筑波大学
University of Tsukuba

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筑波大学
University of Tsukuba

1. Department of Hematology

Principal Investigator: Shigeru Chiba
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Other Faculty Members
Assistant Professor: Naoshi Obara
Assistant Professor: Mamiko Sakata-Yanagimoto

Major Scientific Interests

We are focusing on molecular mechanisms underlying normal and abnormal hematopoiesis, with particular interests in genetic and epigenetic abnormalities in hematologic malignancies and stromal cell abnormalities in the bone marrow failure syndromes.

Projects for Regular Students in Doctoral or Master's Programs

- Role of Tet2 in normal hematopoiesis and hematologic malignancies
- Identification of stromal cells involved in the bone marrow failure syndromes including
  myelodyspoastic syndrome

Programs for Short Stay Students (one week ~ one trimester)

- Learn procedures for analyzing progenitor cells from mouse bone marrow by flowcytometry
- Learn blood cell transplantation in mouse model

Recent Publications

1) Yoshida K, Sanada M, et al., Obara N, Sakata-Yanagimoto M, et al., **Chiba S**, Nakauchi H, Miyano S, Ogawa S. Frequent pathway mutations of splicing machinery in myelodysplasia. ***Nature*** 478:64-69, 2011

2) Sakata-Yanagimoto M, Sakai T, Miyake Y, Saito TI, et al., Yasutomo K, **Chiba S**. Notch2 signaling is required for proper mast cell distribution and mucosal immunity in the intestine. ***Blood*** 117;128-134, 2011

3) Nakahara F, Sakata-Yanagimoto M, et al., **Chiba S**. Hes1 immortalizes committed progenitors and plays a role in blast crisis transition in chronic myelogenous leukemia. ***Blood*** 115:2872-2881, 2010

4) Sanada M, et al., Sakata-Yanagimoto M, et al., **Chiba S**, et al., Ogawa S. Gain-of-function of mutated c-Cbl tumor suppressor associated with myeloid neoplasms having 11q UPD. ***Nature*** 460:904-908, 2009

4) Yokoyama Y, Suzuki T, Sakata-Yanagimoto M, et al., **Chiba S**. Derivation of functional mature neutrophils from human embryonic stem cells. ***Blood*** 113:6584-6592, 2009

5) Kato M, Sanada M, et al., **Chiba S**, et al., Ogawa S. Frequent inactivation of A20 in B-cell lymphomas. ***Nature*** 459:712-716, 2009

6) Sakata-Yanagimoto M, Nakagami-Yamaguchi E, Saito T, Kumano K, Yasutomo K, Ogawa S, Kurokawa M, **Chiba S**. Coordinated regulation of transcription factors through Notch2 is an important mediator of mast cell fate. ***Proc Natl Acad Sci USA*** 105:7839–7844, 2008

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2. Gene Regulation

Principal Investigator: Koji Hisatake
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Major Scientific Interests of the Group

Our group studies the regulation of eukaryotic gene expression, focusing on how transcription regulates cell differentiation. In particular, we are studying the roles of transcription factors and epigenetic changes in regulating iPS cell induction and adipocyte differentiation.

Projects for Regular Students in Doctoral or Master's Programs

1) Mechanistic analyses of the roles for Oct4, Sox2, Klf4 and c-myc during iPS cell induction.
2) Analyses of epigenetic mechanisms of iPS cell induction.
3) Identification and functional analyses of transcription factors involved in adipocyte commitment.
4) Role of non-coding RNA in epigenetic regulation during adipocyte differentiation.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Analysis of transcriptional regulation during white and brown adipocyte differentiation.
2) Induction of iPS cells using a Sendai virus-based vector.

Recent Publications

1) Shimada M, Nakadai T, Fukuda A, **Hisatake K**. cAMP-response element-binding protein (CREB) controls MSK1-mediated phosphorylation of histone H3 at the c-fos promoter in vitro. **J. Biol. Chem.** 285, 9390-9401, 2010
2) Chen Y, Yamaguchi Y, Tsugeno Y, Yamamoto J, Yamada T, Nakamura M, **Hisatake K**, Handa H. DSIF, the Paf1 complex, and Tat-SF1 have nonredundant, cooperative roles in RNA polymerase II elongation. **Genes Dev.** 23, 2765-2777, 2009.
3) Fukuda A, Nakadai T, Shimada M, **Hisatake K**. Heterogeneous nuclear ribonucleoprotein R enhances transcription from the naturally configured c-fos promoter in vitro. **J. Biol. Chem.** 284, 23472-23480, 2009.
4) Yamagata K, Daitoku H, Takahashi Y, Namiki K, **Hisatake K**, Kako K, Mukai H, Kasuya Y, Fukamizu A. Arginine methylation of FOXO transcription factors inhibits their phosphorylation by Akt. **Mol. Cell** 32, 221-231, 2008.
5) Fukuda A, Nakadai T, Shimada M, Tsukui T, Matsumoto M, Nogi Y, Meisterernst M, **Hisatake K**. Transcriptional coactivator PC4 stimulates promoter escape and facilitates transcriptional synergy by GAL4-VP16. **Mol. Cell. Biol.** 24, 6525-6535, 2004.

3. Molecular Parasitology

Investigators: Kiong Ho
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Major Scientific Interests of the Group

Our primary research interest is to understand the gene expression of eukaryotic parasites with a goal in identifying parasite-specific processes that can be exploited as targets for novel therapeutic interventions. We have focused on how messenger RNA acquire 5' cap in the protozoan parasites that responsible for malaria and sleeping sickness. The structure and mechanism of protozoan capping enzyme is completely different from human host, and thus, capping is an attractive target for anti-protozoal drug discovery. We are also investigating the mechanism of RNA repair and recombination. RNA ligase is the key enzyme that joins the broken RNAs together. We are characterized three separate types of RNA ligases from various species and our immediate goal is to define how these ligases recognize the breaks in the RNA and to identify what types of RNA are repaired in the cell.

Projects for Graduate Students

1) Dissecting the mechanism of hypermethylated cap 4 synthesis in *Trypanosome brucei*.
2) Characterization of *T.brucei* capping enzyme complex with transcription and RNA processing factors.
3) Defining the physiological targets for RNA ligase through genome wide screening.

Study Programs for Short Stay Students

1) Screening of small molecule inhibitor against malaria and sleeping sickness.
2) Biochemical characterization of novel RNA capping activities.
3) Defining the optimal RNA substrates for RNA ligase.

Selected Publications

Torchea C, Takagi Y and Ho CK. Archaea RNA Ligase is a Homodimeric Protein that Catalyzes Intramolecular Ligation of Single-Stranded RNA and DNA. ***Nucleic Acid Res.*** 2008; 36: 6218 - 6227.

Takagi Y, Sindkar S, Ekonomidis D, Hall MP and Ho CK. *Trypanosoma brucei* Encodes a Bifunctional Capping Enzyme Essential for Cap 4 Formation on the Spliced Leader RNA. ***J. Biol. Chem***. 2007; 282: 15995-16005.

Hall MP and Ho CK. Functional Characterization of a 48-kDa *Trypanosoma brucei* Cap 2 RNA Methyltransferase. ***Nucleic Acid Res.*** 2006 34: 5594 - 5602.

Pfeffer S, Sewer A, Lagos-Quintana M, Sheridan R, Sander C, Grässer FA, van Dyk LF, Shuman S, Ho CK, Chien M, Russo JJ, Ju J, Randall G, Lindenbach BD, Rice CM, Simon V, Ho DD, Zavolan M, and Tuschl T. Identification of the MicroRNAs of the Herpesvirus Family. ***Nature Method*** 2005; 2: 269-276.

Ho CK, Wang LK, Lima CD and Shuman S. Structure and Mechanism of RNA Ligase. ***Structure*** 2004;12: 327-339.

Chiu YL, Ho CK, Saha N, Schwer B, Shuman S, and Rana TM. Tat Stimulates Cotranscriptional Capping of HIV-1 mRNA. ***Molecular Cell*** 2002; 10: 585-597.

Ho CK and Shuman S. A Yeast-like mRNA Capping Apparatus in *Plasmodium falciparum*. ***Proc. Natl. Acad. Sci. USA*** 2001; 98: 3050-3055

Ho CK and Shuman S. Distinct Roles for CTD Ser2 and Ser5 Phosphorylation in the Recruitment and Allosteric Activation of Mammalian mRNA Capping Enzyme. ***Molecular Cell*** 1999; 3: 405-411.

