



7th Summer Research Program in Tsukuba

July 25- August 5, 2016

List of Laboratories
University of Tsukuba



筑波大学生命環境系
Faculty of Life and
Environmental Sciences
University of Tsukuba



Participating Laboratories

- 1. Tokie Anme**
International Community Care and Lifespan Development: Empowerment Science
- 2. Shigeru Chiba**
Hematology
- 3. Koji Hisatake**
Gene Regulation
- 4. Kiong Ho**
Molecular Parasitology
- 5. Masao Ichikawa**
Global Public Health
- 6. Kenji Irie**
Molecular Cell Biology
- 7. Yasunori Kanaho**
Physiological Chemistry
- 8. Mitsuyasu Kato**
Experimental Pathology and Cancer Signaling
- 9. Atsushi Kawaguchi**
Infectious Biology
- 10. Makoto Kobayashi**
Molecular and Developmental Biology
- 11. Masayuki Masu**
Molecular Neurobiology
- 12. Masafumi Muratani**
Genome Biology
- 13. Masayuki Noguchi**
Diagnostic Surgical Pathology
- 14. Osamu Ohneda**
Regenerative Medicine and Stem Cell Biology
- 15. Akira Shibuya**
Immunology
- 16. Takashi Shiga**
Neurobiology
- 17. Hitoshi Shimano**
Endocrinology and Metabolism
- 18. Fumihiro Sugiyama**
Laboratory Animal Science
- 19. Satoru Takahashi**
Anatomy and Embryology / Laboratory Animal Resource Center
- 20. Koji Tsuboi**
Radiation Biology
- 21. Naoyuki Tsuchiya**
Molecular and Genetic Epidemiology
- 22. Michael Lazarus**
Systems Sleep Biology
- 23. Kaspar Vogt**
Neural Network Analysis in Sleep and Wakefulness
- 24. Toshiharu Enomae**
Paper device and eco-friendly materials
- 25. Hiroshi Ezura**
Olericulture and Floriculture
- 26. Yooichi Kainoh**
Applied Entomology and Zoology
- 27. Yutaka Kitamura**
Food and Biomass Process Engineering
- 28. Yasuhiro Ishiga**
Molecular Plant Pathology
- 29. Sumiko Sugaya**
Pomology
- 30. Hiromi Yanagisawa**
Vascular Matrix Biology
- 31. Yukio Nagasaki**
Biomaterials and Nano-medicines

1. International Community Care and Lifespan Development: Empowerment Sciences



Principal Investigator Tokie Anme

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Major Scientific Interests

The notion of empowerment is a useful concept and method, which can cross national and cultural boundaries to be utilized in many different situations. Our lab designed such a framework of community empowerment for life span development, and applied to programs in other countries, with special attention to local cultural values.

Participation by and empowerment of the people in areas of health promotion, family caregiving, housing, and community development will be examined. This is offered in the hope that we may be able to create communities that can meet their own needs, in an interdependent manner that draws on many levels of contribution to make lives worth living across the lifespan, regardless of where we live.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Cross-Cultural Perspectives on Community Care and Health-Social Services
- 2) Lifespan Development and Environment
- 3) Health Promotion and Community Empowerment
- 4) Child and Elderly Abuse Prevention
- 5) Human Interface with Universal Design: Assistive devices, Housing, and Community Environments

Study Programs for Short Stay Students

- 1) Learning skills how to enhance and evaluate empowerment.
- 2) Field visit on health social settings and implementing empowerment skills.

Recent Publications:

- 1) Gan-Yadam A, Anme T, et al. Factors Associated with Health Service Utilization in Ulaanbaatar, Mongolia: A Population-Based Survey, *Journal of Epidemiology*, Jul 6, 2013
- 2) Mochizuki Y, Anme T, et al. Effects of Wood Education in a Nursery School with a Focus on Changes in Children and Caregivers' Drawings, *Journal of Psychology and Behavioral Sciences*, 3(6), 2013
- 3) Sugisawa Y, Anme T, et al. Strengths and Difficulties of 30-month-olds and Features of the Caregiver-Child Interaction, *Journal of Health Science*, 3(2), 2013
- 4) Anme T, et al. Validity and Reliability of the Social Skill Scale (SSS) as an Index of Social Competence for Preschool Children, *Journal of Health Science*, 3(1), 2013
- 5) Anme T, Kawashima Y et al. Social Interaction and Dementia Prevention : Six-year Follow-up Study, *Public Health Frontier*, 2(2) , 2013
- 6) Anme T, et al. Validity and Reliability of the Index of Child Care Environment (ICCE), *Public Health Frontier*, 2(6), 2013
- 7) Anme T, et al. Wood products Improve the Quality of Life of Elderly People in Assisted Living, *International Multidisciplinary Scientific GeoConference*, 6, 2013
- 8) Anme T, et al. Validity and Reliability of the Index of Active Listening (IAL), *Journal of Applied Medical Sciences*, 2(2), 2013

2. Hematology

Principal Investigator Shigeru Chiba

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Other Faculty Members

Associate Professor Naoshi Obara

Associate Professor Mamiko Sakata-Yanagimoto



Major Scientific Interests

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

Projects for Regular Students in Doctoral or Master's Programs

- Analysis of molecular mechanisms in hematologic malignancies
- Analysis of stromal cells involved in the bone marrow failure

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

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

Recent Publications

- 1) Nishikii H, Kanazawa Y, Umemoto T, Goltsev Y, Matsuzaki Y, Matsushita K, Yamato M, Nolan GP, Negrin R, Chiba S. Unipotent megakaryopoietic pathway bridging hematopoietic stem cells and mature megakaryocytes. *Stem Cells* 33(7):2196-207, 2015
- 2) Nguyen TB, Sakata-Yanagimoto M, Nakamoto-Matsubara R, Enami T, Ito Y, Kobayashi T, Obara N, Hasegawa Y, Chiba S. Double somatic mosaic mutations in TET2 and DNMT3A-origin of peripheral T cell lymphoma in a case. *Ann Hematol* 94(7):1221-3, 2015
- 3) Kato T, Sakata-Yanagimoto M, Nishikii H, Miyake Y, Yokoyama Y, Asabe Y, Kamada Y, Ueno M, Obara N, Suzukawa K, Hasegawa Y, Kitabayashi I, Uchida K, Hirao A, Yagita H, Kageyama R, Chiba S. Hes1 suppresses acute myeloid leukemia development through FLT3 repression. *Leukemia* 29(3):576-85, 2015
- 4) Muto H, Sakata-Yanagimoto M, Nagae G, Shiozawa Y, Miyake Y, Enami T, Kamada Y, Kato T, Yoshida K, Uchida K, Nanmoku T, Sanada M, Obara N, Suzukawa K, Nakamura N, Aburatani H, Ogawa S, Chiba S. Reduced TET2 Function Leads to T-cell Lymphoma with Follicular Helper T cell-like Features in mice. *Blood Cancer J* 4:e264, 2014
- 5) Nakamoto-Matsubara R, Sakata-Yanagimoto M, Enami T, Yoshida K, Yanagimoto S, Shiozawa Y, Nanmoku T, Satomi K, Muto H, Obara N, Kato T, Kurita N, Yokoyama Y, Izutsu K, Ota Y, Sanada M, Shimizu S, Komeno T, Sato Y, Ito T, Kitabayashi I, Takeuchi K, Nakamura N, Ogawa S, Chiba S. Detection of the G17V RHOA mutation in angioimmunoblastic T-cell lymphoma and related lymphomas using quantitative allele-specific PCR. *PLoS ONE* 9(10):e109714, 2014
- 6) Sakata-Yanagimoto M, Enami T, Yoshida K, Shiraishi Y, Ishii R, Miyake Y, Muto H, Tsuyama N, Sato-Otsubo A, Okuno Y, Sakata S, Kamada Y, Nakamoto-Matsubara R, Tran NB, Izutsu K, Sato Y, Ohta Y, Furuta J, Shimizu S, Komeno T, Sato Y, Ito T, Noguchi M, Noguchi E, Sanada M, Chiba K, Tanaka H, Suzukawa K, Nanmoku T, Hasegawa Y, Nureki O, Miyano S, Nakamura N, Takeuchi K, Ogawa S, Chiba S. Somatic RHOA mutation in angioimmunoblastic T cell lymphoma. *Nat Genet* 46(2):171-5 2014

3. Gene Regulation

Principal Investigator Koji Hisatake

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Major Scientific Interests

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) **Fukuda A**, Shimada M, Nakadai T, **Nishimura K**, **Hisatake K**: Heterogeneous Nuclear Ribonucleoprotein R Cooperates with Mediator to Facilitate Transcription Reinitiation on the c-Fos Gene. **PLoS ONE** 8(8): e72496. doi:10.1371/journal.pone.0072496 (2013).
- 2) 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).
- 3) 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).
- 4) **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).
- 5) 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).

