" 2nd Gordon Research Conference on Transglutaminases in Human Disease Processes, Davidson, NC, USA, July, 2012.
3. Yamaguchi Y. "Toward the understanding of site-specific N-glycosylation and maturation", GlycoT2012, Hannover, June 2012.
4. Saito T. "Spatiotemporal regulation of T cell activation and co-stimulation" 2012 Gordon Research Conference -Immunochemistry & Immunobiology, Les Diablerets, Switzerland, June 2012.

<Patent>

1. Kojima, S., Dohmae, N., and Kondo, W. "Methodes of use of antibodies which recognize a protease cleavage site of an LAP fragment of TGF- β ." US 8,198,412 (June 12, 2012)

Department of Pharmacovigilance

1. Staffs and Students (April, 2012)

Professor	Masayoshi Harigai	
Associate Professor	Ryuji Koike,	Toshihiro Nanki
Assistant Professor	Kaori Watanabe,	Ryoko Sakai
Graduate Student	Hayato Yamazaki,	Fumio Hirano,
	Mari Kihara,	Masako Hongo,
	Sayoko Harada,	Shoko Kasai
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. Safety of biologics in clinical use in Japanese patients with rheumatoid arthritis in long-term (SECURE study)
3. Pulmonary infections in patients receiving immunosuppressive treatment for rheumatic diseases (PREVENT)
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. Clinical characteristics and risk factors for *Pneumocystis jirovecii* pneumonia in patients with rheumatoid arthritis receiving TNF inhibitors
8. Evaluation of co-morbidities in rheumatoid arthritis (COMORA study)
9. Clinical epidemiological study of treat-to-target strategy in rheumatoid arthritis patients with moderate to high disease activity
10. Efficacy and safety of programmed intensive treatment with methotrexate in patients with active rheumatoid arthritis
11. Analysis of pulmonary images on thoracic computed tomography in patients with microscopic polyangiitis
12. Clinical outcomes of Japanese rheumatoid arthritis patients in real world commencing targeted therapy (CORRECT)
13. 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).

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. Harigai M, Takeuchi T, Tanaka Y, Matsubara T, Yamanaka H, Miyasaka N. Discontinuation of adalimumab treatment in rheumatoid arthritis patients after achieving low disease activity. *Mod Rheumatol.* 22: 814-822, 2012.
2. Harigai M, Tanaka Y, Maisawa S. Safety and efficiency of various dosages of ocrelizumab in Japanese rheumatoid arthritis patients with an inadequate response to methotrexate therapy: a placebo-controlled, double-blind, parallel-group study. *J Rheumatol.*39: 486-495, 2012.
3. Sakai R, Tanaka M, Nanki T, Watanabe K, Yamazaki H, Koike R, Nagasawa H, Amano K, Saito K, Tanaka Y, Ito S, Sumida T, Ihata A, Ishigatsubo Y, Atsumi T, Koike T, Nakajima A, Tamura N, Fujii T, Dobashi H, Tohma S,

- Sugihara T, Ueki Y, Hashiramoto A, Kawakami A, Hagino N, Miyasaka N, Harigai M; for the REAL Study Group. Drug retention rates and relevant risk factors for drug discontinuation due to adverse events in rheumatoid arthritis patients receiving anticytokine therapy with different target molecules. *Ann Rheum Dis.* 71: 1820-1826, 2012.
4. Arai A, Imadome K, Wang L, Wu N, Kurosu T, Wake A, Yamamoto H, Ota Y, Harigai M, Fujiwara S, Miura O. Recurrence of chronic active Epstein-Barr virus infection from donor cells after achieving complete response through allogeneic bone marrow transplantation. *Intern Med.* 51: 777-782, 2012.
 5. Sakai R, Komano Y, Tanaka M, Nanki T, Koike R, Nagasawa H, Amano K, Nakajima A, Atsumi T, Koike T, Ihata A, Ishigatubo Y, Saito K, Tanaka Y, Ito S, Sumida T, Tohma S, Tamura N, Fujii T, Sugihara T, Kawakami A, Hagino N, Ueki Y, Hashiramoto A, Nagasaka K, Miyasaka N, Harigai M; for the REAL Study Group. Time-dependent increased risk for serious infection from continuous use of tumor necrosis factor antagonists over three years in patients with rheumatoid arthritis. *Arthritis Care Res (Hoboken). Arthritis Care Res (Hoboken).* 64: 1125-1134, 2012.
 6. Tanaka M, Sakai R, Koike R, Komano Y, Nanki T, Sakai F, Sugiyama H, Matsushima H, Kojima T, Ohta S, Ishibe Y, Sawabe T, Ota Y, Ohishi K, Miyazato H, Nonomura Y, Saito K, Tanaka Y, Nagasawa H, Takeuchi T, Nakajima A, Ohtsubo H, Onishi M, Goto Y, Dobashi H, Miyasaka N, Harigai M. *Pneumocystis jirovecii* pneumonia associated with etanercept treatment in patients with rheumatoid arthritis: a retrospective review of 15 cases and analysis of risk factors. *Mod Rheumatol.* 22: 849-858, 2012.
 7. Nishimura K, Omori M, Sato E, Katsumata Y, Gono T, Kawaguchi Y, Harigai M, Yamanaka H, Ishigooka J. Risperidone in the treatment of corticosteroid-induced mood disorders, manic/mixed episodes, in systemic lupus erythematosus: a case series. *Psychosomatics.* 53: 289-293, 2012.
 8. Yamazaki H, Nanki T, Harigai M, Miyasaka N. Successful treatment of refractory Takayasu arteritis with tacrolimus. *J. Rheumatol.* 39: 1487-1488, 2012.
 9. Suzuki F, Kubota T, Miyazaki Y, Ishikawa K, Ebisawa M, Hirohata S, Ogura T, Mizusawa H, Imai T, Miyasaka N, Nanki T. Serum level of soluble CX3CL1/fractalkine is elevated in patients with polymyositis and dermatomyositis, which is correlated with disease activity. *Arthritis Res Ther.* 14: R48, 2012.
 10. Komano Y, Yagi N, Onoue I, Kaneko K, Miyasaka N, Nanki T. Arthritic joint-targeting small interfering RNA-encapsulated liposome: Implication for treatment strategy for rheumatoid arthritis. *J Pharmacol Exp Ther.* 340: 109-113, 2012.

Department of Nanomedicine (DNP)

1. Staffs and Students

Associate Professor	Motohiro KOMAKI, D.D.S., Ph.D.
Assistant Professor	Kengo IWASAKI, D.D.S., Ph.D
Visiting Researcher	Naoki YOKOYAMA (DNP), Hirohito AYAME (DNP)

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 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 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.
- 6) The regeneration of periodontal tissues by PDLSC_ conditioned medium.

4. Clinical Services

Our department members are working in periodontology clinic of Tokyo Medical and Dental University dental hospital. We provide periodontal treatments to patients and are instructors for dental hygienist and dentist.