4. Global Public Health

Principle Investigator: Masao Ichikawa
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Major Scientific Interests of the Group

"The existing gross inequality in the health status of the people, particularly between developed and developing countries as well as within countries, is politically, socially, and economically unacceptable and is, therefore, of common concern to all countries." (The Declaration of Alma-Ata, September 1978) With this statement in mind, we have conducted action-oriented researches into global public health problems among socially disadvantaged and vulnerable population. We know that making change happen is difficult but possible through scientifically sound research. Our research interests fall in various aspects of injury prevention and control in Asian countries. To date, we have conducted injury researches in Japan, Thailand, Laos, Cambodia, Vietnam, Nepal and Sri Lanka in cooperation with local researchers.

Projects for Regular Students in Doctoral or Master's Programs

- Safe and active transport and outdoor physical activity in rapidly motorized Asian cities
- Intimate partner violence during pregnancy and its health outcomes in Laos
- Injury surveillance system development and trauma care training in Asian countries
- A cohort study on mobility and health among older drivers in Japan

Study Program for Short Stay Students

Secondary data analysis using Epi Info™ 7of publicly available epidemiological data to develop health policy recommendations

Pre-requisite: Basic understanding of epidemiological and statistical principles

Recent Publications

1. Nakahara S, Matsuoka T, Ueno M, Mizushima Y, Ichikawa M, Yokota J. Triage protocol modifications to reduce undertriage. ***J Trauma*** 2011;71:267-268.
2. Nakahara S, Ichikawa M. Effects of high-profile collisions on drink-driving penalties and alcohol-related crashes in Japan. ***Injury Prevention*** 2011;17:182-188.
3. Nakahara S, Ichikawa M, Kimura A. Population strategies and high-risk individual strategies for road safety in Japan. ***Health Policy*** 2011;100:247-255.
4. Nakahara S, Ichikawa M, Kimura A. Simplified alternative to the TRISS method for resource-constrained settings. ***World Journal of Surgery*** 2011;35:512-519.

5. Molecular Cell Biology

Principal Investigator: Kenji Irie
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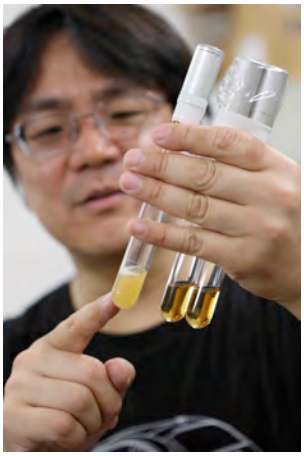

Other Faculty Members
Assistant Professor Tomoaki Mizuno: mizuno@md.tsukuba.ac.jp

Major Scientific Interests of the Group

Post-transcriptional regulation of gene expression by RNA-binding proteins
Molecular mechanism of mRNA localization and local translation regulating cell polarity, asymmetric cell division, and cell-fate
Regulation of myogenic differentiation by RNA-binding protein

Projects for Regular Students in Doctoral or Master's Programs

1) Stability control of MTL1 mRNA by the RNA-binding protein Khd1 in yeast
2) Post-transcriptional regulation of gene expression by Khd1, Ccr4, and Pbp1
3) Stau1 negatively regulates myogenic differentiation in C2C12 cells.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Yeast genetic approaches including the isolation and characterization of mutants, tetrad analysis, complementation, and mitotic recombination.
2) Molecular genetic techniques including yeast transformation, gene knockout, and generation of mutations in cloned genes.
3) Imaging yeast cells using indirect immunofluorescence and GFP-protein fusions.
4) Yeast two-hybrid screening

Recent Publications

1) Pbp1 is involved in the Ccr4 and Khd1-mediated regulation of cell growth through the association with ribosomal proteins, Rpl12a and Rpl12b. Kimura Y, Irie K, Irie K. Eukaryot Cell. 2013 in press.
2) Stau1 regulates Dvl2 expression during myoblast differentiation. Yamaguchi Y, Naiki T, Irie K. Biochem Biophys Res Commun. 2012 Jan 6;417(1):427-32.
3) RNA-binding protein Khd1 and Ccr4 deadenylase play overlapping roles in the cell wall integrity pathway in Saccharomyces cerevisiae. Ito W, Li X, Irie K, Mizuno T, Irie K. Eukaryot Cell. 2011 Oct;10(10):1340-7.
4) Stability control of MTL1 mRNA by the RNA-binding protein Khd1p in yeast. Mauchi N, Ohtake Y, Irie K. Cell Struct Funct. 2010;35(2):95-105.
5) hnRNP K interacts with RNA binding motif protein 42 and functions in the maintenance of cellular ATP level during stress conditions. Fukuda T, Naiki T, Saito M, Irie K. Genes Cells. 2009 Feb;14(2):113-28.
6) Distinct roles for Khd1p in the localization and expression of bud-localized mRNAs in yeast. Hasegawa Y, Irie K, Gerber AP. RNA. 2008 Nov;14(11):2333-47.
7) Stau1 negatively regulates myogenic differentiation in C2C12 cells. Yamaguchi Y, Oohinata R, Naiki T, Irie K. Genes Cells. 2008 Jun;13(6):583-92.

6. Physiological Chemistry

Principal Investigator: Yasunori Kanaho
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biochem/kanaholab/index.html

Other Faculty Members
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Assistant Professor Tsunaki Hongu: thongu@md.tsukuba.ac.jp

Major Scientific Interests of the Group

Studies on regulatory mechanisms and physiological functions of cell signaling systems, especially through the phospholipid-metabolizing enzymes and the small G protein Arf6.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanisms through which the small G protein Arf6 regulates each isozyme of the lipid kinase PIP5K.
2) Physiological functions of the phospholipid-metabolizing enzymes, PIP5K and PLD, and of their regulatory protein Arf6 at cellular and whole animal levels.
3) Human diseases caused by the disruption of the signaling systems through the lipid-metabolizing enzymes and the small G protein Arf6.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Enzyme assay, immunohistochemistry, and immunofluorescent staining of signaling molecules
2) Assays for cell functions such as cell proliferation, cell motility, focal adhesion, secretion, endocytosis, exocytosis, etc.

Recent Publications

1) Unoki T., Matsuda S., Kakegawa W., Van TBN., Kohda K., Suzuki A., Funakoshi Y., Hasegawa H., Yuzaki M., and Kanaho Y. NMDA receptor-mediated PIP5K activation to produce PI(4,5)P2 is essential for AMPA receptor endocytosis during LTD. *Neuron* **73**, 135-148 (2012)
2) Nakano-Kobayashi A., Yamazaki M., Unoki T., Hongu T., Murata C., Taguchi R., Katada T., Frohman M.A., Yokozeki T. and **Kanaho Y**. Role of activation of PIP5Kg661 by AP-2 complex in synaptic vesicle endocytosis. **EMBO J.** 26, 1105-1116 (2007)
3) Suzuki T., Kanai Y., Hara T., Sasaki J., Sasaki T., Kohara M., Maehama T., Taya C., Shitara H., Yonekawa H., Frohaman M.A., Yokozeki T. and **Kanaho Y**. Crucial role of the small GTPase ARF6 in hepatic cord formation during liver development. **Mol. Cell. Biol.** 26, 6149-6156 (2006)
4) Honda A., Nogami M., Yokozeki T., Yamazaki M., Nakamura H., Watanabe H., Kawamoto K., Nakayama K., Morris A.J., Frohman M.A., and **Kanaho Y**. Phosphatidylinositol 4-phosphate 5-kinase a is a downstream effector of the small G protein ARF6 in membrane ruffle formation. **Cell** 99,521-532 (1999)

7. Experimental Pathology

Principal Investigator: Mitsuyasu Kato
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Other Faculty Members
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Assistant Professor Yukihide Watanabe: y-watanabe@md.tsukuba.ac.jp

Major Scientific Interests of the Group

Experimental studies, using murine models and cultured cells, for elucidation of the roles of transforming growth factor-β related molecules in stem cell biology, tissue formation and carcinogenesis. Our aim is to establish novel molecular targeting therapies useful for the prevention of cancer.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanisms of TGF-β related molecules (TMEPAI, MafK etc.) in colonic stem cells maintenance and carcinogenesis using gene-manipulated mice and three dimensional histopathological analysis.
2) Molecular mechanisms of TGF-β related molecules (THG1 etc.) in squamous cell carcinoma formation

Study Programs for Short Stay Students (one week ~ one trimester)

1) Pathological tissue preparation, Immunohistochemistry and 3D reconstruction
2) In vitro tumorigenic assays (cell proliferation, sphere forming assay, scratch assay, matrigel invasion assay, 3D culture invasion assay etc.)

