Research Fields	PI	page
University of Tsukuba		
1. Anatomy and Embryology	Takahashi S	1
2. Laboratory Animal Science	Yagami K	2
3. Physiological Chemistry	Kanaho Y	3
4. Molecular Cell Biology	Irie K	4
5. Gene Regulation	Hisatake K	5
6. Molecular Cell Physiology	Okamura N	6
7. Molecular Neurobiology	Masu M	7
8. Medical Genetics	Arinami T	8
9. Diagnostic Pathology	Noguchi M	9
10. Experimental Pathology	Kato M	10
11. Kidney and Vascular Pathology	Nagata M	11
12. Infection Biology	Nagata K	12
13. Immunology	Shibuya A	13
14. Regenerative Medicine and Stem Cell Biology	Ohneda O	14
15. Environmental Medicine	Kumagai Y	15
16. Genetic Epidemiology/ Public Health Medicine	Tsuchiya N	16
17. Occupational Psychiatry/ Space Medicine	Matsuzaki I	17
18. Radiation Biology	Tsuboi K	18
19. Medical Physics	Sakae T	19
20. Infection Biology	Kawaguchi A	20
21. Microbiology	Ohniwa R	21
22. Neurophysiology	Koganezawa T	22
23. Cellular Reprogramming and Biotechnology	Nishimura K	23
24. Molecular Pharmacology	Yanagisawa M	24
25. Functional neuroanatomy	Hiromasa Funato	25
26. Medicinal Chemistry, Organic Chemistry	Hiroshi Nagase, Noriki Kutsumura	26
27. Biochemistry and Molecular Genetics	Qinghua Liu	27
28. Sleep and Memory	Masanori Sakaguchi	28
29. Systems Sleep Biology	Michael Lazarus	29

Cooperative Graduate Programs

30. Functional Genomics	Ishii S	30
31. International Medicine	Kano S	31
32. Virology	Kurane I	32
33. Experimental Hematology	Nakamura Y	33
34. Biochemistry and Molecular Biology	Tanaka K	34

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 in vivo functions of sugar chains on molecules.
In addition to these themes, we are also analyzing functions of sugar chains on molecules in vivo by using genetically manipulated mice.

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) Kudo T, Sato T, Hagiwara K, Kozuma Y, Yamagami T, Ikehara Y, Hamada M, Matsumoto K, Ema M, Murata S, Ohkohchi N, Narimatsu H, **Takahashi S.** C1galt1-deficient mice exhibit thrombocytopenia due to abnormal terminal differentiation of megakaryocytes. **Blood.** 122, 1649-1657, 2013.
2) 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, 2012.
3) 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.
4) 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.
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

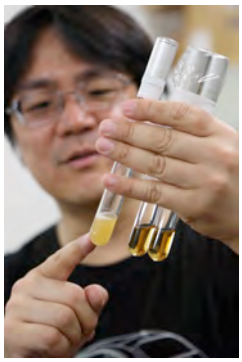
1) Molecular mechanisms through which the small G protein Arf6 regulates each isozyme of the lipid kinase PIP5K.
2) Physiological functions of the phospholipid-metabolizing enzymes, PIP5K and PLD, and of their regulatory protein Arf6 at cellular and whole animal levels.
3) Human diseases caused by the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

Projects for Regular Students in Doctoral or Master's Programs

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

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) Pbp1 is involved in Ccr4- and Khd1-mediated regulation of cell growth through association with ribosomal proteins Rpl12a and Rpl12b. Kimura Y, Irie K, **Irie K.** **Eukaryot Cell.** 2013 June;12(6):864-74.

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.

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
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.