5. Publications

1. 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*. 2012 Dec 14. [Epub ahead of print]
2. Expression of angiogenesis-related factors and inflammatory cytokines in placenta and umbilical vessels in pregnancies with preeclampsia and chorioamnionitis/funisitis. Taki A, Abe M, Komaki M, Oku K, Iseki S, Mizutani S, Morita I. *Congenit Anom (Kyoto)*. 2012 Jun; 52(2): 97-103.
3. Comparative Temporospatial Expression Profiling of Murine Amelotin Protein during Amelogenesis. Somogyi-Ganss E, Nakayama Y, Iwasaki K, Nakano Y, Stolf D, McKee MD, Ganss B. *Cells Tissues Organs*. 2012;195(6):535-49
4. Cementum protein 1 (CEMP1) induces a cementoblastic phenotype and reduces osteoblastic differentiation in periodontal ligament cells. Komaki M, Iwasaki K, Arzate H, Narayanan AS, Izumi Y, Morita I. *J Cell Physiol*. 2012; 227(2): 649-57.

Department for Hepatitis Control

1. Staffs and Students

Professor	Yasuhiro ASAHINA (04/2012-)	
Associate Professor	Naoya SAKAMOTO (-02/2012),	
Senior Associate Professor	Sei KAKINUMA	
Graduate Student (collaboration with Department of Gastroenterology and Hepatology in TMDU)	Akiko KITAZUME (-03/2012), Kei KIYOHASHI (-03/2012), Sayuri NITTA (-03/2012), Miyako MURAKAWA, Kouhei YOSHINO, Junko FUJIKI, Fukiko KAWAI, Hideto YAMANAKA, Satoshi OHTANI, Fumio GOTOH (04/2012-)	

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, Muraoka M, Tanaka K, Suzuki Y, Tamaki N, Hoshioka Y, Yasui Y, Katoh T, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M, Enomoto N, Nitta S, Sakamoto N, Izumi N: Association of gene expression involving innate immunity and genetic variation in interleukin 28B with antiviral response. *Hepatology*. 55: 20- 29, 2012.
2. 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: 46-58, 2013.
3. 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: 2502-2513, 2013.
4. Izumi N, Asahina Y, Kurosaki M, Yamada G, Kawai T, Kajiwaru 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 *a* 2a in patients with chronic hepatitis C: a nationwide multi-center cooperative study. *J Gastroenterol*. (Epub ahead of print) 2012.
 5. Kurosaki M, Hiramatsu N, Sakamoto M, Suzuki Y, Iwasaki M, Tamori A, Matsuura K, Kakinuma S, Sugauchi F, Sakamoto N, Nakagawa M, Yatsushashi H, Izumi N: Age and total ribavirin dose are independent predictors of relapse after interferon therapy in chronic hepatitis C revealed by data mining analysis. *Antivir Ther*. 17: 35- 43, 2012.
 6. Kusano-Kitazume A, Sakamoto N, Okuno Y, Sekine-Osajima Y, Nakagawa M, Kakinuma S, Kiyohashi K, Nitta S, Murakawa M, Azuma S, Nishimura-Sakurai Y, Hagiwara M, Watanabe M: Identification of novel N-(morpholine-4-carbonyloxy) amidine compounds as potent inhibitors against hepatitis C virus replication. *Antimicrob Agents Chemother*. 56:1315-1323, 2012.
 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*. 2012; in press.
 8. Nishida N, Sawai H, Matsuura K, Sugiyama M, Ahn SH, Park JY, Hige S, Kang JH, Suzuki K, Kurosaki M, Asahina Y, Mochida S, Watanabe M, Tanaka E, Honda M, Kaneko S, Orito E, Ttoh Y, Mita E, Tamori A, Murawaki Y, Hiasa Y, Sakaida I, Korenaga M, Hino K, Ide: Genome-wide association study confirming association of HLA-DP with protection against chronic hepatitis B and viral clearance in Japanese and Korean. *PLoS One* 7(6):e39175, 2012.
 9. Ozeki R, Kakinuma S, Asahina K, Simizu-Saito K, Arai S, Tanaka Y, Teraoka H: Hepatic stellate cells mediate differentiation of dendritic cells from monocytes. *J Med Dent Sci*. 59: 39- 48, 2012.
 10. Sawai H, Nishida N, Mbarek H, Matsuda K, Mawatari Y, Yamaoka M, Hige S, Kang JH, Abe K, Mochida S, Watanabe M, Kurosaki M, Asahina Y, Izumi N, Honda M, Kaneko S, Tanaka E, Matsuura K, Itoh Y, Mita E, Korenaga M, Hino K, Murawaki Y, Hiasa Y, Ide T, Ito K: No association for Chinese HBV-related hepatocellular carcinoma susceptibility SNP in other East Asian populations. *BMC Med Genet*. 13: 47 2012.
 11. 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 CN. (Epub ahead of print) *J Viral Hepat*. 20:72-76, 2012.
 12. 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*. 2012; in press.

Department of Advanced GI Therapeutics

1. Staffs and Students (2012)

Associate Professor	Ryuichi OKAMOTO,	Tetsuya NAKAMURA
Junior Associate Professor	Kiichiro TSUCHIYA	
Assistant Professor	Shigeru OSHIMA	
Medical Fellow	Shiro YUI,	Tomohiro MIZUTANI
Graduate Student	Hikomichi SHIMIZU,	Tatsuro MURANO,
	Naoto TSUGE,	Masayoshi FUKUDA,
	Yu MATSUZAWA,	Kengo NOZAKI,
	Yuki YAMAUCHI	

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. Araki A, Suzuki S, Tsuchiya K, Oshima S, Okada E, Watanabe M: Modified single-operator method for double-balloon endoscopy. **Digestive Endoscopy**. 24(6): 470-474, 2012
2. Araki A, Tsuchiya K, Oshima S, Okada E, Suzuki S, Morio-Akiyama J, Fujii T, Okamoto R, Watanabe M: Endoscopic ultrasound with double-balloon endoscopy for the diagnosis of inverted Meckel's diverticulum: a case report. **Journal of Medical Case Reports**. 6(1): 328, 2012
3. 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. **Biochem Biophys Res Commun**. (Epub ahead of print), 2013.
4. Kiyohashi K, Kakinuma S, Kamiya A, Sakamoto N, Nitta S, Yamanaka H, Yoshino K, Fijiki 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**. (in press), 2013.
5. Mizutani T, Nakamura T, Morikawa R, Fukuda M, Mochizuki W, Yamauchi Y, Nozaki K, Yui S, Nemoto Y, Nagaishi T, Okamoto R, Tsuchiya K, Watanabe M: Real-time analysis of P-glycoprotein-mediated drug transport across primary intestinal epithelium three-dimensionally cultured in vitro. **Biochem Biophys Res Commun**. 419:238-243, 2012.
 6. 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**. (Epub ahead of print) 2012
 7. Ono Y, Kanai T, Sujino T, Nemoto Y, Kanai Y, Mikami Y, Hayashi A, Matsumoto A, Takaishi H, Ogata H, Matsuoka K, Hisamatsu T, Watanabe M, Hibi T: T-helper 17 and interleukin-17-producing lymphoid tissue inducer-like cells make different contributions to colitis in mice. **Gastroenterology**. 143(5): 1288-1297, 2012
 8. 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: 125-128, 2012
 9. 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, 2012
 10. 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. **Inflammatory Bowel Dis**. (in press), 2012
 11. Watanabe T, Sasaki I, Sugita A, Fukushima K, Futami K, Hibi T, Watanabe M: Interval of less than 5 years between the first and second operation is a risk factor for a third operation for Crohn's disease. **Inflamm Bowel Dis**. 18: 17- 24, 2012
 12. Watanabe T, Sasaki I, Sugita A, Fukushima K, Futami K, Hibi T, Watanabe M: Time trend and risk factors for reoperation in Crohn's disease in Japan. **Hepatogastroenterology**. 59: 1081- 1086, 2012
 13. 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): 2524-2536, 2012
 14. Yui S, Nakamura T, Sato T, Nemoto Y, Mizutani T, Zheng X, Ichinose S, Nagaishi T, Okamoto R, Tsuchiya K, Clevers H, Watanabe M: Functional engraftment of colon epithelium expanded in vitro from a single adult Lgr5+ stem cell. **Nat Med**. 18:618-623, 2012.