Recent Publications

1) Itoh F, Itoh S, Adachi T, Ichikawa K, Matsumura Y, Takagi T, Festing M, Watanabe T, Weinstein M, Karlsson S, and **Kato M**. Smad2/Smad3 in endothelium is indispensable for vascular stability via S1PR1 and N-cadherin expressions. **Blood** 119: 5320-5328, 2012
2) Watanabe Y, Itoh S, Goto T, Ohnishi E, Inamitsu M, Itoh F, Satoh K, Wiercinska E, Yang W, Shi L, Tanaka A, Nakano N, Mommaas AM, Shibuya H, ten Dijke P and **Kato M**. TMEPAI, a transmembrane TGF-β-inducible protein, sequesters Smad proteins from active participation in TGF-b signaling. **Mol. Cell** 37: 123-134, 2010.
3) Nakano N, Itoh S, Watanabe Y, Maeyama K, Itoh F, and **Kato M**. Requirement of TCF7L2 for TGF-β-dependent transcriptional activation of the TMEPAI gene. **J Biol Chem**. 285: 38023-38033, 2010.
4) Tanaka A, Itoh F, Takezawa T, Itoh S and **Kato M**. bHLH Protein E2-2 inhibits VEGFR2 expression and blocks endothelial cell activation. **Blood**, 115: 4138-4147, 2010.
5) Shi L, Itoh F, Itoh S, Takahashi S, Yamamoto M and **Kato M**. Ephrin-A1 promotes the malignant progression of intestinal tumors in $Apc^{min/+}$ mice. **Oncogene** 27(23): 3265-3273, 2008.

8. Environmental Medicine

Principal Investigator: Yoshito Kumagai
E-mail address: yk-em-tu@md.tsukuba.ac.jp
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Other Faculty Members
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Major Scientific Interests of the Group

This laboratory addresses the mechanisms by which chemicals causing oxidative stress and environmental electrophiles such as polycyclic aromatic hydrocarbon quinones, methylmercury and arsenic affect living systems by interacting with sensor proteins with reactive thiols (thiolate ions) through chemical modification. The observations obtained by this group regarding environmental electrophiles have lent new insight into mechanisms of redox-dependent cell signalings such as cell servival, cell proliferation and cell damage.

Projects for Regular Students in Doctoral or Master's Programs

1) Activation of electrophilic signal transduction pathways (e.g., PTP1B/EGFR-, Keap1/Nrf2-, HSP/HSF-1-signalings) during exposure to environmental electrophiles such as 1,2-naphthoquinone and methylmercury.

2) Search for cellular systems regulating sensor proteins covalently modified by the environmental electrophiles.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Detection of cellular proteins modified by environmental electrophiles by Western blot analysis with specific antibodies against the electrophiles.

2) Proteomics analysis by using 2D-SDS/PAGE and MALDI-TOF/MS.

Recent Publications

1) Nishida M, Sawa T, Kitajima N, Ono K, Inoue H, Ihara H, Motohashi H, Yamamoto M, Suematsu M, Kurose H, Van der Vliet A, Freeman BA, Shibata T, Uchida K, **Kumagai Y**, Akaike T. Hydrogen sulfide anion regulates redox signaling via electrophile sulfhydration. **Nature Chem Biol** 2012, in press.

2) **Kumagai Y**, Shinkai Y, Miura T, Cho AK. The chemical biology of naphthoquinones and its environmental implications. **Annu Rev Pharmacol Toxicol** 52: 221-247, 2012.

3) Toyama T, Shinkai Y, Yasutake A, Uchida K, Yamamoto M, **Kumagai Y**. Isothiocyanates reduce mercury accumulation via an Nrf2-dependent mechanism during exposure of mice to methylmercury. **Environ Health Perspect 119**: 1117-1121, 2011.

4) Yoshida E, Toyama T, Shinkai Y, Sawa T, Akaike T, **Kumagai Y**. Detoxification of methylmercury by hydrogen sulfide producing enzyme in mammalian Cells. **Chem Res Toxicol** 24: 1633-1635, 2011.

5) Iwamoto N, Sumi D, Ishii T, Uchida K, Cho AK, Froines JR, **Kumagai Y**. Chemical knockdown of protein tyrosine phosphatase 1B by 1,2-naphthoquinone through covalent modification causes persistent transactivation of epidermal growth factor receptor. **J Biol. Chem.** 282: 33396-33404, 2007.

9. Molecular Neurobiology

Principal Investigator: Masayuki Masu
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Other Faculty Members
Lecturer: Kensuke Shiomi: kshiomi@md.tsukuba.ac.jp
Lecturer: Kazuko Keino-Masu: kazumasu@md.tsukuba.ac.jp
Assistant Professor: Takuya Okada: okada.takuya.gw@u.tsukuba.ac.jp

Major Scientific Interests of the Group

Our main research focus is to study the molecular mechanisms that regulate the neural circuit formation and higher brain functions. Using integrative approaches including molecular biology, biochemistry, pharmacology, developmental biology, and neuroanatomy, we have been investigating how complex networks are formed in the developing brain and how the mature brain functions are acquired and regulated. We are particularly interested in the molecules that play a role in neural differentiation, cell migration, axon guidance, and synaptogenesis.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular study on neural differentiation
2) Molecular study on axon guidance
3) Molecular study on neural cell migration

Training Programs for Short Stay Students (one week ~ one trimester)

1) Immunohistochemistry, microscopy, and 3D imaging of neural network
2) In situ hybridization

Recent Publications

1) Nagamine S et al. Organ-Specific Sulfation Patterns of Heparan Sulfate Generated by Extracellular Sulfatases Sulf1 and Sulf2 in Mice. **J Biol Chem** 287: 9579-9590, 2012.
2) Koike S, Yutoh Y, Keino-Masu K, Noji S, **Masu M**, and Ohuchi H. Autotaxin is required for the cranial neural tube closure and establishment of the midbrain-hindbrain boundary during mouse development. **Dev Dyn** 240: 413-421, 2011.
3) Koike S, Keino-Masu K, Ohto T, Sugiyama F, Takahashi S, and **Masu M**. Autotaxin/lysophospholipase D-mediated LPA Signaling is Required to Form Distinctive Large Lysosomes in the Visceral Endoderm Cells of the Mouse Yolk Sac. **J Biol Chem** 284: 33561-33570, 2009.
4) Okada T, Keino-Masu K, and **Masu, M**. Migration and nucleogenesis of mouse precerebellar neurons visualized by *in utero* electroporation of a green fluorescent protein gene. **Neurosci Res** 57: 40-49, 2007.
5) Keino-Masu K, **Masu M**, et al. *Deleted in Colorectal Cancer* (*DCC*) Encodes a Netrin Receptor. **Cell** 87: 175-185, 1996.

10. Bacteriology, Molecular Biology

Investigators: Kazuya Morikawa
E-mail: morikawa.kazuya.ga@u.tsukuba.ac.jp
URL:
http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/microbiology/english.html

Major Scientific Interests of the Group

We study how pathogenic bacteria (especially, *Staphylococcus aureus*) cope with bactericidal factors form host and environment.

Study Programs for Short Stay Students

1) Basic techniques of bacteriology.
2) AFM analysis of DNA-protein interaction.

Academic Publications

1) Ryosuke L. Ohniwa, Kana Kitabayashi, and Kazuya Morikawa. Alternative cardiolipin synthase Cls1 compensates for stalled Cls2 function in *Staphylococcus aureus* under conditions of acute acid stress. **FEMS Microbiol Lett** 388, 141-146. 2012.
2) Kazuya Morikawa, Aya J Takemura, Yumiko Inose, Melody Tsai, Le Thuy Nguyen Thi, Toshiko Ohta, and Tarek Msadek. Expression of a cryptic secondary sigma factor gene unveils natural competence for DNA transformation in *Staphylococcus aureus*. **PLoS Pathogen** 8:e1003003. 2012.
3) Melody Tsai, Ryosuke L. Ohniwa, Yusuke Kato, Sayaka L. Takeshita, Toshiko Ohta, Shinji Saito, Hideo Hayashi, and Kazuya Morikawa. *Staphylococcus aureus* requires cardiolipin for survival under conditions of high salinity. **BMC Microbiol.** 11, 13. 2011.
4) Ryosuke L. Ohniwa, Yuri Ushijima, Shinji Saito, and Kazuya Morikawa Proteomic Analyses of Nucleoid-Associated Proteins in *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis,* and *Staphylococcus aureus*. **PLoS One** 6:e19172. 2011.
5) Kazuya Morikawa, Ryosuke L. Ohniwa, Toshiko Ohta, Yoshikazu Tanaka, Kunio Takeyasu, and Tarek Msadek. Adaptation beyond the Stress Response: Cell Structure Dynamics and Population Heterogeneity in *Staphylococcus aureus*. **Microb Environ** 25, 75-82. 2010. *Review*

11. Infection Biology

Principal Investigator: Atsushi KAWAGUCHI
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URL: http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/virology/index_english.html

Other Faculty Members:
Associate Professor; Mitsuru OKUWAKI
Assistant Professor; Shoko SAITO, Kohsuke KATO
(Nagata Special Lab.; Kyosuke NAGATA)

Major Scientific Interests of the Group:
The research aim of this group is to understand the molecular mechanism of replication and pathogenicity of animal viruses such as influenza viruses, measles virus, adenovirus, human cytomegalovirus, etc. The structure and function of virus-encoded factors and host cell-derived factors involved in the above processes are being studied at the atomic, molecular, cellular, and body levels. In addition, we are particularly interested in clarifying the physiological function of identified host factors such as chromatin regulators, molecular chaperones, etc. as well as their roles in infection.

