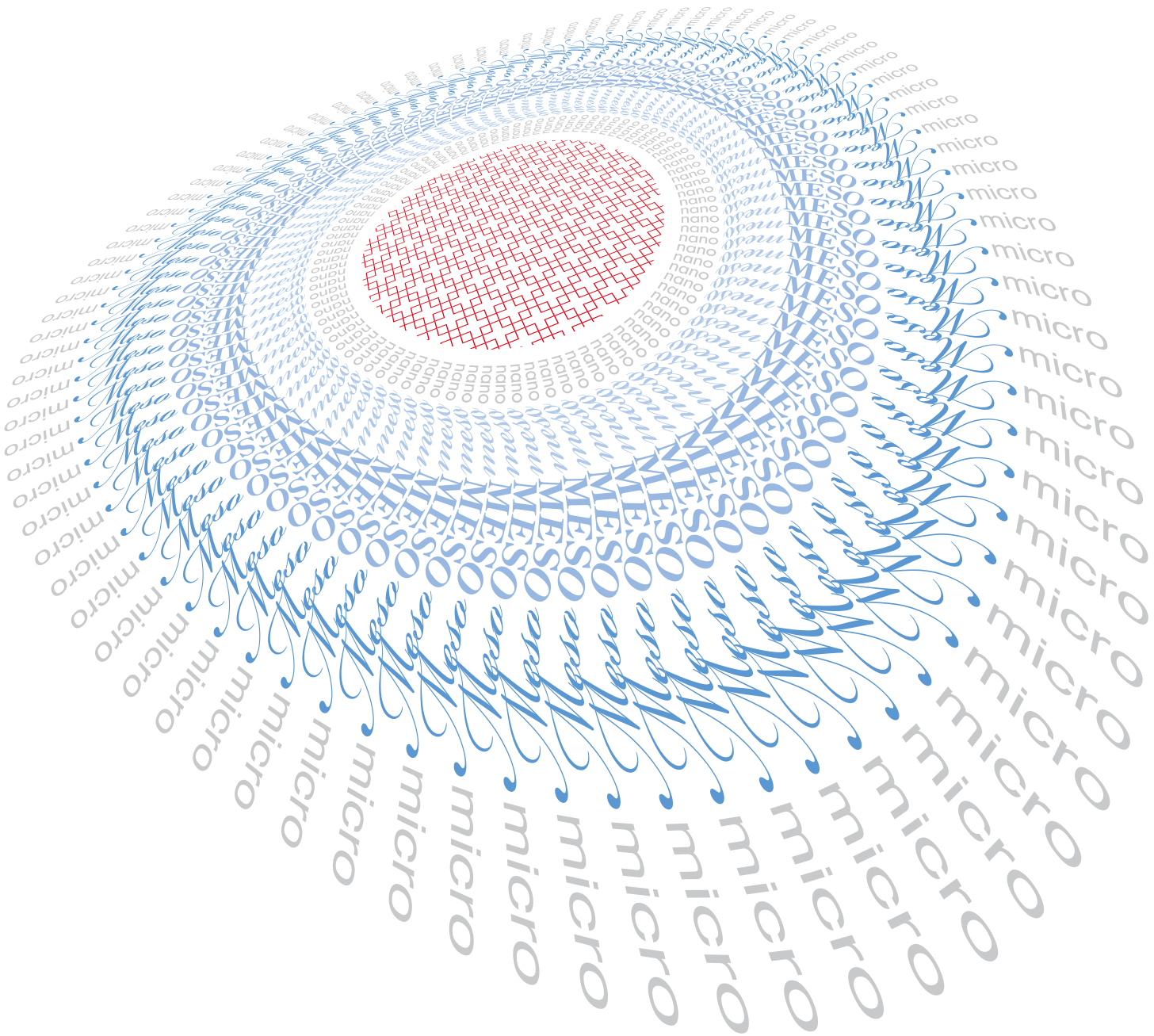


MESO CONTROL | STEM CELLS

Institute for Integrated Cell-Material Sciences, Kyoto University

KYOTO UNIVERSITY FOUNDED 1897

wpi
World Premier International Research Center Initiative

iCeMS
KYOTO UNIVERSITY
WPI Research Center

Table of Contents

Message from the Director

Norio Nakatsuji

Director

Institute for Integrated Cell-Material Sciences, Kyoto University

The Japanese government's **World Premier International Research Center (WPI) Initiative**, launched in 2007, aims to forge a new model for scientific institutions, helping Japan lead the world in a broad range of advanced research. Coordinated by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), this program seeks to have the world's best minds combine the skills of many, varied disciplines to create a space where the most talented and promising young scientists — the great researchers of tomorrow — can be nurtured.

Our Institute for Integrated Cell-Material Sciences (iCeMS) here at Kyoto University is one of these WPI centers. By merging **materials science** and **cell biology**, both fields of great strength at this university, we are in fact creating a new cross-discipline, supported by an advanced research environment and infrastructure that are unprecedented in Japan. We are keenly aware of our leadership role in science as we aim for a truly global level of excellence.

The institute's focus is on two main areas: **meso-control** and **stem cells**. Our pioneering work draws from the life sciences, chemistry, materials science, as well as physics, constantly expanding the boundaries of technological innovation.

The **mesoscale**, as its name implies, exists between two well-scrutinized realms: nano space (atoms and molecules at most several nanometers in size) and bulk space (our everyday world, consisting of everything larger than one micron). In meso space, from handfuls and up to several dozen biopolymers within cells are in constant motion — sharing an existence with the cell membrane and other organelle structures — ceaselessly buffeted by smaller molecules as they fulfill signaling roles and execute intricate cellular functions.

In materials science, whereas conventional research into porous and other new functional materials has (for reasons of convenience) favored the bulk scale, recent high-profile research at the iCeMS has led to the development of crystalline particles and functional architectures in the mesoscale. Individual molecules at the nano-level, as well as solids larger than one micron, both

tend to have singular, clearly defined functions. However mesoscale crystals with soft properties are able to adapt their functions to the physical chemistry of the meso environment, creating flexible and reciprocal relationships that precisely match the fluctuating architectures inside living cells.

Until now, both the analytical tools of nano space — quantum mechanics — and of bulk space — classical and statistical mechanics coupled with everyday experience — have been unable to tackle the complexities of the meso world. An ability to decipher the primary interactive mechanisms of meso space and predict and even control the complex multi-functional workings of mesoscale molecular complexes will lead to innovations in science and technology with wide applications for fields ranging from medicine to industry. In this light, the promise of meso space is truly an unexplored treasure trove.

Cells — and in particular **stem cells**, which possess such diverse and broad significance — have evolved the tools for **meso-control** through natural selection: tools which a solid and less flexible mechanism would have to expend vast quantities of resources in order to wield. Yet cells are able to complete their multitude of functions, performing their chemistry cleanly and precisely, in water solutions and at standard temperatures and pressures, all while continuously adapting to outside conditions. And incredibly all cell functions, from extremely efficient energy conversion to the control of cell proliferation and differentiation, result from the cumulative, ceaseless, and often error-prone movements of countless molecules inside and outside the cell.

While studying the marvelous system that enables the meso-control of cells, another goal is the control of molecular complexes in artificial nano-meso spaces. An ability to freely design, build, and employ functional meso materials will lead to unprecedented new technologies with applications in the control of stem cells and for development of new environmental and energy-related technologies. We are striving for nothing less than the realization of an entirely new form of meso-control through the fusion of cell and material sciences, leading to a future generation of technological innovation and ultimately advancing human well-being through improvements in medicine, pharmaceutical research, and industry.

Today, however, progress of science in Japan faces a very real challenge to its future success in that this country is regarded neither as possessing a borderlessness that might cause the world's top researchers to naturally coalesce here, nor as having a research environment supportive of promising young researchers eager to broaden their careers. Without reversing these trends, Japanese science faces the distinct possibility of not only falling behind the level of other developed countries, but even of losing its lead to some developing nations as well. The iCeMS is working to break with conventional thinking and solve these problems by 1) strengthening the director's authority to make executive decisions, 2) have English be the institute's official language, and 3) have open offices and laboratories as well as other flexible approaches.

Finally, the iCeMS seeks to have its researchers acquire the skills to effectively and adequately relay the latest advances in science and technology to society at large, along with maintaining the highest level of each researcher's own **scientific integrity**. We consider it our mission to identify the role that scientists should play in modern society, and train ourselves to exercise sound judgment accordingly. Our efforts urging researchers to strengthen their science communication and social literacy skills illustrate the iCeMS' dedication to fostering future generations.

May 2010

WPI Initiative

Launched in 2007 by the Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT) in order to establish globally visible research centers, the WPI program seeks to 1) advance leading edge research, 2) create new interdisciplinary domains, 3) establish truly international research environments, and 4) reform existing research organizations.

wpi World Premier International Research Center Initiative

The MEXT grants average ¥1.4 billion (approximately US$14 million) annually per center over 10–15 years, and interim evaluations are conducted at 5-year intervals. Each center is required to meet the following global visibility criteria: 1) 10–20 world-class principal investigators, 2) over 30% overseas researchers, and 3) a staff of over 200 total.

WPI research centers (as of May 2010)

- Advanced Institute for Materials Research (AIMR), Tohoku University
- Institute for the Physics and Mathematics of the Universe (IPMU), The University of Tokyo
- Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University
- Immunology Frontier Research Center (IFReC), Osaka University
- International Center for Materials Nanoarchitectonics (MANA), National Institute for Materials Science

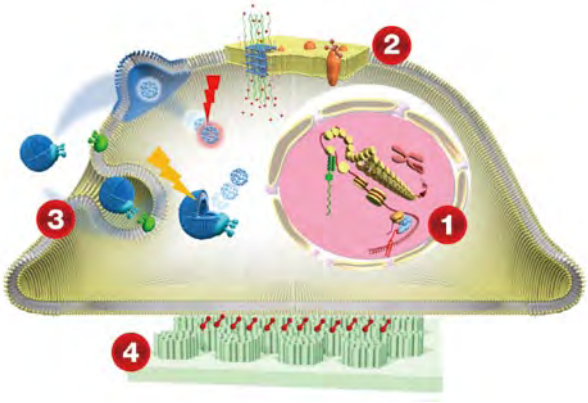
Research Areas and Objectives

The iCeMS aims to create **new cross-disciplinary fields** through the **integration of cell and material sciences**, focusing on two main areas: **meso-control** and **stem cells**.

Between our everyday world and the nanoscale world of atoms and small molecules exists the **mesoscale**: a realm occupied by molecules, molecular complexes, and architectures within cells. The iCeMS seeks not only to understand the processes at work and the means of controlling meso space (i.e., meso-control), but also to design, build, and manipulate **functional architectures** in manufactured meso spaces.

Reaping the benefits of this new knowledge will result in the development of meso technologies applicable to the control of **stem cell systems**, with the promise of applications in medical science, drug research, energy and the environment, and industry. A future increase in human well-being is a certain outcome of this exploration of meso space, mastering of meso-control, and harnessing of stem cells.

New cross-disciplinary fields through the integration of cell and material sciences



❶ Chromatin architecture/function and meso-control
➢Gene expression control with bio-functional chemicals/materials

❷ Cell membrane architecture/function and meso-control
➢Ion channel/transporter/receptor with bio-functional chemicals/materials

❸ Intracellular delivery of bio-functional materials
➢Control by external signals

❹ Cellular environment architecture/function and meso-control
➢Nano/meso/micro-engineered materials with bio-functional molecules

Timeline

2007	**Sep. 12**	The iCeMS is selected for the World Premier International Research Center (WPI) Initiative by the Ministry of Education, Culture, Sports, Science and Technology (MEXT).
	Oct. 1	The iCeMS is established at Kyoto University with Prof. Norio Nakatsuji as founding director.
2008	**Jan. 22**	The Center for iPS Cell Research and Application (CiRA) is established under the auspices of the iCeMS with Prof. Shinya Yamanaka as founding director.
	Feb. 19	iCeMS inauguration ceremony held at the Kyoto University Clock Tower Centennial Hall.
	Apr. 28	New iCeMS laboratory opened on the Katsura Campus of Kyoto University.
2009	**Mar. 3**	The Center for Meso-Bio Single-Molecule Imaging (CeMI) is established within the iCeMS with Prof. Akihiro Kusumi as founding director.
	Apr. 28	iCeMS Complex 1 opening ceremony held at the iCeMS Main Building.
	Jun. 26	iCeMS Gifu University Satellite opening ceremony.
	Nov. 1	Chemical Screening Center opened in the Main Building.
2010	**Apr. 1**	The Center for iPS Cell Research and Application (CiRA) is re-established as a sibling institute to the iCeMS with Prof. Shinya Yamanaka as founding director.