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

No lectures in our department.

3. Research Subjects

- Effects of NMDA-type glutamate receptor co-agonist on gamma oscillations and sleep in schizophrenia.
- Open-label trial of ramelteon for diabetes mellitus with sleep disorder.
- The effect of chronotherapy with the angiotensin-antagonist in hypertension with sleep apnea syndrome.
- The efficacy of home-oxygen therapy in patients with sleep apnea and pulmonary fibrosis.
- Development of the evaluation system for the efficacy of oral appliances on obstructive sleep apnea syndrome.
- Open-label trial of hyperbaric oxygen therapy on sleep quality.

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 (Health Service Center)
Wednesday:	AM	Dr. Miyazaki (Health Service Center)
Thursday:	AM	Dr. Tamaoka (Sleep Modulatory Medicine)
	PM	Dr. Tamaoka (Sleep Modulatory Medicine)
Friday:	AM	Dr. Uezato (Psychiatry)
	AM	Dr. Tateishi (Pulmonary Medicine)
	PM	Dr. Tateishi(Pulmonary Medicine)

5. Publication

Department of Women's Health

1. Staffs

Associate Professor	Masakazu Terauchi (April 2012~)
Assistant Professor	Kimio Wakana (April 2012~, concurrent)

2. Education

As a branch of the Department of Obstetrics and Gynecology, we shared responsibility in the education of Obstetrics and Gynecology, Maternal Nursing, 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 2012, 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

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 between Anxiety, Depression and Insomnia in Peri- and Post-Menopausal Women. *Maturitas* 72(1): 61-65, 2012
2. Terauchi M, Honjo H, Mizunuma H, Aso T. Effects of oral estradiol and levonorgestrel on cardiovascular risk markers in postmenopausal women. *Arch Gynecol Obstet* 285(6): 1647-1656 2012
3. 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* (in press)

Poster Presentation

1. Masakazu Terauchi, Shiro Hiramitsu, Mihoko Akiyoshi, Yoko Owa, Kiyoko Kato, Satoshi Obayashi, Eisuke Matsushima, Toshiro Kubota. "Associations among Depression, Anxiety, and Somatic Symptoms in Peri- and Postmenopausal Women". 23rd North American Menopause Society Annual Meeting, Orlando, FL, 2012-10-4

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 department is to provide the students opportunities to study the 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 students in the another vocational schools for medical technologists.

Besides the students, eleven 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. Four clinical laboratory technicians in the other hospital were 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. Items of emergency laboratory tests have been in increase, including smear test for tubercle bacillus and cell counting of the cerebrospinal fluid. Since November 2011, blood-taking and analysis have been started at 8:05, 30 minutes earlier than before. It results in shortening the waiting time of patients and in more speedy reporting the results of analysis. The results of physiological examinations are online reported quickly and correctly. 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.

5. Publications

Original Article

1. Arai A, Nogami A, Imadome K, Kurata M, **Murakami N**, Fujiwara S, Miura O. Sequential monitoring of serum IL-6, TNF- α , and IFN- γ levels in a CAEBV patient treated by plasma exchange and immunotherapy. *Int J Haematol.* 2012;96:669-673.
2. Kanamori E, Itoh M, **Tojo N**, Koyama T, Nara N, **Tohda S**. Flow cytometric analysis of Notch1 and Jagged1 expression in normal blood cells and leukemia cells. *Exp Ther Med.* 2012;4:397-400.
3. Kitamura Y, Sawabe E, Ohkusu K, **Tojo N**, **Tohda S**. First report of sepsis caused by *Rhodococcus corynebacterioides* in a patient with myelodysplastic syndrome. *J Clin Microbiol.* 2012;50:1089-1091.
4. Kobayashi M, Yokota T, Tomimitsu H, Ishibashi S, Sekiguchi T, **Kanouchi T**, Ishikawa K, Mizusawa H. Motor-dominant chronic inflammatory demyelinating polyradiculoneuropathy with Uhthoff-like phenomenon is a distinct clinical entity? *Muscle Nerve.* 2012;46(1):140-142.
5. Ono A, Okuhashi Y, Takahashi Y, Itoh M, Nara N, **Tohda S**. Advantages of the quenching probe method over other PCR-based methods for detection of the JAK2 V617F mutation. *Oncol Lett.* 2012;4:205-208.
6. Takahashi Y, Ishigaki T, Okuhashi Y, Ono A, Itoh M, Nara N, **Tohda S**. Effect of BMP4 on the growth and clonogenicity of human leukemia and lymphoma cells. *Anticancer Res.* 2012;32:2813-2817.

Review Article

1. **Kanouchi T**, Ohkubo T, Yokota T. Can regional spreading of amyotrophic lateral sclerosis motor symptoms be explained by prion-like propagation? *J Neurol Neurosurg Psychiatry*. 2012;83(7):739-45.

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 2012)

1) The amount of blood products used

Red cell component products	12,305	Units	(6,207 bags)
Platelet concentration	26,236	Units	(2,183 bags)
Fresh frozen plasma	8,177.5	Units	(3,850 bags)

2) Autologous blood collection and transfusion

Autologous blood collection	395	cases	(525times, 1,017Units)
Autologous blood transfusion	351	cases	(869Units)

3) The number of clinical tests of transfusion

Blood typing	8,496
Anti red blood cell antibody test	3,774
Cross match	10,045

4) Hematopoietic stem cell harvest

Autologous peripheral blood stem cell harvest	9 cases	19 times
Allogenic peripheral blood stem cell harvest	5 cases	6 times
Autologous peripheral mononuclear cell harvest	1 case	1 time
Allogenic bone marrow harvest	11 cases	11 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	12 cases	12 times
Allogenic peripheral blood stem cell transplantation	4 cases	4 times
Autologous peripheral mononuclear cell transplantation	1 case	1 time
Allogenic bone marrow transplantation	9 cases	9 times
Allogenic umbilical cord blood transplantation	6 cases	6 times

5. Publications

Original articles

1. Fujihara H, Watanabe H, Yamada C, Ohtomo N, Oshida M, Tomoda Y, Yurugi K, Hoshi Y, Takahashi K, Maekawa M, Ohto H, Takeshita H. Situation and problems of education in transfusion medicine in Japanese university hospitals: the 2009 transfusion conference of Japanese university hospitals surveillance report on medical education (2). *Jpn J Transf Cell Ther* 58:492-499, 2012.