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

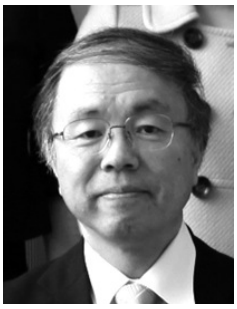
1) Molecular study on neural differentiation
2) Molecular study on axon guidance
3) Molecular study on neural cell migration

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
4) 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

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
Assistant Professor Markus Dahl: carlaxelmarkus@gmail.com

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, Gpnmb etc.) in stem cell maintenance and carcinogenesis using gene-manipulated mice and three dimensional histopathological analysis.
2) Molecular mechanisms of TGF-β related molecules (THG-1) 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)Okita Y, Kamoshida A, Suzuki H, Itoh K, Motohashi H, Igarashi K, Yamamoto M Ogami T, Koinuma D, and **Kato M**. Transforming Growth Factor-β induces transcription factors MafK and Bach1 to suppress expression of the heme oxygenase-1 gene. J. Biol. Chem, *in press*
2)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.
3)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-β signaling. **Mol. Cell** 37: 123-134, 2010.
4)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.
5)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.
6)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.

Infection Biology

Principal Investigator: Atsushi KAWAGUCHI
E-mail address: ats-kawaguchi@md.tsukuba.ac.jp
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
(President Special Lab.; President 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.

Microbiology

Principal Investigator: Ryosuke Ohniwa (Assistant Professor)
E-mail address: ohniwa@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/
infectionbiology/microbiology/english.html

Other Faculty Members
Associate Professor Kazuya Morikawa:
morikawa.kazuya.ga@u.tsukuba.ac.jp
Associate Professor Shinji Saito: sinsaito@md.tsukuba.ac.jp

Major Scientific Interests of the Group

The research aim of our lab is to understand how *Staphylococcus aureus* and other pathogens have evolved to cope with bactericidal factors from host and environment.

Projects for Regular Students in Doctoral or Master's Programs
(including the projects in Microbiology group)

1) Dynamics of cellular structures: nucleoid and membrane
2) Population heterogeneity: stochastic gene expression
3) Natural genetic competence in gram positive pathogens
4) Host-pathogen interaction *in vitro*

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

1) Molecular genetic and biochemical techniques in bacteria
2) Single molecule analysis using atomic force microscopy

Recent Publications:

1) **Ohniwa RL**, Muchaku H, **Saito S**, Wada C and **Morikawa K**. "Atomic force microscopy analysis of the role of major DNA-binding proteins in organization of the nucleoid in *Escherichia coli*." ***PLoS ONE***. **8**, e72954 (2013)
2) **Ohniwa RL**, Kitabayashi K, **Morikawa K**. Alternative cardiolipin synthase Cls1 compensates for stalled Cls2 function in *Staphylococcus aureus* under conditions of acute acid stress. ***FEMS Microbiol Lett***. **338**:141-6 (2013)
3) **Morikawa K**, Takemura A, Inose Y, Tsai M, Nguyen Thi le T, Ohta T and Msadek T. "Expression of a cryptic secondary sigma factor gene unveils natural competence for DNA transformation in *Staphylococcus aureus*". ***PLoS Pathog***, **8**:e1003003. (2012)
4) **Ohniwa RL**, Ushijima Y, **Saito S** and **Morikawa K**, "Proteomic Analyses of Nucleoid-Associated Proteins in *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*." ***PLoS ONE***, **6**, e19172 (2011)
5) Tsai M, **Ohniwa RL**, Kato Y, Takeshita SL, Ohta T, **Saito S**, Hayashi H and **Morikawa K** "*Staphylococcus aureus* requires cardiolipin for survival under high salinity conditions." ***BMC Microbiology***, **11**:13 (2011)

Neurophysiology

Principal Investigator: Tadachika Koganezawa
E-mail address: t-kogane@md.tsukuba.ac.jp
URL: http://www.md.tsukuba.ac.jp/basic-med/physiology/t-kogane/

Major Scientific Interests of the Group

We are studying mechanisms of cardiovascular and respiratory regulation by the central nervous system. Especially, we are paying attention to the autonomic nervous system for the circulatory and respiratory system.

Projects for Regular Students in Doctoral or Master's Programs

Cardiovascular and respiratory regulation by the central nervous system plays crucial roles in homeostasis. Disorder of this system causes serious problems in a living body. Despite this, it has been remained that lots of unknown mechanisms in the cardiovascular and respiratory center. Now, we are studying cardiovascular and respiratory regulation by the autonomic nervous system using electrophysiological methods *in situ* and *in vivo*, and trying to investigate relationship between disorder of the neurogenic regulation and cardiovascular and respiratory diseases.

