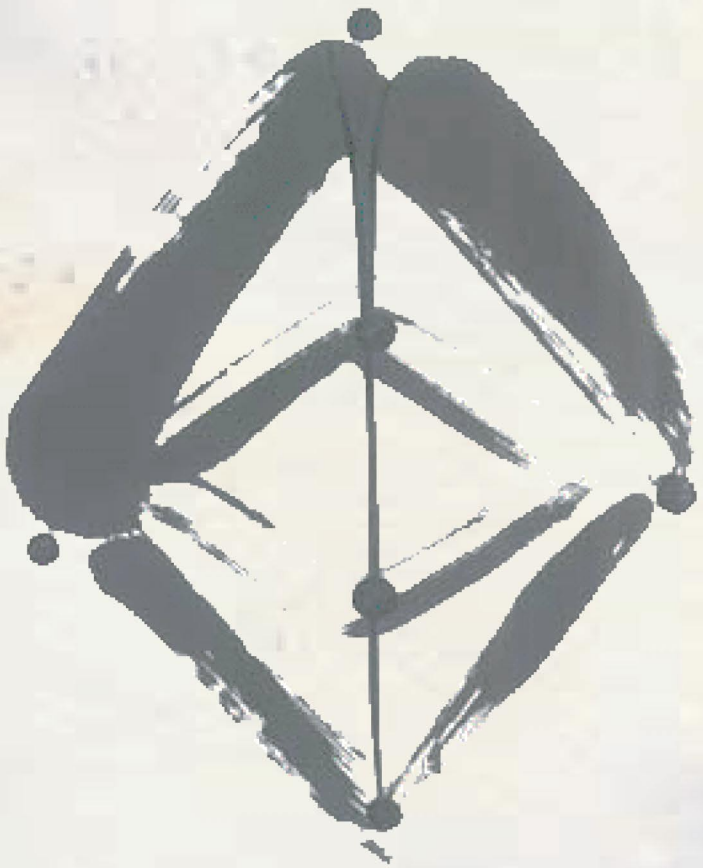
University of Tsukuba

2012

Biomedical Research Activities

University of Tsukuba



Creativity

Integrity

Friendliness

Strength

Enthusiasm

Intelligence

Name of the Field: 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

1) Molecular mechanism of the development of pancreatic endocrine cells and macrophages.
We are researching the molecular mechanisms of the development of pancreatic endocrine cells and macrophages. 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.
2) Analysis about molecular mechanism of stem cell pluripotency.
In addition to these themes, we are also analyzing molecular mechanism of stem cell pluripotency.

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) Takase H, Yamadera R, Matsumoto K, Kubota Y, Ohtsu A, Suzuki R, Kojima T, Mochizuki H, Ishitobi H, Takano S, Uchida K, **Takahashi S,** Ema M. Genome-wide identification of vascular endothelial-specific genes during development in the mouse. **Blood.** 120, 914-923.
2) Kusakabe M, Hasegawa K, Hamada M, Nakamura M, Ohsumi T, Suzuki H, Kudo T, Uchida K, Ninomiya H, Chiba S, **Takahashi S.** c-Maf is indispensable for the microenvironment of definitive erythropoiesis as it forms erythroblastic islands in fetal liver. **Blood.** 118, 1374-1385, 2011.
3) Hishida T, Nozaki Y, Nakachi Y, Mizuno Y, Okazaki Y, Ema M, **Takahashi S,** Nishimoto M, Okuda A. Indefinite self-renewal of ES cells through Myc/Max transcriptional complexes-independent mechanisms. **Cell Stem Cell.** 9, 37-49, 2011.
4) Morito N, Yoh K, Maeda A, Nakano T, Fujita A, Kusakabe M, Hamada M, Kudo T, Yamagata K, **Takahashi S.** A novel transgenic mouse model of the human multiple myeloma chromosomal translocation t(14;16)(q32;q23). **Cancer Res.** 71, 339-348, 2011.
5) Nishikawa K, Nakashima T, Takeda S, Isogai M, Hamada M, Kimura A, Kodama T, Yamaguchi A, Owen MJ, **Takahashi S,** Takayanagi H. Maf mediates the age-related switch in mesenchymal cell differentiation. ***J Clin Invest.*** 120, 3455-3465, 2010.

Research Field: Laboratory Animal Science
Principal Investigator: Prof. Ken-ichi Yagami
E-mail address: kenyagam@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/yagami/index.html

Other Faculty Members
Associate Professor Fumihiro Sugiyama: bunbun@md.tsukuba.ac.jp
Assistant Professor Satoshi Kunita: kunitasa@md.tsukuba.ac.jp

Major Scientific Interests of the Group

The aims of our research are development, characterization and quality control of genetically induced animal models for human diseases. We focus on the following research themes:

1) We are creating a variety of mice in which genes regulating blood pressure (BP) are altered. Characterization of these mice allows us to develop hypertension models as well as to evaluate unknown functions of the genes. Additionally, quantitative trait loci (QTL) mapping of BP regulating genes is in progress by using spontaneously hypertensive mice to search novel genes associated with BP regulation.