Department of Blood Purification

Associate Professor	Tatemitsu RAI	
Assistant Professor	Eisei SOHARA,	Katsumasa OI
Hospital Staff	Miyuki YOSHIZAKI,	Keita KUSAKA

(1) Education

The Department of Blood Purification 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 Blood Purification 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 Blood Purification in 2011 are as follows:

Total number of blood purification sessions	5294
Number of hemodialysis (HD) sessions	4299
Number of plasma exchange (PE) sessions	145
Number of plasma adsorption sessions	99
Number of continuous hemodiafiltration (CHDF) sessions	526
Number of leukapheresis sessions	62
Number of endotoxin adsorption sessions	35
Number of cell-free concentrated ascites reinfusion (CART) sessions	6

(4) Publications

【Original articles】

1. Hara-Chikuma M, Sugiyama Y, Kabashima K, Sohara E, Uchida S, Sasaki S, Inoue S, Miyachi Y. Involvement of aquaporin-7 in the cutaneous primary immune response through modulation of antigen uptake and migration in dendritic cells. *FASEB J.* 26:211-8, 2012.
2. Hossain Khan MZ, Sohara E, Ohta A, Chiga M, Inoue Y, Isobe K, Wakabayashi M, Oi K, Rai T, Sasaki S, Uchida S. Phosphorylation of Na-Cl cotransporter by OSR1 and SPAK kinases regulates its ubiquitination. *Biochem. Biophys. Res. Commun.* 425:456-61, 2012.
3. Nishida H, Sohara E, Nomura N, Chiga M, Alessi DR, Rai T, Sasaki S, Uchida S. Phosphatidylinositol 3-kinase/Akt signaling pathway activates the WNK-OSR1/SPAK-NCC phosphorylation cascade in hyperinsulinemic db/db mice. *Hypertension.* 60:981-90, 2012.
4. Ohta E, Akazawa M, Noda Y, Mandai S, Naito S, Ohta A, Sohara E, Okado T, Rai T, Uchida S, Sasaki S. Severe hyperparathyroidism in a pre-dialysis chronic kidney disease patient treated with a very low protein diet. *J. Bone Miner. Metab.* 30:238-42, 2012.
5. Oi K, Sohara E, Rai T, Misawa M, Chiga M, Alessi DR, Sasaki S, Uchida S. A minor role of WNK3 in regulating phosphorylation of renal NKCC2 and NCC co-transporters in vivo. *Biol. Open.* 1:120-7, 2012.
6. Susa K, Kita S, Iwamoto T, Yang SS, Lin SH, Ohta A, Sohara E, Rai T, Sasaki S, Alessi DR, Uchida S. Effect of heterozygous deletion of WNK1 on the WNK-OSR1/ SPAK-NCC/NKCC1/NKCC2 signal cascade in the kidney and blood vessels. *Clin. Exp. Nephrol.* 16:530-8, 2012.
7. Susa K, Sohara E, Isobe K, Chiga M, Rai T, Sasaki S, Uchida S. WNK-OSR1/SPAK-NCC signal cascade has circadian rhythm dependent on aldosterone. *Biochem. Biophys. Res. Commun.* 427:743-7, 2012.

8. Uchida S, Chiga M, Sohara E, Rai T, Sasaki S. Does a β 2-adrenergic receptor-WNK4-Na-Cl co-transporter signal cascade exist in the in vivo kidney? *Nat. Med.* 18:1324-5, 2012.

【Scientific meetings】

1. Hossain Khan MZ, Sohara E, Ohta A, Chiga M, Inoue Y, Isobe K, Wakabayashi M, Naito S, Oi K, Rai T, Sasaki S, Uchida S. Phosphorylation of Na-Cl cotransporter by OSR1 and SPAK kinases regulates its ubiquitination. The 45th Annual meeting of American Society of Nephrology, San Diego, November, 2012.
2. Iimori S, Naito S, Eto K, Sohara E, Okado T, Noda Y, Rai T, Uchida S, Sasaki S. The effect of Educational Hospitalization (EH) on the progression of CKD. 1st Chronic Kidney Disease Frontier Meeting, Nagoya, February 2012.
3. Inoue Y, Sohara E, Kobayashi K, Rai T, Ishibashi K, Sasaki S, Shinichi U. Impaired trafficking of polycystin-1 may be a key mechanism of cyst formation in the aquaporin-11 knockout mouse. The 45th Annual Meeting of American Society of Nephrology, San Diego, November, 2012.
4. Isobe K, Sohara E, Rai T, Sasaki S, Uchida S. Development of sandwich enzyme linked immunosorbent assay (ELISA) for measurement of urinary total and phosphorylated Na-Clcotransporter (NCC) protein. The 45th Annual meeting of American Society of Nephrology, San Diego, November, 2012.
5. Kikuchi E, Mori T, Isobe K, Sohara E, Rai T, Sasaki S, Uchida S. Chemical library screening for direct SPAK inhibitors by a newly developed ELISA system. The 45th Annual Meeting of American Society of Nephrology, San Diego, November, 2012.
6. Mori T, Sohara E, Rai T, Sasaki S, Uchida S. Generation and analysis of WT-WNK4 transgenic mice revealed the physiological role of WNK4. The 45th Annual Meeting of American Society of Nephrology, San Diego, November, 2012.
7. Susa K, Sohara E, Isobe K, Chiga M, Rai T, Sasaki S, Uchida S.. WNK4-OSR1/SPAK-NCC signal cascade has circadian rhythm dependent on aldosterone. The 45th Annual Meeting of American Society of Nephrology, San Diego, November, 2012.
8. Zeniya M, Sohara E, Oi K, Chiga M, Susa K, Mori T, Rai T, Sasaki S, Uchida S. Dietary salt intake and angiotensin II regulates WNK-SPAK-NKCC1 phosphorylation cascade in mouse aorta. The 45th Annual Meeting of American Society of Nephrology, San Diego, November, 2012.

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	Shizuko Minegishi (to June 2012), Yuri Kohno, Naomi Terada(from May 2012), Akane Miyasaka (from May 2012)	
Technicians (From Collaborative Research)	Takashi Kosaka	
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. Clinical study on ex-vivo expanded donor T-cell infusion for patients who underwent hematopoietic stem cell transplantation (HSCT)
4. Development of multi-virus specific T lymphocytes for adoptive immunotherapy
5. Development of short tandem repeat method as a molecular ID for personal identification
6. Research on a regeneration system of the cartilage bone from the synovial membrane (Department of Orthopedic Surgery)
7. Development of novel peptide-pulsed dendritic therapy for adult T-cell leukemia (Department of Immunotherapeutics)

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 1,593 samples in year 2012 in total.