Projects for Regular Students in Doctoral or Master's Programs:
1) Identification and characterization of novel factors in virus replication
2) Control of virus diseases based on the knowledge of host defense systems, or through development of novel anti-viral drugs
3) Regulatory mechanism for the structure and function of chromatin
4) Leukemogenic mechanism by chromosomal translocation

Study Programs for Short Stay Students (one week ~ one trimester):
1) Molecular mechanism of host factors involved in influenza virus replication
2) Action mechanism of an anti-virus drug
3) *Cell-free* reconstitution of a nucleus
4) Molecular function of a fusion gene product(s) in oncogenesis

Selected Recent Publications:

1) Kawaguchi A, Matsumoto K, Nagata K. YB-1 functions as a porter to lead influenza virus ribonucleoprotein complexes to microtubules. ***J. Virol.***, 2012; 86: 11086-11095.

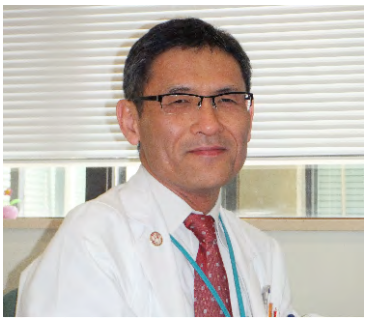
2) Kato K, Okuwaki M, Nagata K. Involvement of Template Activating Factor-I as a chaperone in linker histone dynamics. ***J. Cell Sci.***, 2011; 124: 3254-3265.

3) Sugiyama K, Obayashi E, Kawaguchi A, Tame J R H, Nagata K, Park S-Y. Structural insight into a novel subunit contact within influenza virus RNA polymerase. ***EMBO J.***, 2009; 28: 1803-1811.

4) Obayashi E, Yoshida H, Kawai F, Shibayama N, Kawaguchi A, Nagata K, Tame J R H, Park S-Y. The structural basis for an essential subunit interaction in influenza virus RNA polymerase. ***Nature***, 2008; 454: 1127-1131.

5) Naito T, Kiyasu Y, Sugiyama K, Kimura A, Nakano R, Matsukage A, Nagata K. A novel influenza virus replicon system in yeast identified Tat-SF1 as a stimulatory host factor for viral RNA synthesis. ***Proc. Natl. Acad. Sci. USA***, 2007; 104: 18235-18240.

6) Kawaguchi A, Nagata K. *De novo* replication of the influenza virus RNA genome is regulated by a DNA replicative helicase, MCM. ***EMBO J.***, 2007; 26: 4566-4575.



12. Diagnostic Surgical Pathology

Principal Investigator: Masayuki Noguchi
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Other Faculty Members
Associate Professor Yuko Minami: minami-y@md.tsukuba.ac.jp
Assistant Professor Junko Kano: junkano@md.tsukuba.ac.jp
Assistant Professor Masato Sugano: suganomd@gmail.com
Assistant Professor Kaishi Satomi: kaishis@md.tsukuba.ac.jp
Assistant Professor Aya Shiba-Ishii: Aya_Shiba@md.tsukuba.ac.jp

Major Scientific Interests of the Group
1) Molecular pathology of multistep carcinogenesis
2) Studies of the initial genetic alterations of precancerous lesions and early carcinoma
3) Studies of the interactions between cancer cells and interstitial cells

Projects for Regular Students in Doctoral or Master's Programs
1) Analysis for the molecular mechanisms of pulmonary adenocarcinogenesis. Screening of the differentially expressed genes and proteins between early adenocarcinoma of the lung (*in situ* adenocarcinoma) and early advanced tumors.
2) Produce monoclonal antibodies against fetal swine to screen for specific antibodies against human carcinomas.
3) *In vitro* and *in vivo* studies of the molecular mechanisms of the reproduction of liver tissue.

Study Programs for Short Stay Studies (one week ～ one trimester)
1) Basic techniques of immunohistochemistry, *in situ* hybridization, and FISH
2) Basic techniques of tissue micro-dissection

Recent Publications
1) Nakazato Y, Maeshima MA, Ishikawa Y, Yatabe Y, Fukuoka J, Yokose T, Tomita Y, Minami Y, Asamura Y, Tachibana K, Goya T, **Noguchi M**. Inter observer agreement in the nuclear grading of primary pulmonary adenocarcinoma. **J Thorac Oncol** (in press)
2) Shiba-Ishii A and **Noguchi M**. Aberrant Stratifin overexpression is regulated by tumor-associated CpG demetylation in lung adenocarcinoma. **Am J Pathol** 180:1653-1662, 2012.
3) Tachibana K, Minami Y, Shiba-Ishii A, Kano J, Nakazato Y, Sato Y, Goya T and **Noguchi M**. Abnormality of the hepatocyte growth factor/MET pathway in pulmonary adenocarcinogenesis. **Lung Cancer** 75:181-188, 2012.
4) Satomi K, Morishita Y, Sakashita S, Kondou Y Furuya S, Minami Y and **Noguchi M**. Specific expression of ZO-1 and N-cadherin in rosette structures of various tumor: possible recapitulation of neural tube formation in embryogenesis and utility as a potentially novel immunohistochemical marker of rosette formation in pulmonary neuroendocrine tumors. **Virchow Arch** 459:399-407, 2011.
5) Li D, Sakashita S, Morishita Y, Kano J, Shiba A, Sato T and **Noguchi M**. Binding of lactoferrine to IGBP1 triggers apoptosis in a lung adenocarcinoma cell line. **ANTICANCER RESEARCH** 31:529-534, 2011.
6) Kobayashi H, Minami Y, Anami Y, Kondou Y, Iijima T, Kano J, Morishita Y, Tsuta K, Hayashi S and **Noguchi M**. Expression of the GA733 gene family and its relationship to prognosis in pulmonary adenocarcinoma. **Virchows Arch** 457:69-76, 2010.
7) Nakazato Y, Minami Y, Kobayashi H, Satomi K, Anami Y, Tsuta K, Tanaka R, Okada M, Goya T and **Noguchi M**. Nuclear Grading of Primary Pulmonary Adenocarcinomas -Correlation of nuclear size with prognosis-. **Cancer** 116:2011-2019, 2010.
8) Anami Y, Iijima T, Suzuki K, Yokota J, Minami Y, Kobayashi H, Satomi K, Nakazato Y, Okada M and **Noguchi M**. Bronchioloalveolar carcinoma (lepidic growth) component is a more useful prognostic factor than lymph node metastasis. **J Thorac Oncol** 4:951-8, 2009.