4. Molecular Parasitology

Principal Investigator Kiong Ho

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Major Scientific Interests

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

Projects for Graduate Students

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

Study Programs for Short Stay Students

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

Selected Publications

- 1) Gu H, Yoshinari S, Ghosh R, Murakami KS, Ignatochkina AV, Gollnick P and Ho CK. (2016) Structural and Mutational Analysis of Archaeal ATP-dependent RNA ligase Identifies Amino Acid Required for RNA Binding and Catalysis. *Nucleic Acid Res.* 44: 2337 - 2347.
- 2) Smith P, Ho CK, Takagi Y, Djaballah H, and Shuman S. (2016) Nanomolar Inhibitors of Trypanosoma brucei RNA Triphosphatase. *mBIO* 7: e000058-16
- 3) Ignatochkina AV, Takagi Y, Liu Y, Nagata K, and Ho CK. (2015) The Messenger RNA Decapping and Recapping Pathway in *Trypanosoma*. *Proc. Natl. Acad. Sci. USA*
- 4) Torchea C, Takagi Y and Ho CK. Archaea RNA Ligase is a Homodimeric Protein that Catalyzes Intramolecular Ligation of Single-Stranded RNA and DNA. (2008) *Nucleic Acid Res.* 36: 6218 - 6227.
- 5) Takagi Y, Sindkar S, Ekonomidis D, Hall MP and Ho CK. (2007) *Trypanosoma brucei* Encodes a Bifunctional Capping Enzyme Essential for Cap 4 Formation on the Spliced Leader RNA. *J. Biol. Chem.* 282: 15995-16005.
- 6) Hall MP and Ho CK. (2006) Functional Characterization of a 48-kDa *Trypanosoma brucei* Cap 2 RNA Methyltransferase. *Nucleic Acid Res.* 2006 34: 5594 - 5602.
- 7) Pfeffer S, Sewer A, Lagos-Quintana M, Sheridan R, Sander C, Grässer FA, van Dyk LF, Shuman S, Ho CK, Chien M, Russo JJ, Ju J, Randall G, Lindenbach BD, Rice CM, Simon V, Ho DD, Zavolan M, and Tuschl T. Identification of the MicroRNAs of the Herpesvirus Family. *Nature Method* 2005; 2: 269-276..

5. Global Public Health

Principal Investigator Masao Ichikawa
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Major Scientific Interests

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

Projects for Regular Students in Doctoral or Master’s Programs

Child burn prevention in Mongolia; Health systems analysis in Uzbekistan; Effects of nutritional status on surgical outcomes among cancer patients in Vietnam; Psychological impact of cervical cancer screening; Prehospital care/EMS; Food dessert and undernutrition among older adults

Study Program for Short Stay Students*

Systematic Review Workshop. Find “What is Systematic Review” at:

<http://www.cochranelibrary.com/>

<http://www.campbellcollaboration.org/>

*Participants are expected to have basic understanding (undergraduate level) of epidemiological and statistical principles.

Recent Publications

- 1) Nakahara S, Tomio J, Ichikawa M, Nakamura F, Nishida M, Takahashi H, Morimura N, Sakamoto T. Association of bystander interventions with neurologically intact survival among patients with bystander-witnessed out-of-hospital cardiac arrest in Japan. *JAMA* 2015;314:247-54.
- 2) Ichikawa M, Nakahara S, Taniguchi A. Older drivers' risks of at-fault motor vehicle collisions. *Accid Anal Prev* 2015;81:120-3.
- 3) Ichikawa M, Nakahara S, Inada H. Impact of mandating a driving lesson for older drivers at license renewal in Japan. *Accid Anal Prev* 2015;75:55-60.
- 4) Nakahara S, Ichikawa M, Nakajima Y. Effects of increasing child restraint use in reducing occupant injuries among children aged 0-5 years in Japan. *Traffic Inj Prev* 2015;16:55-61.
- 5) Ichikawa M, Inada H, Kumeji M. Reconsidering the effects of blue-light installation for prevention of railway suicides. *J Affect Disord* 2014;152-154:183-5.

6. Molecular Cell Biology

Principal Investigator Prof. Kenji Irie

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Other Faculty Members

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Assistant Professor Yasuyuki Suda: ysuda@md.tsukuba.ac.jp

Assistant Professor Yuichi Kimura: kimura@md.tsukuba.ac.jp



Major Scientific Interests

- 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 endoplasmic reticulum stress response
- Prospore membrane formation by vesicle docking

Projects for Regular Students in Doctoral or Master's Programs

- 1) Stability control of *MTL1* mRNA by the RNA-binding protein Khd1 in yeast
- 2) Post-transcriptional regulation of gene expression by Khd1, Ccr4, and Pbp1
- 3) Regulation of cell growth by an yeast ortholog of ATXN2, Pbp1, and ribosomal proteins.
- 4) Regulation of 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) The *Saccharomyces cerevisiae* AMPK, Snf1, Negatively Regulates the Hog1 MAPK Pathway in ER Stress Response. Mizuno T, Masuda Y, Irie K. *PLoS Genet.* 11(9):e1005491, 2015.
- 2) Pbp1 is involved in the Ccr4 and Khd1-mediated regulation of cell growth through the association with ribosomal proteins, Rpl12a and Rpl12b. Kimura Y, Irie K, Irie K. *Eukaryot Cell.* 2013 Jun;12(6):864-74.
- 3) Stau1 regulates Dvl2 expression during myoblast differentiation. Yamaguchi Y, Naiki T, Irie K. *Biochem Biophys Res Commun.* 2012 Jan 6;417(1):427-32.
- 4) 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.
- 5) 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.

7. Physiological Chemistry

Principal Investigator Yasunori Kanaho

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Other Faculty Members

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Assistant Professor Yuji Funakoshi: funa@md.tsukuba.ac.jp

Assistant Professor Naohiro Katagiri: nkatagiri@md.tsukuba.ac.jp



Major Scientific Interests

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) Hongu T, Funakoshi Y, Fukuhara S, Suzuki T, Sakimoto S, Takakura N, Ema M, Takahashi S, Itoh S, Kato M, Hasegawa H, Mochizuki N, **Kanaho Y**. Arf6 regulates tumour angiogenesis and growth through HGF-induced endothelial $\beta 1$ integrin recycling. *Nat Commun.* 6, 7925, 2015
- 2) Akiyama M, Hasegawa H, Hongu T, Frohman MA, Harada A, Sakagami H, **Kanaho Y**. Trans-regulation of oligodendrocyte myelination by neurons through small GTPase Arf6-regulated secretion of fibroblast growth factor-2. *Nat. Commun.* 5:4744 (2014).
- 3) 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)
- 4) 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)
- 5) 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)

8. Experimental Pathology and Cancer Signaling

Principal Investigator Mitsuyasu Kato

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Major Scientific Interests

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

Projects for Regular Students in Doctoral or Master's Programs

- 1) Molecular mechanisms of TGF- β related molecules (TMEMPAI, MafK, GPNMB) in tissue stem cell maintenance and carcinogenesis.
- 2) Molecular mechanisms of TGF- β related molecules (THG-1 etc.) in squamous cell carcinoma formation.
- 3) Macrocyclic peptides screening for the establishment of live imaging probes and molecular targeting therapy.

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

- 1) Tissue preparation, Immunohistochemistry and 3D reconstruction analysis
- 2) *In vitro* tumorigenic assays (cell proliferation, sphere forming assay, matrigel invasion assay, 3D culture assay etc.)

Recent Publications

- 1) Yoon JH, Sudo K, Kuroda M, **Kato M**, Lee IK, Han JS, Nakae S, Imamura T, Kim J, Ju JH, Kim DK, Matsuzaki K, Weinstein M, Matsumoto I, Sumida T, Mamura M. Phosphorylation status determines the opposing functions of Smad2/Smad3 as STAT3 cofactors in TH17 differentiation. **Nat Commun.** 6: 7600, 2015.
- 2) Vo Nguyen TT, Watanabe Y, Shiba A, Noguchi M, Itoh S and **Kato M**. TMEMPAI/PMEPA1 enhances tumorigenic activities in lung cancer cells. **Cancer Sci.** 105: 334-341, 2014.
- 3) 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**, 288: 20658-20667, 2013.
- 4) 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.
- 5) 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**. TMEMPAI, a transmembrane TGF- β -inducible protein, sequesters Smad proteins from active participation in TGF- β signaling. **Mol. Cell** 37: 123-134, 2010.
- 6) Nakano N, Itoh S, Watanabe Y, Maeyama K, Itoh F, and **Kato M**. Requirement of TCF7L2 for TGF- β -dependent transcriptional activation of the TMEMPAI gene. **J Biol Chem.** 285: 38023-38033, 2010.
- 7) 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.

9. Infection Biology

Principal Investigator Atsushi Kawaguchi

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Other Faculty Members

Associate Professor Mitsuru Okuwaki

Assistant Professor Shoko Saito, Kohsuke Kato

(Nagata Special Lab.; Kyosuke Nagata)



Major Scientific Interests

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.