Management

According to the principles of the WPI program, the iCeMS is implementing a new system of management which is unprecedented for a Japanese university.

Management Reform Initiatives

- Rapid, institute director-centered decision-making process
- An Executive Board, Board of PIs, and committee structure supporting the director
- A pay scale not based solely on seniority
- Hiring not limited by the retirement age

Initiatives Aimed at Meeting International Standards

- Establishment of the Internationalization Committee
- Use of English as the official language
- Global staff recruitment and over 30% non-Japanese researchers
- Strengthening of International Public Relations and Overseas Affairs and Planning staff
- Establishment of the Overseas Researchers Support Office
- Over 50% English-speaking administrative staff
- Active exchange with numerous overseas partner institutions
- Active overseas outreach via the Institutional Program for Young Researcher Overseas Visits
- iCeMS Seminars regularly conducted by noted international researchers (approx. 30 annually)

Promoting Ground-Breaking, Cross-Disciplinary Research

- 18 world-class principal investigators (PIs)
- iCeMS Kyoto Fellow (junior PI) positions
- Strategic Committee for Cross-Disciplinary Research
- Facilities Management Committee and the implementation of open offices and shared laboratories
- A research environment including break areas designed to promote active exchanges across disciplines
- Promotion of cross-disciplinary research through the common use of large facilities, such as apparatuses in the Center for Meso-Bio Single-Molecule Imaging (CeMI)
- A Cross-Disciplinary Seminar series
- International symposia (approx. 3 annually)
- Exploratory Grants for Junior Investigators, promoting cross-disciplinary research among young iCeMS scientists
- Support for collaborative projects with other young Kyoto University researchers via the iCeMS Cross-Disciplinary Research Promotion Project

Other Efforts

- Development of science communication theory hand-in-hand with an active outreach program
- A reading club aiming to enhance participants' sense of scientific ethics
- Development of innovation management theory coupled with a vigorous public and private sector linkage effort

Organization Chart

As of May 1, 2010

Executive Board

Director

Norio Nakatsuji

Deputy Director

Susumu Kitagawa

Chairman of the Board of PIs

Motonari Uesugi

Administrative Director

Shinji Tomita

Principal Investigators (PIs)


Konstantin Agladze


Yong Chen


Mitsuru Hashida


Takashi Hiiragi


Hiroshi Imahori


Mineko Kengaku


Makoto Kiso


Susumu Kitagawa


Norio Nakatsuji


Hiroshi Sugiyama


Mikio Takano


Kazumitsu Ueda


CeMI Director
Akihiro Kusumi


Yoshie Harada


John Heuser


Koichiro Tanaka


Motonari Uesugi


Shinya Yamanaka

Center for Meso-Bio Single-Molecule Imaging (CeMI)

iCeMS Kyoto Fellows (junior PIs)


Peter Carlton


Ziya Kalay


Tatsuya Murakami


Takuya Yamamoto

Administration

Deputy Administrative Director
Takeshi Yamazaki

- General Affairs — Hiroyuki Shintoku
- Overseas Affairs and Planning — Daisuke Yamada
  - Overseas Researchers Support
- International Public Relations — Yutaka Iijima
- Finance — Katsumi Sakamoto
- Funding Management — Sadahiro Naka
- Facilities and Environment — Tetsuo Tanaka
- IT Support — Yoshitaka Morimura

Satellite at Gifu University


Makoto Kiso

Innovation Management


Shintaro Sengoku

Science Communication


Kazuto Kato (Adjunct)

Adjunct Faculty

- Hiroshi Kageyama (Graduate School of Engineering, Kyoto Univ)
- Hiroshi Kitagawa (Graduate School of Science, Kyoto Univ)
- Tamio Hayashi (Graduate School of Science, Kyoto Univ)
- Mitinori Saitou (Graduate School of Medicine, Kyoto Univ)
- Takashi Shinohara (Graduate School of Medicine, Kyoto Univ)
- Masahiro Shirakawa (Graduate School of Engineering, Kyoto Univ)

Partner Institutions

- California NanoSystems Institute, UCLA
- Max Planck Institute of Molecular Cell Biology and Genetics
- National Centre for Biological Sciences, India
- Purdue University Center for Basic and Applied Membrane Sciences
- RIKEN Center for Developmental Biology
- Wellcome Trust Centre for Stem Cell Research, The University of Cambridge

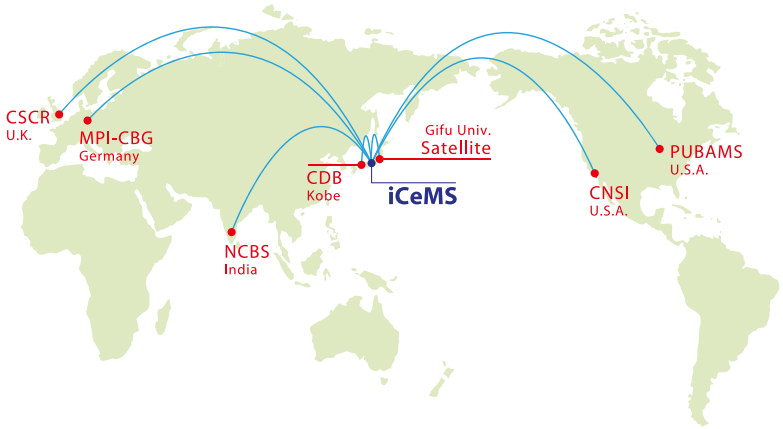
Advisory Committee

- Barbara Baird (Cornell University)
- Daniel Choquet (Université de Bordeaux 2)
- Lee Eng-Hin (The University of Singapore)
- Keiji Morokuma (Kyoto University)
- Noriko Osumi (Tohoku University)
- Kenneth R. Poeppelmeier (Northwestern University)
- Ferdi Schüth (Max-Planck-Institut für Kohlenforschung)
- Masatoshi Takeichi (RIKEN Center for Developmental Biology)
- Fiona Watt (The University of Cambridge)

Partner Institutions & Satellite

The iCeMS enriches its research through close contact with the following domestic and international partners:

- California Nanosystems Institute (CNSI), UCLA, USA
- Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG), Germany
- National Centre for Biological Sciences (NCBS), Bangalore, India
- Purdue University Center for Basic and Applied Membrane Sciences (PUBAMS), USA
- Riken Center for Developmental Biology (CDB), Kobe, Japan
- Wellcome Trust Centre for Stem Cell Research (CSCR), The University of Cambridge, UK
- Satellite at Gifu University, Japan



Institutional Program for Young Researcher Overseas Visits

With support from the Japan Society for the Promotion of Science (JSPS), the iCeMS funds two initiatives intended to assist scientists seeking to expand their future career possibilities. During their time overseas, participants are also expected to act as evangelists for the iCeMS.

(1) Long-Term: International Seminar Tour Mainly for Senior Lecturers and Assistant Professors

4–6 researchers annually, 2–3 month overseas stays each, for the purpose of promoting collaborative work and building networks. Supporting those seeking to become truly global scientists by planting and nurturing the seeds of international cooperation.

(2) Short-Term: Overseas Interview Tour Mainly for Research Associates and Graduate Students

6–9 researchers annually, 2–3 week overseas stays each, for the purpose of an interview tour to enhance future overseas job prospects. Participants receive thorough pre-departure presentation training as well as post-return debriefings.

Exploratory Grants for Young Researchers

The following grant programs have been established to promote cross-disciplinary research:

iCeMS Exploratory Grants for Junior Investigators

Every year the most promising, new cross-disciplinary joint research projects by iCeMS junior investigators are selected to receive startup grants. Young iCeMS researchers working in different research groups are eligible to apply. Moreover, with an aim to promote increased scientific inquiry crossing the boundaries between numerous fields, researchers outside of the iCeMS are also encouraged to participate as collaborators. In FY 2010, 28 projects were selected for funding.

iCeMS Cross-Disciplinary Research Promotion Project

Started in FY 2010, the wide scope of this project accepts applications from young Kyoto University scientists taking part in cross-disciplinary research with partner researchers within the iCeMS. This effort seeks to attract and provide startup funding to research efforts initiated by a range of departments outside of the iCeMS. Funds are also provided to partner researchers within the institute. In FY 2010, 19 projects were selected for funding.

Konstantin Agladze Lab

Biophysics, Non-Linear Science

Faculty Members

Konstantin Agladze (Professor)

Nobuyuki Magome (Assistant Professor)

Research Overview

Our highly diverse group of researchers includes biophysicists, chemists, biochemists, material scientists, as well as computational scientists, advancing the interdisciplinary field of physics and **bio-physics** of **excitable** and **self-organizing systems**. Special attention is paid to the mechanisms of **transition to a chaotic state** in cardiac tissue, which might be lethally dangerous. Understanding how a heart can lose its orchestrated function allows for the development of efficient methods to **fight cardiac arrhythmia**. As a rule, the precursors of such a dangerous state in the heart muscle are rotating **spiral waves** or **reentries**. Currently, the following four directions of study are being developed:

1. Study of fundamental mechanisms of reentry (or spiral waves) originating in the heart based on the **curvature-related failure** of the propagating wave.

2. Development of a novel method for controlling cardiac activity based on **reversible sensibilization** of voltage-gated ion channels of cardiomyocytes to **light** and subsequent **meso-scale changes** in **membrane-protein complexes** responsible for cardiomyocytes functioning.

3. Development of **nanofiber-based scaffolds** for **cardiac tissue engineering** employing a meso-scale approach in investigation of single-cell and single-fiber attachment. These scaffolds will allow us to construct functional artificial cardiac tissue patches with **well-controlled structures**.

4. Study of **interaction** and **common network formation** of **primary** culture cardiomyocytes with cardiomyocytes descended from **pluripotent cells**, as a generic experimental model for cardiac tissue repair.

Selected Papers

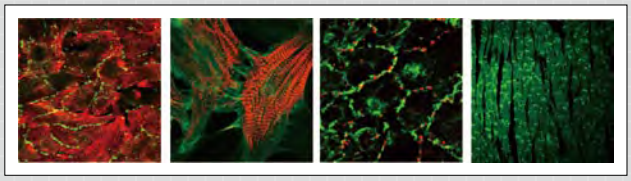
Magome, N. and Agladze, K. Patterning and excitability control in cardiomyocyte tissue culture. *Phys. D* **239**, 1560–1566 (2010).

Horning, M., Isomura, A., Agladze, K. and Yoshikawa, K. Liberation of a pinned spiral wave by a single stimulus in excitable media. *Phys. Rev. E* **79**, 026218 (2009).

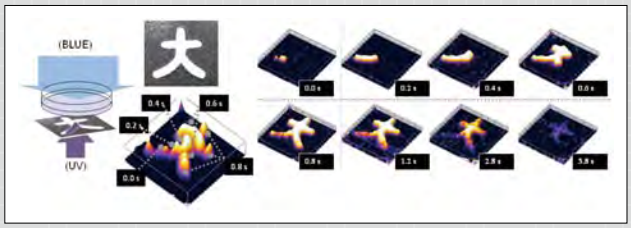
Isomura, A., Horning, M., Agladze, K. and Yoshikawa, K. Eliminating spiral waves pinned to an anatomical obstacle in cardiac myocytes by high-frequency stimuli. *Phys. Rev. E* **78**, 066216 (2008).

Pumir, A., Nikolski, V., Horning, M., Isomura, A., Agladze, K., Yoshikawa, K., Gilmour, R., Bodenschatz, E. and Krisky, V. Wave emission from heterogeneities opens a way to controlling chaos in the heart. *Phys. Rev. Lett.* **99**, 208101 (2007).

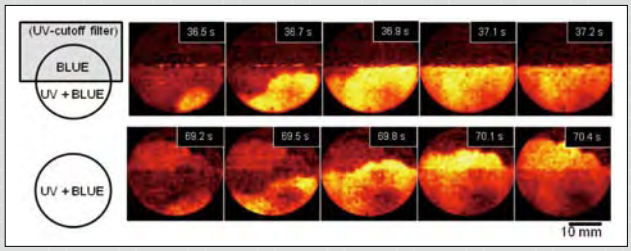
Agladze, K., Kay, M. W., Krinsky, V. and Sarvazyan, N. Interaction between Spiral and Paced Waves in Cardiac Tissue. *Am. J. Physiol. Heart Circ. Physiol.* **293**, H503–H513 (2007).