5. Publications

Original articles

1. 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*. (in press) 2012.
2. 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*. (in press), 2012.
3. Kamae C, Nakagawa N, Sato H, Honma K, Mitsui N, Ohara O, Kanegane H, Pasic S, Pan-Hammerstrom Q, van Zelm M.C., **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.* (in press), 2012
 4. Isoda T, Takagi M, Piao J, Nishii R, Masaki S, Masuda K, Ikawa T, Azuma M, **Morio T**, Kawamoto H, Mizutani S: Process for immune defect and chromosomal translocation during early thymocyte development lacking ATM. *Blood*.120:789-799, 2012.
 5. Nozaki T, Takada H, Ishimura M, Ihara K, Imai K, **Morio T**, Kobayashi M, Nonoyama S, Hara T: Endocrine complications in primary immunodeficiency diseases in Japan. *Clinical Endocrinol.* 77:628-634, 2012.
 6. Nakajima K. Hayashi M. Tanuma N. **Morio T**: An autopsy case of polymicrogyria and intracerebral calcification with death by intracerebral hemorrhage. *Neuropathology.* 32:207-10, 2012.
 7. Honda F, Kano H, Kanegane H, Nonoyama S, Kim E-S, Lee S-K, Takagi M, Mizutani S, **Morio T**: Btk negatively regulates ROS production and stimulation-induced apoptosis in human neutrophils. *Nature Immunol.* 13: 369-378, 2012.
 8. Jang SH, Lim JW, **Morio T**, Kim H: Lycopene inhibits Helicobacter pylori-induced ATM/ATR-dependent DNA damage response in gastric epithelial AGS cells. *Free Radical Biol. Med.* 52: 607-615, 2012.
 9. Kuramitsu M, Sato-Otsubo A, **Morio T**, Takagi M, Toki T, Terui K, RuNan W, Kanno H, Ohga S, Ohara A, Kojima S, Kitoh T, Goi K, Kudo K, Matsubayashi T, Mizue N, Ozeki M, Masumi A, Momose H, Takizawa K, Mizukami T, Yamaguchi K, Ogawa S, Ito E: Extensive gene deletions in Japanese patients with Diamond-Blackfan anemia. *Blood.* 119:2376-84, 2012.
 10. Sato R, Iizumi S, Kim E-S, Honda F, Lee S-K, Adachi N, Koyama H, Mizutani S, **Morio T**: Impaired cell adhesion, apoptosis, and signaling in WASP-gene disrupted Nalm-6 pre-B cells and recovery of cell adhesion using a transducible form of WASp. *Int. J. Hematol.* 95:299-310, 2012.
 11. Uchida Y, Matsubara K, **Morio T**, Kasawaki Y, Iwata A, Yura K, Kamimura K, Nigami H, Fukaya T: Acute cerebellitis and concurrent encephalitis associated with parvovirus B19 infection. *Pediatr. Infect. Dis. J.* 31:427, 2012.
 12. Lee SW, Kim JH, Park MC, Park YB, Chae WJ, **Morio T**, Lee DH, Yang SH, Lee SK, Lee SK, Lee SK: Alleviation of rheumatoid arthritis by cell-transducible methotrexate upon transcutaneous delivery. *Biomaterials* 33:1563-72, 2012.
 13. Honda F, Hane Y, Toma T, Yachie A, Kim E-S, Lee S-K, Takagi M, Mizutani S, **Morio T**: Transducible form of p47phox and p67phox compensate for defective NADPH oxidase activity in neutrophils of patients with chronic granulomatous disease. *Biochem. Biophys. Res. Comm.* 417:162-168, 2012.
 14. Nakamura K. Du L. Tunuguntla R. Fike F. Cavaliere S. **Morio T**. Mizutani S: Brusco A. Gatti RA. Functional characterization and targeted correction of ATM mutations identified in Japanese patients with ataxia-telangiectasia. *Hum Mutat.* 33:198-208, 2012.
 15. Uchida Y, Matsubara K, Wada T, Oishi K, **Morio T**, Takada H, Iwata A, Yura K, Kamimura K, Nigami H, Fukaya T: Recurrent bacterial meningitis by three different pathogens in an isolated asplenic child. *J Infect Chemother.* 52:607-15, 2012.
 16. Otabe K, Muneta T, Kawashima N, Suda H, Tsuji K, **Sekiya I**: Comparison of Gingiva, Dental Pulp, and Periodontal Ligament Cells From the Standpoint of Mesenchymal Stem Cell Properties. *Cell Medicine* 4(1): 13-21, 2012
 17. Nakamura T, **Sekiya I**, Muneta T, Hatsushika D, Horie M, Tsuji K, Kawarasaki T, Watanabe A, Hishikawa S, Fujimoto Y, Tanaka H, Kobayashi E: Arthroscopic, histological and MRI analyses of cartilage repair after a minimally invasive method of transplantation of allogeneic synovial mesenchymal stromal cells into cartilage defects in pigs. *Cytotherapy.* 14(3): 327-338, 2012.
 18. Horie M, Driscoll MD, Sampson HW, **Sekiya I**, Caroom CT, Prockop DJ, Thomas DB: Implantation of allogeneic synovial stem cells promotes meniscal regeneration in a rabbit meniscal defect model. *J Bone Joint Surg Am.* 18:94(8):701-12, 2012.Apr.
 19. Horie M, Choi H, Lee RH, Reger RL, Ylostalo J, Muneta T, **Sekiya I**, Prockop DJ: Intra-articular injection of human mesenchymal stem cells (MSCs) promote rat meniscal regeneration by being activated to express Indian hedgehog that enhances expression of type II collagen. *Osteoarthritis Cartilage.* 20(10):1197-207, 2012.Oct.
 20. **Sekiya I**, Ojima M, Suzuki S, Yamaga M, Horie M, Koga H, Tsuji K, Miyaguchi K, Ogishima S, Tanaka H, Muneta T: Human mesenchymal stem cells in synovial fluid increase in the knee with degenerated cartilage and osteoarthritis. *J Orthop Res.* 30(6):943-9, 2012.
 21. Suzuki S, Muneta T, Tsuji K, Ichinose S, Makino H, Umezawa A, **Sekiya I**: Properties and usefulness of aggregates of synovial mesenchymal stem cells as a source for cartilage regeneration. *Arthritis Res Ther.*;14(3):R136, 2012.