2) In order to elucidate the molecular mechanisms associated with pathogenesis of infectious agents, such as parvovirus and Helicobacter, we are analyzing the interaction between infectious agents and host genes. Additionally, we continue to develop technology for creating genetically-induced mice and to survey microbiological infection in laboratory animals.

Projects for Regular Students in Doctoral or Master's Programs

1) Development of embryonic stem cells in mice and rats.
2) Development of monoclonal antibody-based antigen detection methods for diagnosing infectious diseases in mice (such as *Helicobacter hepaticus* and murine norovirus infections).

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

1) Manipulation of mouse preimplantation embryos.
2) Multiplex serologic tests for infectious diseases in mice and rats by microsphere fluorescent immunoassay.

Recent Publications

1) Feng M, Deerhake ME, Keating R, Thaisz J, Xu L, Tsaih SW, Smith R, Ishige T, **Sugiyama F**, Churchill GA, DiPetrillo K.Genetic analysis of blood pressure in 8 mouse intercross populations. **Hypertension.** 2009 Oct;54(4):802-9. Epub 2009 Aug 3.
2) 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.
3) 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)
4) Nishihara E, Tsaih SW, Tsukahara C, Langley S, Sheehan S, DiPetrillo K, **Kunita S**, **Yagami K**, Churchill GA, Paigen B, **Sugiyama F**. Quantitative trait loci associated with blood pressure of metabolic syndrome in the progeny of NZO/HILtJxC3H/HeJ intercrosses. **Mamm Genome.** 2007 Aug;18(8):573-83.
5) **Kunita S**, Chaya M, Hagiwara K, Ishida T, Takakura A, Sugimoto T, Iseki H, Fuke K, **Sugiyama F**, **Yagami K**. Development of ELISA using recombinant antigens for specific detection of mouse parvovirus infection. **Exp Anim.** 2006 Apr;55(2):117-24.
6) 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.
7) Iseki H, Shimizukawa R, **Sugiyama F**, **Kunita S**, Iwama A, Onodera M, Nakauchi H, **Yagami K**. Parvovirus nonstructural proteins induce an epigenetic modification through histone acetylation in host genes and revert tumor malignancy to benignancy. **J Virol.** 2005 Jul;79(14):8886-93.
8) 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.

Physiological Chemistry

Principal Investigator: Yasunori Kanaho
E-mail address: ykanaho@md.tsukuba.ac.jp
URL:http: //www.md.tsukuba.ac.jp/basic-med/biochem/kanaholab/index.html

Other Faculty Members
Associate Professor Hiroshi Hasegawa: h.hasegawa@md.tsukuba.ac.jp
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.

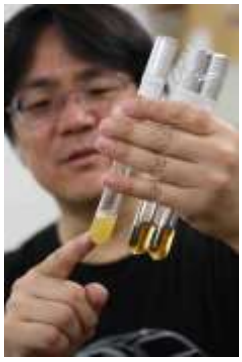
Study Programs for Short Stay Students (one week ~ one trimester)

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)

Molecular Cell Biology



Principal Investigator: Kenji Irie
E-mail address: kirie@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/public/basic-med/molcellbiol/index.html

Other Faculty Members
Assistant Professor Takahiro Naiki: taknaiki@md.tsukuba.ac.jp
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 Khd1p 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.

Recent Publications

1) Stau1 regulates Dvl2 expression during myoblast differentiation. Yamaguchi Y, Naiki T, **Irie K. Biochem Biophys Res Commun.** 2012 Jan 6;417(1):427-32.

2) 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.

3) 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.

4) 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.

5) 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.

6) Stau1 negatively regulates myogenic differentiation in C2C12 cells. Yamaguchi Y, Oohinata R, Naiki T, **Irie K**. **Genes Cells.** 2008 Jun;13(6):583-92.

Gene Regulation

Principal Investigator: Koji Hisatake
E-mail address: kojihisa@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/biochem/gene/

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.

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

9) 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.

10) 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.

11) **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.

Research Field: Molecular Neurobiology
Principal Investigator: Prof. Masayuki Masu
E-mail address: mmasu@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/duo/molneurobiol/

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
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.

Medical Genetics

Principal Investigator: Tadao Arinami
E-mail address: tarinami@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/m-genetics/

Major Scientific Interests of the Group

1) Genetic study of neuropsychiatric disorders. Linkage and association analyses, expression profiles from human and animal tissues, and animal model study of schizophrenia, depression, substance abuse/dependence, developmental disorders.
2) Genetic study of asthma/allergy. Linkage and association analyses, expression profiles from human and animal tissues, and animal model study of bronchial asthma, allergic rhinitis and atopic dermatitis.
3) Genetic diagnosis and counseling

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular pathophysiology and therapeutic trials for schizophrenia, depression and developmental disorders based on genetic evidence.
2) Identification of novel genomic mutations associated with asthma/atopy and development of genetic markers and therapeutic materials for personalized medicine of asthma and pollinosis.