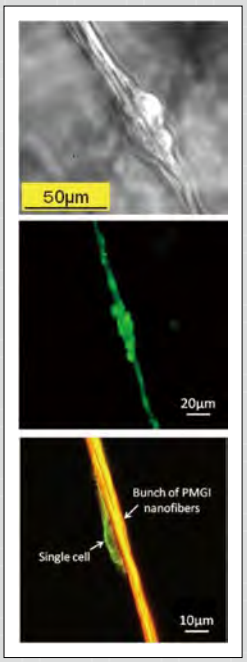
Cardiac tissue culture – immunostaining



Fluorescence images of propagating excitation waves in a light-controlled path



Light controlled excitation in a cardiac tissue culture



Single cardiac cell-PMGI nanofiber interaction

Yong Chen Lab

Nanobiotechnology

Faculty Members

Yong Chen (Professor)

Research Overview

We explore **microfluidic** and **nanofabrication technologies** in cell biological studies for both control of cellular microenvironments and high throughput screenings. New methods and tools are developed for the control of soluble factors, extracellular matrices and cell-cell interactions. As one example, we investigated the formation of functional **neural networks** derived from stem cells which can serve as model systems for both fundamental research and advanced applications.

Whereas conventional nanofabrication techniques are used for the manufacturing of different types of substrata and microelectrode arrays, microfluidic techniques can also be applied for highly precise administration of cell culture media and secretion factors. Particular attention is paid to cell-material interaction at nano and meso length scales as well as to the function of designed cellular networks at different levels of complexity.

We have been working on embryonic stem cells (ESCs) and other types of cells cultured on nanofabricated substrata or nano-scaffolds, demonstrating interesting features such as the formation of quasi-three dimensional ESC colonies with significantly extended stability without unexpected differentiation.

More recently, we have achieved cellular network formation on patterned substrates, showing particular signal propagation recorded by both microelectrode arrays and fluorescence images. The ultimate goal is to use derived stem cells for the construction of functional **neural networks** with the capability of responding to both chemical and electrical stimuli with high spatial and temporal resolution by using microfluidic and microelectrode array techniques.

We are also developing **artificial cell models** by using cell-sized **liposomes** for the incorporation of gene-expression systems. In particular, we are interested in the expression of functional membrane proteins with liposomes: a crucial step toward providing a more realistic model for cell biological studies.

At the iCeMS, we have been collaborating with other research groups on a variety of interdisciplinary projects:

1. Creation of nano-substrata and microfluidic chambers to perform culture and differentiation (Nakatsuji Lab).
2. Fabrication of nano-scaffolds for cardiomyocyte analyses (Agladze Lab).
3. Development of micro- and nanofluidic tools for guided growth of neural cells (Kenkagu Lab).
4. Creation of nanoinjectors for high resolution stimuli and single cell imaging (Kusumi Lab).
5. Fabrication of magnetic nanoparticles containing fibers for cell manipulation (Takano Lab).

Selected Papers

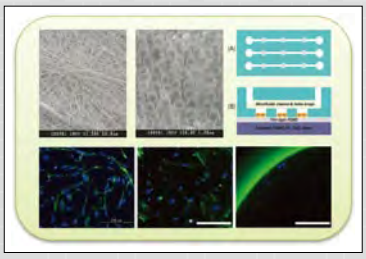
Liu, L., Luo, C. X., Ni, X. F., Wang, L., Yamauchi, K., Nomura, S. M., Nakatsuji, N. and Chen, Y. A micro-channel-well system for culture and differentiation of embryonic stem cells on different types of substrate. *Biomed. Microdevices* **12**, 505–11 (2010).

Hu, J., Shi, J., Zhang, F., Lei, L., Li, X., Wang, L., Liu, L. and Chen, Y. High resolution and hybrid patterning for single cell attachment, *Microelectron. Eng.* **87**, 726–729 (2010).

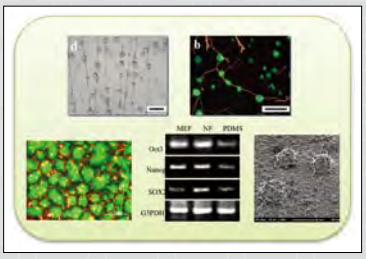
Luo, C. X., Ni, X. F., Liu, L., Nomura, S. M. and Chen, Y. Degassing-Assisted Patterning of Cell Culture Surfaces. *Biotechnol. Bioeng.* **105**, 854–859 (2010).

Zhou, X. T., Shi, J., Zhang, F., Hu, J., Li, X., Wang, L., Ma, X. M. and Chen, Y. Reversed cell imprinting, AFM imaging and adhesion analyses of cells on patterned surfaces. *Lab Chip* **10**, 1182–1188 (2010).

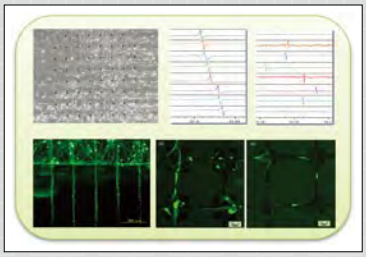
Yamaji, K., Kanai, T., Nomura, S. I. M., Akiyoshi, K., Negishi, M., Chen, Y., Atomi, H., Yoshikawa, K. and Imanaka, T. Protein synthesis in giant liposomes using the in vitro translation system of Thermococcus kodakaraensis. *IEEE Trans. Nanobiosci.* **8**, 325–331 (2009).



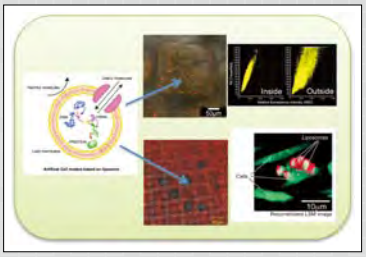
Nano-scaffolds and microfluidics



Embryonic stem cells on nanoscafolds



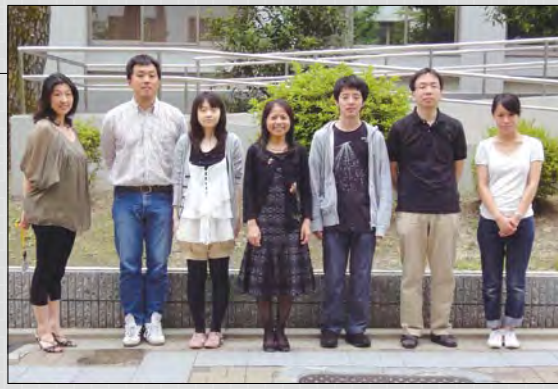
Cardiac and neural networks



Vesicle based gene expression

Yoshie Harada Lab

Single-Molecule Physiology



Faculty Members

Yoshie Harada (Professor)
Mariko Ariyoshi (Associate Professor)
Hiroaki Yokota (Senior Lecturer)
Yong-Woon Han (Assistant Professor)

Research Overview

The biomolecules functioning in our bodies vary in size from several nanometers to several hundreds of nanometers. This size is exactly the "meso" range at the junction between micro and macro. The critical difference between the environment in which biomolecules live and the environment in which we live is that biomolecules cannot ignore thermal fluctuations. Biomolecules are constantly exposed to large thermal fluctuations. Therefore, biomolecules differ from artificial machines in that they make skillful use of thermal fluctuations while functioning. For example, RNA polymerase is one-dimensionally diffused on DNA when searching for a promoter site on DNA. Our ultimate goal is to understand these skilled molecular functions of biomolecules.

Observing the motions of individual molecules and manipulating molecules directly are very useful for learning the working mechanisms of biomolecules. Therefore, we have developed techniques such as **single-molecule imaging microscopy** capable of directly observing the motion and structural changes of individual molecules, a method of manipulating molecules by grabbing molecules with **optical** or **magnetic tweezers**, and an apparatus for measuring the minute forces generated by molecules. Today, we use these techniques to investigate the functions of proteins related to **DNA replication**, **repair**, and **recombination**.

DNA replication, repair, and recombination are the most important mechanisms for guaranteeing the genetic continuity of a species. DNA replication is surprisingly complex because DNA information must be transmitted accurately to descendents. The dynamics of how various proteins actually interact when replicating DNA to catalyze a reaction quickly and with exquisite precision are not understood.

Therefore, our goal is to further develop **single-molecule measurement** techniques to understand DNA replication, repair, and recombination at the single-molecule level by single-molecule imaging of interactions between DNA and proteins, among different proteins, and simultaneous mechanical measurement of one interacting DNA molecule.

Selected Papers

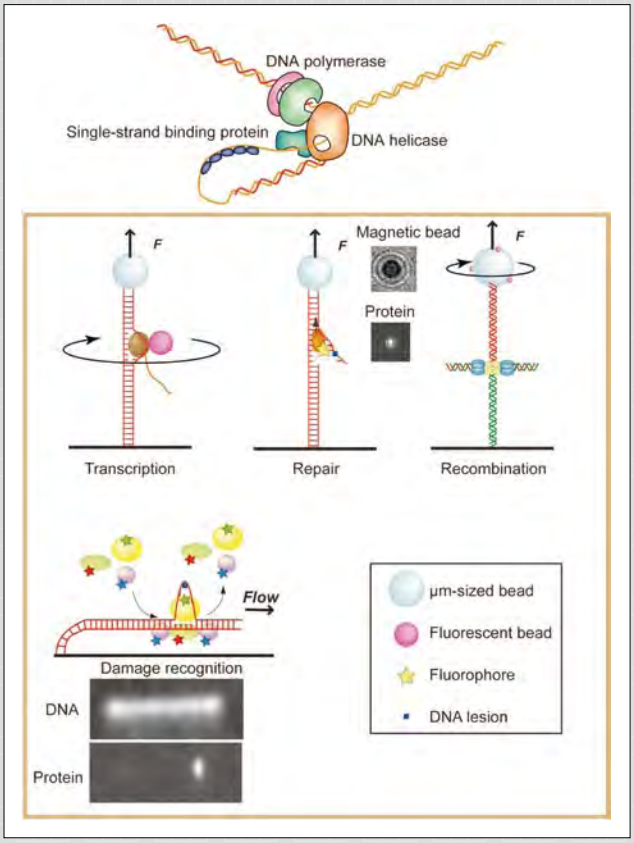
Miyazono, Y., Hayashi, M., Karagiannis, P., Harada, Y. and Tadakuma, H. Strain through the neck linker ensures processive runs: a DNA-kinesin hybrid nanomachine study. *EMBO J.* **29**, 93–106 (2009).

Sasuga, Y., Iwasawa, T., Terada, K., Oe, Y., Sorimachi, H., Ohara, O. and Harada, Y. Single-cell chemical lysis method for analyses of intracellular molecules using an array of picoliter-scale microwells. *Anal. Chem.* **80**, 9141–9149 (2008).

Hayashi, M. and Harada, Y. Direct observation of the reversible unwinding of a single DNA molecule caused by the intercalation of ethidium bromide. *Nucleic Acids Res.* **35**, e125 (2007).

Han, Y., Tani, T., Hayashi, M., Hishida, T., Iwasaki, H., Shinagawa H. and Harada, Y. Direct observation of DNA rotation during branch migration of Holliday junction DNA by Escherichia coli RuvA-RuvB protein complex. *Proc. Natl. Acad. Sci. U.S.A.* **103**, 11544–11548 (2006).

Sasuga, Y., Tani, T., Hayashi, M., Yamakawa, H., Ohara, O. and Harada, Y. Development of a microscopic platform for real-time monitoring of biomolecular interactions. *Genome Res.* **16**, 132–139 (2006).



Mitsuru Hashida Lab

Drug Delivery Systems (DDS)

Faculty Members

Mitsuru Hashida (Professor)

Research Overview

The use of **drug delivery systems** is a novel concept involving administration technology for optimizing chemotherapy to control the distribution of drugs. It is one of the most important fields and basic technologies supporting drug discovery and development in the pharmaceutical sciences associated with biomedicine and gene medicine. One of the main emphases of this group is **the development of drug and gene carriers** using new materials with unique characteristics. We are also studying the application of **carbon nanotubes (CNTs)** to drug delivery systems. One of the key steps in using CNTs *in vivo* is solubilization of this material into water, and we employ the approach using peptides as a dispersing agent to clear this subject. Currently, we are working on functionalization of CNTs for drug delivery. In this study, the physicochemical evaluation of CNTs is carried out collaboratively with the Imahori Lab, and functionalization of CNTs with sugar moiety is conducted in collaboration with the Kiso Lab. We are also developing new drug carrier collaborations with the Kiso Lab. A carbohydrate-cholesterol conjugate was synthesized through an electronically neutral linkage and is applied to the development of new drug carriers with improved cell-specific targeting properties.