10. Molecular and Developmental Biology

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Major Scientific Interests

- Gene regulation in the cellular defense mechanisms against a variety of stresses
- Gene regulation in the cell-fate determination especially in hematopoiesis

Projects for Regular Students in Doctoral or Master's Programs

- 1) Stress sensors in the Keap1-Nrf2 system
- 2) Gene regulation of Nrf2-dependent cytoprotective genes
- 3) Determination of hematopoietic and endothelial cell fate
- 4) Determination of erythropoietic and myelopoietic cell fate
- 5) Relationship between cell differentiation and energy pathways
- 6) Use of zebrafish to study gerontology

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

- 1) Gene expression analyses using zebrafish embryos by whole-mount *in situ* hybridization
- 2) Examination of toxicity/medicinal effects of oxidants and/or anti-oxidants using zebrafish embryos

Recent Publications

- 1) Takeuchi, M., Fuse, Y., Watanabe, M., Andrea, C.S., Takeuchi, M., Nakajima, H., Ohashi, K., Kaneko, H., Kobayashi-Osaki, M., Yamamoto, M. and **Kobayashi, M.** (2015) LSD1/KDM1A promotes hematopoietic commitment of hemangioblasts through downregulation of Etv2. *Proc. Natl. Acad. Sci. USA* 112: 13922-13927.
- 2) Fuse, Y., Nakajima, H., Nakajima-Takagi, Y., Nakajima, O. and **Kobayashi, M.** (2015) Heme-mediated inhibition of Bach1 regulates the liver specificity and transience of the Nrf2-dependent induction of zebrafish heme oxygenase 1. *Genes Cells* 20: 590-600.
- 3) Mukaigasa, K., Nguyen, L.T.P., Li, L., Nakajima, H., Yamamoto, M. and **Kobayashi, M.** (2012) Genetic evidence of an evolutionarily conserved role for Nrf2 in the protection against oxidative stress. *Mol. Cell. Biol.* 32: 4455-4461.
- 4) Nakajima, H., Nakajima-Takagi, Y., Tsujita, T., Akiyama, S., Wakasa, T., Mukaigasa, M., Kaneko, H., Tamaru, Y., Yamamoto, M. and **Kobayashi, M.** (2011) Tissue-restricted induction of Nrf2 and its target genes in zebrafish with gene-specific variations in the induction profiles. *PLoS ONE* 6: e26884.
- 5) Tsujita, T., Li, L., Nakajima, H., Iwamoto, N., Nakajima-Takagi, Y., Ohashi, K., Kawakami, K., Kumagai, Y., Freeman, B. A., Yamamoto, M. and **Kobayashi, M.** (2011) Nitro-fatty acids and cyclopentenone prostaglandins share strategies to activate the Keap1-Nrf2 system: a study using green fluorescent protein transgenic zebrafish. *Genes Cells* 16: 46-57.
- 6) Takeuchi, M., Kaneko, H., Nishikawa, K., Kawakami, K., Yamamoto, M. and **Kobayashi, M.** (2010) Efficient transient rescue of hematopoietic mutant phenotypes in zebrafish using *Tol2*-mediated transgenesis. *Dev. Growth Differ.* 52: 245-250.

11. Molecular Neurobiology

Principal Investigator Masayuki Masu

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Lecturer: Kazuko Keino-Masu: kazumasu@md.tsukuba.ac.jp

Assistant Professor: Takuya Okada: okada.takuya.gw@u.tsukuba.ac.jp



Major Scientific Interests

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) Confocal microscopy
- 3) 3D imaging of neural network
- 4) Transparent brain technique
- 5) In situ hybridization

Recent Publications

- 1) **Masu M**. Proteoglycans and axon guidance: a new relationship between old partners. **J Neurochem** doi: 10.1111/jnc.13508.
- 2) Freeman SD, Keino-Masu K, **Masu M** and Ladher RK. Expression of the heparan sulfate 6-O-endosulfatases, Sulf1 and Sulf2, in the avian and mammalian inner ear suggests a role for sulfation in inner ear development. **Dev Dyn** 244: 168-180, 2015.
- 3) 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.
- 4) 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.
- 5) 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.
- 6) Keino-Masu K, **Masu M**, et al. *Deleted in Colorectal Cancer (DCC)* Encodes a Netrin Receptor. **Cell** 87: 175-185, 1996.

12. Genome Biology

Principal Investigator Masafumi Muratani

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Major Scientific Interests

We develop methods for genome and epigenome analysis of limited samples. Main area of application is characterization of clinical tissue samples from Tsukuba Human Tissue Bank. We try to link histopathological features of human diseases to regulatory status of the genome.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Clinical sample analysis using chromatin immunoprecipitation combined with 2nd generation sequencing (ChIPseq) and RNAseq, data analysis and validation of potential disease biomarkers.
- 2) Genomics and epigenomics analysis of human and experimental mouse samples at single-cell resolution.

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

- 1) Access to genomics databases, integrative analysis of regulatory regions, gene expression and genetic variations.
- 2) Genomics and epigenomics assays, chromatin immunoprecipitation, RNA assays and genotyping.

Selected Publications

- 1) Kumar V*, Rayan NA*, Muratani M*, Lim S, Elanggovan B, Lixia X, Lu T, Makhija H, Poschmann J, Lufkin T, Ng HH, Prabhakar S. Comprehensive benchmarking reveals H2BK20 acetylation as a distinctive signature of cell-state-specific enhancers and promoters. *Genome Res.* pii: gr.201038.115, 2016. (*Equal contribution)
- 2) Kakran M*, Muratani M*, Tng WJ, Liang H, Trushina DB, Sukhorukov GB, Ng HH, Antipina MN. Layered polymeric capsules inhibiting the activity of RNases for intracellular delivery of messenger RNA. *J. Mater. Chem. B.* Vol.3, 5842-5848, 2015. (*Equal contribution)
- 3) Muratani M, Deng N, Ooi WF, Lin SJ, Xing M, Xu C, Qamra A, Tay ST, Malik S, Wu J, Lee MH, Zhang S, Tan LL, Chua H, Wong WK, Ong HS, Ooi LL, Chow PK, Chan WH, Soo KC, Goh LK, Rozen S, Teh BT, Yu Q, Ng HH, Tan P. Nanoscale chromatin profiling of gastric adenocarcinoma reveals cancer-associated cryptic promoters and somatically acquired regulatory elements. *Nat Commun.* 5:4361, 2014.
- 4) V. Kumar, M. Muratani, N.A. Rayan, P. Kraus, T. Lufkin, H.H. Ng, S. Prabhakar. Uniform, optimal signal processing of mapped deep-sequencing data. *Nature Biotechnology*, Vol.31(7), 615-22, 2013
- 5) J.H. Ng*, V. Kumar*, M. Muratani*, P. Kraus, J.C. Yeo, L.P. Yaw, K. Xue, T. Lufkin, S. Prabhakar, H.H. Ng: In vivo epigenomic profiling of germ cells reveals germ cell molecular signatures, *Developmental Cell*, Vol.24(3), 324-33, 2013 (*Equal contribution)

13. Diagnostic Surgical Pathology

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Major Scientific Interests

Molecular pathology of multistep carcinogenesis

Studies of the initial genetic alterations of precancerous lesions and early carcinoma

Studies of the interactions between cancer cells and interstitial cells

Projects for Regular Students in Doctoral or Master's Programs

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.

Produce monoclonal antibodies against fetal swine to screen for specific antibodies against human carcinomas.

In vitro and *in vivo* studies of the molecular mechanisms of the reproduction of liver tissue.

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

Basic techniques of immunohistochemistry, *in situ* hybridization, and FISH

Basic techniques of tissue micro-dissection

Recent Publications

- 1) Shiba-Ishii A and **Noguchi M**. Aberrant Stratifin overexpression is regulated by tumor-associated CpG demethylation 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 lactoferrin 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.

14. Regenerative Medicine and Stem Cell Biology

Principal Investigator Osamu Ohneda

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Dr. Masumi Kuma Nagano (Assistant Professor) naganom@md.tsukuba.ac.jp



Major Scientific Interests

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

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

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

Summer School Course (2016)

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

Recent Publications:

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

15. Immunology

Principal Investigator Akira Shibuya

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Major Scientific Interests

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) Honda, et al. Marginal zone B cells exacerbate endotoxic shock via interleukin-6 secretion induced by Fca/mR-coupled TLR4 signaling. *Nature Commun*, in press (2016)
- 2) Nakahashi-Oda C, et al. Apoptotic epithelial cells control regulatory T cell expansion. *Nature Immunol*, 2016 Feb 8. doi: 10.1038/ni.3345.
- 3) Totsuka N, et al. Toll-like receptor 4 and MAIR-II/CLM-4/LMIR2 immunoreceptor regulate VLA-4-mediated inflammatory monocyte migration. *Nature Commun*, 5:4710, 2014
- 4) Kim YG, et al. Gut dysbiosis promotes M2 macrophage polarization and allergic airway inflammation via fungi-induced PGE₂. *Cell Host & Microbe*, 15(1):95–102, 2014
- 5) Nakahashi-Oda C, et al. Apoptotic cells suppress mast cell inflammatory responses via the CD300a immunoreceptor. *J. Exp. Med.* 209, 1493-1503, 2012
- 6) Nakano-Yokomizo T, et al. The immunoreceptor adapter protein DAP12 suppresses B lymphocyte-driven adaptive immune responses. *J. Exp. Med.* 208, 1661-1671, 2011.
- 7) Hitomi K, et al. An immunoglobulin-like receptor, Allergin-1, inhibits immunoglobulin E-mediated immediate hypersensitivity reactions. *Nature Immunol.* 11: 601-607, 2010
- 8) Nabekura T, et al. Critical role of DNAX accessory molecule-1 (DNAM-1) in the development of acute graft-versus-host disease in mice. *Proc Natl Acad Sci USA*, 107(43):18593-18598, 2010