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

1) Genetic testing, genotyping, expression analyses,
2) Genetic informatics

Recent Publications

1) Tanaka S, Syu A, Ishiguro H, Inada T, Horiuchi Y, Ishikawa M, Koga M, **Noguchi E**, Ozaki N, Someya T, Kakita A, Takahashi H, Nawa H, **Arinami T**. DPP6 as a candidate gene for neuroleptic-induced tardive dyskinesia. **Pharmacogenomics J**. in press
2) **Noguchi E**, Sakamoto H, Hirota T, Ochiai K, Imoto Y, Sakashita M, Kurosaka F, Akasawa A, Yoshihara S, Kanno N, Yamada Y, Shimojo N, Kohno Y, Suzuki Y, Kang MJ, Kwon JW, Hong SJ, Inoue K, Goto Y, Yamashita F, Asada T, Hirose H, Saito I, Fujieda S, Hizawa N, Sakamoto T, Masuko H, Nakamura Y, Nomura I, Tamari M, **Arinami T**, Yoshida T, Saito H, Matsumoto K. Genome-wide association study identifies HLA-DP as a susceptibility gene for pediatric asthma in Asian populations. **PLoS Genet** 7:e1002170, 2011
3) Syu A, Ishiguro H, Inada T, Horiuchi Y, Tanaka S, Ishikawa M, Arai M, Itokawa M, Niizato K, Iritani S, Ozaki N, Takahashi M, Kakita A, Takahashi H, Nawa H, Keino-Masu K, Arikawa-Hirasawa E, and **Arinami T**. Association of the HSPG2 gene with neuroleptic-induced tardive Dyskinesia. **Neuropsychopharmacology.** 35:1155-1164, 2010

Ishiguro H, Horiuchi Y, Ishikawa M, Koga M, Imai K, Suzuki Y, Morikawa M, Inada T, Watanabe Y, Takahashi M, Someya T, Ujike H, Iwata N, Ozaki N, Onaivi ES, Kunugi H, Sasaki T, Itokawa M, Arai M, Niizato K, Iritani S, Naka I, Ohashi J, Kakita A, Takahashi H, Nawa H, and **Arinami T**. Brain cannabinoid CB2 receptor in schizophrenia. **Biol Psychiatry.** 67:974-982. 2010

Name of the Field: Molecular Pharmacology
Principal Investigator: Masashi Yanagisawa, M.D., Ph.D.
E-mail address: yanagisawa.masa.fu@u.tsukuba.ac.jp
URL: http://sleepymouse.tsukuba.ac.jp/
Other Faculty Member:
Associate Professor Hiromasa Funato, M.D., Ph.D.

Major Scientific Interests of the Group

1) Exploring genes regulating sleep/wake
2) Real-time visualization and manipulation of neuronal mechanisms controlling sleep/wake
3) 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) Chemical biology for orexin receptor agonists
3) Analysis of sleep and wakefulness in genetically modified mice
4) In vivo real-time imaging of neuronal activities in the hypothalamus and other deep brain structures in freely behaving mice

Training 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
4) Cell-based assay for GPCR activation

Recent Publications

1) 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. 2010 Oct 19;107(42):18155-60. Epub 2010.
2) 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.
3) 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.
4) 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.
5) 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.

Diagnostic Surgical Pathology

Principal Investigator: Masayuki Noguchi
E-mail address: nmasayuk@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/diagpatho/

Other Faculty Members
Associate Professor Yukio Morishita:ymorishi@md.tsukuba.ac.jp
Associate Professor Yuko Minami: minami-y@md.tsukuba.ac.jp
Assistant Professor Junko Kano: junkano@md.tsukuba.ac.jp
Assistant Professor Shingo Sakashita: sakashingo@hotmail.com
Assistant Professor Kaishi Satomi: kaishis@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) 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.
2) 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.
3) 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.
4) 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.
5) 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.
6) 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.
7) 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.

Experimental Pathology

Principal Investigator: Mitsuyasu Kato
E-mail address: mit-kato@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/epatho/

Other Faculty Members
Associate Professor Hiroyuki Suzuki: h-suzuki@md.tsukuba.ac.jp
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** *in press*.
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.

Research Field: Kidney and Vascular Pathology
Principal Investigator: Prof. Michio Nagata
E-mail address: nagatam@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/rvpatho/

Major Scientific Interests of the Group

Kidney pathology is the main issue in our group.
Current interests include podocyte pathology, pathophysiology of FSGS, systemic vasculitis (ANCA-related) and cystogenesis in polycystic kidney.
Vascular pathology in chronic kidney disease is another focus in our group.

Projects for Regular Students in Doctoral or Master's Programs

1) Pathophysiology and molecular mechanisms of focal segmental glomerulosclerosis from the view of podocyte and parietal cell transdifferentiation.
2) Morphologic investigation in systemic vascular changes and kidney injury.