Our current research projects are listed below:

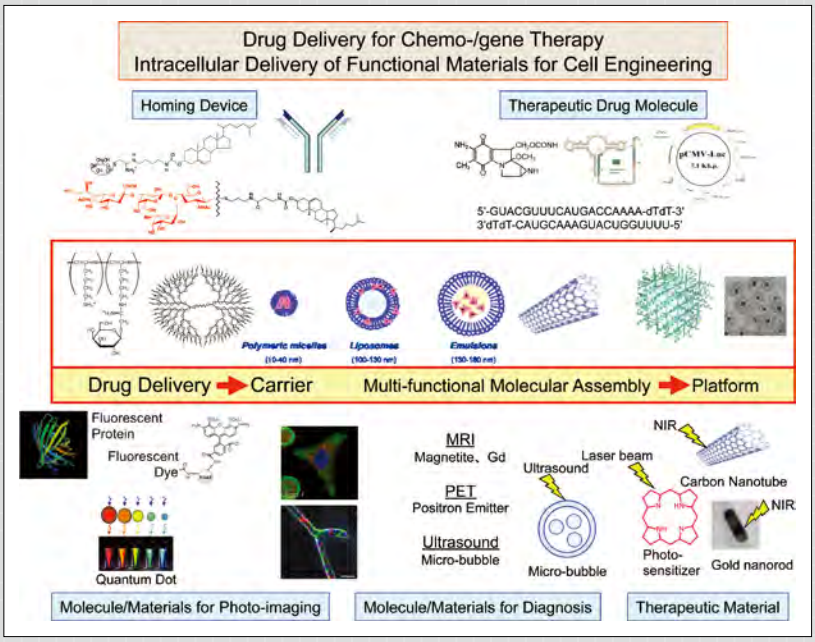
1. Rational design of macromolecular and particulate carriers for drug targeting
2. *In vivo* disposition control and targeting of proteins by chemical modification
3. Cell specific delivery of genes
4. Development of carrier systems employing new materials such as carbon nanotubes
5. *In silico* prediction of mucosal and skin absorption of drugs

Selected Papers

Nakanishi, H., Higuchi, Y., Kawakami, S., Yamashita, F. and Hashida, M. PiggyBac transposon-mediated long-term gene expression in mice. *Mol. Ther.* **18**, 707–14 (2010).

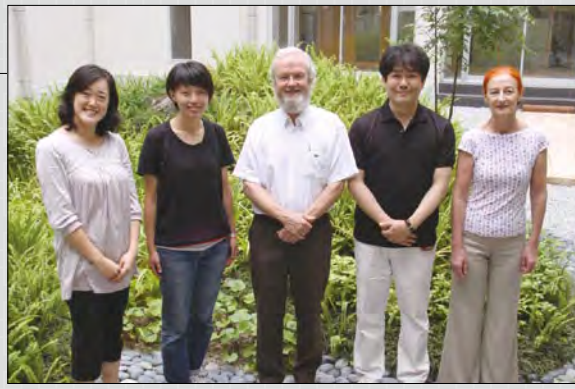
Un, K., Kawakami, S., Suzuki, R., Maruyama, K., Yamashita, F. and Hashida, M. Enhanced transfection efficiency into macrophages and dendritic cells by a combination method using mannosylated lipoplexes and bubble liposomes with ultrasound exposure. *Hum. Gene Ther.* **21**, 65–74 (2010).

Higuchi, Y., Kawakami, S., Yamashita, F. and Hashida, M. The potential role of fucosylated cationic liposome/NFkappaB decoy complexes in the treatment of cytokine-related liver disease. *Biomaterials* **28**, 532–9 (2007).



John Heuser Lab

Biophysics, Cell Biology



Faculty Members

John Heuser (Professor)
Nobuhiro Morone (Senior Lecturer)
Tatyana Tenkova-Heuser (Assistant Professor)

Research Overview

The key goal of this laboratory has long been to develop advanced new procedures for preserving the living appearance of the **meso-scaled molecular machinery** found inside cells. Our basic procedure is the "**quick-freeze/deep-etch**" method of **electron microscopy**, which we originally developed to visualize the mechanisms involved in the quantal release of neural transmitter substances from brain synapses and neuromuscular junctions. This we found involved secretion of the **meso-scaled entities** called "**synaptic vesicles**". Subsequently, our freeze-etch techniques were disseminated and reproduced all around the world, as other electron microscopists sought to visualize the structures and living dynamics of many different **meso-machines** found inside cells, including receptor and signaling complexes, cytoskeletal actomyosin networks, and a whole variety of cell-membrane differentiations, including clathrin-coated pits, caveolae, and endocytotic organelles of all sorts.

Overall, our "**quick-freeze/deep-etch**" techniques have been used to capture, visualize, and understand several important cellular processes that occur far too rapidly, and on too small a scale, to visualize in any other way – not only neural transmission, but also muscular contraction, viral infection, immune-cell synapse formation, vesicular transport, and cell migration during neurogenesis.

Additionally, we have modified the "**quick-freeze/deep-etch**" technique so that we can visualize isolated and purified protein and DNA macromolecules, in order to better understand the molecular mechanisms that underlie cellular functioning on the **meso-scale**. In all of our studies of macromolecules, as well as our studies of cell organelles, our TEM and SEM-imaging techniques have provided exceedingly true-to-life views that retain the full meso-architecture of cells and organelles, and thus are best viewed by modern methods of 3D-imaging including **tomography** and **stereology**.

At the present, we are well along in a further development of **cryo-scanning electron microscopy** for directly visualizing frozen cells without any further manipulation. In this way, we intend to make our EM laboratory in the iCeMS the world leader in 3D electron microscopy at the **meso-scale**.

The cross-disciplinary projects that we have already initiated with other iCeMS researchers include the following:

1. EM visualization of the pathological **meso-scale entities** that form in and around nerve and glial cells in various neurodegenerative diseases, including the "**plaques and tangles**" that develop in Alzheimer's disease, as well as the various other intracellular-fibril "**amyloid**" aggregates that form in Parkinson's disease, Huntington's disease, ALS, etc. Here we are working closely with the Nakatsuji Lab to develop and analyze various **ES and iPS** cell-lines that are genetically engineered to recapitulate these diseases by forming intracellular fibril-aggregates, with the goal of determining what can be done to prevent their formation or assist the affected cells in ridding themselves of them.

2. The above project also involves close collaboration with the Kusumi Lab, in order to **correlate our EM observations with their high-speed single-molecule imaging of fibril-formation**, in a further effort to determine the effects this has on membrane and organellar dynamics in living cells. Indeed, we are seeking to determine the EM-equivalents of many different aspects of the advanced high-speed single-molecule imaging that is always being done, on many different fronts, in the Kusumi Lab.

3. Finally, we are seeking to provide EM support for a number of other multidisciplinary research projects going on within the iCeMS, including the development of "**smart nanoporus materials**" with the Takano and Kitagawa Labs, the development of new imaging methods to visualize lipid transport and the formation of **mesoscale lipid-assemblies** with the Ueda and Kusumi Labs, and the spatial and temporal organization of organelles (everything from the mundane mitochondria to the most mysterious bit of 'nuage'), which the Hiiragi, Kengaku, and Nakatsuji Labs are studying to determine the special roles they play during **embryonic and neural development**.

Selected Papers

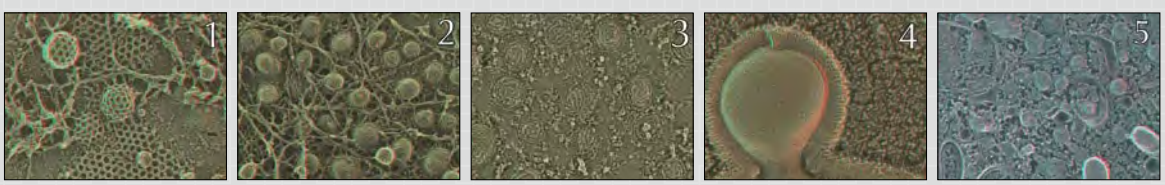
Hanson, P. I., Roth, R., Lin, Y. and Heuser, J. E. Plasma membrane deformation by circular arrays of ESCRT-III protein filaments. *J. Cell Biol.* **180**, 389–402 (2008).

Morone, N., Nakada, C., Umemura, Y., Usukura, J. and Kusumi, A. Three-dimensional molecular architecture of the plasma-membrane-associated cytoskeleton as reconstructed by freeze-etch electron tomography. *Methods Cell Biol.* **88**, 207–36 (2008).

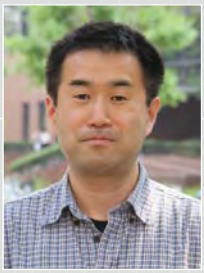
Heuser, J. Evidence for recycling of contractile vacuole membrane during osmoregulation in Dictyostelium amoebae – A tribute to Gunther Gerisch. Eur. *J. Cell Biol.* **85**, 859–871 (2006).

Morone, N., Fujiwara, T., Murase, K., Kasai, R. S., Ike, H., Yuasa, S., Usukura, J. and Kusumi, A. Three-dimensional reconstruction of the membrane skeleton at the plasma membrane interface by electron tomography. *J. Cell Biol.* **174**, 851–862 (2006).

Heuser, J. Deep-etch EM reveals that the early poxvirus envelope is a single membrane bilayer stabilized by a geodetic "honeycomb" surface coat. *J. Cell Biol.* **169**, 269–283 (2005).



Samples:
1. Clathrin-coated pits
2. Actin MSK/Cavelae
3. Caveolae
4. Yeast
5. Intestine



Takashi Hiiragi Lab

Developmental Biology

Faculty Members

Takashi Hiiragi (Professor)

Research Overview

The ultimate goal of the research in our laboratory is the understanding of **totipotency**: what defines totipotency and what makes a cell totipotent. Germ-line cells, oocytes and sperm, are highly differentiated but nevertheless able to regain totipotency by forming zygotes, thereby initiating embryonic development in the next generation. A prerequisite for understanding totipotency is the knowledge of developmental mechanisms during transition from oocyte to embryo and early embryogenesis. Our current research thus focuses on understanding the principles underlying early mammalian development.

We have so far characterized the following key features:

1. Mechanical and structural context plays a key role in morphogenesis and **embryonic patterning** (Motosugi et al. 2005; Motosugi et al. 2006; Honda et al. 2008);
2. An asymmetry may emerge autonomously in an equivalent cellular population with no need for a priori intrinsic differences (Honda et al. 2008);
3. Early mouse development involves **stochastic processes** (Dietrich and Hiiragi 2007; Dietrich and Hiiragi 2008).

These features suggest that, in order to fully understand the mechanisms of early mammalian development, it will be essential to address how the diverse inputs acting on every individual cell are integrated in the embryo **at the systems level**. We thus adopt a wide variety of experimental approaches in order to understand the development at a molecular, cellular and systems level; in particular, 4D live-imaging, fluorescence-based gene-trap screens, gene expression profiling of individual blastomeres, experimental micromanipulation and computer simulation of the blastocyst morphogenesis. An emerging hypothesis is that early mammalian embryogenesis may be a random and stochastic process in a particular structural context that eventually leads to **self-organization**. This principle of embryonic patterning may underlie the highly regulative capacity that is unique to mammalian pre-implantation embryos.

At the iCeMS, we are further exploring multi-disciplinary approaches including:

1. Characterization of the stochastic patterning process at the meso-scale level. Gene expression profiles of individual blastomeres in the mouse pre-implantation embryo will be established by single-cell cDNA amplification, while spatio-temporal gene expression patterns will be visualized by Fluorescence Correlation Spectroscopy (FCS). This collaboration may identify a shift from “stochastic” to “consolidated” patterns of gene expression upon lineage commitment in vivo (Harada Lab, CeMI, Saitou Lab).
2. Potential contributions of cellular geometry to cell fate specification. **Mechanical contexts** will be applied to the embryo or the isolated cell culture using a micro-device, in order to examine if geometrical information can drive lineage specification (Chen Lab).

Selected Papers

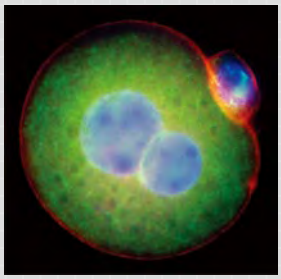
Honda, H., Motosugi, N., Nagai, T., Tanemura, M. and Hiiragi, T. Computer simulation of emerging asymmetry in the mammalian blastocyst. *Development* **135**, 1407–1414 (2008).