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

1) Recording of cardiovascular and respiratory parameters in human and rodent.

2)Physiological analysis of cardiovascular and respiratory parameters in human and rodent.

Recent Publications

1) Sabino-Silva R, Ceroni A, **Koganezawa T**, Michelini LC, Machado UF, Antunes VR Baroreceptor-mediated activation of sympathetic nerve activity to salivary glands. **Physiol Behav**, 107(3), 390-396 (2012)

2) Koganezawa T, Okada Y, Terui N, Paton JF, Oku Y A μ-opioid receptor agonist DAMGO induces rapid breathing in the arterially perfused in situ preparation of rat. **Respir Physiol Neurobiol**, 177(2), 207-211 (2011)

3) Koganezawa T, Shimomura Y, Terui N. The viscerosympathetic response in rabbits is mediated by GABAergic and glutamatergic inputs into the sympathetic premotor neurons of the rostral ventrolateral medulla. **Exp Physiol**, 95(11), 1061-1070 (2010)

4) Wang R, **Koganezawa T**, Terui N. Different responses of symapthetic premotor neurons in the rostral ventrolateral medulla to stimulation of the dorsomedial hypothalamus in rabbits. **Brain Res**, 1356, 44-53 (2010)

5) Nishimaru H, **Koganezawa T**, Kakizaki M, Ebihara T, Yanagawa Y. Inhibitory synaptic modulation of Renshaw cell activity in the lumbar spinal cord of neonatal mice. **J Neurophysiol**, 103(6), 3437-3447. (2010)

6) Koganezawa T, Shimomura Y, Teuri N. The role of the RVLM neurons in the viscero-sympathetic reflex: A mini review. **Auton Neurosci**, 142(1-2), 17-19. (2008)

7)Koganezawa T, Terui N. Differential responsiveness of RVLM sympathetic premotor neurons to hypoxia in the rabbit. **Am J Physiol Heart Circ Physiol**., 292, H408-414 (2007)

Cellular Reprogramming and Biotechnology

Principal Investigator: Ken Nishimura
E-mail address: ken-nishimura@md.tsukuba.ac.jp
URL: http://ttweb.sec.tsukuba.ac.jp/nishimura.html

Major Scientific Interests of the Group

Our group studies the molecular mechanism of the cell reprogramming to establish an efficient method of the production of well-reprogrammed iPS cells by using our unique gene transfer system (SeVdp vectors). We are also trying to apply these vector to establish safe cell-differentiation systems.

Projects for Regular Students in Doctoral or Master's Programs

1) Molecular mechanism of iPS cell production by analyzing series of partially reprogrammed cells induced by SeVdp vectors.
2) Establishment of iPS cell production methods with novel factors which improve cell reprogramming.
3) Development of SeVdp vector-based methods to produce differentiated tissues without contaminating undifferentiated cells.

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

1) Production of mouse and human iPS cells using SeVdp vectors.
2) Cell biology and molecular biology experiments for analysis of gene expression.