16. Neurobiology

Principal Investigator Takashi Shiga

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Other Faculty Members

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Major Scientific Interests

We are examining the mechanisms underlying the formation of neural network by multidisciplinary approaches from molecules to behavior, using mouse and rat embryos.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Monoamines in the dendrite formation and synaptogenesis
- 2) Environmental factors affecting development of brain and behavior
- 3) Axon guidance mechanisms of sensory neurons with special reference to Runx transcription factors and axon guidance molecules
- 4) Effects of gravitational stress (hypergravity, microgravity) on gene expression in the brain

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

- 1) Effects of serotonin and its receptor on gene expression of Ht22 cells which are derived from mouse hippocampus: quantitative PCR analysis

Recent Publications

- 1) Akatsu S, Ishikawa C, Takemura K, Ohtani A, Shiga T. Effects of prenatal stress and neonatal handling on anxiety, spatial learning and serotonergic system of male offspring mice. *Neurosci. Res.* 101(2015)15-23.
- 2) Ohtani A, Kozono N, Senzaki K, **Shiga T**. Serotonin 2A receptor regulates microtubule assembly and induces dynamics of dendritic growth cones in rat cortical neurons *in vitro*. **Neurosci. Res.** 81-82(2014)11-20.
- 3) Li F, Ohtani A, Senzaki K, **Shiga T**. Receptor-dependent regulation of dendrite formation of noradrenaline and dopamine in non-GABAergic cerebral cortical neurons. **Dev. Neurobiol.** 73, 370-383, 2013.
- 4) Kobayashi A, Senzaki K, Ozaki S, Yoshikawa M, **Shiga T**. Runx1 promotes neuronal differentiation in dorsal root ganglion. **Mol. Cell Neurosci.** 49, 223-31, 2012.
- 5) Yoshida H, Kanamaru C, Ohtani A, Li F, Senzaki K, **Shiga T**. Subtype specific roles of serotonin receptors in the spine formation of cortical neurons *in vitro*. **Neurosci. Res.** 71, 311-314, 2011.
- 6) Hayashi, T., Ohtani, A., Onuki, F., Natsume, M., Li, F., Satou, T., Yoshikawa, M., Senzaki, K., **Shiga, T**. Roles of serotonin 5-HT3 receptor in the formation of dendrites and axons in the rat cerebral cortex: An *in vitro* study. **Neurosci. Res.** 66, 22-28, 2010.

17. Endocrinology and Metabolism

Principal Investigator Hitoshi Shimano

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Major Scientific Interests

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

Projects for Regular Students in Doctoral or Master's Programs

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

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

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

Recent Publications

- 1) Kuba M, Matsuzaka T, Matsumori R, Saito R, Kaga N, Taka H, Ikehata K, Okada N, Kikuchi T, Ohno H, Han SI, Takeuchi Y, Kobayashi K, Iwasaki H, Yatoh S, Suzuki H, Sone H, Yahagi N, Arakawa Y, Fujimura T, Nakagawa Y, Yamada N, **Shimano H**. Absence of Elovl6 attenuates steatohepatitis but promotes gallstone formation in a lithogenic diet-fed Ldlr(-/-) mouse model. *Sci Rep*. 5:17604, 2015.
- 2) Nakagawa Y, Satoh A, Yabe S, Furusawa M, Tokushige N, Tezuka H, Mikami M, Iwata W, Shingyouchi A, Matsuzaka T, Kiwata S, Fujimoto Y, Shimizu H, Takeuchi Y, Iwasaki H, Shimada M, Kawakami Y, Urayama O, Sone H, Takekoshi K, Kobayashi K, Yatoh S, Takahashi A, Yahagi N, Suzuki H, Yamada N, **Shimano H**. Hepatic CREB3L3 controls whole-body energy homeostasis and improves obesity and diabetes. *Endocrinology*. 155:4706-19, 2014.
- 3) Izumida Y, Yahagi N, Takeuchi Y, Nishi M, Shikama A, Takarada A, Masuda Y, Kubota M, Matsuzaka T, Nakagawa Y, Iizuka Y, Itaka K, Kataoka K, Shioda S, Nijima A, Yamada T, Katagiri H, Nagai R, Yamada N, Kadowaki T, **Shimano H**. Glycogen shortage during fasting triggers liver-brain-adipose neurocircuitry to facilitate fat utilization. *Nat Commun*. 4:2316, 2013.
- 4) Matsuzaka T, Atsumi A, Matsumori R, Nie T, Shinozaki H, Suzuki-Kemuriyama N, Kuba M, Nakagawa Y, Ishii K, Shimada M, Kobayashi K, Yatoh S, Takahashi A, Takekoshi K, Sone H, Yahagi N, Suzuki H, Murata S, Nakamuta M, Yamada N, **Shimano H**. Elovl6 promotes nonalcoholic steatohepatitis. *Hepatology*. 56(6):2199-208, 2012.

18. Laboratory Animal Science

Principal Investigator Fumihiro Sugiyama

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Major Scientific Interests

Laboratory animals are essential and important bio-resources for the advancement of medical sciences. Gene-modified animals are used very often to study *in vivo* function of genes and proteins in development, homeostasis and disease. In particular, we focus on 1) development of genome editing technology for developmental engineering and 2) creation of mouse models for elucidating biological function and human diseases.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Development of the advanced cre-loxP system in mice.
- 2) Development of mouse models for *in vivo* imaging.
- 3) Elucidating biological function of gene leading to early embryonic lethality.

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

- 1) Mouse embryo manipulation.
- 2) Mouse genome editing with the CRISPR/Cas9 system.

Recent Publications

- 1) Hasegawa Y, Hoshino Y, Abdelaziz E. Ibrahim, Kato K, Daitoku Y, Tanimoto Y, Ikeda Y, Oishi H, Takahashi S, Yoshiki A, Yagami K, Iseki H, Mizuno S, Sugiyama F. Generation of CRISPR/Cas9-mediated bicistronic knock-in Ins1-cre driver mice. *Exp Anim.* 65: *In pressed*, 2016
- 2) Mizuno S, Takami K, Daitoku Y, Tanimoto Y, Dinh TT, Mizuno-Iijima S, Hasegawa Y, Takahashi S, Sugiyama F (Corresponding Author), Yagami K. Peri-implantation lethality in mice carrying megabase-scale deletion on 5q33.3 is caused by Exoc1 null mutation. *Sci. Rep.* 5:13632. 2015
- 4) Mizuno S, Dinh TT, Kato K, Mizuno-Iijima S, Tanimoto Y, Daitoku Y, Hoshino Y, Ikawa M, Takahashi S, Sugiyama F (Corresponding Author), Yagami K. Simple generation of albino C57BL/6J mice with G291T mutation in the tyrosinase gene by the CRISPR/Cas9 system. *Mamm. Genome* 25:327-334. 2014
- 5) Hasegawa Y, Daitoku Y, Mizuno S, Tanimoto Y, Mizuno-Iijima S, Matsuo M, Kajiwara N, Ema M, Oishi H, Miwa Y, Mekada K, Yoshiki A, Takahashi S, Sugiyama F (Corresponding Author), Yagami K. Generation and characterization of Ins1-cre-driver C57BL/6N for exclusive pancreatic beta cell-specific Cre-loxP recombination. *Exp. Anim.* 63:183-191. 2014

19. Anatomy and Embryology/ Laboratory Animal Resource Center

Principal Investigator Satoru Takahashi

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Major Scientific Interests

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

Projects for Regular Students in Doctoral or Master's Programs

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

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

- 1) Histological analysis of genetically manipulated mice.
- 2) Handling skill for mouse embryos.

Recent Publications

- 1) Ohmura S, Mizuno S, Oishi H, Ku CJ, Hermann M, Hosoya T, Takahashi S, Engel JD. Lineage-affiliated transcription factors bind the Gata3 Tce1 enhancer to mediate lineage-specific programs. *J Clin Invest*. 2016 Mar 1;126(3):865-78.
- 2) Hamada M, Nakamura M, Tran MT, Moriguchi T, Hong C, Ohsumi T, Dinh TT, Kusakabe M, Hattori M, Katsumata T, Arai S, Nakashima K, Kudo T, Kuroda E, Wu CH, Kao PH, Sakai M, Shimano H, Miyazaki T, Tontonz P, Takahashi S. MafB promotes atherosclerosis by inhibiting foam-cell apoptosis. *Nat Commun*. 5, 3147, 2014.
- 3) Shinagawa T, Takagi T, Tsukamoto D, Tomaru C, Huynh LM, Sivaraman P, Kumarevel T, Inoue K, Nakato R, Katou Y, Sado T, Takahashi S, Ogura A, Shirahige K, Ishii. Histone variants enriched in oocytes enhance reprogramming to induced pluripotent stem cells. *Cell Stem Cell*. 14, 217-227, 2014.
- 4) Katsumata T, Oishi H, Sekiguchi Y, Nagasaki H, Daassi D, Ema M, Kudo T, Takahashi S. In vivo monitoring of pancreatic b-cell mass and intrahepatic insulin gene activity in Ins1-luc BAC transgenic mice by bioluminescence imaging. *Plos One*. 8, e60411, 2013.
- 5) 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.