Dietrich, J. E. and Hiiragi, T. Stochastic patterning in the mouse pre-implantation embryo. *Development* **134**, 4219–4231 (2007).

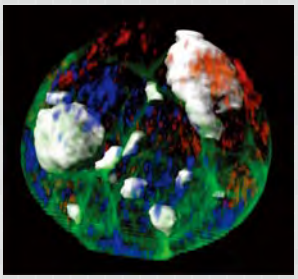
Hiiragi, T., Louvet-Vallee, S., Solter, D. and Maro, B. Does prepatterning occur in the mouse egg? *Nature* **442**, E3–4 (2006).

Motosugi, N., Dietrich, J. E., Polanski, Z., Solter, D. and Hiiragi, T. Space asymmetry directs preferential sperm entry in the absence of polarity in the mouse oocyte. *PLoS Biology* **4**, e135 (2006).

Motosugi, N., Bauer, T., Polanski, Z., Solter, D. and Hiiragi, T. Polarity of the mouse embryo is established at blastocyst and is not prepatterned. *Gene. Dev.* **19**, 1081–1092 (2005).

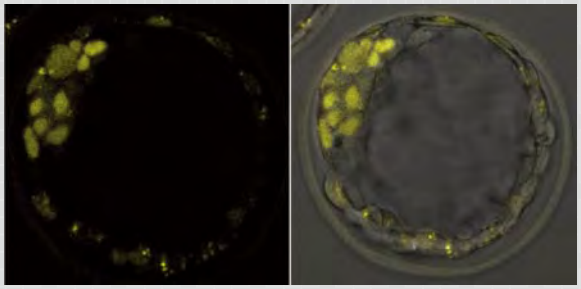


Totipotent egg



Blastocyst morphogenesis

Computer simulation of blastocyst morphogenesis



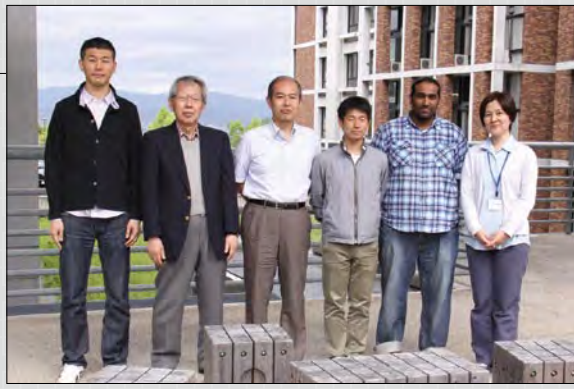
ICM-specific reporter expression in a gene-trap mouse

Hiroshi Imahori Lab

Organic Chemistry, Photochemistry, Drug Delivery Systems

Faculty Members

Hiroshi Imahori (Professor)



Research Overview

Our laboratory has been working on development of **artificial photosynthetic** and **solar energy conversion systems**. In particular, we have demonstrated small reorganization energies of fullerenes, which is favorable for efficient solar energy conversion. Namely, they have made it possible to produce a long-lived charge-separated state with a high quantum yield in donor-acceptor systems. The elucidation of basic electron transfer properties of fullerenes has provided us with an important basis for high performance of fullerene-based organic electronics including organic solar cells. The papers published during this period are highly cited in the fields of chemistry and material science.

The shortage of fossil fuels and the degradation of the global environment have focused research attention on solar cells, which can convert sustainable solar energy into electricity. However, the cost of electricity from inorganic solar cells (silicon-based photovoltaics) is presently much higher than that generated by hydroelectric power and nuclear or fossil fuels. Therefore, it is necessary to develop low-cost solar cells with high power conversion efficiencies. **Organic solar cells** would be promising candidates if they fulfill their potential, especially as they bear unique advantages over inorganic solar cells, that is, they are flexible, lightweight, and colorful.

Our group has been creating various organic solar cells including **dye-sensitized**, **bulk heterojunction**, and **novel organic solar cells**. Specifically, we have developed a novel hybrid solar cell possessing both characteristics of dye-sensitized and bulk heterojunction devices. Currently, a power conversion efficiency of >8% has been achieved on our solar cells.

At the iCeMS, we have initiated new multidisciplinary research projects based on organic chemistry and photochemistry through collaboration with other research groups of the institute, including:

1. Development of **light-harvesting mesomaterials** for phototherapy and multifunctional **light-emitting mesomaterials** for cell imaging (Murakami Fellow and Hashida Lab).

2. Development of **artificial transporters** made by photofunctional mesomaterials to elucidate cellular functions and control stem cells (Ueda Lab).

Selected Papers

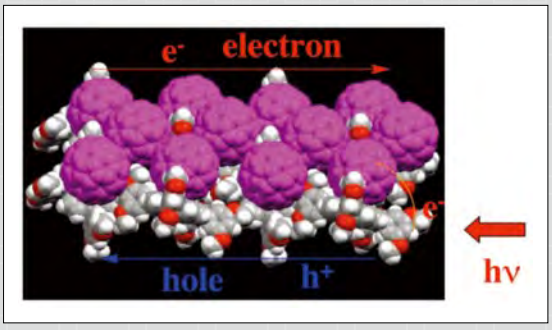
Sagawa, T., Yoshikawa, S. and Imahori, H. One-dimensional nanostructured semiconducting materials for organic photovoltaics. *J. Phys. Chem. Lett.* **1**, 1020–1025 (2010).

Imahori, H., Umeyama, T. and Ito. S. Large π aromatic molecules as potential sensitizers in dye-sensitized solar cells. *Acc. Chem. Res.* **42**, 1809–1818 (2009).

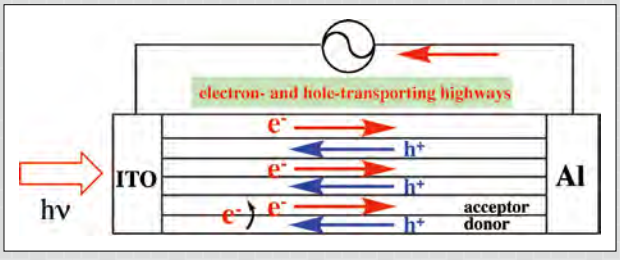
Matano, Y. and Imahori, H. Phosphole-containing calixpyrroles, calixphyrins, and porphyrins: Synthesis and coordination chemistry. *Acc. Chem. Res.* **42**, 1193–1204 (2009).

Imahori, H. and Umeyama, T. Donor-acceptor nanoarchitecture on semiconducting electrodes for solar energy conversion. *J. Phys. Chem. C* **113**, 9029–9039 (2009).

Kira, A., Umeyama, T., Matano, Y., Yoshida, K., Isoda, S., Park, J.-K., Kim, D. and Imahori, H. Supramolecular donor-acceptor heterojunctions by vectorial stepwise assembly of porphyrins and coordination-bonded fullerene arrays for photocurrent generation. *J. Am. Chem. Soc.* **131**, 3198–3200 (2009).



Highly efficient hole and electron transportation by molecule-level bicontinuous donor-acceptor network



Schematic illustration of ideal bulk heterojunction solar cell

Photocurrent generation in porphyrin-sensitized solar cell

Mineko Kengaku Lab

Developmental Neurobiology, Cell Biology

Faculty Members

Mineko Kengaku (Associate Professor)

Research Overview

Control of **cell shapes and positions** is critical for the formation and function of multicellular tissues in living organisms. In the mammalian brain, 10–100 billion **neurons** with intricate branches are orderly arranged for integration into specific neural circuits. Differentiating neurons are highly motile cells that migrate long distances from the germinal layer to their destinations within the brain. They then extend cellular processes and arborize well-patterned dendrites and axons in order to contact their specific synaptic counterparts. These dynamic cellular movements are regulated by conformational and biochemical activity changes in **cell membranes** and **cytoskeletal proteins**. However, the spatiotemporal dynamics of molecules in motile neurons are largely unknown. The major goal of our research is to clarify the dynamics and mechanisms of **molecular interaction in meso-space** during **neuronal migration** and **dendrite branching**. We also aim to develop imaging techniques for real-time observation of molecular and cellular dynamics of neurons in the developing brain.

Three main research directions are as follows:

1. Live imaging analyses of **cytoskeletal dynamics** during **organelle transport** in migrating neurons
2. Biological and physical bases of **branch patterning** in differentiating dendrites
3. Development of **imaging techniques** for molecular analysis of neuronal motility

Selected Papers

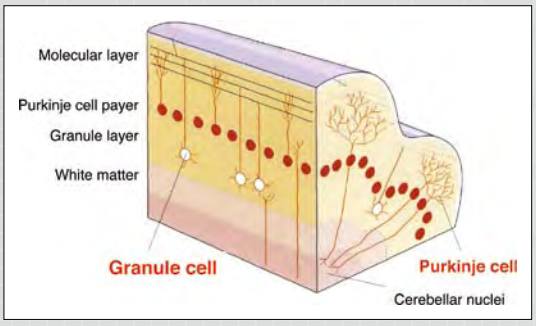
Kurisu. J., Fukuda. T., Yokoyama. S., Hirano, T. and Kengaku, M. Polarized targeting of DNER into dendritic plasma membrane in hippocampal neurons depends on endocytosis. *J. Neurochem.* **113**, 1598–1610 (2010).

Fukazawa, N., Yokoyama, S., Eiraku, M., Kengaku, M. and Maeda, N. Receptor type protein tyrosine phosphatase zeta-pleiotrophin signaling controls endocytic trafficking of DNER that regulates neuritogenesis. *Mol. Cell. Biol.* **28**, 4494–4506 (2008).

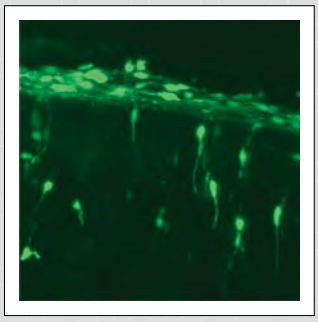
Umeshima, H., Hirano, T. and Kengaku, M. Microtubule-based nuclear movement occurs independently of centrosome positioning in migrating neurons. *Proc. Natl. Acad. Sci. U.S.A.* **104**,16182–7 (2007).

Fujishima, K., Kiyonari, H., Kurisu, J., Hirano, T. and Kengaku, M. Targeted disruption of Sept3, a heteromeric assembly partner of Sept5 and Sept7 in axons, has no effect on developing CNS neurons. *J. Neurochem.* **102**, 77–92 (2007).

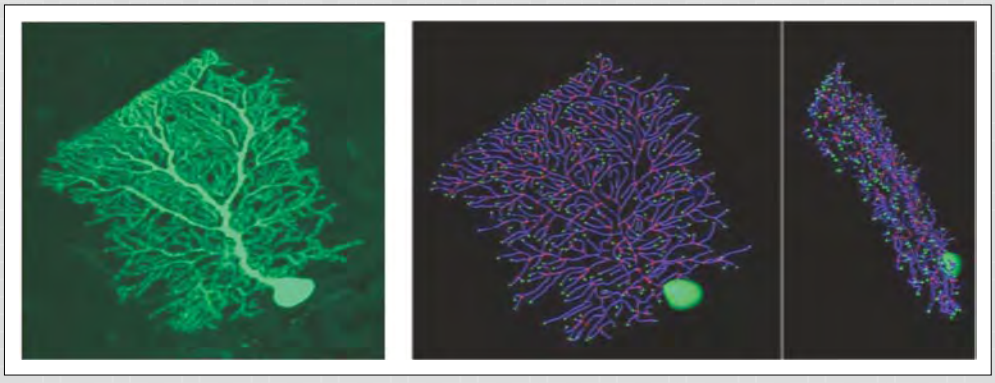
Eiraku, M., Tohgo, A., Ono, K., Fujishima, K., Kaneko, M., Hirano, T. and Kengaku, M. DNER acts as a neuron-specific Notch ligand during Bergmann glial development. *Nat. Neurosci.* **8**, 873–880 (2005).



Cytoarchitecture of the cerebellar cortex of mammals



Time-lapse imaging of migrating granule cells in the developing cerebellum



Microscopic and graphic images of the cerebellar Purkinje cell transduced with GFP gene

Makoto Kiso Lab

Glycotechnology

Faculty Members

Makoto Kiso (Professor)

Hiromune Ando (Associate Professor)

Research Overview

The iCeMS Gifu University satellite pursues the elucidation of the molecular basis underlying the multifunctions of carbohydrates (especially those called "**glycans**") in various biological processes by chemical methods and their applications in medicine. Our research is focused on the development of a versatile and powerful synthetic methodology of glycans, and the creation of a **Glycobank** possessing a wide spectrum of biologically-significant glycans and functionalized glycan probes. Utilizing the full entries of the Glycobank, we will conduct cross-disciplinary studies with molecular biology, developmental biology, structural biology, and biophysics in order to understand and apply the biological functions of glycans.