13. Department of Surgery

Chairman : Prof. Nobuhiro Ohkohchi, MD, PhD
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Major Clinical activities

1) Surgical resection of esophageal, gastrointestinal, hepatobiliary and pancreatic tumor
2) Computer-assisted 3D-CT hepatectomy simulation
3) Chemoradiation of Esophageal cancer
4) Neoadjuvant chemoradiation of rectal cancer
5) Surgical treatment of Inflammatory bowel disease
6) Living donor liver transplantation
7) Cadaveric donor kidney transplantation

Major Scientific Interests

1) Liver regeneration and prevention of liver cirrhosis by platelet
2) Hepatic ischemia reperfusion injury
3) Anatomy of liver
4) DDS of anti-cancer drug
5) sense/anti sense RNA of cancer and liver disease
6) Mechanism of wound healing

Projects for Regular Students in Doctoral or Master's Programs

1) Research on platelet effects on liver regeneration and fibrosis
2) Research on prevention of hepatic ischemia reperfusion injury
3) Research on DDS of anti-cancer drug of gastrointestinal tract
4) Research on function of anti-sense RNA in cancer
5) Research on mechanism of wound healing of intestine

Programs for Short Stay Students (one week ~ one trimester)

1) Handling of abdominal organs of small animals
2) Handling of cell culture
3) Techniques of molecular biology

1) Matsuo R, Nakano Y, Ohkohchi N. Platelet administration via the portal vein promotes liver regeneration in rats after 70% hepatectomy. Annals of surgery. 235;1-5.2011
2) Kobayashi A, Oda T, Fukunaga K, Sasaki R, Minami M, Ohkohchi N. MR Imaging of Reactive Lymphoid Hyperplasia of the liver. Journal of Gastrointestinal Surgery. Epub ahead of print.Feb
3) Hisakura K, Murata S, Matsuo R, Paku S, Ikeda N, Kawasaki T, Kohno K, Myronovych A, Nakano Y, Ikeda O, Watanabe M, Ohkohchi N. Platelets Prevent Acute Hepatitis Induced by

Anti-Fas Antibody. Journal of Gastroenterology and Hepatology. 26(2);348-355.2011

4) Ohkohchi N. Platelets play an important role in the recovery of liver dysfunction after hepatic resection. Annals of surgery. 252(4);708-709.2010

5) Yamaguchi R, Terashima H, Yoneyama S, Tadano S, Ohkohchi N. Effects of Platelet-Rich Plasma on Intestinal Anastomotic Healing in Rats: PRP Concentration is a Key Factor. Journal of Surgical Research. Epub ahead of print. 2-Nov.2010

6) Kohno K, Chiba M, Murata S, Pak S, Nagai K, Yamamoto M, Yanagisawa K, Kobayashi A, Yasue H, Ohkohchi N. Identification of natural antisense transcripts involved in human colorectal cancer development. International Journal of Oncology. 37(6);1425-1432.2010

7) Murata S, Yanagisawa K, Fukunaga K, Oda T, Kobayashi A, Sasaki R, Ohkohchi N. Fatty acid synthase cerulenin suppresses liver metastasis of colon cancer in mice. Cancer Science. 101(8);1861-1865.2010

8) Kawasaki T, Murata S, Takahashi K, Nozaki R, Ohshiro Y, Ikeda N, Paku S, Myronovych A, Hisakura K, Fukunaga K, Oda T, Sasaki R, Ohkohchi N. Activation of human liver sinusoidal endothelial cell by human platelets induces hepatocyte proliferation. Journal of Hepatology. 53(4);648-654.2010

9) Matsuda A, Kuno A, Kawamoto T, Ohkohchi N, Shoda J, Hirabayashi J, Naarimatsu H. Wisteria floribunda agglutinin-positive mucin 1 is a sensitive biliary marker for human cholangiocarcinoma. Hepatology. 52(1);174-182.2010

10) Hashimoto S, Oda T, Yamada K, Takagi M, Enomoto T, Ohkohchi N, Takagi T, Kanamori T, Ikeda H, Yanagihara H, Kita E, Tasaki A. The measurement of small magnetic signals from magnetic nanoparticles attached to the cell surface and surrounding living cells using a general-purpose SQUID magnetometer. Physics in Medicine and Biology. 54(8);2571-2583.2009

11) Nakano Y, Kondo T, Matsuo R, Murata S, Fukunaga K, Ohkohchi N. Prevention of leukocyte activation by the neutrophil elastase inhibitor, sivelestat, in the hepatic microcirculation after ischemia-reperfusion. Journal of Surgical Research. 155(2);311-317.2009

12) Watanabe M, Murata S, Hashimoto I, Nakano Y, Ikeda O, Aoyagi Y, Matsuo R, Fukunaga K, Yasue H, Ohkohchi N. Platelets contribute to the reduction of liver fibrosis in mice. Journal of Gastroenterology and Hepatology. 24(1);78-89.2009

14. Regenerative Medicine and Stem Cell Biology

Principle Investigator: Osamu Ohneda
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Staffs:

Dr. Mami Matsuo Takasaki (Assistant Professor), mamimt@md.tsukuba.ac.jp
Dr. Toshiharu Yamashita (Assistant Professor), t-yama@md.tsukuba.ac.jp
Dr. Masumi Kuma Nagano (Assistant Professor), naganom@md.tsukuba.ac.jp

Major Scientific Interests of the Group:

1) Identification and analyses of functional stem cells for cell therapy in human tissues
2) Hypoxic responses in stem cell development and tumor development

Projects for Regular Students in Doctoral or Master's Programs:

1) Analysis of functional stem cells (MSC and EPC) for clinical application
2) Analysis of how hypoxic inducible factors (HIFs) are involved in stem cell development
3) Analysis of how HIFs are involved in tumor development (tumor and tumor endothelial cell)

♦Summer School Course (2013)♦

1) Analysis of Mesenchymal Stem Cells
2) Neural Differentiation of human iPS

Recent Publications:

1) Akimoto K, Kimura K, Nagano M, Takano S, Salazar G, Yamashita T, and Ohneda O. Umbilical cord blood-derived mesenchymal stem cells inhibit, but adipose tissue-derived mesenchymal stem cells promote, glioblastoma multiforme proliferation. **Stem Cells and Dev.** 2013; 22: 1370-1386.
2) Tu T, Kimura K, Nagano M, Yamashita T, Ohneda K, Sugimori H, Sato F, Sakakibara Y, Hamada H, Yoshikawa H, Son H , and Ohneda O. Identification of human placenta-derived mesenchymal stem cells involved in re-endothelialization. **J Cell Physiol**. 2011; 226: 224-235.
3) Nagano M, Kimura K, Yamashita T, Ohneda K, Nozawa D, Hamada H, Yoshikawa H, Ochiai N, and Ohneda O. Hypoxia responsive mesenchymal stem cells derived from human umbilical cord blood are effective for bone repair. **Stem Cells and Dev.** 2010; 19: 1195-1210.
4) Yamashita T, Ohneda O, Sakiyama A, Iwata F, Ohneda K, and Fujii-Kuriyama Y. The microenvironment for erythropoiesis is regulated by HIF-2alpha through VCAM-1 in endothelial cells. **Blood** 2008; 112: 1482-1492.
5) Yamashita T, Ohneda K. Nagano M, Miyoshi C, Kaneko N, Miwa Y, Yamamoto M, Ohneda O, and Fujii-Kuriyama Y. HIF-2alpha in endothelial cells regulates tumor neovascularization through activation of ephrin A1. **J Biol Chem** 2008; 283: 18926-18936.
6) Nagano M, Yamashita T, Hamada H, Ohneda K, Kimura K, Nakagawa T, Shibuya M, Yoshikawa H, and Ohneda O. Identification of functional endothelial progenitor cells suitable for the treatment of ischemic tissue using human umbilical cord blood. **Blood** 2007; 110: 151-160.

15. Molecular Cell Physiology / Reproductive Biochemistry

Principal Investigator: Naomichi Okamura
E-mail address: naooka@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/
biochem/reproductive_biochem/index.html

Other Faculty Members
Assistant Professor: Manabu Matsuda,
Akihiro Kawashima

Major Scientific Interests of the Group
1. Molecular mechanisms involved in the spermatogenesis and sperm maturation in mammals
2. Signal transduction in germ cells
3. Biology of mammogenesis, milkstasis and secretion

Projects for Regular Students in Doctoral or Master's Programs
1) Proteome analysis of calcium-binding proteins expressed in the spermatogenic cells.
2) Molecular mechanisms of the sperm maturation during transit through epididymis.
3) Role of the protein tyrosine phosphorylation in capacitation.

Study Programs for Short Stay Students (one week ~ one trimester)
1) Technology for proteome analysis.
2) Assessment of mammalian sperm fertilizing activities.
3) In vitro studies on functions of monoamines in secretion.

Recent Publications
1) Osman B, **Kawashima A**, Tamba M, Satoh E, Kato Y, Iki A, Konishi K, **Matsuda M** and **Okamura N**. Localization of a Nobel RNA-binding Protein, SKIV2L2, to the Nucleus in the Round Spermatids of Mice. J. Reprod. Develop., 57, 457-467, 2011.
2) Ogushi Y, Akabane G, Hasegawa T, Mochida H, **Matsuda M**, Suzuki M, Tanaka S. Water adaptation strategy in anuran amphibians: molecular diversity of aquaporin. Endocrinology 151(1), 165-173, 2010.
3) **Kawashima A**, Osman B, Takashima M, Kikuchi A, Kohch S, Satoh E, Tamba M, **Matsuda M** and **Okamura N**. CABS1 is a novel calcium-binding protein specifically expressed in elongate spermatids of mice. Biol. Reprod.,80, 1293-1304, 2009.