20. Radiation Biology

Principal Investigator **Koji Tsuboi**

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Major Scientific Interests

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 Programs

- 1) Particle beam induced DNA damage and repair
- 2) Radiation induced tumor immunological reactions
- 3) Biological effects of x-ray micro beams,

Study Program for Short Stay Student (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) Abei M, Okumura T, Fukuda K, Hashimoto T, Araki M, Ishige K, Hyodo I, Kanemoto A, Numajiri H, Mizumoto M, Sakae T, Sakurai H, Zenkoh J, Ariungerel G, Sogo Y, Ito A, Ohno T, Tsuboi K. A phase I study on combined therapy with proton-beam radiotherapy and in situ tumor vaccination for locally advanced recurrent hepatocellular carcinoma. *Radiat Oncol.* 2013 Oct 16;8(1):239.
- 2) Suzuki K, Gerelchuluun A, Hong Z, Sun L, Zenkoh J, Moritake T, Tsuboi K. Celecoxib enhances radiosensitivity of hypoxic glioblastoma cells through endoplasmic reticulum stress. *Neuro Oncol.* 2013 Sep;15(9):1186-99.
- 3) Sun L, Moritake T, Zheng YW, Suzuki K, Gerelchuluun A, Hong Z, Zenkoh J, Taniguchi H, Tsuboi K: In vitro stemness characterization of radioresistant clones isolated from a medulloblastoma cell line ONS-76. *J Radiat Res.* 2013 Jan;54(1):61-9.
- 4) Hong Z, Kase Y, Moritake T, Gerelchuluun A, Sun L, Suzuki K, Terunuma T, Yasuoka K, Kumada H, Anzai K, Sakurai H, Sakae T, Tsuboi K: Lineal energy-based evaluation of oxidative DNA damage induced by proton beams and X-rays. *Int J Radiat Biol.* 2013 Jan;89(1):36-43.
- 5) 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.]

21. Molecular and Genetic Epidemiology

Principal Investigator Naoyuki Tsuchiya

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Other Faculty Members

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Major Scientific Interests of the Group

Genetics of human autoimmune rheumatic diseases, including systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis and ANCA-associated vasculitis

Projects for Regular Students in Doctoral or Master's Programs

Detection and functional analyses of the polymorphisms associated with development and clinical manifestations of human autoimmune diseases in the Japanese population.

Study Program for Short Stay Student (1 weeks – 1 trimester)

Functional analysis of disease associated polymorphisms using animal models.

Recent Publications

- 1) **Oka S, Furukawa H**, Shimada K, Sugii S, Hashimoto A, Komiya A, Fukui N, Suda A, Tsunoda S, Ito S, Nakamura T, Saisho K, Sano H, Migita K, Nagaoka S, **Tsuchiya N**, Tohma S. Association of human leukocyte antigen alleles with chronic lung diseases in rheumatoid arthritis. *Rheumatology* 2016;doi:10.1093/rheumatology/kew025.
- 2) **Oka S, Furukawa H, Kawasaki A**, Shimada K, Sugii S, Hashimoto A, Komiya A, Fukui N, Ito S, Nakamura T, Saisho K, Kayatama M, Tsunoda S, Sano H, Migita K, Suda A, Nagaoka S, **Tsuchiya N**†, Tohma S† (†equal senior authors). Protective effect of the HLA-DRB1*13:02 allele in Japanese rheumatoid arthritis patients. *PLOS ONE* 2014;9:e99453.
- 3) **Kawasaki A, Furukawa H**, Nishida N, Warabi E, Kondo Y, Ito S, Matsumoto I, Kusaoi M, Amano H, Suda A, Nagaoka S, Setoguchi K, Nagai T, Hirohata S, Shimada K, Sugii S, Okamoto A, Chiba N, Suematsu E, Tokunaga K, Takasaki Y, Hashimoto H, Sumida T, Tohma S, **Tsuchiya N**. Association of functional polymorphisms in Interferon Regulatory Factor 2 (*IRF2*) with susceptibility to systemic lupus erythematosus: A case-control association study. *PLOS ONE* 2014;9: e109764.
- 4) **Furukawa H, Kawasaki A, Oka S**, Ito I, Shimada K, Sugii S, Hashimoto A, Komiya A, Fukui N, Kondo Y, Ito S, Hayashi T, Matsumoto I, Kusaoi M, Amano H, Nagai T, Hirohata S, Setoguchi K, Kono H, Okamoto A, Chiba N, Suematsu E, Katayama M, Migita K, Suda A, Ohno S, Hashimoto H, Takasaki Y, Sumida T, Nagaoka S, **Tsuchiya N***, Tohma S*. (*equal senior authors) Human leukocyte antigens and systemic lupus erythematosus: A protective role for the HLA-DR6 alleles *DRB1*13:02* and **14:03*. *PLOS ONE* 2014; 9: e87792.
- 5) Gazal S, Sacre K, Allanore Y, Teruel M, Goodall AH (The CARDIOGENICS consortium), Tohma S, Alfredsson L, Okada Y, Xie G, Constantin A, Balsa A, **Kawasaki A**, Nlicaise P, Amos C, Rodriguez-Rodriguez L, Chiocchia G, Boileau C, Zhang J, Vittecoq O, Barnetche T, Gonzalez-Gay MA, **Furukawa H**, Cantagrel A, Le Loet X, Sumida T, Hurtado-Nedelec M, Richez C, Chollet-Martin S, Schaeveerbecke T, Combe B, Khoriaty L, Coustet B, El-Benna J, Siminovitsh K, Plenge R, Padyukov L, Martin J, **Tsuchiya N**, Dieude P. Identification of secreted phosphoprotein 1 gene as a new rheumatoid arthritis susceptibility gene. *Ann Rheum Dis* Published Online First: 21st Jan 2014 doi:10.1136/annrheumdis-2013-204581.
- 6) **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* 2013;72:153-155.
- 7) **Kawasaki A**, Inoue N, Ajimi C, Sada K, Kobayashi S, Yamada H, **Furukawa H**, Sumida T, Tohma S, Miyasaka N, Matsuo S, Ozaki S, Hashimoto H, Makino H, Harigai M, **Tsuchiya N**. Association of *IRF5* polymorphism with MPO-ANCA positive vasculitis in a Japanese population. *Genes Immun* 2013; 14: 527–529.

22. Systems Sleep Biology

Principal Investigator Dr. rer. nat. **Michael Lazarus**

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Other Lab Members

Researcher Yo Oishi, Ph.D.

Researcher Yoko Takata, Ph.D.



Major Scientific Interests

Use of genetically engineered systems to dissect neural circuitry regulating behavioral states

The mesolimbic brain system in the control of sleep and wakefulness

Motivated behavior as a sleep-regulating factor

Projects for Regular Students in Doctoral or Master's Programs

- 1) Neuronal mechanisms of dopamine in sleep-wake regulation
- 2) Characterization of neuronal activity in the nucleus accumbens during sleep-wake states
- 3) Identification of novel brain circuits for the control of sleep and wakefulness

Study 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) Oishi Y, Takata Y, Taguchi Y, Kohtoh S, Urade Y, Lazarus M*. Polygraphic recording procedure for measuring sleep in mice. **J Vis Exp** 2016; e53678, doi:10.3791/53678.
- 2) Fuller PM, Yamanaka A, Lazarus M*. How genetically engineered systems are helping to define, and in some cases redefine, the neurobiological basis of sleep and wake. **Temperature** 2015; 2: 406-417.
- 3) Oishi Y, Yoshida K, Scammell TE, Urade Y, Lazarus M*, Saper CB*. The roles of prostaglandin E2 and D2 in lipopolysaccharide-mediated changes in sleep. **Brain Behav Immun** 2015; doi: 10.1016/j.bbi.2014.11.019. *Co-senior author.
- 4) 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.
- 5) 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.
- 6) 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).

23. Neural Network Analysis in Sleep and Wakefulness



Principal Investigator Kaspar Vogt (MD-PhD.)

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Other Lab Members

Robby Greene (part time, UT Southwestern Dallas, Texas US)

Kaoru Ohyama PhD., Francois Grenier PhD.

Major Scientific Interests

In the transition from wakefulness to sleep the brain undergoes a dramatic functional reorganization. We are interested in understanding the mechanisms that control this transition and in the functional aspects of the synchronous oscillations in sleep. We are using functional in-vivo imaging and in-vivo electrophysiology and slice physiology and imaging for more detailed analysis.

Projects for Regular Students in Doctoral or Master's Programs

- 1) In-vivo long-term recordings of EEG, EMG and local field potentials and single unit activity to investigate cortical network function during waking and sleep
- 2) In-vivo imaging of neural activity in head-fixed mice that undergo wake-sleep transitions
- 3) In-vitro slice physiology to study cortical neural network function and verify optogenetic and pharmacogenetic tools

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

- 1) Preparative surgery, virus injection into the cortex of mice and electrode implantation and recording
- 2) Mouse handling and adaptation to head fixation, imaging of identified neurons.