Our synthesized glycans have been utilized in diverse biological research such as those related to immune systems, virus entry, and cancer migration. At the iCeMS, we have launched new cross-disciplinary projects using the entries of the Glycobank, including:

1. Creation of the **glyco-director** system for stem cell engineering, which is comprised of arrays of homogenous synthetic glycans that direct the differentiation and proliferation of stem cells (ES and iPS cells), in collaboration with stem cell science (Nakatsuji and Yamanaka Labs) and nanomaterial science (Chen Lab).
2. Development of glycan probes for **single molecule tracking** of cell membranes to understand the formation and functions of **raft domains**, a functionalized complex of membrane constituents, in collaboration with single-molecule cell biophysics (Kusumi Lab).
3. Innovation of **drug delivery systems** (**DDS**) by creating new drug carriers using carbon nanotubes and lyposomes functionalized with glycans, in collaboration with biopharmaceuticals (Hashida Lab) and nanomaterial and biomaterial sciences (Kitagawa and Imahori Labs).

Selected Papers

Fujikawa, K., Nohara, T., Imamura, A., Ando, H., Ishida, H. and Kiso, M. A cyclic glucosyl ceramide acceptor as a versatile building block for complex ganglioside synthesis. *Tetrahedron Lett.* **51**, 1126–1130 (2010).

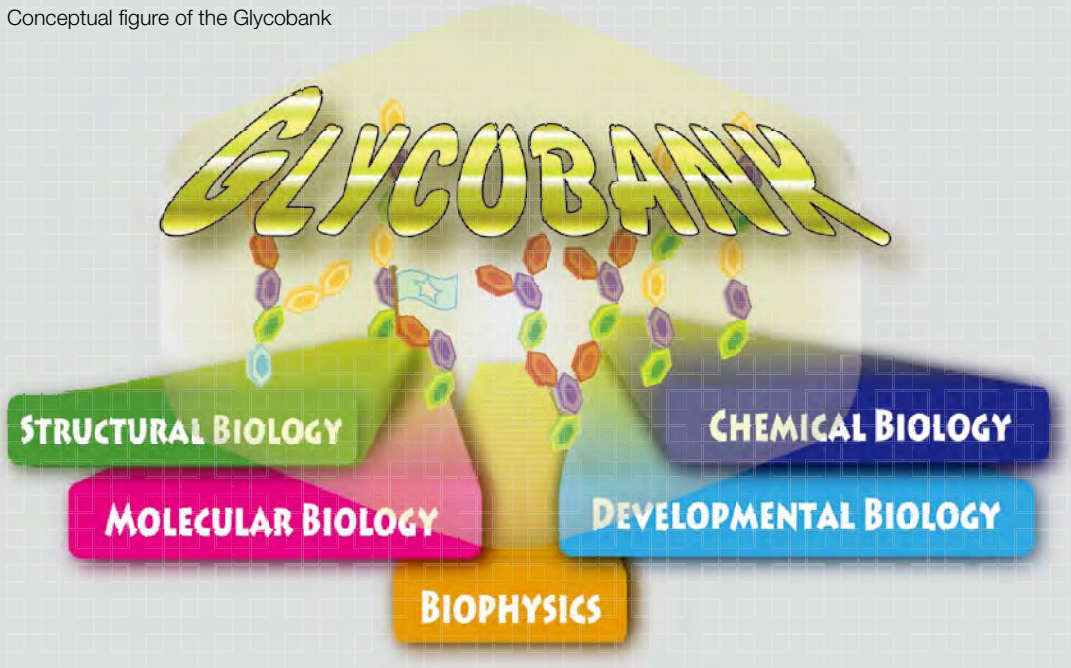
Iwayama, Y., Ando, H., Ishida, H. and Kiso, M. A first total synthesis of ganglioside HLG-2. *Chem. Eur. J.* **15**, 4637–4648 (2009).

Imamura, A., Ando, H., Ishida, H. and Kiso, M. Ganglioside GQ1b: Efficient total synthesis and the expansion to synthetic derivatives to elucidate its biological roles. *J. Org. Chem.* **74**, 3009–3023 (2009).

Stenmark, P., Dupuy, J., Imamura, A., Kiso, M. and Stevens, R. C. Crystal structure of botulinum neurotoxin type a in complex with the cell surface co-receptor GT1b–insight into the toxin–neuron interaction. *PLoS Pathog.* **4**, 1–10 (2008).

Abdu-Allah, H. H. M., Tamanaka, T., Yu, J., Lu, Z., Sadagopan, M., Adachi, T., Tsubata, T., Kelm, S., Ishida, H. and Kiso, M. Design, synthesis, and structure-affinity relationships of novel series of sialosides as CD22-specific inhibitors. *J. Med. Chem.* **51**, 6665–6681 (2008).

Conceptual figure of the Glycobank



Susumu Kitagawa Lab

Coordination Chemistry, Biological Inorganic Chemistry, Biomaterial Science

Faculty Members

Susumu Kitagawa (Professor)
Takafumi Ueno (Associate Professor)
Shuhei Furukawa (Associate Professor)
Ryotaro Matsuda (Associate Professor)
Hirokazu Kobayashi (Assistant Professor)
Stéphane Diring (Assistant Professor)

Research Overview

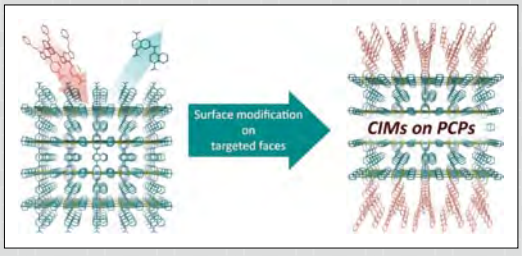
We are developing a chemistry of new organic-inorganic porous materials with pores or also channels in a scale ranging from tenths of nanometers to several nanometers in size. So-called **smart microporous materials**, these have controllable properties *ad arbitrium* adjustable in response to surrounding environments. This new field will likely contribute to the alleviation of energy and environment issues as well as to an increase in human welfare by developing (a) low-pressure gas storage and high-efficiency separation systems, (b) molecular- and ion-transport and controlled-release microvessels working in cells, and (c) environmentally friendly chemical reaction systems. These materials being studied in our lab are called **Porous Coordination Polymers** (**PCPs**) and **Metal-Organic Frameworks** (**MOFs**). Moreover, we are interested in **mesoscale** (5-100nm) crystals of our materials because these have properties unique from their bulk counterparts. The mesoscale domain is particularly important in that vital physical and chemical phenomena of cells occur in this range. Our materials open the door to a new field combining cell biology and porous material science.

1. Development of PCPs: We synthesize functional PCPs not only for gas storage but also for separations with higher capacity than conventional materials. Low molecular weight molecules, such as carbon dioxide (CO_2), methane (CH_4), and alkanes (C_2-C_3) are important gases for sustaining life, and are contained in natural gas and biogas as well. In order to obtain highly purified CH_4, the key question is how to separate CH_4 from a mixture gas containing carbon dioxide (CO_2) impurities without expending a large amount of energy. Succeeding in this would provide us with a new industrial technology independent of petroleum oil resources.

2. Delivery of functional molecules, such as drugs and ions, using porous materials: carbon monoxide (CO), nitric oxide (NO), and ammonia (NH_3) have attracted attention as important molecules involved in many physiological and pathological processes. We are synthesizing new porous materials which can absorb and release these gas molecules and ions in physiological environments for detoxication and control of cell functions.

3. Porous materials integrated with cell membranes: We are working to construct new artificial membranes conjugated with porous materials having various functions such as gas storage and ion channels. These bio-integrated materials can serve as new drug delivery systems and bio-imaging reagents, as well as aiding in the elucidation of cell functions.

4. Bio-compatible materials using proteins: In many biological systems, protein assembly cages and channels can deliver various organic molecules and metal ions. We are working on reconstruction of porous materials made from protein assemblies or protein crystals for development of highly biocompatible materials.



Surface modification of PCPs

Selected Papers

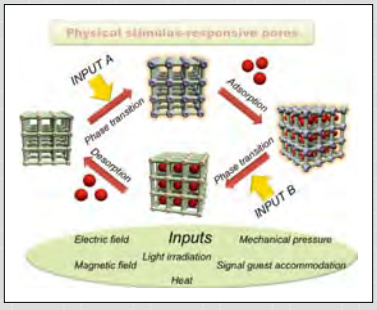
Horike, S., Shimomura, S. and Kitagawa, S. Soft porous crystals. *Nat. Chem.* **1**, 695–704 (2009).

Bureekaew, S., Horike, S., Higuchi, M., Mizuno, M., Kawamura, T., Tanaka, D., Yanai, N. and Kitagawa, S. One-dimensional imidazole aggregate in aluminium porous coordination polymers with high proton conductivity. *Nat. Mater.* **8**, 831–836 (2009).

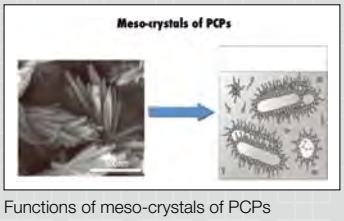
Abe, S., Hirata, K., Ueno, T., Morino, K., Shimizu, N., Yamamoto, M., Takata, M., Yashima, E. and Watanabe, Y. Polymerization of Phenylacetylene by Rhodium Complexes within a Discrete Space of apo-Ferritin. *J. Am. Chem. Soc.* **131**, 6958–6960 (2009).

Maji, T. K., Matsuda, R. and Kitagawa, S. A Flexible Interpenetrating Coordination Framework with a Bimodal Porous Functionality. *Nat. Mater.* **6**, 142–148 (2007).

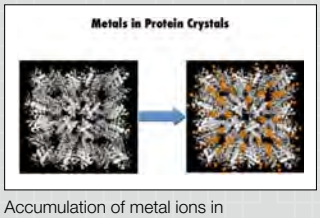
Matsuda, R., Kitaura, R., Kitagawa, S., Kubota, Y., Belosludov, R. V., Kobayashi, T. C., Sakamoto, H., Chiba, T., Takata, M., Kawazoe, Y. and Mita, Y. Highly controlled acetylene accommodation in a metal–organic microporous material. *Nature* **436**, 238–241 (2005).



External stimuli for controlling PCP functions



Functions of meso-crystals of PCPs



Accumulation of metal ions in porous protein crystals

Akihiro Kusumi Lab

Single-Molecule Cell Biophysics

Faculty Members
Akihiro Kusumi (Professor)
Kenichi Suzuki (Senior Lecturer)

Research Overview

Our laboratory is dedicated to understanding **membrane mechanisms** and developing ultra-speed **single-molecule** observation and manipulation nano-methodologies applicable to the studies of living cells. These methodologies are initially employed to reveal the structures, dynamics, and functions of mesoscale (1–100 nm, slightly expanded from the iCeMS' definition of 5–100 nm) domains in the plasma membrane, which are investigated in the context of cellular **signal transduction** and **neuronal network remodeling**. A smooth melding of physics, engineering, and biomedicine is the key to the research conducted in our laboratory. Based on these single-molecule insights into mesoscale processes occurring in the cell, we intend to develop **systems molecular biology** to understand the mechanisms for the formation and function of meso-scale membrane domains, including membrane compartments, raft domains, and transient protein oligomers.

Fig. 1, left. **Single-molecule tracking** techniques. A fluorescent or colloidal gold tag is attached to a specific target membrane protein or lipid, and its movements in the cell membrane are visualized. **The fastest imaging** ever has been achieved for single gold particles and single fluorescent molecules (6 and 100 microseconds/frame with a spatial precision of 17 and 35 nm, respectively).

Fig. 1, right. Using laser tweezers, a gold-tagged membrane molecule is moved at will along the membrane.

Fig. 2. A signaling molecule, a small G protein Ras (green), undergoes diffusion on the cytoplasmic surface of the plasma membrane (yellow trajectories). The activation of this single Ras molecule was imaged (green color changed to red, center of this image), which entails the first successful observation of the activation of a single molecule. Furthermore, many other cytoplasmic molecules are recruited to this activated Ras molecule to form activated Ras signaling complexes, which last, surprisingly, for only a fraction of a second, suggesting the possibility that the basic unit of the cellular signal occurs like a digital pulse in such transient molecular complexes.