22. Futami I, Ishijima M, Kaneko H, Tsuji K, Ichikawa-Tomikawa, N., Sadatsuki R, Muneta T, Arikawa-Hirasawa, E, **Sekiya I**, Kaneko K: Isolation and characterization of multipotential mesenchymal cells from the mouse synovium. *PLoS One* 7, e45517, 2012.
23. Ogawa M, Sugita S, **Shimizu N**, Watanabe K, Nakagawa I, Mochizuki M: Broad-range real-time PCR assay for detection of bacterial DNA in ocular samples from infectious endophthalmitis. *Jpn J Ophthalmol.* 56(6):529-535, 2012.
24. Sugita S, **Shimizu N**, Watanabe K, Ogawa M, Maruyama K, Usui N, Mochizuki M: Virological analysis in patients with human herpes virus 6-associated ocular inflammatory disorders. *Invest Ophthalmol Vis Sci.* 2012 Jul 12;53(8):4692-8. Print 2012 Jul.
25. Ogawa M, Sugita S, Watanabe K, **Shimizu N**, Mochizuki M: Novel diagnosis of fungal endophthalmitis by broad-range real-time PCR detection of fungal 28S ribosomal DNA. *Graefes Arch Clin Exp Ophthalmol.* 250(12):1877-1883, 2012.
26. Sugita S, Kamoi K, Ogawa M, Watanabe K, **Shimizu N**, Mochizuki M: Detection of Candida & Aspergillus species DNA using broad-range real-time PCR for fungal endophthalmitis. *Graefes Arch Clin Exp Ophthalmol.* 250:391-398, 2012.

Hyperbaric Medical Center

1. Staffs

Center Chief and Junior Associate Professor

Kazuyoshi YAGISHITA

Tokunin Junior Associate Professor Mitsuihiro 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) Yagishita K, Muneta T, Ju YJ, Morito T, Yamazaki J, Sekiya I. High-flex posterior cruciate-retaining vs posterior cruciate-substituting designs in simultaneous bilateral total knee arthroplasty. A prospective randomized study. *J Arthroplasty*. 2012, 27(3):368-74.
- 2) Enomoto M, Ukegawa D, Sakaki K, Tomizawa S, Arai Y, Kawabata S, Kato T, Yoshii T, Shinomiya K, Okawa A. Increase in paravertebral muscle activity in lumbar kyphosis patients by surface electromyography compared with lumbar spinal canal stenosis patients and healthy volunteers. *J Spinal Disord Tech*. 2012, 25(6):E167-73.
- 3) Hirai T, Enomoto M, Machida A, Yamamoto M, Kuwahara H, Tajiri M, Hirai Y, Sotome S, Mizusawa H, Shinomiya K, Okawa A, Yokota T. Intrathecal shRNA-AAV9 inhibits target protein expression in the spinal cord and dorsal root ganglia of adult mice. *Hum Gene Ther Methods*. 2012, 23(2):119-27.

- 4) Hirai T, Kato T, Kawabata S, Enomoto M, Tomizawa S, Yoshii T, Sakaki K, Shinomiya K, Okawa A. Adhesive arachnoiditis with extensive syringomyelia and giant arachnoid cyst after spinal and epidural anesthesia: a case report. *Spine*. 2012, 37(3):E195-8.
- 5) Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. Surgical management of grade 3 medial knee injuries combined with cruciate ligament injuries. *Knee Surg Sports Traumatol Arthrosc*. 2012, 20(1):88-94.
- 7) Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. The effects of graft fixation angles on anteroposterior and rotational knee laxity in double-bundle anterior cruciate ligament reconstruction: Evaluation using computerized navigation. *Am J Sports Med*. 2012, 40(3):615-23.
- 8) Li W, Enomoto M, Ukegawa M, Hirai T, Sotome S, Wakabayashi Y, Shinomiya K, Okawa A. Subcutaneous injections of platelet-rich plasma into skin flaps modulate proangiogenic gene expression and improve survival rates. *Plast Reconstr Surg*. 2012, 129(4):858-66.
- 9) Uchida A, Sasaguri H, Kimura N, Tajiri M, Ohkubo T, Ono F, Sakaue F, Kanai K, Hirai T, Sano T, Shibuya K, Kobayashi M, Yamamoto M, Yokota S, Kubodera T, Tomori M, Sakaki K, Enomoto M, Hirai Y, Kumagai J, Yasutomi Y, Mochizuki H, Kuwabara S, Uchihara T, Mizusawa H, Yokota T. Non-human primate model of amyotrophic lateral sclerosis with cytoplasmic mislocalization of TDP-43. *Brain*. 2012, 135:833-46.

Clean Room, University Hospital, Faculty of Dentistry

1. Staffs and Students (April, 2012)

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. Tomoatsu Kaneko, Uraivan Chokuchanachaisakul, Jun Kawamura, Yusuke Yamanaka, Takafumi Ito, Mitsuhiro Sunakawa, Hideaki Suda, Takashi Okiji: Upregulation of p38 mitogen-activated protein kinase during pulp injury-induced glial cell/neuronal interaction in the rat thalamus. *J. of Endod.* (Accepted 2012. 11.07)

[Meeting]

1. Uraivan Chokuchanachaiakul, Tomoatsu Kaneko, Yusuke Yamanaka, Mitsuhiro Sunakawa, Takashi Okiji and Hideaki Suda: Immuno-laser capture microdissection analysis of dental pulp macrophages in a whole-tooth culture model. The 14th International Congress of Histochemistry and Cytochemistry (ICHO 2012), Kyoto, 2012.8.28-29
2. Uraivan Chokuchanachaisakul, Tomoatsu Kaneko, Yusuke Yamanaka, Reika Kaneko, Mitsuhiro Sunakawa, Takashi Okiji and Hideaki Suda: Expression of p38 MAP kinase family in the rat central nervous system is regulated by signals from the tooth pulp. The 136th JSCD Annual Meeting, Okinawa, 2012.6.28-29
3. Jun Kawamura, Tomoatsu Kaneko, Uraivan Chokuchanachaisakul, Yusuke Yamanaka, Takashi Ito, Mitsuhiro Sunakawa, Takashi Okiji, Hideaki Suda: p38 MAPK-upregulation/activation during pulp injury-related glial-neuronal interaction in rat thalamus. The 60th JADR Annual Meeting, 2012.12.15 Niigata Convention Center.

Center for Development of Devices and Drugs in Dentistry

1. Staffs (April, 2012)

Director	Junji TAGAMI	
Co-Director	Hidekazu TAKAHASHI,	Hideki HARASAWA,
	Naoko HARADA	
Member	Miwako WAGAI (CRC),	Emiko NAGAE (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, 2012).

The 152 consultation services concerning dental devices were performed in 2012.