Recent Publications

- 1) Jaafari N, Vogt KE, Saggau P, Leslie LM, Zecevic D, Canepari M. Combining Membrane Potential Imaging with Other Optical Techniques. *Adv Exp Med Biol*. 2015; 859:103-25.
- 2) Vogt K. Diversity in GABAergic signaling. *Adv Pharmacol*. 2015; 73:203-22.
- 3) Willadt S, Canepari M, Yan P, Loew LM, Vogt KE. Combined Optogenetics and voltage sensitive dye imaging at single cell resolution. *Front. Cell. Neurosci*. 2014
- 4) Marowsky A, Vogt KE. Delta-subunit-containing GABAA-receptors mediate tonic inhibition in paracapsular cells of the mouse amygdala. *Front Neural Circuits*. 2014 Mar 25; 8:27.
- 5) Willadt S, Nenniger M, Vogt KE. Hippocampal feedforward inhibition focuses excitatory synaptic signals into distinct dendritic compartments. *PLoS One*. 2013 8:e80984.
- 6) Baudouin SJ, Gaudias J, Gerharz S, Hatstatt L, Zhou K, Punnakkal P, Tanaka KF, Spooren W, Hen R, De Zeeuw CI, Vogt K, Scheiffele P. Shared synaptic pathophysiology in syndromic and nonsyndromic rodent models of autism. *Science*. 2012 338:128-32.
- 7) Deogracias R, Yazdani M, Dekkers MP, Guy J, Ionescu MC, Vogt KE, Barde YA. Fingolimod, a sphingosine-1 phosphate receptor modulator, increases BDNF levels and improves symptoms of a mouse model of Rett syndrome. *Proc. Natl. Acad. Sci. USA* 2012 109:14230-5.

24. Paper device and eco-friendly materials

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Major Scientific Interests

For effective utilization of bio-materials and new technology derived from paper science, "super paper-application" is a promising field into the future. Paper is a simple and familiar material, and thus greatly expected to be applied to electronics, biosensors, and power generators. Technologies of papermaking processes can alter paper properties and provide superior performances. In addition, we proposed a simple method-immersion in salt water- for flood-damaged important books and documents to rescue them by inhibiting mold growth.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Triboelectric power generation from paper vibration induced by sonic waves
- 2) Development of paper-based copper ion sensor for drinking water test
- 3) Comparison between electronic and paper media in educational effects
- 4) Creation of bacterial culture system on paper by application of inkjet printing
- 5) Application of the saltwater immersion method for rescuing paper-based documents damaged by flood or tsunami: salt-paper interaction and desalination processes

Study Programs for Short Stay Students

- 1) Fiber shape characterization and quantification of filler contents of paper by X-ray diffract.
- 2) Fabrication of microfluidic channels with hydrophobic resin by ink jet printing
- 3) Fabrication of paper-based electronics with conductive ink by ink jet printing

Recent Publications

- 1) Oktavia, E., Morii, M., Enomae, T., "Triboelectric power generation from paper vibration induced by sonic waves, **Energy Harvesting and Systems**, 3(2), 189-196 (2016).
- 2) Srimongkon, T., Mandai, S., Enomae, T., "Application of biomaterials and inkjet printing to develop bacterial culture system", **Advances in Materials Sci & Eng**, Vol. 2015, 290790(2015).
- 3) Bunyaphiphat, T., Nakagawa-Izumi, A., Enomae, T., "Influences of saltwater immersion on properties of wood-cellulosic paper", **Carbohydrate polymers**, 116, 255-260 (2015).
- 4) Srimongkon, T., Ishida, T., Igarashi, K., Enomae, T., "Development of a bacterial culture system using a paper platform to accommodate media and an ink-jet printing to dispense bacteria", **Am. J. Biochem Biotechnol**, 10, 81-87(2014).
- 5) Xu, Y., Enomae, T., "Paper substrate modification for rapid capillary flow in microfluidic paper-based analytical devices", **RSC Advances**, 4, 12867-12872(2014).
- 6) Dogome, K., Enomae, T., Isogai, A., "Method for controlling surface energies of paper substrates to create paper-based printed electronics", **Chem Eng Proces: Process Intens**, 68, 21-25(2013).
- 7) Higashijima, K., Hori, C., Igarashi, K., Enomae, T., Isogai, A., "First aid for flood-damaged paper using saltwater: The inhibiting effect of saltwater on mold growth", **Stud Conserv**, 57(3), 164-171(2012).
- 8) Enomae, T., Dogome, K. and Isogai, A., "Evaluation of absorption of micro-droplets on paper for creation of paper-based microstructures", **Journal of Materials Science**, 47, 8, 3554-3563(2012).

25. Olericulture and Floriculture

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Other Faculty Member:

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Associate Professors Naoya Fukuda, Ph.D., Kang Seungwon, Ph.D. Tohru Ariizumi, Ph.D., Kyoko Tanase-Hiwasa Ph.D.

Assistant Professors Satoko Nonaka, Ph.D., Kanna Izawa-Sato, Ph.D., Ken Hoshikawa, Ph.D., Ryoichi Yano Ph.D., Yoshihiro Okabe Ph.D.



Major Scientific Interests

- Exploring genes regulating tomato fruit development
- Analysis of the mechanism for sugar and GABA metabolism in tomato
- Creation of genetic modified tomato accumulating functional materials benefit for human health
- Innovating crop transgenic and genome editing technologies for crop breeding
- Improving cultivation method for increasing sugar accumulation in tomato fruit
- Identification of genes controlling pigment accumulation in ornamental plant

Projects for Regular Students in Doctoral or Master's Programs

- 1) Forward genetic screening of genes that influence fruit development in tomato
- 2) Reverse genetic screening of novel mutations that increase fruit shelf-life of tomato
- 3) Functional analysis of GABA metabolism genes in tomato

Study Programs for Short Stay Students (one week)

- 1) DNA/RNA purification from plants
- 2) DNA amplification by PCR reaction, digestion by restriction enzymes, and electrophoresis
- 3) cDNA synthesis and RT-PCR reaction

Recent Publications

- 1) Shikata M, Hoshikawa K, Ariizumi T, Fukuda N, Yamazaki Y, Ezura H (2016) TOMATOMA Update: Phenotypic and metabolite information of Micro-Tom mutant resource. *Plant Cell Physiol.* 57(1): 1-10.
- 2) Takayama M, Koike S, Kusano M, Matsukura C, Saito K, Ariizumi T, Ezura H. (2015) Tomato glutamate decarboxylase genes SIGAD2 and SIGAD3 play key roles in regulation of γ -aminobutyric acid level in tomato (*Solanum lycopersicum*). *Plant Cell Physiol.* 56(8): 1533-1545.
- 3) Shinozaki Y, Hao S, Kojima M, Sakakibara H, Oseki-Iida Y, Zhen Y, Fei Z, Zhong S, Giovannoni J, Rose JKC, Okabe Y, Heta Y, Ezura H, Ariizumi T. (2015) Ethylene suppresses tomato fruit set through modification of gibberellin metabolism. *Plant J.* 83(2): 237-251.
- 4) Ariizumi T, Kishimoto S, Kakami R, Maoka T, Hirakawa H, Suzuki Y, Ozeki Y, Shirasawa K, Bernillon S, Okabe Y, Moing A, Asamizu E, Rothan C, Ohmiya A, Ezura H (2014) Identification of the Carotenoid Modifying Gene *PALE YELLOW PETAL 1* as an Essential Factor in Xanthophyll Esterification and Yellow Flower Pigmentation in Tomato (*Solanum lycopersicum*). *Plant J* 79:453-465.
- 5) Chusreeaom K, Ariizumi T, Asamizu E, Okabe Y, Shirasawa K, Ezura H (2014) A novel tomato mutant, *Solanum lycopersicum elongated fruit1 (Slefl1)*, exhibits an elongated fruit shape caused by increased cell layers in the proximal region of the ovary. *Mol Genet Genomics* 289:399-409.
- 6) Kimbara J, Yoshida M, Ito H, Kitagawa M, Takada W, Hayashi K, Shibutani Y, Kusano M, Okazaki Y, Nakabayashi R, Mori T, Saito K, Ariizumi T, Ezura H (2013) Inhibition of *CUTIN DEFICIENT 2* causes defects in cuticle function and structure and metabolite changes in tomato fruit. *Plant Cell Physiol* 54: 1535-1548.
- 7) Koike S, Matsukura C, Takayama M, Asamizu E, Ezura H (2013) Suppression of γ -amino butyric acid (GABA) transaminases induces prominent GABA accumulation, dwarfism and infertility in the tomato (*Solanum lycopersicum* L.). *Plant Cell Physiol* 54: 793-807.

26. Applied Entomology and Zoology

Principal Investigator Yooichi Kainoh

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Other Faculty Members

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Assistant Professor Natsuko Kinoshita: kinoshita.natsuko.gf@u.tsukuba.ac.jp



Major Scientific Interests

Experimental studies using insects, spiders and ticks for elucidation of behavioral and physiological mechanisms underlining host location behavior, physiology of reproduction and immunity, innate immune response to various infections, and molecular mechanisms inducing the release of plant volatiles from herbivore-infested plants.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Flight response of parasitic wasps to the plant infested by host insect.
- 2) Endocrinological and nutritional regulation of tick and spider ecdysis, reproduction and immunity.
- 3) Molecular mechanisms in the regulation of insect immunity
- 4) Visualization and modeling of volatile compound mediated plant-plant and plant-insect interaction.