Recent Publications

1) Wakao H, Yoshikiyo K, Koshimizu U, Furukawa T, Enomoto K, Matsunaga T, Tanaka T, Yasutomi Y, Yamada T, Minakami H, Tanaka J, Oda A, Sasaki T, Wakao R, Lantz O, Udagawa T, Sekiya Y, Higuchi K, Harada N, **Nishimura K**, Ohtaka M, Nakanishi M, Fujita H: Expansion of Functional Human Mucosal-Associated Invariant T Cells via Reprogramming to Pluripotency and Redifferentiation. ***Cell Stem Cell,*** 12: 546-558, 2013
2) Nishimura T, Kaneko S, Kawana-Tachikawa A, Tajima Y, Goto H, Zhu D, Nakayama -Hosoya K, Iriguchi S, Uemura Y, Shimizu T, Takayama N, Yamada D, **Nishimura K**, Ohtaka M, Watanabe N, Takahashi S, Iwamoto A, Koseki H, Nakanishi M, Eto K, Nakauchi H: Generation of rejuvenated antigen-specific T cells by reprogramming to pluripotency and redifferentiation. ***Cell Stem Cell,*** 12: 114-126, 2013
3) **Nishimura K**, Sano M, Ohtaka M, Furuta B, Umemura Y, Nakajima Y, Ikehara Y, Kobayashi T, Segawa H, Takayasu S, Sato H, Motomura K, Uchida E, Kanayasu-Toyoda T, Asashima M, Nakauchi H, Yamaguchi T, Nakanishi M: Development of Defective and Persistent Sendai Virus Vector: a Unique Gene Delivery/Expression System Ideal for Cell Reprogramming. ***J. Biol. Chem.,*** 286: 4760-4771, 2011
4) **Nishimura K**, Segawa H, Goto T, Morishita M, Masago A, Takahashi H, Ohmiya Y, Sakaguchi T, Asada M, Imamura T, Shimotono K, Takayama K, Yoshida Y, Nakanishi M: Persistent and stable gene expression by a cytoplasmic RNA replicon based on a noncytopathic variant Sendai virus. ***J. Biol. Chem.,*** 282: 27383-27391, 2007

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

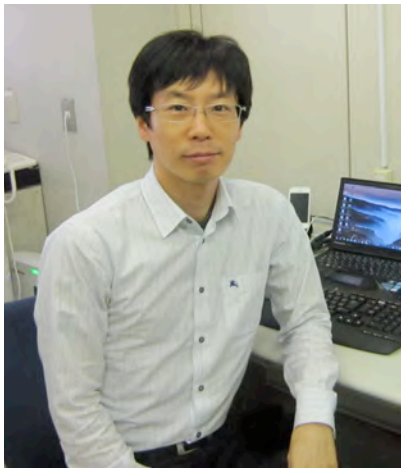
1) Large-scale, forward genetic screening of genes responsible for sleep/wake regulation in mutagenized mice
2) Chemical biology for orexin receptor agonists
3) Analysis of sleep and wakefulness in genetically modified mice
4) In vivo real-time imaging of neuronal activities in the hypothalamus and other 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) 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 $GABA_B$ receptors in orexin-producing neurons results in disrupted sleep/wakefulness architecture. *Proc. Natl. Acad. Sci. USA* **106**:4459-4464, 2009.
2) Funato, H., Tsai, A.L., Willie, J.T., Kisanuki, Y., Williams, S.C., Sakurai, T., Yanagisawa, M. Enhanced orexin receptor-2 signaling prevents diet-induced obesity and improves leptin sensitivity. *Cell Metab.* **9**:64-76, 2009.
3) Funato, H., Sato, M., Sinton, C.M., Gautron, L., Williams, S.C., Skach, A., Elmquist, J.K., Skoultchi, A.I., 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. USA* **107**:18155-18160, 2010.
4) Chang, L., Bramall, N.A., Baynash, G.A., Rattner, A., Rakheja, D., Post, M., McKerlie, J.S., Stewart, J.D., McInnes, R.R., Yanagisawa, M. Endothelin-2 deficiency causes growth retardation, hypothermia, and emphysema in mice. *J.Clin. Invest.* **123**:2643-2653, 2013.
5) Suzuki, A., Sinton, M.C., Green, W.R., Yanagisawa, M. Behavioral and biochemical dissociation of arousal and homeostatic sleep need influenced by prior wakeful experience in mice. *Proc. Natl. Acad. Sci. USA* **110**:10288-10293, 2013.
6) Ikeda, Y., Kumagai, H., Skach, A., Sato, M., Yanagisawa, M. Modulation of circadian glucocorticoid oscillation through adrenal opioid-CXCR7 signaling alters emotional behavior. *Cell* 2013, in press.



Name of the Field: Functional neuroanatomy

Principal Investigator:. Hiromasa Funato
E-mail address: funato.hiromasa.km@u.tsukuba.ac.jp

Major Scientific Interests of the Group

1) Identification of novel genes that regulate sleep/wakefulness behavior using forward genetic approach.