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 Mitsuihiro ENOMOTO

Chief of Athletic Rehabilitation Junya AIZAWA

Researcher 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 trial 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) Yagishita K, Muneta T, Ju YJ, Morito T, Yamazaki J, Sekiya I. High-flex posterior cruciate-retaining vs posterior cruciate-substituting designs in simultaneous bilateral total knee arthroplasty. A prospective randomized study. *J Arthroplasty*. 2012, 27(3):368-74.
- 2) Nakajima K, Takeda T, Kurokawa K, Hasegawa K, Narimatsu K, Kajima T, Sato T, Shimada A, Kondo Y, Ishigami K : Influence of mouthguard on single-tooth root distortion. *Int J Sports Dent* 2012, 5:7-12.
- 3) Mishima O, Amemiya A, Kurokawa K, Nakajima K, Takeda T, Ishigami K : Effect of clenching and pinching force on activation on cortex involved in motor brain activity: an fMRI study. *Int J Sports Dent* 2012, 5:35-43.
- 4) Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. Surgical management of grade 3 medial knee injuries combined with cruciate ligament injuries. *Knee Surg Sports Traumatol Arthrosc*. 2012, 20(1):88-94.
- 5) Koga H, Muneta T, Yagishita K, Ju YJ, Sekiya I. The effects of graft fixation angles on anteroposterior and rotational knee laxity in double-bundle anterior cruciate ligament reconstruction: Evaluation using computerized navigation. *Am J Sports Med*, 2012, 40(3):615-23.
- 6) Li W, Enomoto M, Ukegawa M, Hirai T, Sotome S, Wakabayashi Y, Shinomiya K, Okawa A. Subcutaneous injections of platelet-rich plasma into skin flaps modulate proangiogenic gene expression and improve survival rates. *Plast Reconstr Surg*. 2012, 129(4):858-66.
- 7) Uchida A, Sasaguri H, Kimura N, Tajiri M, Ohkubo T, Ono F, Sakaue F, Kanai K, Hirai T, Sano T, Shibuya K, Kobayashi M, Yamamoto M, Yokota S, Kubodera T, Tomori M, Sakaki K, Enomoto M, Hirai Y, Kumagai J, Yasutomi Y, Mochizuki H, Kuwabara S, Uchihara T, Mizusawa H, Yokota T. Non-human primate model of amyotrophic lateral sclerosis with cytoplasmic mislocalization of TDP-43. *Brain*. 2012, 135:833-46.

Lifetime Oral Health Care Science

1. Staffs and Students (April, 2012)

Professor Shinichi ARAKAWA (July~)
Junior Associate Professor Keiko KONDO (April~)

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. Hayakumo S, Arakawa S, Mano Y, Izumi Y. 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.* 2012. (DOI: 10.1007/s 00784-012-0711-7).

Oral Care for Systemic Health Support

1. Staffs and Student(April,2012)

Professor Hidemi YOSHIMASU

Junior Associate Professor Mitsue ONODERA

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

- 1) YOSHIMASU,H., SATO, Y., MISHIMAGI, T., NEGISHI: Postoperative evaluation of the folded pharyngeal flap operation for cleft palate patients with velopharyngeal insufficiency. Balaji, S.M. ed.: Management of cleft and craniofacial deformities - current techniques, research and future directions, Transactions of The 7th Congress of the International Cleft Palate Foundation,7-11 June, 2012, Seychelles, p336-340.

Preventive Oral Health Care Science

1. Staffs and Students (2012)

Professor	Kayoko SHINADA	
Associate Professor	Keiko ENDO	
Assistant Professor	Hiromi OTSUKA	
Part-time Lecturer	Yuki OHARA,	Chizuru TAZAWA,
	Akie KOUNO,	Miyuki YAMASAKI,
	Masako OKADA,	Noriko IIDA,
	Masayo YASUDA	
Graduate Students Master Course	Yuka SHIZUMA,	Ayako KUBOTA

2. Purpose of Education

In order to cultivate students' abilities to prevent and detect oral diseases at an early stage, which are important to maintain and improve the nation's health, we help students acquire deep academic knowledge and high standard skills in preventive oral health care such as skills to check over the condition of oral cavities. Additionally, we help students develop skills to provide oral health counseling and oral health promotion, and nurture human resources who can actively contribute the development of oral health promotion.

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. Pham TA, Ueno M, Shinada K, Kawaguchi Y : Factors affecting oral malodor in periodontitis and gingivitis patients. *J Investig Clin Dent* 3: 284-290, 2012.
2. Mori C, Hakuta C, Endo K, Nariai T, Ueno M, Shinada K, Kawaguchi Y. : The effects of professional oral health care on patients in the subacute stage of emergent neurosurgical disorders. *Spec Care Dentist* 32: 259-264, 2012.
3. Pham TA, Ueno M, Shinada K, Kawaguchi Y : Comparison between self-perceived and clinical oral malodor. *Oral Surg Oral Med Oral Pathol Oral Radiol* 113:70-80, 2012.
4. Takeuchi S, Ueno M, Takehara S, Pham TA, Hakuta C, Morishima S, Shinada K, Kawaguchi Y : The relationship between turbidity of mouth-rinsed water and oral health status. *J Investig Clin Dent* 3: 23-29, 2012.
5. Ohnuki M, Shinada K, Ueno M, Zaitzu T, Wright FA, Kawaguchi Y : Exploring taste hyposensitivity in Japanese senior high school students. *Acta Odontol Scand* 70: 426-431, 2012.
6. Ueno M, Shinada K, Zaitzu T, Yokoyama S, Kawaguchi Y : Effects of an oral health education program targeting oral malodor prevention in Japanese senior high school students. *Acta Odontol Scand* 70: 426-431, 2012.

Oral Health Care Science for Community and Welfare

1. Staffs and Student

Professor	Chiyoko Hakuta (April,2012)
Junior Associate Professor	Keiko Endo (July, 2012)
Student	Rena Nakayama (April,2012)

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, 2012)

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. Staff.

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.
- 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. Spatial relationships between the morphologies and innervations of the scalene and anterior vertebral muscles. *Annals of Anatomy* 194: 381- 388, 2012.
2. Himeno-Ando A, Izumi Y, Yamaguchi A, Iimura T. Structural differences in the osteocyte network between the calvaria and long bone revealed by three-dimensional fluorescence morphometry, possibly reflecting distinct mechano-adaptations and sensitivities. *Biochem Bioph Res Co* 417: 765-770, 2012
3. Sakamoto K, Fujii T, Kawachi H, Miki Y, Omura K, Morita K, Kayamori K, Khanom R, Katsube K, Yamaguchi A. Reduction of NOTCH1 expression pertains to maturation abnormalities of keratinocytes in squamous neoplasms. *Lob Invest* 92: 688-702, 2012
4. Khanom R, Sakamoto K, Pal SK, Shimada Y, Morita K-i, Omura K, Miki Y, Yamaguchi A. Expression of basal cell keratin 15 and keratin 19 in oral squamous cell carcinoma represent diverse pathophysiologicals. *Histol Histopathol* 27: 949-959, 2012
5. Aizawa R, Yamada A, Suzuki D, Iimura T, Kassai H, Harada T, Tsukasaki M, Yamamoto G, Tachikawa T, Nakao K, Yamamoto M, Yamaguchi A, Aiba A, Kamiyo R. Cdc42 is required for chondrogenesis and interdigital programmed cell death during limb development. *Mech Dev* 129: 38-50, 2012
6. Michikawa C, Uzawa N, Kayamori K, Sonoda I, Ohya Y, Okada N, Yamaguchi A, Amagasa T. Clinical significance of lymphatic and blood vessel invasion in oral tongue squamous cell carcinomas. *Oral Oncol* 48: 320-324, 2012
7. Umehara K, Iimura T, Sakamoto K, Lin Z, Kasugai S, Igarashi Y, Yamaguchi A. Canine oral mucosal fibroblasts differentiate into osteoblastic cells in response to BMP-2. *Anat Rec* 295: 1327-1335, 2012
8. Watanabe T, Tamamura Y, Hoshino A, Makino Y, Nishimura R, Kamioka H, Yoneda T, Amagasa T, Yamaguchi A, Iimura T. Increasing participation of Sclerostin in postnatal bone development revealed by three-dimensional immunofluorescence morphometry. *BONE* 51: 447-458, 2012
9. Sakamoto K, Khanom R, Hamagaki M, Yamaguchi A. Ectopic production of hair keratin constitutes Rushton's hyaline bodies in association with hematogenous deposits. *J Oral Pathol Med* 27: 949-959, 2012
10. Oue E, Lee JW, Sakamoto K, Iimura T, Aoki K, Kayamori K, Miki Y, Yamashiro M, Yamaguchi A. CXCL2 synthesized by oral squamous cell carcinoma is involved in cancer-associated bone destruction. *Biochem Bioph Res Co* 424: 456-461, 2012