Study Programs for Short Stay Students

- 1) Head space volatile collection and olfactometer study using the volatile extract.
- 2) Measurement of insect immune activity against infection by molecular techniques.
- 3) Molecular mechanism of plant-insect interaction by expression analyses and bio-imaging

Recent Publications:

- 1) Piyasaengthong, N., Y. Sato, N. Kinoshita and Y. Kainoh (2016) Oviposition preference for leaf age in the smaller tea tortrix *Adoxophyes honmai* (Lepidoptera: Tortricidae) as related to performance of neonates. *Applied Entomology and Zoology*. 10.1007/s13355-016-0408-5
- 2) Deshpande, S. A. and Y. Kainoh (2012) Herbivore egg deposition induces tea leaves arresting the egg-larval parasitoid *Ascogaster reticulata* Watanabe (Hymenoptera: Braconidae). *Entomol. Exp. Appl.* 144:172-180.
- 3) Ogihara, M.H., J. Hikiba, Y. Suzuki, D. Taylor and H. Kataoka (2015) Ovarian Ecdysteroidgenesis in Both Immature and Mature Stages of an Acari, *Ornithodoros moubata*. *PLOS ONE* 10(4): e0124953. doi:10.1371/journal.pone.0124953.
- 4) Ogihara, M.H. and D. Taylor (2013) Female Reproductive System: Anatomy, Physiology and Molecular Biology, Chapter 17. In D.E. Sonenshine and R.M. Roe (Editors). *Biology of Ticks*, Volume 1. Second Edition, Oxford University Press, New York, USA. pp. 449-483.
- 5) Furukawa, S., H. Tanaka, A. Sagisaka, J. Ishibashi, and M. Yamakawa. (2012) Both kB and C/EBP binding sites are indispensable for full expression of a nitric oxide synthase gene in the silkworm, *Bombyx mori*. *J. Seric. Sci. Jpn.* 81:13-20.
- 6) Furukawa, S., K. Tanaka, T. Ikeda, T. Fukatsu and T. Sasaki. (2012) Quantitative analysis of the lytic cycle of WO phages infecting *Wolbachia*. *Appl. Entomol. Zool.* 47:449-456.
- 7) Kinoshita, N., H. Wang, H. Kasahara, J. Liu, C. MacPherson, Y. Machida, Y. Kamiya *et al.* (2012) *IAA-Ala Resistant 3 (LAR3)*, a new evolutionarily conserved target of miR167, mediates *Arabidopsis* root architecture changes during high osmotic stress. *Plant Cell* 24: 3590-602.
- 8) Kinoshita, N., A. Berr, C. Belin, R. Chappuis *et al.* (2010) Identification of *growth insensitive to ABA3 (gia3)*, a recessive mutation affecting ABA signaling for the control of early post-germination growth in *Arabidopsis thaliana*. *Plant Cell Physiol.* 51: 239-251.

27. Food and Biomass Process Engineering

Principal Investigator Yutaka Kitamura

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Other Faculty Members

Assistant Professor Mito Kokawa



Major Scientific Interests

Focusing on agricultural products, food, unused resources and biomass as local biological materials, process development and characteristics for utilization and conversion of these resources are investigated to produce food, energy and industrial materials. By implementing the advanced technology for the local biological resources, we have the goal to contribute widely to the promotion of agriculture, energy conservation, environmental protection and industry creation in local and global view point.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Development of Florescence Fingerprint Monitoring System for Microbial Content of Beef
- 2) Processing of Orange Juice (*Citrus sinensis*) Powder by Micro Wet Milling and Vacuum Spray Drying Process
- 3) Study on Production of Mugwort with Bio-active Compounds
- 4) Process Characteristics of Whole Fruit Brewed Wine of Strawberry
- 5) Anaerobic Fermentation for Biogas from Agricultural and Food Waste

Study Programs for Short Stay Students

- 1) Development of hydro gel beads for functional foods
- 2) Processing of rice milk and rice milk products

Recent Publications

- 1) Dheni Mita Mala, Masatoshi Yoshimura, Susumu Kawasaki, Mizuki Tsuta, Mito Kokawa, Vipavee Trivittayasil, Junichi Sugiyama, Yutaka Kitamura, Fiber optics fluorescence fingerprint measurement for aerobic plate count prediction on sliced beef surface, *LWT - Food Science and Technology*, 68, 14-20, 2016
- 2) M.Z. Islam, Yutaka Kitamura, Yoshitsugu Yamano, Mai Kitamura, Effect of vacuum spray drying on the physicochemical properties, water sorption and glass transition phenomenon of orange juice powder, *Journal of Food Engineering*, 169, 131-140, 2016
- 3) Masaru Koyama, Yutaka Kitamura, Development of a new rice beverage by improving the physical stability of rice slurry, *Journal of Food Engineering*, 131, 89-95, 2014
- 4) Kenji Takisawa, Kazuyo Kanemoto, Tatsuo Miyazaki, Yutaka Kitamura, Hydrolysis for direct esterification of lipids from wet microalgae, *Bioresource Technology*, 144, 38-43, 2013
- 5) C. Song, Y. Kitamura, S. Li, J. Lu. Deposition CO₂ Capture Process Using a Free Piston Stirling Cooler. *Industrial & Engineering Chemistry Research*, 52 (42), 14936–14943, 2013
- 6) Chunfeng Song, Yutaka Kitamura, Shuhong Li. Energy analysis of the cryogenic CO₂ capture process based on Stirling coolers. *Energy*. 65, 580-589, 2014

28. Molecular Plant Pathology

Principal Investigator Yasuhiro Ishiga

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Other Faculty Members

Plant Parasitic Mycology Laboratory; Professor Yuichi Yamaoka

Associate Professor Izumi Okane, Assistant Professor Junichi P Abe



Major Scientific Interests

The research aim of our group is to understand the molecular mechanisms of plant immunity and pathogenicity of plant pathogens in the interactions of plant and microbes. Our primary target pathosystem is soybean and soybean rust interactions. Soybean rust caused by *Phakopsora pachyrhizi* is one of the most devastating foliar diseases affecting soybean production worldwide. In addition, we are interested in bacterial pathosystem, such as *Pseudomonas syringae*-tomato interactions. By working on the molecular basis of plant-microbe interactions, we are trying to establish the sustainable disease control strategies.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Multi-omics approached to study host-resistance on soybean against soybean rust using *Rpp* near-isogenic lines (NILs)
- 2) Development of Host Induced Gene Silencing (HIGS) in the interactions of soybean and soybean rust towards crop protection
- 3) Functional analysis of retrograde signaling in plant immunity
- 4) Reactive Oxygen Species (ROS)-mediated plant-microbe interactions

Study Programs for Short Stay Students

- 1) Molecular mechanism of plant immunity against fungal and bacterial pathogens
- 2) Functional analysis of pathogenicity related genes in bacterial and fungal pathogens.

Selected Recent Publications

- 1) **Ishiga, Y.**, Ishiga, T., Ikeda, Y., Matsuura, T. and Mysore, K.S. (2016) NADPH-dependent thioredoxin reductase C plays a role in nonhost disease resistance against *Pseudomonas syringae* pathogens by regulating chloroplast-generated reactive oxygen species. *PeerJ*.
- 2) **Ishiga, Y.** and Ichinose, Y. (2015) *Pseudomonas syringae* pv. tomato OxyR is required for virulence in tomato and Arabidopsis. *Mol. Plant-Microbe Interact.* 29:119-31.
- 3) **Ishiga, Y.**, Uppalapati, S.R., Gill, U.S., Huhman, D., Tang, Y. and Mysore, K.S. (2015) Transcriptomic and metabolomic analyses identify a role for chlorophyll catabolism and phytoalexin during *Medicago* nonhost resistance against Asian soybean rust. *Scientific Reports* 12;5:13061
- 4) **Ishiga, Y.**, Ishiga, T., Uppalapati, S.R. and Mysore, K.S. (2013) Jasmonate ZIM-domain (JAZ) protein regulates host and nonhost pathogen-induced cell death in tomato and *Nicotiana benthamiana*. *PLoS ONE* 8: e75728.
- 5) Uppalapati, S.R., **Ishiga, Y.**, Doraiswamy, V., Bedair, M., Mittal, S., Chen, J., Nakashima, J., Tang, Y., Tadege, M., Ratet, P., Chen, R., Schultheiss, H. and Mysore K.S. (2012) Loss of abaxial leaf epicuticular wax in *Medicago truncatula* *irg1/palm1* mutants results in reduced spore differentiation of anthracnose and nonhost rust pathogens. *The Plant Cell* 24: 353-370.
- 6) **Ishiga, Y.**, Ishiga, T. Wangdi, T., Mysore, K.S. and Uppalapati, S.R. (2012) NTRC and chloroplast-generated reactive oxygen species regulate *Pseudomonas syringae* pv. *tomato* disease development in tomato and Arabidopsis. *Mol. Plant-Microbe Interact.* 25: 294-306.

29. Pomology

Principal Investigator Sumiko Sugaya, Ph.D.

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Other Faculty Member:

Assistant Professor Yoshihiko Sekozawa, Ph.D.



Major Scientific Interests

- 1) Molecular mechanism underlying fruit quality involving coloring, taste and flavor in fruit trees.
- 2) Mechanism of bud dormancy in deciduous trees and role of chilling in winter.
- 3) Postharvest physiology in fruits to develop technologies for prolonging shelf life.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Carbohydrate metabolism in dormancy of Japanese pear under mild winter condition.
- 2) Effects of the joint training system on phytohormone metabolism and flowering in fruit trees.
- 3) Effects of heat treatment on ripening and quality during storage of fruits.

Study Programs for Short Stay Students (one week)

- 1) Determination of fruit quality with sugar analysis in fruits.
- 2) Analysis of flavor compounds in fruits.
- 3) Extraction of DNA/RNA from fruits and amplification by PCR.