2) Molecular mechanism underlying feeding and body weight homeostasis, anxiety and depressive behavior

Projects for Regular Students in Doctoral or Master's Programs

1) Functional characterization of novel sleep-regulating genes

2) Combined approaches using viral vectors and gene-modified mice to uncover neural circuits underlying sleep/wakefulness behavior, feeding and body weight homeostasis, and anxiety and depressive behavior

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

1) Basic skills for EEG/EMG-based sleep analysis

2) Histological analysis using immunohistochemistry and *in situ* hybridization

3) Behavioral analysis of viral vector-injected mice.

Recent Publications

1) Kenkichi Takase, Satoko Oda, Masaru Kuroda, *__Hiromasa Funato.__ Monoaminergic and neuropeptidergic neurons have distinct expression profiles of histone deacetylases. PLoS One 8:e58473, 1-15, 2013.

2)**Hiromasa Funato**, Makito Sato, Christopher M. Sinton, Laurent Gautron, S. Clay Williams, Amber Skach, Joel K. Elmquist, Arthur I. Skoultchi, Masashi Yanagisawa. Loss of Goosecoid-like and DiGeorge syndrome critical region 14 in interpeduncular nucleus results in altered regulation of rapid eye movement sleep. Proceedings of the National Academy of Sciences of the United States of America 107:18155-18160, 2010.

3)**Hiromasa Funato**, Allen L. Tsai, Jon T. Willie, Yasushi Kisanuki, S. Clay Williams, Takeshi Sakurai, Masashi Yanagisawa. Enhanced orexin receptor-2 signaling prevents diet-induced obesity and improves leptin sensitivity. Cell Metabolism 9:64-76, 2009.

Medicinal Chemistry, **Organic Chemistry**

Principal Investigator: Prof. Hiroshi Nagase, Ph.D.
Associate Prof. Noriki Kutsumura, Ph.D.
E-mail address: nagase.hiroshi.gt@u.tsukuba.ac.jp
kutsumura.noriki.gn@u.tsukuba.ac.jp
URL: http://nagase.wpi-iiis.tsukuba.ac.jp
Other Faculty Members:
Assistant Prof. Naoshi Yamamoto, Ph.D.: yamamoto.naoshi.gu@u.tsukuba.ac.jp
Assistant Prof. Takayuki Ohyoshi, Ph.D.: oyoshi.takayuki.gb@u.tsukuba.ac.jp
Assistant Prof. Tsuyoshi Saitoh, Ph.D.: tsuyoshi-saito.gf@u.tsukuba.ac.jp

Major Scientific Interests of the Group:

1) Design and Synthesis of Orexin Agonists
2) Design and Synthesis of Opioid Receptor Agonists and Antagonists
3) Clarification of Mechanism of Drug Resistance and Dependence

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

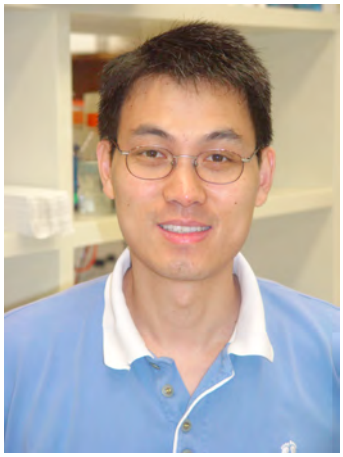
1) Study of Medicinal Chemistry 2) Study of Organic Chemistry
3) Research Development of New Drugs

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

1) Organic Synthesis of Opioid Compounds 2) Organic Synthesis of Orexin Ligands
3) Purification and Separation Technique 4) Basic Drug Design

Selected Recent Publications:

1) Watanabe, Y.; Kitazawa, S.; Nemoto, T.; Hirayama, S.; Iwai, T.; Fujii, H.; **Nagase, H.**, Design and synthesis of novel opioid ligands with an azabicyclo[2.2.2]octane skeleton having a 7-amide chain and their pharmacologies, *Bioorg. Med. Chem*. **2013**, *21*, 3032-3050.
2) **Kutsumura, N.**; Matsubara, Y.; Niwa, K.; Ito, A.; Saito, T., Novel One-pot Method for Regioselective Bromination and Sequential Carbon−Carbon Bond-forming Reactions of Allylic Alcohol Derivatives, *Eur. J. Org. Chem.* **2013**, 3337-3346.
3) Nemoto, T.; Yamamoto, N.; Wada, N.; Harada, Y.; Tomatsu, M.; Ishihara, M.; Hirayama, S.; Iwai, T.; Fujii, H.; **Nagase, H.**, The effect of 17-N substituents on the activity of the opioid κ receptor in nalfurafine derivatives, *Bioorg. Med. Chem. Lett.* **2013**, *23*, 268-272.
4) **Nagase, H.**; Imaide, S.; Hirayama, S.; Nemoto, T.; Fujii, H., Essential structure of opioid κ receptor agonist nalfurafine for binding to the κ receptor 2: Synthesis of decahydro(iminoethano) phenanthrene derivatives and their pharmacologies, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 5071-5074.
5) **Nagase, H.**; Akiyama, J.; Nakajima, R.; Hirayama, S.; Nemoto, T.; Gouda, H.; Hirono, S.; Fujii, H., Synthesis of new opioid derivatives with a propellane skeleton and their pharmacology. Part 2: Propellane derivatives with an amide side chain, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 2775- 2779.
6) **Kutsumura, N.**; Kiriseko, A.; Saito, T., Total Synthesis of (+)-heteroplexisolide E, *Heterocycles* **2012**, *86*, 1367-1378.
7) **Kutsumura, N.**; Kiriseko, A.; Saito, T., First total synthesis of (+)-heteroplexisolide E, *Tetrahedron Lett.* **2012**, *53*, 3274-3276.
8) **Nagase, H.**; Imaide, S.; Yamada, T.; Hirayama, S.; Nemoto, T.; Yamaotsu, N.; Hirono, S.; Fujii, H., Essential Structure of Opioid κ Receptor Agonist Nalfurafine for Binding to κ Receptor 1: Synthesis of Decahydroisoquinoline Derivatives and Their Pharmacologies, *Chem. Pharm. Bull.* **2012**, *60*, 945-948.



Name of the Field: Biochemistry and Molecular Genetics
Principal Investigator: Qinghua Liu, Ph.D.
E-mail address: qinghua.liu@utsouthwestern.edu
URL: http://profiles.utsouthwestern.edu/profile/50723/qinghua-liu.html
Other Faculty Member: None

Major Scientific Interests of the Group
1) RNA Interference and MicroRNAs
2) Sleep Research
3) Odor-induced Innate Fear

Projects for Regular Students in Doctoral or Master's Programs
1) We use genetic screen and biochemical fractionation to identify novel factors (e.g. R2D2, C3PO, and others) and characterize their precise functions in the RNA Interference (RNAi) and MicroRNA pathways.
2) We will understand the molecular circuits of Sleep/Wake control, a fundamental mystery in neuroscience, by integrating mouse genetic screen, quantitative mass spectrometry, and biochemical reconstitution.
3) We are conducting the first genetic screen in mice in search of the "fearless" mutants to understand the molecular circuits of odor-induced innate fear (of predator).

Training Programs for Short Stay Students (one week ~ one trimester)
1) Molecular cloning
2) Fear screen
3) Sleep recording

Recent Publications
1) C. Liang et al. and **Q. Liu.** Sjogren Syndrome Antigen B (SSB)/La promotes global microRNA expression by binding microRNA precursors through stem-loop recognition. ***J Biol Chem,*** 288:723-36 (2013)
2) Y. Liu, H. Tan, H. Tian, C. Liang, S. Chen, **Q. Liu**. Autoantigen La promotes RNAi, antiviral response, and transposon silencing by facilitating multi-turnover RISC catalysis, ***Molecular Cell*** 44:502-8 (2011).
3) X. Ye, N. Huang, Y. Liu, Z. Paroo, C. Huerta, P. Li, S. Chen, **Q. Liu***, H. Zhang* (co-corresponding authors). Structure of C3PO and mechanism of human RISC activation. ***Nat Struct Mol Biol.*** 18:650-657 (2011)
4) Paroo, X. Ye, S. Chen, and **Q. Liu**. Phosphorylation of the human micro-RNA generating complex mediates MAPK/Erk signaling. ***Cell*** 139:112-122 (2009)
5)Y. Liu, X. Ye, F. Jiang, C. Liang, D. Chen, J. Peng, L.N. Kinch, N.V. Grishin, and **Q. Liu**. C3PO, an endoribonuclease that promotes RNAi by facilitating RISC activation. ***Science***,325:750-753 (2009)