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

1) Diagnosis of human kidney biopsy samples according to the specific interest.
2) Immunohistochemistry and molecular biologic techniques using podocyte-specific transgenic animals.

Recent Publications

1) Aita K, Yamaguchi Y, Horita S, Ohno M, Tanabe K, Fuchinoue S, Teraoka S, Toma H, **Nagata M**. : Thickening of the peritubular capillary basement membrane is a useful diagnostic marker of chronic rejection in renal allografts. **Am J Transplant.** 2007 Apr;7(4):923-9.
2) Aita K, Etoh M, Hamada H, Yokoyama C, Takahashi A, Suzuki T, Hara M, **Nagata M**. Acute podocyte loss is the possible mechanism of heavy proteinuria in preeclampsia. **Nephron Clin Prac** 2009;112(2):c65-70.
3) Suzuki T, Matsusaka T, Nakayama M, Asano T, Watanabe T, Ichikawa I, **Nagata M**. Genetic podocyte lineage reveals progressive podocytopenia with parietal cell hyperplasia in a murine model of focal segmental glomerulosclerosis. **Am J Pathol** 2009May;174(5):1675-82.
4) Sekine Y, Nishibori Y, Akimoto Y, Kudo A, Ito N, Fukuhara D, Kurayama R, Higashihara E, Babu E, Kanai Y, Asanuma K, **Nagata M**, Majumdar A, Tryggvason K, Yan K. Amino acid transporter LAT3 is required for podocyte development and function. **J Am Soc Nephrol.** 2009 Jul;20(7):1586-96
5) Kobayashi A, Goto Y, **Nagata M**, Yamaguchi Y Granular swollen epithelial cells: a histological and diagnostic marker for mitochondrial nephropathy **Am J Sur Pathol** 34: 262-70, 2010

Infection Biology

Principal Investigator: Professor Kyosuke Nagata
E-mail address: knagata@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/infectionbiology/virology/index_english.html

Other Faculty Members:
Associate Professor; Kaoru Takeuchi, Mitsuru Okuwaki
Assistant Professor; Shoko Saito, Kohsuke Kato, Atsushi Kawaguchi

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) Discovery of novel factors using an influenza virus replicon system in yeast
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) Kohsuke Kato, Mitsuru Okuwaki, **Nagata K**. Involvement of Template Activating Factor-I as a chaperone in linker histone dynamics. ***J. Cell Sci.***, 2011; 124: 3254-3265.

2) 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.

3) 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.

4) 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.

5) 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.

6) Haruki H, Okuwaki M, Miyagishi M, Taira K, **Nagata K**. Involvement of TAF-I/SET in transcription of adenovirus early genes as a positively acting factor. ***J. Virol.***, 2006; 80: 794-801.

Immunology

Principal Investigator (Professor): Akira Shibuya, M.D., Ph.D
E-mail address: ashibuya@md.tsukuba.ac.jp
URL:http://www.md.tsukuba.ac.jp/basic-med/immunology/immunol.index.html

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

Regenerative Medicine and Stem Cell Biology

Principle Investigator: Osamu Ohneda
E-mail address: oohneda@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/remed/

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
Dr. Georgina Salazar (Assistant Professor), georgina.salazar@gmail.com

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 itself and tumor endothelial cell)

♦Summer School Course (2012)♦

1) Basic Radiobiology for Mesenchymal stem cells
2) Neural Differentiation of human iPS for clinical use

Recent Publications:

1) 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.
2) 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.
3) 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.
4) 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.
5) Yamashita T, Ohneda O, Nagano M, Iemitsu M, Makino Y, Tanaka H, Miyauchi H, Goto K, Ohneda K, Fujii-Kuriyama Y, Lorenz Poellinger, and Yamamoto M. Abnormal heart development and lung remodeling in mice lacking a HIF-related bHLH-PAS protein NEPAS. **Mol. Cell. Biol.** 2008; 28: 1285-1297.
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.

Name of the Field: Environmental Medicine
Principal Investigator: Yoshito Kumagai
E-mail address: yk-em-tu@md.tsukuba.ac.jp
URL:http://www.md.tsukuba.ac.jp/community-med/environmental_medicine/main/toppage.html

Other Faculty Members
Assistant Professor Yasuhiro Shinkai: ya_shinkai@md.tsukuba.ac.jp

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.

Molecular and Genetic Epidemiology/Public Health Medicine

Principal Investigator: Naoyuki Tsuchiya
E-mail addresses: tsuchiya@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/community-med/publicmd/index.html

Other Faculty Members;
Associate Professor Jun Ohashi, juno-tky@umin.ac.jp
Assistant Professor Kazumasa Yamagishi, k-yamagishi@umin.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)
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)
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)

Selected Recent Publications

1) Furukawa H, Oka S, Shimada K, 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** doi:10.1136/annrheumdis-2012-201944
2) Hasebe N, Kawasaki A, Ito I, Kawamoto M, Hasegawa M, Fujimoto M, Furukawa H, Tohma S, Sumida T, Takehara K, Sato S, Kawaguchi Y, **Tsuchiya N**. Association of *UBE2L3* polymorphisms with diffuse cutaneous systemic sclerosis in a Japanese population. **Ann Rheum Dis** 2012;71:1259-1260.
3) 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.
4) **Ohashi J**, Naka I, **Tsuchiya N**. The impact of natural selection on an *ABCC11* SNP determining earwax type. **Mol Biol Evol** 2011;28:849-857.
5) Chei CL, **Yamagishi K**, Kitamura A, Kiyama M, Imano H, Ohira T, et al. C-reactive protein levels and risk of stroke and its subtype in Japanese: the Circulatory Risk in Communities Study (CIRCS). **Atherosclerosis** 2011;217:187-193.
6) 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.