Recent Publications

- 1) Chutinantakun, T., J.S. Maninang, Sugaya Sumiko, Y. Sekozawa, Gemma H. 2014. Tree jointing and branch bending influence endogenous levels of hormones and flowering in Japanese plum 'Kiyō'. *Acta Horticulturae* 1042: 57-63.
- 2) Yooyongwech, S., A. K. Horigane, M. Yoshida, Y. Sekozawa, S. Sugaya, S. Cha-um and H. Gemma. 2012. Hydrogen cyanamide enhances MRI-measured water status in flower buds of peach (*Prunus persica* L.) during winter. *Plant Omics Journal* 5: 400-404.
- 3) Boonkorn, P., H. Gemma, S. Sugaya, S. Setha, J. Uthabultra and K. Wangchai. 2012. Impact of high-dose, short periods of ozone exposure on green mold and antioxidant enzyme activity of tangerine fruit. *Postharvest Biology and Technology* 67: 25-28.
- 4) Kondo, S., S. Sugaya, S. Sugawa, M. Ninomiya, M. Kittikorn, K. Okawa, H. Ohara, K. Ueno, Y. Todoroki, M. Mizutani and N. Hirai. 2012. Dehydration tolerance in apple seedlings is affected by an inhibitor of ABA 8'-hydroxylase CYP707A. *Journal of Plant Physiology* 169: 234-241.
- 5) Maninang, J. S., C. Wong-Aree, S. Kanlayanarat, S. Sugaya, and H. Gemma. 2011. Influence of maturity and postharvest treatment on the volatile profile and physiological properties of the durian (*Durio zibethinus* Murray) fruit. *International Food Research Journal* 18: 1067-1075.
- 6) Pongprasert, N., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. A novel postharvest UV-C treatment to reduce chilling injury (membrane damage, browning and chlorophyll degradation) in banana peel. *Scientia Horticulturae* 130: 73-77.
- 7) Pongprasert, N., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. The role and mode of action of UV-C hormesis in reducing cellular oxidative stress and the consequential chilling injury of banana fruit peel. *International Food Research Journal* 18: 741-749.
- 8) Pathirana, U. A. P., Y. Sekozawa, S. Sugaya and H. Gemma. 2011. Effect of combined application of 1-MCP and low oxygen treatments on alleviation of chilling injury and lipid oxidation stability of avocado (*Persea americana* Mill.) under low temperature storage. *Fruits* 66: 161-170.

30. Vascular Matrix Biology

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Major Scientific Interests:

The maintenance of proper extracellular environment—comprised of extracellular matrices (ECM), ECM degrading enzymes, cytokines/growth factors, and physical factors—is crucial for normal development and cellular functions. The long-term goal of my laboratory is to elucidate how extracellular environment modulates intracellular signaling, cellular functions, and stem cell maintenance. In particular, we focus on the vessel wall and ECM. We aim to identify novel ECM proteins and characterize their biochemical and physiological functions by taking molecular, biochemical, and genetic engineering approaches.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Molecular mechanism of aortic aneurysm
- 2) Identification of vascular and skin niche for stem/progenitor cells
- 3) Novel ECM and renal calcification

Study Programs for Short Stay Students

- 1) Genetic and phenotypic identification of mutant mice with defective ECM
- 2) Preparation of histological sections and immunostaining

Recent Publications:

- 1) Y. Yamashiro, C.L. Papke*, J. Kim*, L.-J. Ringuette*, Q.-J. Zhang, Z.-P. Liu, H. Mirzaei, J. Wagenseil, E.C. Davis, and **H. Yanagisawa**: Abnormal mechanosensing and cofilin activation promotes the progression of ascending aortic aneurysms in mice. *Science Signaling*, 8(399): ra105 (2015).
- 2) C. L. Papke and **H. Yanagisawa**: Fibulin-4 and fibulin-5 in elastogenesis and beyond: insights from mouse and human studies. *Invited mini review to Matrix Biology*. 37:142-9. (2014).
- 3) J. Huang, Y. Yamashiro*, C. L. Papke*, Y. Ikeda*, Y. Lin, M. Patel, T. Inagami, V. P. Le, E. Wagenseil and **H. Yanagisawa**: Angiotensin converting enzyme-induced activation of local angiotensin signaling is required for ascending aortic aneurysms in fibulin-4 deficient mice. *Science Transl. Med.* 5, 183ra58 (2013).
- 4) M. Budatha, S. Roshanravan, Q. Zheng, C. Weislander, S. L. Chapman, E. C. Davis, B.C. Starcher, R. A. Word* and **H. Yanagisawa***: Extracellular matrix proteases contribute to progression of pelvic organ prolapse in mice and humans. *J Clin Invest.* 121(5):2048-59 (2011). (Featured in Commentaries in *JCI*, Featured in “Clinical Implication of Basic Research” in *N. Eng. J. Med.*)
- 5) J. Huang, E. C. Davis, S. L. Chapman, L. Y. Budatha, M., Marmorstein, R. A. Word and **H. Yanagisawa**: Fibulin-4 deficiency results in ascending aortic aneurysms: a potential link between abnormal smooth muscle cell phenotype and aneurysm progression. *Circ Res.* 106(3):583-592 (2010).

31. Biomaterials and Nanomedicines

Principal Investigator Yukio Nagasaki

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Major Scientific Interests

Our group is focusing on design of functionality materials, which can be utilized in biological environments. Versatile kinds of end-functionalized poly(ethylene glycol)s (PEG) have been newly synthesized as a surface modification agent of biosensor chips and biodevices and also for protein modifications (PEGylations). Some of them are already commercialized from several companies. Synthesis of PEG derivatives is now expanding polymer nanoparticles as vehicles for drug delivery system and nanomedicines. For example, we have recently prepared amphiphilic polymers, which scavenge reactive oxygen species (ROS). This redox active amphiphilic polymers spontaneously form self-assembling polymer micelle in aqueous media (Redox nanoparticle, RNP). We confirmed that RNP can be applicable for cerebral, myocardial and renal ischemic reperfusion injuries, cancers, liver fibrosis, Alzheimer's diseases, bowel inflammatory diseases and so on. Very recently, new nanoparticles, which generates nitric oxides in response to activated macrophages in tumor environments, have been also developed from our group. Control of gaseous molecules by our nanoparticle design is promising approach but not many groups have been done yet in the world.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Design of functionality polymeric materials as biomaterials
- 2) Nanoparticles as a novel nanomedicines, which control gaseous molecules in vivo.

Study Programs for Short Stay Students

- 1) Design of functionality polymeric materials as biomaterials.
- 2) Preparation of nanoparticles, physicochemical characterization and in vitro evaluation
- 3) Preparation of tumor-bearing mice and evaluation of anti-tumor activity of nanoparticle

Recent Selected Publications:

- 1) Shiro Ishii, Junya Kaneko, Yukio Nagasaki, Development of a long-acting, protein-loaded, redox-active, injectable gel formed by a polyion complex for local protein therapeutics, *Biomaterials*, Volume 84, page 210-218(2016) (doi: 10.1016/j.biomaterials.2016.01.029)
- 2) Makiko Saita, et al., Novel antioxidative nanotherapeutics in a rat periodontitis model: Reactive oxygen species scavenging by redox injectable gel suppresses alveolar bone resorption, *Biomaterials*, Volume 76, January 2016, Pages 292-301 (doi: 10.1016/j.biomaterials.2015.10.077).
- 3) Shinpei Kudo, Yukio Nagasaki, A Novel Nitric Oxide-based Anticancer therapeutics by Macrophage-targeted Poly(L-Arginine)-based Nanoparticles, *Journal of Controlled Release*, Vol. 217, 256–262(2015) (doi: 10.1016/j.jconrel.2015.09.019)
- 4) Sindhu Thangavel, Toru Yoshitomi, Meena Kishore Sakharkar and Yukio Nagasaki, Redox nanoparticles inhibit curcumin oxidative degradation and enhance its therapeutic effect on prostate cancer, *Journal of Controlled Release*, Volume 209, 10 July 2015, Pages 110-119 (doi: 10.1016/j.jconrel.2015.04.025)
- 5) Hiroyuki Nakagawa, Yoko Matsumoto, Yu Matsumoto, Yoshihiro Miwa, Yukio Nagasaki, Design of high-performance anti-adhesion agent using injectable gel with an anti-oxidative stress function, *Biomaterials*, Vol. 69,165-173 (2015) (doi: 10.1016/j.biomaterials.2015.08.018).
- 6) Pennapa Chonpathompikunlert, Toru Yoshitomi, Long Binh Vong, Natsuka Imaizumi, Yuki Ozaki, Yukio Nagasaki, Recovery of Cognitive Dysfunction via Orally Administered Redox-polymer Nanotherapeutics in SAMP8 mice, *PLoS ONE*, 10(5): e0126013 (2015). (doi: 10.1371/journal.pone.0126013)
- 7) Long Binh Vong, Tsutomu Tomita, Toru Yoshitomi, Hirofumi Matsui, Yukio Nagasaki, An Orally Administered Redox Nanoparticle that Accumulates in the Colonic Mucosa and Reduces Colitis in Mice, *Gastroenterology*, Vol.143, No.4, 1027-1036(2012).(doi:10.1053/j.gastro.2012.06.043)

See: http://www.ims.tsukuba.ac.jp/~nagasaki_lab/publications_and_proceedings/publications.htm in detail