16. Immunology

Principal Investigator (Professor): Akira Shibuya, M.D., Ph.D
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Other Faculty Members
Associate Professor: Kazuko Shibuya, M.D., Ph.D (kazukos@md.tsukuba.ac.jp)
Shinichiro Honda, M.D., Ph.D (shonda@md.tsukuba.ac.jp)
Assistant Professor: Satoko Tahara, Ph.D（tokothr@md.tsukuba.ac.jp）
Chigusa Oda, M.D., Ph.D（chigusano@md.tsukuba.ac.jp）

Major Scientific Interests of the Group

The molecular mechanisms of tumor immunity, autoimmunity, infectious immunity and allergy and clinical applications of our basic research findings

Projects for Regular Students in Doctoral or Master's Programs

1) In vivo and in vitro function of the immunoreceptors DNAM-1, Fca/mR, MAIR-I, MAIR-II, and Allergin-1, all of which were identified in our laboratory, in immune responses
2) The pathophysiological roles of the immunoreceptors in tumors, autoimmune diseases, allergy and infectious disease

Study Programs for Short Stay Students (one week ~ one trimester)

1) Generation of monoclonal antibodies and their application for expression analyses by flow cytometry and immunohistochemistry
2) Cell separation by sorting on flow cytometry or magnetic beads and analyses of cytokine production or proliferation upon antigen stimulation

Recent Publications

1) Nakahashi-Oda C, Tahara-Hanaoka S, Shoji M, Okoshi Y, Nakano-Yokomizo T, Ohkohchi N, Yasui T, Kikutani H, Honda S, Shibuya K, Nagata S, Shibuya A. Apoptotic cells suppress mast cell inflammatory responses via the CD300a immunoreceptor. ***J. Exp. Med.*** in press (2012)
2) Nakano-Yokomizo T, Tahara-Hanaoka S, Nakahashi-Oda C, Nabekura T, Tchao N K, Kadosaki M, Totsuka N, Kurita N, Nakamagoe K, Tamaoka A, Takai T, Yasui T, Kikutani H, Honda S, Shibuya K, Lanier L L and **Shibuya A**. The immunoreceptor adapter protein DAP12 suppresses B lymphocyte-driven adaptive immune responses. ***J. Exp. Med.*** **208**, 1661-1671, 2011.
3) Hitomi K, Tahara-Hanaoka S, Someya S, Fujiki A, Tada H, Sugiyama T, Shibayama S, Shibuya K and **Shibuya A**. An immunoglobulin-like receptor, Allergin-1, inhibits immunoglobulin E-mediated immediate hypersensitivity reactions. ***Nat Immunol.*** 11: 601-607, 2010
4) Honda S, Miyamoto A, Cho Y, Usui K, Kurita N, Takeshita K, Takahashi S, Kinoshita T, Fujita T, Tahara-Hanaoka S, Shibuya K, **Shibuya A**. Enhanced humoral immune responses against T-independent antigens in Fcα/μR-deficient mice. **Proc Natl Acad Sci USA.** 106:11230-11235, 2009

17. Endocrinology and Metabolism

Principal Investigator: Hitoshi Shimano
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Other Faculty Members
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Assistant Professor: Takahsi Matsuzaka (t-matsuz@md.tsukuba.ac.jp)
Research Associate: Kiyoaki Ishii (kishii@md.tsukuba.ac.jp)

Major Scientific Interests of the Group

We are working to understand the molecular mechanisms of energy metabolism using the newest technologies, such as molecular and cellular biology, gene-engineered animals, genome informatics. We also extend our investigations to understand the molecular basis of metabolic disease, and try to develop new therapeutic approaches for preventing obesity, diabetes, and cardiovascular disease.

Projects for Regular Students in Doctoral or Master's Programs

1) Research on energy metabolism and transcription factors.
2) Research on lipid metabolism for various metabolic diseases.
3) Research on pathogenic mechanisms and treatment of diabetes.
4) Research on pathogenic mechanisms and treatment of atherosclerosis.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Transfection and Luciferase assay for analyzing the function of transcription factors.
2) Experimental procedures for mouse metabolic disease model.

Recent Publications

1) Kumadaki S, Karasawa T, Matsuzaka T, Ema M, Nakagawa Y, Nakakuki M, Saito R, Yahagi N, Iwasaki H, Sone H, Takekoshi K, Yatoh S, Kobayashi K, Takahashi A, Suzuki H, Takahashi S, Yamada N, **Shimano H**. Inhibition of ubiquitin ligase F-box and WD repeat domain-containing 7α (Fbw7α) causes hepatosteatosis through Krüppel-like factor 5 (KLF5)/peroxisome proliferator-activated receptor γ2 (PPARγ2) pathway but not SREBP-1c protein in mice. **J Biol Chem.** 286(47):40835-46, 2011.
2) Saito R, Matsuzaka T, Karasawa T, Sekiya M, Okada N, Igarashi M, Matsumori R, Ishii K, Nakagawa Y, Iwasaki H, Kobayashi K, Yatoh S, Takahashi A, Sone H, Suzuki H, Yahagi N, Yamada N, **Shimano H**. Macrophage Elovl6 deficiency ameliorates foam cell formation and reduces atherosclerosis in low-density lipoprotein receptor-deficient mice. **Arterioscler Thromb Vasc Biol.** 31(9):1973-9, 2011.
3) Amemiya-Kudo M, Oka J, Takeuchi Y, Okazaki H, Yamamoto T, Yahagi N, Matsuzaka K, Okazaki S, Osuga J, Yamada N, Murase T, **Shimano H**. Suppression of the pancreatic duodenal homeodomain transcription factor-1 (Pdx-1) promoter by sterol regulatory element-binding protein-1c (SREBP-1c). **J Biol Chem**. 286(32):27902-14, 2011.

18. Anatomy and Embryology/ Laboratory Animal Resource Center

Principal Investigator: Satoru Takahashi
E-mail address: satoruta@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/anatomy/embryology/index.html

Major Scientific Interests of the Group

We are working on the functional analysis of transcription factors in the body by employing developmental engineering techniques such as the generation of transgenic mice.

Projects for Regular Students in Doctoral or Master's Programs

Molecular mechanism of the development of organs.

We are researching the molecular mechanisms of the development of organs by analyzing the function of the large Maf family of transcription factors. In both human and mouse, four large Maf transcription factors, MafA, MafB, c-Maf and Nrl, have been identified. We genetically manipulate mice about these genes and analyze their in vivo function.

Study Programs for Short Stay Students (one week ~ one trimester)

3) Histological analysis of genetically manipulated mice.
4) Handling skill for mouse embryos.

Recent Publications

1) Bourane S, Garces A, Venteo S, Pattyn A, Hubert T, Fichard A, Puech S, Boukhaddaoui H, Baudet C, **Takahashi S**, Valmier J, Carroll P. Low-threshold mechanoreceptor subtypes selectively express MafA and are specified by Ret signaling. **Neuron.** 64, 857-870, 2009.
2) Kato T, Shimano H, Yamamoto T, Yokoo T, Endo Y, Ishikawa M, Matuzaka T, Nakagawa Y, Kumadaki S, Yahagi N, Takahashi A, Sone H, Suzuki H, Toyoshima H, Hasty AH, **Takahashi S**, Gomi H, Izumi T, Yamada N. Granuphilin is activated by SREBP-1c and involved in impaired insulin secretion in diabetic mice. **Cell Metab.** 2, 143-154, 2006.
3) Moriguchi T, Hamada M, Morito N, Terunuma T, Hasegawa K, Zhang C, Yokomizo T, Esaki R, Kuroda E, Yoh K, Kudo T, Nagata M, Greaves DR, Engel JD, Yamamoto M, **Takahashi S**. MafB is essential for renal development and F4/80 expression in macrophage. **Mol Cell Biol.** 26, 5715-5727, 2006.
4) Morito N, Yoh K, Fujioka Y, Nakano T, Shimohata H, Yamada A, Maeda A, Matsuno F, Hata H, Suzuki A, Imagawa S, Mitsuya H, Esumi H, Koyama A, Yamamoto M, Mori N, **Takahashi S**. Overexpression of c-Maf contributed to T cell lymphoma. **Cancer Res.** 66, 812-819, 2006.
5) Zhang C, Moriguchi T, Kajihara M, Esaki R, Harada A, Shimohata H, Oishi H, Hamada M, Morito N, Hasegawa H, Kudo T, Engel JD, Yamamoto M, **Takahashi S**. MafA is a key regulator of glucose-stimulated insulin secretion. **Mol Cell Biol.** 25, 4969-4976, 2005.