Name of the Field: Sleep and Memory
Principal Investigator: Masanori Sakaguchi
E-mail address: masanori.sakaguchi@gmail.com
URL: http://researchmap.jp/masanorisakaguchi/

Major Scientific Interests of the Group

After receiving my medical degree from the University of Tsukuba in 2001, I continued to pursue a research-oriented career in neuroscience, focusing on regenerative medicine, adult neurogenesis and memory in particular. My experience abroad and career thereafter provided me with a firm grasp of world-class techniques (optogenetics, neuronal tracing, behavioral neuroscience, etc.) but furthermore, with an open-mindedness in understanding both Western and Eastern cultures and sufficient communication abilities (fluent English and intermediate-level Chinese) all so vital in scientific research today.

Currently, at IIIS our group strives to investigate the relation between sleep and memory. We hope to clarify the still unanswered questions regarding narcoleptic and cataplectic attacks, neuronal networks possibly involved in sleep-wake transitions as well as the further elucidation of sleep stages, REM, non-REM and slow wave sleep and its significance towards memory consolidation. I welcome motivated and self-driven students and researchers interested in sleep and memory anytime.

Projects for Regular Students in Doctoral or Master's Programs

1) Function of sleep in memory consolidation
2) Sleep regulation by GABA neurons in the VLPO
3) Mapping brain regions activated in each sleep stages

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

1) Optogenetic stimulation of target brain regions
2) Tracing neuronal circuit using virus vectors
3) Analyzing memory trace using mouse genetics

Recent Publications (25 in total, 9 first-author publications)

1) Sakaguchi M and Hayashi Y, Catching the engram: strategies to examine the memory trace, **Mol. Brain** 2012Oct, 5:32(359 viewed in the first 10days, 6th best viewed during the 1st month)
2) Hirota Y, Sawada M, Kida Y, Huang SH, Yamada O, Sakaguchi M, Ogura T, Okano H, Sawamoto K, Roles of planar cell polarity signaling in maturation of neuronal precursor cells in the postnatal mouse olfactory bulb, **Stem Cells**, 2012 Aug;30(8):1726-33.
3) Sakaguchi M, Okano H. Neural stem cells, adult neurogenesis and galectins: from bench to bedside, **Dev. Neurobiol.**, 2012 Jul;72(7):1059-67. doi: 10.1002/dneu.22023.
4) Stone S, Teixeira CM, Zaslavsky K, Wheeler AL, Canabal1 AM, Wang AH, Sakaguchi M, Lozano AM, Frankland PW, Functional Convergence of Developmentally- and Adult-Generated Granule Cells in Dentate Gyrus Circuits Supporting Hippocampus-Dependent Memory, **Hippocampus**. 2011 Dec;21(12):1348-62.
5) Arruda-Carvalho M*., Sakaguchi M*, Akers KG., Josselyn SA., Frankland PW., Post-training ablation of adult-generated neurons degrades previously-acquired memories., **J. Neurosci**. 2011 Oct 19;31(42):15113-27., *The authors contributed equally

Name of the Field: Systems Sleep Biology
Principal Investigator: Michael Lazarus, Ph.D.
E-mail address: lazarus.michael.ka@u.tsukuba.ac.jp
Other Lab Members:
Researcher Yo Oishi, Ph.D.
Researcher Yoko Takata, Ph.D.