Research Field: Occupational Psychiatry / Space Medicine [#1]
Longevity medicine Endowed Chair [#2]
Principal Investigator: Prof. Ichiyo Matsuzaki [#1]
E-mail address: ZAW00312@nifty.com
URL: http://www.md.tsukuba.ac.jp/community-med/envhlth/

Other Faculty Members;
Assistant Professor: Shin-ichiro Sasahara [#1, #2],s-sshara@md.tsukuba.ac.jp
Assistant Professor: Satoshi Yoshino [#1], satoshi-yoshino.gm@u.tsukuba.ac.jp

Major Scientific Interests of the Group

Environmental and occupational prevention of work-related diseases.
Empirical and epidemiological study on risk factors for work-related diseases and prevention.

Projects for Regular Students in Doctoral or Master's Programs

1) Various mental disorder patients' treatment in occupational health.
Training of psychiatric clinical ability demanded on site of industrial medicine.
2) Techniques for managing working people's mental/physical health (industrial physicians).
3) Research by use of epidemiological techniques.

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

1) Health care for workers focusing on their mental health
2) Clinical psychiatry (major depressive disorder, adjustment disorder etc.)
3) Return-to-work support

Recent Publications

1) **I.Matsuzaki**, T. Sagara, Y. Ohshita, H. Nagase, K. Ogino, A. Eboshida, **S. Sasahara**, H. Nakamura : Psychological factors including sense of coherence and some lifestyles are related to General Health Questionnaire-12 (GHQ-12) in elderly workers in Japan. **Environ. Health Prev. Med.**, Vol.12, 71-77, 2007
2) **S. Yoshino**, **S. Sasahara**, T. Maeno, K. Kitaoka-Higashiguchi, Y. Tomotsune, K. Taniguchi, E. Tomita, K. Usami , T. Haoka, H. Nakamura, **I. Matsuzaki** : Relationship between mental health of Japanese residents and the quality of medical service. **Journal of Physical Fitness, Nutrition and Immunology**, Vol. 17(1), 3-11, 2007
3) H. Tatsukawa, **S. Sasahara**, **S. Yoshino**, Y Tomotsune, K Taniguchi, H. Nakamura, **I. Matsuzaki** : Influence of the stress coping ability of supervisors on the stress situation of their subordinates. Journal of Physical Fitness, **Nutrition and Immunology**, Vol.15(2), 82-87, 2005
4) **Sasahara S**, **Matsuzaki I**, Nakamura H, Ozasa K, Endo T, Imai T, Honda Y, Hatta K, Ide T, Motohashi Y, Eboshida A : Environmental factors and lifestyles as risk factors for Japanese cedar pollinosis in recent urban areas. **Arch Complex Environ Studies Arch. Com. Eff. Study**, 15,20-25,2003

Radiation Biology
Principal Investigator: Koji Tsuboi
E-mail address: tsuboi-k@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/radiation/

Other Faculty Members
Assistant Professor Takashi Moritake:
moritake@pmrc.tsukuba.ac.jp

Major Scientific Interest of the Group:
Radiation biology is a field of medical sciences dealing with research on the biological actions of ionizing radiation on life or living things. In this field, it is essential to establish robust methods to evaluate and measure biological phenomena by physical parameters. The mission of this group is to clarify the biological characteristics of x-rays and proton beams and to improve the safety and efficacy of x-rays and proton beam radiotherapy.

Projects for Regular Students in Doctoral or Master's Program
1) Proton beam induced DNA damage and repair,
2) Radiation induced tumor immunological reactions,
3) Biological effects of x-ray micro beams,
4) Radiation protection.