Fig. 3. A paradigm shift in the concept of plasma membrane structure and function, proposed by us. The entire plasma membrane is partitioned into many small compartments of 30–200 nm due to the actin-based membrane skeleton (membrane-skeleton “fence” model, left) and various transmembrane proteins anchored to the membrane skeleton (anchored transmembrane-protein pickets, right).

Transmembrane proteins anchored to the membrane skeleton and immobilized, lining the membrane skeleton fence, effectively act like rows of diffusion barriers, due not only to the steric hindrance effect but also to the hydrodynamic friction effect at the surfaces of immobile molecules.

Selected Papers

Kusumi, A., Shirai, Y. M., Koyama-Honda, I., Suzuki, K. G. N. and Fujiwara, T. K. Hierarchical organization of the plasma membrane: investigations by single-molecule tracking vs. fluorescence correlation spectroscopy (review). *FEBS Lett.* **584**, 1814–1823 (2010).

Umemura, Y. M., Vrljic, M., Nishimura, S. Y., Fujiwara, T. K., Suzuki, K. G. N. and Kusumi, A. Both MHC class II and its GPI-anchored form undergo hop diffusion as observed by single-molecule tracking. *Biophys. J.* **95**, 435–450 (2008).

Suzuki, K. G. N., Fujiwara, T. K., Sanematsu, F., Iino, R., Edidin, M. and Kusumi, A. GPI-anchored receptor clusters transiently recruit Lyn and Gα for temporary cluster immobilization and Lyn activation: single-molecule tracking study 1. *J. Cell Biol.* **177**, 717–730 (2007).

Morone, N., Fujiwara, T., Murase, K., Kasai, R. S., Ike, H., Yuasa, S., Usukura, J. and Kusumi, A. Three-dimensional reconstruction of the membrane skeleton at the plasma membrane interface by electron tomography. *J. Cell Biol.* **174**, 851–62 (2006).

Kusumi, A., Nakada, C., Ritchie, K., Murase, K., Suzuki, K., Murakoshi, H., Kasai, R. S., Kondo, J. and Fujiwara, T. Paradigm shift of the plasma membrane concept from the two-dimensional continuum fluid to the partitioned fluid: high-speed single-molecule tracking of membrane molecules. *Annu. Rev. Biophys. Biomol. Struct.* **34**, 351–378 (2005).

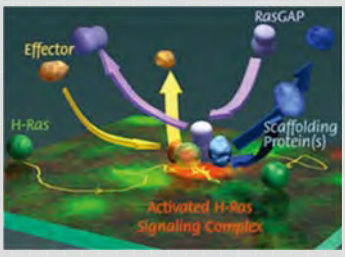


Fig. 2

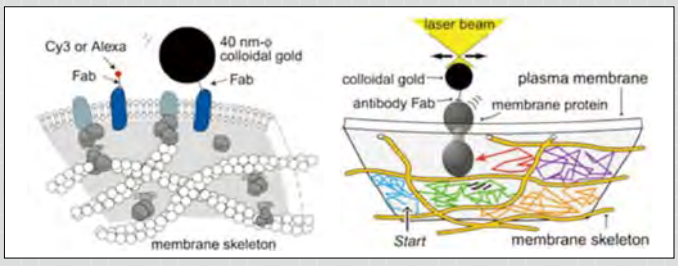


Fig. 1

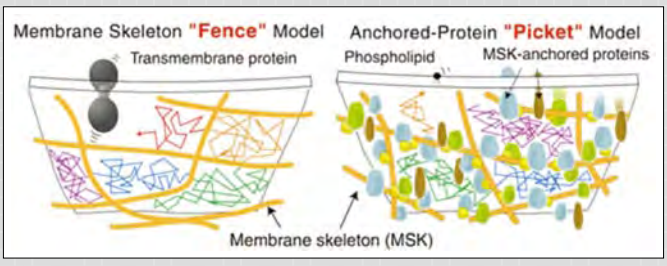


Fig. 3

Norio Nakatsuji Lab

Stem Cell Biology, Developmental Biology

Faculty Members
Norio Nakatsuji (Professor)
Dongju Jung (Senior Lecturer)
Kazuhiro Aiba (Senior Lecturer)

Research Overview

Our research group has been working on development and differentiation of **embryonic stem cells** and **germ cells** in mammals. In particular, we have established mouse, cynomolgus monkey, and **human embryonic stem (ES) cell lines**, and we have been carrying out various aspects of basic and application research using **pluripotent stem cells**. We are still the only group in Japan to have derived and distributed human ES cell lines to numerous other biomedical researchers.

We are developing methods of **genetic modification** in primate and human pluripotent stem cells, including conditional expression such as the Tet-On/Off system, expression of multiple transgenes, and the homologous recombination method. More recently, our group has created normal and disease **model cells** for disease mechanism research and drug discovery tools, which are important applications of pluripotent stem cell lines. These include production of neurodegenerative disease model cells by introduction of mutated genes, toxicology studies using cardiomyocytes, and **chemical screening** for stem cell control.

We have initiated multidisciplinary research projects using **ES and iPS cell lines** in collaboration with other research groups of the iCeMS, as follows:

1. Creation and analysis of model cells for biomedical research by utilizing pluripotent stem cells including human ES and iPS cell lines. The first example is **neurodegenerative disease model** cells produced by genetic modification of stem cell lines and differentiation into relevant cells in each disease. Production of abnormal protein/peptides and disease mechanisms will be examined in collaboration with other research groups including the meso-imaging CeMI group.
2. Control of stem cells by **screening synthetic small molecules** and utilization of **nano/meso/micro-fabricated substrata and chambers** to control differentiation of ES/iPS cells in collaboration with chemical biology (such as the Uesugi Lab) and nano/meso/micro-engineering groups (such as the Chen Lab).
3. Development of **synthetic artificial transcription factors** to regulate important genes for pluripotency maintenance and differentiation into specific cell lineages by collaboration with chemical biology groups (such as the Sugiyama and Uesugi Labs).

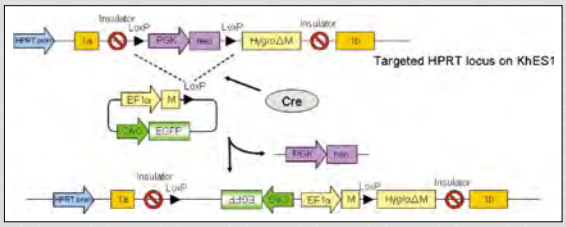
Selected Papers

Sakurai, K., Shimoji, M., Tahimic, C. G. T., Aiba, K., Kawase, E., Hasegawa, K., Amagai, Y., Suemori, H. and Nakatsuji, N. Efficient integration of transgenes into a defined locus in human embryonic stem cells. *Nucleic Acids Res.* **38**, e96 (2010).

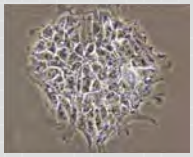
Shoji, M., Tanaka, T., Hosokawa, M., Reuter, M., Stark, A., Kato, Y., Kondoh, G., Okawa, K., Chujo, T., Suzuki, T., Hata, K., Martin, S. L., Noce, T., Kuramochi-Miyagawa, S., Nakano, T., Sasaki, H., Pillai, R. S., Nakatsuji, N. and Chuma, S. The TDRD9-MIWI2 complex is essential for piRNA-mediated retrotransposon silencing in the mouse male germline. *Dev. Cell* **17**, 775–787 (2009).

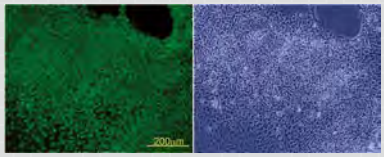
Wada, T., Honda, M., Minami, I., Tooi, N., Amagai, Y., Nakatsuji, N. and Aiba, K. Highly efficient differentiation and enrichment of spinal motor neurons derived from human and monkey embryonic stem cells. *PLoS ONE* **4**, e6722 (2009).

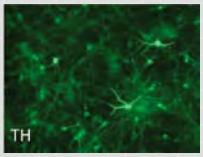
Suzuki, K., Mitsui, K., Aizawa, E., Hasegawa, K., Kawase, E., Yamagishi, T., Shimizu, Y., Suemori, H., Nakatsuji, N. and Mitani, K. Highly efficient transient gene expression and gene targeting in primate embryonic stem cells with helper-dependent adenoviral vectors. *Proc. Natl. Acad. Sci. U.S.A.* **105**, 13781–13786 (2008).



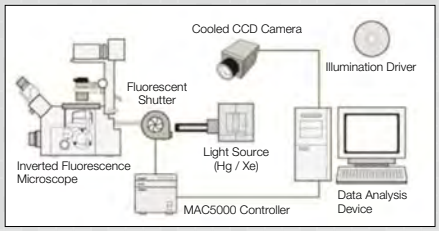
Cre/loxP mediated site-specific gene integration

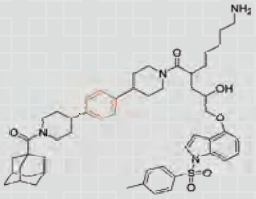

hES cells

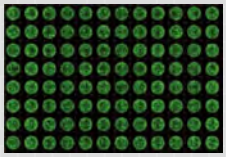

Neural stem/progenitor cells

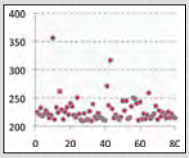


Dopaminergic Neurons

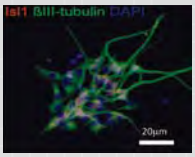



Synthetic Transcription Activator optimized "Wrenchnolol"


96 well plate scanning image GFP fluorescence



Chemical screening of effective compounds



Motor Neurons

Hiroshi Sugiyama Lab

Chemical Biology

Faculty Members
Hiroshi Sugiyama (Professor)
Masayuki Endo (Associate Professor)

Research Overview

The Sugiyama Lab's research interests involve the chemical biology of nucleic acids. Using the tools of organic synthesis and molecular biology, our group seeks to define the chemical principles underlying the recognition, reactivity, and structure of nucleic acids. We utilize a chemical approach in the following areas: design of highly efficient sequence-specific DNA acting agents, design of unnatural nucleic acids to elucidate nucleic acid structures and functions, design of DNA nanostructures to control and observe single molecule dynamics and single reactions, and development of a general method for probing DNA local conformation *in vivo*. Long-range goals are analysis of molecular behaviors involved in epigenetic regulation, and creation of **artificial genetic switches** for iPS cell production and targeted cell differentiation, and treatment of various diseases.

1. Sequence-specific DNA binder pyrrole-imidazole polyamides are developed and applied in cell biology. Using synthetic polyamides, specific gene regulations including gene suppression and activation are carried out by conjugating with alkylating agents and transcription activating small molecules. By constructing the gene regulation system, the method is expanded to create artificial synthetic molecules for cell reprogramming and differentiation.

2. Using the DNA self-assembly system “DNA origami” method, research focuses on the following points: (1) programmed assembly of DNA scaffolds; (2) design and construction of novel 2D and 3D DNA nanostructures; (3) control of biomolecular reactions in the designed nanostructures; and (4) biophysical analysis of single molecule behavior in the designed nanostructure. A real-time AFM imaging system is employed for the analysis of single molecule dynamics and single reactions in the designed nano-space.