19. Environmental Microbiology

Principal Investigator: Associate Professor Kaoru Takeuchi
E-mail address: ktakeuch@md.tsukuba.ac.jp
URL: http://under construction

Other Faculty Members:

Major Scientific Interests of the Group:
The aim of our group is to understand the host-pathogen interactions. We have established reverse genetics system (recovery of infectious viruses from cloned cDNA) of wild-type measles virus. By using the reverse genetics system, we are analyzing molecular mechanism of the pathogenicity of measles virus. We are also interested in applied science. We are developing new multivalent animal vaccines based on bovine parainfluenza type 3 virus and plant-made edible vaccines against norovirus or hepatitis E virus.

Projects for Regular Students in Doctoral or Master's Programs:
5) Identification of host factors required for hepatitis E virus replication
6) Production of edible vaccines in plants
7) Production of recombinant viral vaccines

Study Programs for Short Stay Students (one week ~ one trimester):
5) Expression of virus genes in mammalian cells
6) Cell culture and infection of viruses
7) Detection of viruses by RT-PCR

Selected Recent Publications:
1) Ohkura T, Kokuho T, Konishi M, Kameyama K, **Takeuchi K**. Complete genome sequences of bovine parainfluenza virus type 3 BN-1 and BN-CE vaccine strains. ***Genome A.*** 2013. (in press).

2) Wakimoto H, Shimodo M, Satoh Y, Kitagawa Y, **Takeuchi K**, Gotoh B, Ito M. F-actin modulates measles virus cell-cell fusion and assembly by altering the interaction between the matrix protein and the cytoplasmic tail of hemagglutinin. ***J. Virol.*** 2013; 87(4): 1974-1984.

3) Kato SI, Nagata K, **Takeuchi K**, Cell tropism and pathogenicity of measles virus in monkeys. ***Front. Microbiol***. 2012;3:14 Epub 2012 Jan 30.

4) **Takeuchi K**, Nagata N, Kato SI, Ami Y, Suzaki Y, Suzuki Y, Sato Y, Tsunetsugu-Yokota Y, Mori K, Van Nguyen N, Kimura H, Nagata K. Wild-type measles virus with the hemagglutinin protein of the Edmonston vaccine strain retains wild-type tropism in macaques. ***J. Virol***. 2012; 86(6):3027-3037.

5) Sugiyama H, Onuki K, Ishige K, Baba N, Ueda T, Matsuda S, Takeuchi K, Onodera M, Nakanuma Y, Yamato M, Yamamoto M, Hyodo I, Shoda J. Potent in vitro and in vivo antitumor activity of sorafenib against human intrahepatic cholangiocarcinoma cells. **J Gastroenterol**. 2011; 46:779-789.

20. Molecular and Genetic Epidemiology/ Public Health Medicine

Principal Investigator: Naoyuki Tsuchiya
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Other Faculty Members;
Associate Professor Jun Ohashi, juno-tky@umin.ac.jp
Assistant Professor Kazumasa Yamagishi, k-yamagishi@umin.ac.jp
Junior Assistant Professor Aya Kawasaki, a-kawasaki@md.tsukuba.ac.jp

Major Scientific Interests of the Group

1) Genetics of human rheumatic diseases including systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis and microscopic polyangiitis (Dr. Naoyuki Tsuchiya, Dr. Aya Kawasaki)
2) Genetics of obesity in Oceanic islanders (Dr. Jun Ohashi)
3) Epidemiology and prevention of lifestyle-related diseases (Dr. Kazumasa Yamagishi)

Projects for Regular Students in Doctoral or Master's Programs

1) Polymorphisms associated with rheumatic diseases in Japanese (Dr. Naoyuki Tsuchiya, Dr. Aya Kawasaki)
2) Polymorphisms associated with obesity in Oceanic populations (Dr. Jun Ohashi)

Study Programs for Short Stay Students (one week ~ one trimester)

Genome database (tutorial), SNP typing (laboratory), Preventive medicine activity in the community (a field trip) (optional)

Recent Publications

1) Furukawa H, Oka S, Shimada K, Rheumatoid Arthritis associated Interstitial Lung Disease (RA-ILD) Study Consortium, **Tsuchiya N**, Tohma S. *HLA-A*31:01* and methotrexate-induced interstitial lung disease in Japanese rheumatoid arthritis patients: a multi-drug hypersensitivity marker? **Ann Rheum Dis** 2013;72:153-155.
2) **Yamagishi K**, Iso H, Kokubo Y, Saito I, Yatsuya H, Ishihara J, Inoue M, Tsugane S; for the JPHC Study Group. Dietary intake of saturated fatty acids and incident stroke and coronary heart disease in Japanese communities: The JPHC Study. **Eur Heart J** 2013;34: 1225-1232
3) Naka I, Hikami K, Nakayama K, Koga M, Nishida N, Kimura R, Furusawa T, Natsuhara K, Yamauchi T, Nakazawa M, Ataka Y, Ishida T, Inaoka T, Iwamoto S, Matsumura Y, Ohtsuka R, Tsuchiya N, **Ohashi J**. A functional SNP upstream of the beta-2 adrenergic receptor gene (ADRB2) is associated with obesity in Oceanic populations. **Int J Obes (Lond)** 2012;doi: 10.1038/ijo.2012.206.
4) Hikami K, Kawasaki A, Ito I, Koga M, Ito S, Hayashi T, Matsumoto I, Tsutsumi A, Kusaoi M, Takasaki Y, Hashimoto H, Arinami T, Sumida T, **Tsuchiya N**. Association of a functional polymorphism in the 3' untranslated region of *SPI1* with systemic lupus erythematosus. **Arthritis Rheum** 2011;63:755-763.
5) Ito I, Kawaguchi K, Kawasaki A, Hasegawa M, **Ohashi J**, Kawamoto M, Fujimoto M, Takehara K, Sato S, Hara M, **Tsuchiya N**. Association of the *FAM167A-BLK* region with systemic sclerosis. **Arthritis Rheum** 2010;62:890-895.

筑波大学
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21. Clinical Trial and Clinical Epidemiology

Principle Investigator: Yukiko Wagatsuma
E-mail: ywagats@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/epidemiology/

Major Scientific Interests of the Group:
Current scope of research has much diversified from infectious disease control to population, nutrition, environmental and health systems research. The most challenging initiatives I am involving are in the studies of emerging and re-emerging infections, developmental origins of health and disease and climate change impact on health. I continue to be interested in finding effective and appropriate options for health interventions to control ill and health for the most vulnerable population in the wolrd.

Projects for Regular Students in Doctoral or Master's Programs

1. Cohort studies on children's health in Bangladesh.
2. Patient-oriented clinical researches and their application.
3. Development, evaluation and application of biostatistics theory.
4. Developing methods to extract standardized clinical data from large information systems.

Study Programs for Short Stay Students

1. Clinical epidemiology and its applications.
2. Data analysis by using statistical software.

Recent Publications:

1. Hawkesworth S, Wagatsuma Y, Kahn AI, Hawlader MD, Fulford AJ, Arifeen SE, Persson LÅ, Moore SE. Combined Food and Micronutrient Supplements during Pregnancy Have Limited Impact on Child Blood Pressure and Kidney Function in Rural Bangladesh. J Nutr 2013; 143:728-34.
2. Hawkesworth S, Wagatsuma Y, Kippler M, Fulford AJ, Arifeen SE, Persson LA, Moore SE, Vahter M. Early exposure to toxic metals has a limited effect on blood pressure or kidney function in later childhood, rural Bangladesh. Int J Epidemiol 2013; 42:176-85.
3. Ahmed S, Ahsan KB, Kippler M, Mily A, Wagatsuma Y, Hoque AM, Ngom PT, El Arifeen S, Raqib R, Vahter M. In utero arsenic exposure is associated with impaired thymic function in newborns possibly via oxidative stress and apoptosis.Toxicol Sci 2012; 129:305-14.
4. Persson LÅ, Arifeen S, Ekström EC, Rasmussen KM, Frongillo EA, Yunus M; MINIMat Study Team. Effects of prenatal micronutrient and early food supplementation on maternal hemoglobin, birth weight, and infant mortality among children in Bangladesh: the MINIMat randomized trial. JAMA 2012; 307:2050-9.
5. Takano M, Okada M, Oka S, Wagatsuma Y. The relationship between HIV testing and CD4 counts at HIV diagnosis among newly diagnosed HIV-1 patients in Japan. Int J STD AIDS 2012; 23:262-6.
6. Beatty ME, Stone A, Fitzsimons DW, Hanna JN, Lam SK, Vong S, Guzman MG, Mendez-Galvan JF, Halstead SB, Letson GW, Kuritsky J, Mahoney R, Margolis HS; Asia-Pacific and Americas Dengue Prevention Boards Surveillance Working Group. Best practices in dengue surveillance: a report from the Asia-Pacific and Americas Dengue Prevention Boards. PLoS Negl Trop Dis 2010; 4:e890.
7. Hashizume M, Faruque AS, Wagatsuma Y, Hayashi T, Armstrong B. Cholera in Bangladesh: climatic components of seasonal variation. Epidemiology 2010; 21(5):706-10.