Study Programs for Short Stay Students (2 weeks – 6 months)
1) Cell culture techniques and basic in vitro radio sensitivity assays
2) Methods to evaluate DNA damage in cells and tissues
3) Studies on physical parameters to evaluate biological effects

Recent Publications
1) Zhengshan Hong, Yuki Kase, Takashi Moritake, Ariungerel Gerelchuluun, Lue Sun, Kenshi Suzuki, Toshiyuki Terunuma, Kiyoshi Yasuoka, *Hiroaki Kumada,* Kazunori, Hideyuki Sakurai, Takeji Sakae, and Koji Tsuboi. Lineal energy-based evaluation of oxidative DNA damage induced by proton beams and X-rays. Int. J. Radiat. Biol. in press.
2) Gerelchuluun A, Hong Z, Sun L, Suzuki K, Terunuma T, Yasuoka K, Sakae T, Moritake T, Tsuboi K. Induction of in situ DNA double-strand breaks and apoptosis by 200 MeV protons and 10 MV X-rays in human tumour cell lines. Int J Radiat Biol. 2011 Jan;87(1):57-70.
3) Mizumoto M, Tsuboi K, Igaki H, Yamamoto T, Takano S, Oshiro Y, Hayashi Y, Hashii H, Kanemoto A, Nakayama H, Sugahara S, Sakurai H, Matsumura A, Tokuuye K. Phase I/II Trial of Hyperfractionated Concomitant Boost Proton Radiotherapy for Supratentorial Glioblastoma Multiforme. Int J Radiat Oncol Biol Phys. 2009 Aug 19.
4) Tsuboi K, Moritake T, Tsuchida Y, Tokuuye K, Matsumura A, Ando K. Cell cycle checkpoint and apoptosis induction in glioblastoma cells and fibroblasts irradiated with carbon beam. J Radiat Res (Tokyo). 2007 Jul;48(4):317-25.

Research Field: Functional Genomics
Principal Investigator: Prof. Shunsuke Ishii
E-mail address: sishii@rtc.riken.jp
URL: http://rtcweb.rtc.riken.jp/lab/mg/en/mg.html

Other Faculty Member
Associate Professor Teruaki Nomura: tnomura@rtc.riken.jp

Major Scientific Interests of the Group

Transcriptional control is a key step for development, stress response, and various diseases in human beings. We focus on understanding the molecular mechanisms of transcription control. Our lab has three groups (molecular biology, mouse, and Drosophila), which are using different methods, but focus on the same transcriptional regulators.

Projects for Regular Students in Doctoral or Master's Programs

1) Role of nuclear oncogene products Myb and Ski in cancer
2) Epigenetic regulation by ATF-2 family transcription factors
3) Mechanism of iPSC generation

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

1) Molecular biology experiments for studying transcriptional control
2) Genetic experiments using Drosophila and mice

Recent Publications

1) Seong KH, Li D, Shimizu H, Nakamura R and **Ishii S**. Inheritance of stress-induced, ATF-2-dependent epigenetic change. ***Cell*** in press, 2011.
2) Maekawa T, Kim S, Nakai D, Makino C, Takagi T, Ogura H, Yamada K, Chatton B and **Ishii S**. Social isolation stress induces ATF-7 phosphorylation and impairs silencing of the 5-HT 5B receptor gene. **EMBO J.** 29: 196-208, 2010.
3) Yamauchi T, Ishidao T, Nomura T, Shinagawa T, Tanaka Y, Yonemura S and **Ishii S**. A B-Myb complex containing clathrin and filamin is required for mitotic spindle function. **EMBO J.** 27: 1852-1862, 2008.
4) Jin W, Takagi T, Kanesashi S, Kurahashi T, Nomura T, Harada J and **Ishii S**. Schnurri-2 controls BMP-dependent adipogenesis via interaction with Smad proteins. **Dev. Cell** 10: 461-471, 2006.5) Kanei-Ishii C, Ninomiya-Tsuji J, Tanikawa J, Nomura T, Ishitani T, Kishida S, Kokura K, Kurahashi T, Ichikawa-Iwata E, Kim Y, Matsumoto K and **Ishii S**. Wnt-1 signal induces phosphorylation and degradation of c-Myb protein via TAK1, HIPK2, and NLK. **Genes Dev.** 18, 816-829, 2004.

Research Field: International Medicine
Principal Investigator: Prof. Shigeyuki Kano
E-mail address: kano@ri.ncgm.go.jp
URL: http://www.ncgm.go.jp/rese/top/j/rese_trop.html

Other Faculty Members: none

Major Scientific Interests of the Group

The objectives of our research group are to develop appropriate medical technologies that are transferable to developing countries, in order to promote their primary health status. The following two subjects are our biggest research targets.

1) Research on controlling emerging and re-emerging infectious diseases of international importance.
2) Research on international medical cooperation.

Projects for Regular Students in Doctoral or Master's Programs

1) Biology and pathophysiology of re-emerging infectious diseases
   (a) Basic and clinical research on malaria
   (b) Research on the development of malaria vaccine
2) Social technology development for controlling diseases in developing countries
   (a) Researches on global malaria and parasite control strategy
   (b) Evaluation of international health cooperation projects

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

1) *In vitro* culture of *Plasmodium falciparum* and its drug susceptibility assay
2) Discrimination of parasite species by PCR and other methods, including drug resistant DNA marker detection.