11. Nishimura R, Wakabayashi M, Hata K, Matsubara T, Honma H, Wakisaka S, Kiyonari H, Shioi G, Yamaguchi A, Tsumaki N, Akiyama H, Yoneda T. Osterix regulates calcification and degradation of chondrogenic matrices through matrix metalloproteinase (MMP13) expression in association with transcription factor Runx2 during endochondral ossification. *J Biol Chem* 287: 33179-33190, 2012
12. 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* 258: 28826-28837, 2012
13. 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 1alpha, 25(OH)2D3 and FGF23. *J Nutr Biochem*. 24: 1000-1007, 2013

Review Articles

1. Iimura T, Nakane A, Sugiyama M, Sato H, Makino Y, Watanabe T, Takagi Y, Numano R, Yamaguchi A. A fluorescence spotlight on the clockwork development and metabolism of bone. *J Bone Miner Metab*. 30: 254-269, 2012

5. International meetings

1. Yamaguchi A. Bone destruction by oral cancer, The 6th Global COE international Symposium at TMDU, Tokyo, Japan, Jan. 22, 2012.
2. Sakamoto Y. Spatial relations among the muscles at the boundary region between the oral cavity and the pharynx. *Clinical Anatomy* 25: 950, 2012. Abstract book of 29th annual meeting: AACA, 101, 2012. The 29th annual meeting American Association of Clinical Anatomists, St. George' s, Grenada, July 8-13, 2012.

6. Invited Lectures

1. Yamaguchi A. Bisphosphonate-related osteonecrosis, updates. 2012 Sino-Japan Dental Conference, Chengdu, Sichuan, China, April 27, 2012.

Basic Oral Health Science

1. Staffs and Students

Professor

Kumiko Sugimoto

2. Purpose of Education

Basic oral health 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 Basic oral health 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) Objective assessment of internal stress during dental treatment by analysis of autonomic nervous activities

4. Publications

Original Articles

1. Uehara N, Takagi Y, Miwa Z, Sugimoto K: Objective assessment of internal stress in children during dental treatment by analysis of autonomic nervous activity. *Internatl J Paediatric Dent* 22(6): 331-341, 2012.
2. Tsuchihashi N, Uehara N, Takagi Y, Miwa Z, Sugimoto K: Internal stress in children and parental attitude to dental treatment with passive restraint. *Pediatric Dent J* 22(2): 170-177, 2012.

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 will 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 will provide 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

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.

Clinical Oral 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. Tano E, Otsuki M, Kato J, Sadr A, Ikeda M, Tagami J. Effects of 405 nm diode laser on titanium oxide bleaching activation. *Photomed Laser Surg.* 30(11), 648-54, 2012.
2. Yahagi C, Takagaki T, Sadr A, Ikeda M, Nikaido T, Tagami J. Effect of lining with a flowable composite on internal adaptation of direct composite restorations using all-in-one adhesive systems. *Dent Mater J.* 31(3), 481-8, 2012.
3. Kitasako Y, Sadr A, Hamba H, Ikeda M, Tagami J. Gum containing calcium fluoride reinforces enamel subsurface lesions in situ. *J Dent Res.* 91(4), 370-5, 2012.
4. Nurrohman H, Nikaido T, Takagaki T, Sadr A, Waidyasekera K, Kitayama S, Ikeda M, Tagami J. Dentin bonding performance and ability of four MMA-based adhesive resins to prevent demineralization along the hybrid layer. *J Adhes Dent.* 14(4), 339-48, 2012.

Oral Health Information Technology

1. Staffs and Students

Lecturer

Haruo OKAYASU

2. Purpose of Education

Oral Health Information Technology educates the present conditions of dentistry, the basic manner as the medical person, and a necessary technique as an expert. This section brings up professionals involved in the maintenance and promotion of people's health.

3. Research Subjects

- 1) The role of the dental technician during large-scale disasters

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. Kumagai N, Komada W, Fukui Y, Okada D, Takahashi H, Yoshida K, Miura H. Influence of the flexural modulus of prefabricated and experimental posts on the fracture strength and failure mode of composite resin cores. *Dent Mater J* 2012; 31(1): 202-206
2. Koottathape N, Takahashi H, Finger WJ, Kanehira M, Iwasaki N, Aoyagi Y. Quantification of in vitro produced wear sites on composite resins using contact profilometry and CCD microscopy: A methodological investigation. *J Med & Dent Sci* 2012; 59: 53-56.
3. Chaijareenont P, Takahashi H, Nishiyama N, Arksornnukit M. Effects of silane coupling agents and solutions of different polarity on PMMA bonding to alumina. *Dent Mater J* 2012; 30(4): 610-616.
4. Chaijareenont P, Takahashi H, Nishiyama N, Arksornnukit M. Effect of different amounts of 3-methacryloxypropyltrimethoxysilane on the flexural properties and wear resistance of alumina reinforced PMMA. *Dent Mater J* 2012; 30(4): 623-628.
5. Koottathape N, Takahashi H, Iwasaki N, Kanehira M, Finger WJ. Morphological features of composite resin surfaces after two- and three-body wear simulation. *World J Dent* 2012; 3(3): 221-228.
6. Koottathape N, Takahashi H, Iwasaki N, Kanehira M, Finger WJ. Two- and three-body wear of composite resins. *Dent Mater* 2012; 28(12): 1261-1270.

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, 2012)

Professor	Tetsuya SUZUKI
Research Associate	Kouichi HUKAWA

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. Furuya J, Nakamura S, Ono T, Suzuki T. Tongue pressure production while swallowing water and pudding and during dry swallow using a sensor sheet system. J Oral Rehabil 39:684-691, 2012.
2. Furuya J, Tamada Y, Suzuki T. Effect of mandibular position on three-dimensional shape of the oropharynx in seated posture. J Oral Rehabil 39:277-284, 2012.