Major Scientific Interests of the Group

1) Role of adenosine and dopamine in sleep-wake regulation
2) Motivational state as fundamental regulator of sleep and wake
3) Exploring methamphetamine-sensitive circadian oscillation

Projects for Regular Students in Doctoral or Master's Programs

1) Neuronal mechanisms of dopamine in sleep-wake regulation
2) Characterization of neuronal firing in the nucleus accumbens during sleep-wake states
3) Role of cannabinoid or opioid receptors in the striatum for sleep-wake regulation

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

1) EEG/EMG electrode implantation and recording in mice
2) Engineering and production of adeno-associated viruses
3) Opto-/pharmacogenetic modulation of neural circuitry by using stereotaxic microinjections of viral vectors
4) Immunohistochemistry and in situ hybridization of brain tissue

Recent Publications

1) Lazarus M, Chen J-F, Urade Y, Huang Z-L. Role of the basal ganglia in the control of sleep and wakefulness. Curr Opin Neurobiol 2013; doi: 10.1016/j.conb.2013.02.001
2) Lazarus M, Huang Z-L, Lu J, Urade Y, Chen J-F. How do the basal ganglia regulate sleep-wake behavior? Trends Neurosci 2012, 35: 723-732.
3) Lazarus M, Shen HY, Cherasse Y, Qu WM, Huang ZL, Bass C, Winsky-Sommerer R, Semba K, Fredholm B, Boison D, Hayaishi O, Urade Y, Chen JF. Arousal effect of caffeine depends on adenosine A2A receptors in the shell of the nucleus accumbens. J Neurosci 2011, 31: 10067-10075.
4) Gautron L*, Lazarus M* (Co-first author), Scott MM, Saper CB, Elmquist JK. Identifying the efferent projections of leptin-responsive neurons in the dorsomedial hypothalamus using a novel conditional tracing approach. J Comp Neurol 2010, 518: 2090–2108.
5) Lazarus M, Yoshida K, Coppari R, Bass CE, Mochizuki T, Lowell BB, Saper CB. EP3 prostaglandin receptors in the median preoptic nucleus are critical for fever responses. Nat Neurosci 10(9), 1131-3 (2007).

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.rincgm.jp/department/lab/01/

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) Kimura R, Komaki-Yasuda K, Kawazu S, Kano S. 2-Cys peroxiredoxin of *Plasmodium falciparum* is involved in resistance to heat stress of the parasite. **Parasitol Int** 62:137-43, 2013
2) 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
3) Culleton R, Coban C, Zeyrek FY, et al: The origins of African *Plasmodium vivax*; Insights from mitochondrial genome sequencing. **PLoS ONE** 6(12): e29137, 2011
4) Okudaira N, Goto M, Yanobu-Takanashi R, et al.: Involvement of retrotransposition of long interspersed nucleotide element-1 in skin tumorigenesis induced by 7,12-dimethylbenz[a]anthracene and 12-O-tetradecanoylphorbol-13-acetate. **Cancer Science** 102(11): 2000-6, 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) Kurita, R., Suda, N., Sudo, K., Miharada, K., Hiroyama, T., Miyoshi, H., Tani, K., and Nakamura, Y. Establishment of immortalized human erythroid progenitor cell lines able to produce enucleated red blood cells. ***PLoS ONE*** 8: e59890 (2013)
2) Fujitani, N., Furukawa, J., Araki, K., Fujioka, T., Takegawa, Y., Piao, J., Nishioka, T., Tamura, T., Nikaido, T., Ito, M., Nakamura, Y., and Shinohara, Y. Total cellular glycomics allows characterizing cells and streamlining the discovery process for cellular biomarkers. ***Proc. Natl. Acad. Sci. U.S.A.*** 110: 2105-2110 (2013)
3) Masters, J. R., Alston-Roberts, C., Barrett, T., Burnett, E. C., Cooper, J. R., Dirks, W. G., Freshney, R. I., Healy, L., Kerrigan, L., Kohara, A., Korch, C., MacLeod, R. A. F., Nakamura, Y., Nims, R. W., Reid, Y. A., Storts, D. R., and Capes-Davis, A. (The International Cell Line Authentication Committee) End the scandal of false cell lines. ***Nature*** 492: 186 (2012)
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