Recent Publications

1) Iwagami M, Fukumoto M, Hwang SY, Kim SH, Kho WG, Kano S: Population structure and transmission dynamics of *Plasmodium vivax* in the Republic of Korea based on microsatellite DNA analysis. **PLoS Negl Trop Dis**, 6(4):e1592, 2012
2) Tangpukdee N, Krudsood S, Kano S, Wilairatana P: Falciparum malaria parasitemia index for predicting severe malaria. **Int J Lab Hematol** 34(3): 320-327, 2012
3) Culleton R, Coban C, Zeyrek FY, Cravo P, Kaneko A, Randrianarivelojosia M, Andrianaranjaka V, Kano S, Farnert A, Arez AP, Sharp PM, Carter R, Tanabe K: The origins of African *Plasmodium vivax*; Insights from mitochondrial genpme sequencing. **PLoS ONE** 6(12): e29137, 2011
4) Noriyuki Okudaira, Motohito Goto, Rieko Yanobu-Takanashi, Masato Tamura, Akihiro An, Yukiko Abe, Shigeyuki Kano, Shotaro Hagiwara, Yukihito Ishizaka, Tadashi Okamura: Involvement of Retrotransposition of Long Interspersed Nucleotide Element-1 in DMBA/TPA-induced Skin Tumorigenesis. **Cancer Science** 102(11): 2000-2006, 2011

Reserch Field: Virology
Principal Investigator: Prof. Ichiro Kurane
E-mail address: kurane@nih.go.jp
URL: http://www.nih.go.jp/niid/index.html

Major Scientific Interests of the Group

Elucidation of the pathogenesis of dengue fever and dengue hemorrhagic fever.

Projects for Regular Students in Doctoral or Master's Programs

1) Establishment of animal models of dengue fever.
2) Role of immune responses in the pathogenesis of dengue hemorrhagic fever.

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

None

Recent Publications

1) Moi, M.L., Lim,C.K., Kotaki, A., Takasaki, T. and **Kurane, I.**: Detection of higher levels of dengue viremia using Fc{gamma}R-expressing BHK-21 cells than Fc{gamma}R-negative cells in secondary infection but not in primary infection. Journal of Infectious Diseases. 203(10): 1405-1414, 2011.
2) Fujii, K., Matsutani, T., Kitaura, K., Suzuki, S., Itoh, T., Takasaki, T., Suzuki, R. and **Kurane, I**.: Comprehensive analysis and characterization of the TCR alpha chain sequences in the common marmoset. **Immunogenetics,** 62(6): 383-385, 2010.
3) Tajima, S., Nerome, R., Nukui, Y., Kato, F, Takasaki, T. and **Kurane, I**.: A single mutation in the Japanese encephalitis virus E protein (S123R) increases its growth rate in mouse neuroblastoma cells and its pathogenicity in mice. **Virology** 396(2): 298-304, 2010.
4) Moi, M.L., Lim, C.K., Takasaki, T. and **Kurane, I**.: Involvement of the Fc gamma receptor IIA cytoplasmic domain in antibody-dependent enhancement of dengue virus infection. **Journal of General Virology** 91(Pt 1): 103-111, 2010.
5) Moi, M.L., Lim, C.K., Kotaki, A., Takasaki, T. and **Kurane, I**.: Discrepancy in neutralizing antibody titers between plaque reduction neutralizing tests with Fcgamma receptor (Fcgamma R)-negative and FcgammaR-expressing BHK-21 cells. **Clinical and Vaccine Imunology** 17(3): 402-7,2010.
6) Lim, C.K., Nishibori, T., Watanabe, K., Ito, M., Kotaki, A., Tanaka, K., **Kurane, I**. and Takasaki, T.: Chikungunya virus isolated from a returnee to Japan from Sri Lanka: isolation of two sub-strains with different characteristics. **American Journal of Tropical Medicine and Hygiene** 81(5): 865-8, 2009.
7) Moi, M.L., Lim, C.K., Kotaki, A., Takasaki, T. and **Kurane, I**.: Development of an antibody-dependent enhancement assay for dengue virus using stable BHK-21 cell lines expressing Fc gammaRIIA. **Journal of Virological Methods** 163(2)205-9, 2010.

Research Field: Experimental Hematology
Principal Investigator: Prof. Yukio Nakamura
E-mail address: yukionak@brc.riken.jp
URL: http://www.brc.riken.jp/lab/cell/

Major Scientific Interests of the Group

In vitro production of red blood cells (RBCs) able to be used in the clinic. For this purpose, we are attempting to establish immortalized human RBC progenitor cell lines from various cell sources such as hematopoietic stem cells, ES cells and iPS cells. In addition, we are studying the mechanisms of enucleation of RBC progenitor cells so as to improve the efficiency of in vitro enucleation.

Projects for Regular Students in Doctoral or Master's Programs

1) Cell culture of human ES and iPS cells. Induction of hematopoietic cells from human ES and iPS cells. Establishment of immortalized human hematopoietic cell lines from various cell sources such as hematopoietic stem cells, ES cells and iPS cells.
2) Molecular mechanisms of enucleation of RBC progenitor cells.

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

1) Cell culture of mouse ES or iPS cells.
2) Cell analysis by flow cytometer.