22. Laboratory Animal Science

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Major Scientific Interests of the Group

Laboratory animals are essential and important bio-resources for the advancement of medical sciences. Gene-modified animals are used very often to study *in vivo* function of genes and proteins in development, homeostasis and disease. In particular, we focus on 1) establishment of germline-competent embryonic stem cells from various inbred strains of mice and rats for developing gene-modified animals and 2) generation of bacterial artificial chromosome (BAC) based Cre driver mice and novel photoconversion Cre reporter mice and rats for assembling high specific conditional Knockout systems. In addition, we investigate 3) the mechanisms of embryo implantation and early embryo development on novel mutant and Knockout mouse strains.

Projects for Regular Students in Doctoral or Master's Programs

1) Development of embryonic stem cells in mice and rats.
2) Development of advanced Cre-LoxP system in mice.
3) Investigate peri-implantation development in mutant mice.

Study Programs for Short Stay Students (one week ~ one trimester)

1) Manipulation of mouse preimplantation embryos.

Recent Publications

4) Mizuno S, Iijima S, Okano T, Kajiwara N, Kunita S, Sugiyama F, Yagami K. Retrotransposon-mediated Fgf5(go-Utr) mutant mice with long pelage hair. Exp Anim. 2011;60(2):161-7.
5) Iijima S, Tanimoto Y, Mizuno S, Daitoku Y, Kunita S, Sugiyama F, Yagami K. Effect of different culture conditions on establishment of embryonic stem cells from BALB/cAJ and NZB/BINJ mice. Cell Reprogram. 2010 Dec;12(6):679-88.
6) Mizuno S, Mizobuchi A, Iseki H, Iijima S, Matsuda Y, Kunita S, Sugiyama F, Yagami K. A novel locus on proximal chromosome 18 associated with agenesis of the corpus callosum in mice. Mamm Genome. 2010 Dec;21(11-12):525-33.
7) Tanimoto Y, Iijima S, Hasegawa Y, Suzuki Y, Daitoku Y, Mizuno S, Ishige T, Kudo T, Takahashi S, Kunita S, Sugiyama F, Yagami K. Embryonic stem cells derived from C57BL/6J and C57BL/6N mice. Comp Med. 2008 Aug;58(4):347-52.
8) Shigematsu Y, Yoshida N, Miwa Y, Mizobuti A, Suzuki Y, Tanimoto Y, Takahashi S, Kunita S, Sugiyama F, Yagami K. Novel embryonic stem cells expressing tdKaede protein photoconvertible from green to red fluorescence.(Int J Mol Med. 2007 Oct;20(4):439-44)
9) Shimizu Y, Motohashi N, Iseki H, Kunita S, Sugiyama F, Yagami K. A novel subpopulation lacking Oct4 expression in the testicular side population. Int J Mol Med. 2006 Jan;17(1):21-8.
10) Shimizukawa R, Sakata A, Hirose M, Takahashi A, Iseki H, Liu Y, Kunita S, Sugiyama F, Yagami K. Establishment of a new embryonic stem cell line derived from C57BL/6 mouse expressing EGFP ubiquitously. Genesis. 2005 May;42(1):47-52.

23. Neurobiology of Sleep

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Other Faculty Member:
Professor Hiromasa Funato, M.D., Ph.D., Masanori Sakaguchi, M.D., Ph.D., Michael Lazarus, Ph.D., Yu Hayashi, Ph.D.

Major Scientific Interests of the Group

- Exploring genes regulating sleep/wake
- Real-time visualization and manipulation of neuronal mechanisms controlling sleep/wake
- Finding new drugs for sleep disorders

Projects for Regular Students in Doctoral or Master's Programs

1) Large-scale, forward genetic screening of genes responsible for sleep/wake regulation in mutagenized mice
2) Screening for orexin receptor agonists
3) Analysis of sleep and wakefulness in genetically modified mice
4) in vivo real-time imaging of neuronal activities in hypothalamus and other deep brain structures in freely behaving mice

Study Programs for Short Stay Students (one week ~ one trimester)

1) EEG/EMG electrode implantation and recording in mice
2) patch clamp recording in cells and brain slices
3) imaging of nerve cell activities in brain slices

Recent Publications

1) Suzuki, A, Sinton CM, Greene RW, Yanagisawa M. Behavioral and biochemical dissociation of arousal and homeostatic sleep need influenced by prior wakeful experience in mice. *Proc Natl Acad Sci U S A.* (in press) 2013.
2) Chang, I, Bramall AN, Baynash AG, Rattner A, Rakheja D, Post M, Joza S, McKerlie C, Stewart DJ, McInnes RR, Yanagisawa M. Endothelin-2 deficiency causes growth retardation, hypothermia, and emphysema in mice. *J Clin Invest.* 2013.
3) Funato H, Sato M, Sinton CM, Gautron L, Williams SC, Skach A, Elmquist JK, Skoultchi AI, Yanagisawa M.Loss of Goosecoid-like and DiGeorge syndrome critical region 14 in interpeduncular nucleus results in altered regulation of rapid eye movement sleep. *Proc Natl Acad Sci U S A*. Oct 19;107(42):18155-60. 2010
4) Matsuki. T., Nomiyama, M., Takahira, H., Hirashima. N., Kunita, S., Takahashi, S., Yagami, K., Kilduff, T.S., Bettler, B., Yanagisawa, M. & Sakurai, T. Selective loss of GABAB receptors in orexin-producing neurons results in disrupted sleep/wakefulness architecture. *Proc. Natl. Acad. Sci. USA* **106**:4459-64, 2009.
5) Irukayama-Tomobe, Y., Tanaka, H., Yokomizo, T., Yanagisawa, M. & Sakurai, T. Aromatic D-amino acids act as chemoattractant factors for human leukocytes through a G protein-coupled receptor, GPR109B. *Proc. Natl. Acad. Sci. USA* **106**:3930-4, 2009.
6) Sakakibara,I., Fujino, T., Ishii, M., Tanaka,T., Shimosawa, T., Miura, S., Zhang, W.,Tokutake,8 Y., Yamamoto, J., Awano, M., Iwasaki, S., Motoike, T., Okamura, M., Inagaki, T., Kita, K., Ezaki, O., Naito, M., Kuwaki, T., Chohnan, S., Yamamoto, T., Hammer, R.E., Kodama, T., Yanagisawa, M., and Sakai, J. Fasting-Induced Hypothermia and Reduced Energy Production in Mice Lacking Acetyl-CoA Synthetase 2 *Celll Metabolism* **9**: 191-202. 2009.
7) Funato, H., Tsai, A.L., Willie, J.T., Kisanuki Y., Williams,S.C., Sakurai,T., and Yanagisawa M. Enhanced Orexin Receptor-2 Signaling Prevents Diet-Induced Obesity and Improves Leptin Sensitivity. *Celll Metabolism* **9**: 64-76. 2009.

8) Arruda-Carvalho M*., Sakaguchi M*, Akers KG., Josselyn SA., FranklandPW., Post-training ablation of adult-generated neurons degrades previously-acquired memories., *J. Neurosci.* Oct 19;31(42):15113-27. 2011, *The authors contributed equally
9) Lazarus, M., Yoshida, K., Coppari, R., Bass, C.E., Mochizuki, T., Lowell, B.B., and Saper, C.B. 2007. EP3 prostaglandin receptors in the median preoptic nucleus are critical for fever responses. *Nat Neurosci*. 10:1131-1133. 2007
10) Hayashi, Y., Hirotsu, T., Iwata, R., Kage-Nakadai, E., Kunitomo, H., Ishihara, T., Iino, Y., and Kubo, T. A trophic role for Wnt-Ror kinase signaling during developmental pruning in Caenorhabditis elegans. *Nature Neuroscience*. Aug;12(8):981-7. 2009