Recent Publications

1) Nakamura, Y. ES cell-derived erythroid cell lines able to produce mature red blood cells. InTech "Embryonic Stem Cells-Recent Advances in Pluripotent Stem Cell-Based Regenerative Medicine" (edited by Craig Atwood), Chapter 15, p273-288 (2011)
2) Sudo, K., Yasuda, J., and Nakamura, Y. Gene expression profiles of cryopreserved $CD34^+$ human umbilical cord blood cells are related to their bone marrow reconstitution abilities in mouse xenografts. Biochem. Biophys. Res. Commun. 397: 697-705 (2010)
3) Ishigaki, T., Sudo, K., Hiroyama, T., Miharada, K., Ninomiya, H., Chiba, S., Nagasawa, T., and Nakamura, Y. Human hematopoietic stem cells can survive *in vitro* for several months. *Adv. Hematol.* **2009**: ID936761 (open access journal) (2009)
4) Hiroyama, T., Miharada, K., Sudo, K., Danjo, I., Aoki, N., and Nakamura, Y. Establishment of mouse embryonic stem cell-derived erythroid progenitor cell lines able to produce functional red blood cells. PLoS ONE 3: e1544 (open access journal) (2008)
5) Miharada, K., Hiroyama, T., Sudo, K., Nagasawa, T., and Nakamura, Y. Efficient enucleation of erythroblasts differentiated in vitro from hematopoietic stem and progenitor cells. Nat. Biotechnol. 24: 1255-1256 (2006)

Name of the Field: Biochemistry and Molecular Cell Biology
Principal Investigator: Professor and Director General
Keiji Tanaka
E-mail address: tanaka-kj@igakuken.or.jp
URL: http://www.igakuken.or.jp/
Other Faculty Members: Project leader, Masaaki Komatsu; Chief Researcher, Noriyuki Matsuda; Chief Researcher, Yasushi Saeki; Senior Researcher, Yoko Kimura; Senior Researcher, Yukiko Yoshida

Major Scientific Interests of the Group:

In-depth analyses of ubiquitin-, proteasome-, and autophagy-mediated regulatory proteolysis.

Projects for Graduate Students:

1) Molecular mechanisms for assembly and diversity in eukaryotic proteasomes. 2) Physiological and Pathological roles of the autophagy system. 3) Control of mitochondrial homeostasis by PINK1/Parkin whose impairment causes Parkinson's disease.

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

1) Enzymatic assays and affinity purification of eukaryotic proteasomes. 2) Ubiquitylation assays directed by Parkin and SCFFbs ubiquitin E3 ligases. 3) Assays for monitoring autophagy based on genetically engineered mice.

Recent Publications:

1) Matsuda, N., Sato, S., Shiba, K., Okatsu, K., Saisho, K., Gautier, CA Sou, Y., Saiki, S., Kawajiri, S., Sato, F., Kimura, M., Komatsu, M., Hattori, N., and Tanaka, K. (2010) PINK1 stabilized by depolarization recruits Parkin to damaged mitochondria and activates latent Parkin for mitophagy. ***J Cell Biol.*** 189, 211-221

2) Murata, S., Yashiroda, H., and Tanaka, K. (2009) Molecular mechanisms of proteasome assembly. ***Nat. Rev. Mol. Cell. Biol.*** 10, 104-115

3) Kimura, Y., Yashiroda, H., Kudo, T., Koitabashi, S., Murata, S., Kakizuka, A., and Tanaka, K. (2009) An inhibitor of deubiquitinating enzyme regulates ubiquitin homeostasis. ***Cell*** 137, 549-559

4) Saeki, Y., Toh-e, A., Kudo, T., Kawamura, H., and Tanaka, K. (2009) Multiple proteasome-interacting proteins assist the assembly of the yeast 19S regulatory particle. ***Cell*** 137, 900-913

5) Murata, S., Sasaki, K., Kishimoto, T., Niwa, S., Hayashi, H., Takahama, Y., and Tanaka, K. (2007) Regulation of CD8+ T cell development by thymus-specific proteasomes. ***Science*** 316, 1349-1353

6) Komatsu, M., Waguri, S., Koike, M., Sou, Y., Ueno, T., Hara, T., Mizushima, N., Iwata, J., Ezaki, J., Murata, S., Hamazaki, J., Nishito, Y., Iemura, S., Natsume, N., Yanagawa, T., Uwayama, J., Warabi, E., Yoshida, H., Ishii, T., Kobayashi, A., Yamamoto, M., Yue, Z., Uchiyama, Y., Kominami, E., and Tanaka, K. (2007) Homeostatic levels of p62 control cytoplasmic inclusion body formation in autophagy-deficient mice. ***Cell*** 131, 1149-1163

7) Komatsu, M., Waguri, S., Chiba, T., Murata, S., Iwata, J., Ueno, T., Koike, M., Uchiyama, Y., Kominami, E., and Tanaka, K. (2006) Loss of autophagy in the central nervous system causes neurodegeneration. ***Nature*** 441, 880-884