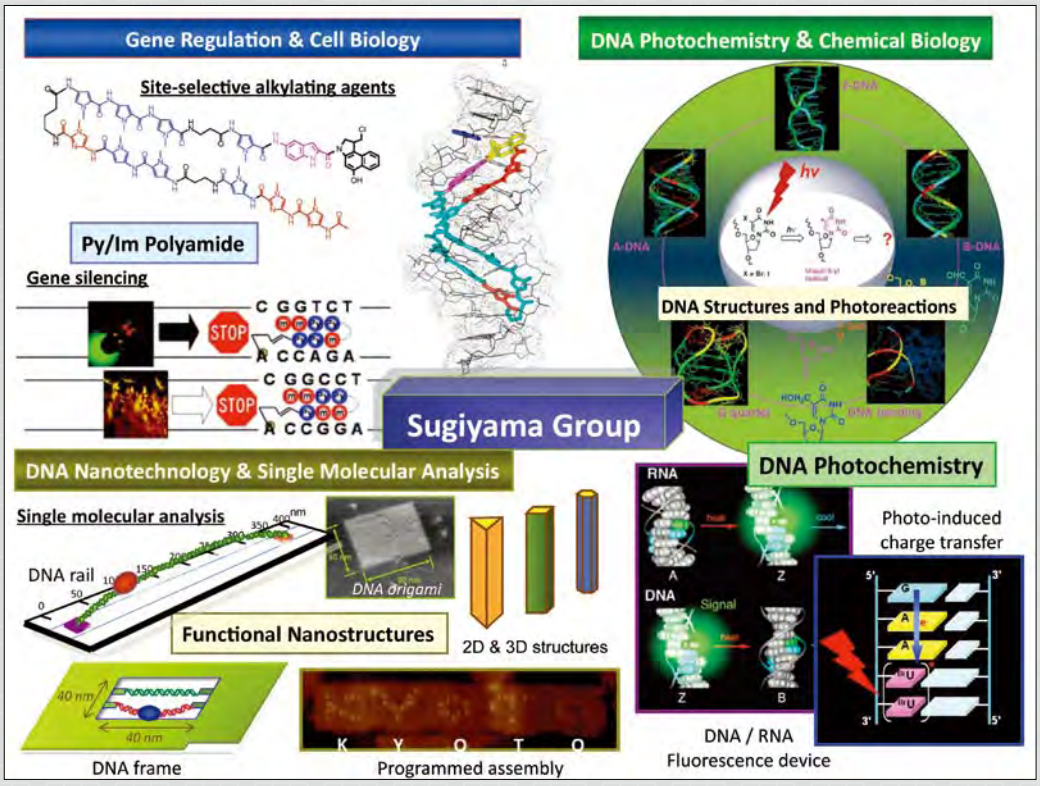
Selected Papers

Endo, M., Sugita, T., Katsuda, Y., Hidaka, K. and Sugiyama, H. Programmed-Assembly System Using DNA Jigsaw Pieces. *Chem. Eur. J.* **16**, 5362–5368 (2010).

Shinohara, K., Sannohe, Y., Kaieda, S., Tanaka, K., Osuga, H., Tahara, H., Xu, Y., Kawase, T., Bando, T. and Sugiyama, H. A Chiral Wedge Molecule Inhibits Telomerase Activity. *J. Am. Chem. Soc.* **132**, 3778–3782 (2010).

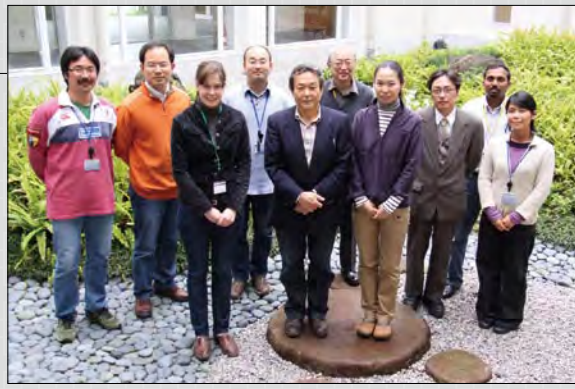
Endo, M., Katsuda, Y., Hidaka, K. and Sugiyama, H. Regulation of DNA Methylation Using Different Tensions of Double Strands Constructed in a Defined DNA Nanostructure. *J. Am. Chem. Soc.* **132**, 1592–1597 (2010).

Endo, M., Hidaka, K., Kato, T., Namba, K. and Sugiyama, H. DNA Prism Structures Constructed by Folding of Multiple Rectangular Arms. *J. Am. Chem. Soc.* **131**, 15570–15571 (2009).



Mikio Takano Lab

Solid State Chemistry



Faculty Members

Mikio Takano (Professor)
Hideki Koyanaka (Associate Professor)
Shinpei Yamamoto (Assistant Professor)
Zhaofei Li (Assistant Professor)

Research Overview

We are carrying out **solid state chemistry** on materials containing **3d transition metals** (3dTM) such as titanium (Ti), manganese (Mn), iron (Fe), and nickel (Ni). The solid state chemistry here includes synthesis, structural analysis, and clarification of physical and chemical properties. These elements are relatively rich in the earth's crust and, therefore, relatively cheap and easily obtained. Thanks to their high chemical activity there exist an uncountable number of compounds. Human society has made use of the superior functionalities of chosen monomers and compounds as coloring materials (α-Fe_2O_3, for example), catalysts (TiO_2, Ni), dielectrics ($BaTiO_3$), magnets (α-Fe, Fe_3O_4), superconductors ($Bi_2Sr_2Ca_2Cu_3O_{10}$), battery electrodes (MnO_2, $LiCoO_2$), etc.

Our activity is multilayered. At the core, or at the most basic level, is the **search for unknown materials** using various synthetic techniques. On the surface are efforts to apply known and new materials to **cross-disciplinary research** with bioscience groups such as the Sugiyama, Chen, and Hashida Labs. Our research ideal is that a new discovery by us will lead to a truly innovative, actual material.

The following are two typical topics included in our studies:

1. **Nano-Sized Magnets**
   We have created corrosion-resistant, shape controlled, and highly dispersible nano-sized magnetic particles applicable to bioscientific and medical research. Very recently we successfully invented a new chemical process that facilitates an organic surface coating needed for biocompatibility and biofunctionality.
   Currently we are working on iron metal (**α-Fe**), one of the best magnets ever known; iron nitride, **$Fe_{16}N_2$**, will also be tried soon. This material is fairly new, exhibiting better magnetic performance than that of α-Fe, although more studies are needed in terms of purification and corrosion control. We intend to make use of our experience and know-how to help realize the full potential practical utility of this new material.

2. **Manganese Oxide for Green Chemistry**
   Photosystem II is the enzyme that gave rise to the big bang of evolution thanks to the success of water splitting using sunlight, $2H_2O \rightarrow 4H^+ + 4e^- + O_2$. The active site contains a cluster made of four Mn ions and one Ca ion, Mn_4Ca. The exact mechanism of water splitting is not yet known, but there is no doubt that it is based on the facility of the cluster to adjust itself to changes in electron count in the reaction process. We are aiming to create simple, cheap, and easy-to-handle 3dTM oxides with such functionalities. Of specific interest to us now is **R-MnO_2**.

Selected Papers

Tamada, Y., Yamamoto, S., Nasu, S. and Ono, T. Fixation of Orientated L1(0)-FePt Nanoparticles on Si Substrates. *Appl. Phys. Express* **2**, 123001 (2009).

Kawakami, T., Tsujimoto, Y., Kageyama, H., Chen, X.-Q., Fu, C. L., Tassel, C., Kitada, A., Suto, S., Hirama, K., Sekiya, Y., Makino, Y., Okada, T., Yagi, T., Hayashi, N., Yoshimura, K., Nasu, S., Podloucky R. and Takano, M. Spin transition in a four-coordinate iron oxide. *Nat. Chem.* **1**, 371–376 (2009).

Kurosaki, F., Koyanaka, H., Tsujimoto, M. and Imamura, Y. Shape-controlled multi-porous carbon with hierarchical micro-meso-macro pores synthesized by flash heating of wood biomass. *Carbon* **46**, 850–857 (2008).

Tsujimoto, Y., Tassel, C., Hayashi, N., Watanabe, T., Kageyama, H., Yoshimura, K., Takano, M., Ceretti, M., Ritter, C. and Paulus, W. Infinite-Layer Iron Oxide with a Square-Planar Coordination. *Nature* **450**, 1062–1066 (2007).

Yamamoto, S., Morimoto, Y., Ono T. and Takano, M. Magnetically superior and easy to handle L1(0)-FePt nanocrystals. *Appl. Phys. Lett.* **87**, 032503 (2005).

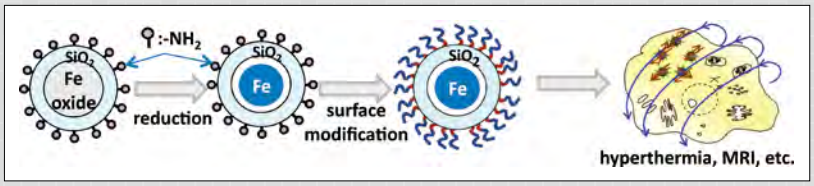


Fig. 1

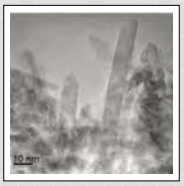


Fig. 3

Fig. 1 Corrosion-resistant, dispersible, organo-funtionalized, and shape-controlled magnetic nanoparticle to be applied to bioscientific and medical studies. The iron-oxide core of the starting particle is reduced at low temperatures of ~200℃ to metallic iron exhibiting better magnetic performance.

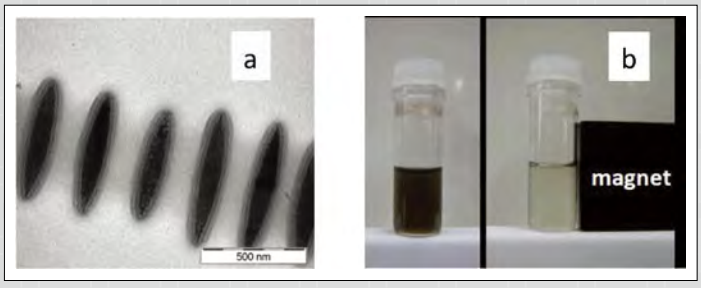


Fig. 2

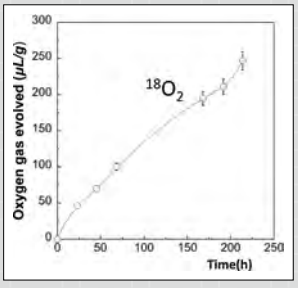


Fig. 4

Fig. 2 a: Spindle-shaped iron-core/silica/organic particles of ~500nm in length.
b: Particles dispersed in a solvent can be collected easily with a pocket magnet.

Fig. 3 TEM image of R-MnO_2 particles, which tend to grow preferentially along a specific crystalline axis.

Fig. 4 Evolution of oxygen, $^{18}O_2$, from water, $H_2{}^{18}O$, exhibiting a specific water splitting capability of R-MnO_2.

Koichiro Tanaka Lab

Teraherz Optical Science

Faculty Members
Koichiro Tanaka (Professor)
Masanobu Shirai (Assistant Professor)

Research Overview

Terahertz (THz) waves, electromagnetic radiation in the frequency region from 0.1 to 10 THz, is the next frontier in optical science and technology*. THz waves have been used to characterize the electronic, vibrational, and compositional properties of solid, liquid, and gas phase materials. In particular, biological sensing and imaging are the most highly anticipated applications of THz waves. Important features of THz waves for biological applications are summarized as follows:

- **Fingerprints**: Many biological molecules have their rotational and vibrational modes in the THz frequency range.
- **Water-sensitivity**: THz radiation is quite sensitive to water and its dynamic behaviors depending on temperatures and interaction with various kinds of solutes.
- **Safety**: THz radiation has low phonon energies (4 meV @ 1 THz) and, therefore, does not ionize biological tissue.

However, compared to well-developed visible light optical technologies and electronics in the microwave region, basic research, new approaches, and advanced technology development in the THz band have been only limited, as THz wave emitters and receivers are not as well developed compared to microwave and optical equipment.

We are developing high-power THz wave generation techniques and their application to the biological sciences. Our method of high power THz wave generation is based on the Cherenkov-type rectification process in $LiNbO_3$ crystals, or the four-wave-mixing process in laser induced gas-plasma with amplified femtosecond lasers (4mJ/pulse). This has allowed us to generate an intense THz wave over 200 kV/cm in the electric field in the repetition rate of 1 KHz. Recently, our group has been exploring **non-linear optical responses** of semiconductors and biological materials and we have found various novel phenomena that have never before been observed. Simultaneously we are developing a near-field THz microscope working at video rate. These technologies will open the doors to new THz sensing and **imaging** applications in the near future.

At the iCeMS, we have initiated new multidisciplinary research projects using high-power THz waves and related THz science and technologies including:

1. Biological applications of **THz near-field microscopy**. We have developed a special sensing crystal that enables us to convert the THz near-field image to a visible image using a non-linear optical process inside the sample mount. The current target for special resolution is below 5 micrometers. Thanks to our high power THz-waves, the microscope will work at video rates. Biological applications are now possible and will be conducted in collaboration with the Harada and Kusumi Labs.
2. Development of novel techniques to control materials with intense THz waves. Intense THz waves have the potential to modify or control optical and electrical properties in various functional materials. For example, non-linear properties in the THz frequency region are important in semiconductors for high-speed switching devices and future hopes in biological materials for new sensing and imaging technologies. Serious photo-blinking and darkening problems in fluorescent semiconductor quantum-dots may be overcome in part using resonant excitation of intense THz waves ranging from hidden dark levels to luminescent levels.
3. Water-material interaction in meso-space is important to understand biological activities in living cells. We are developing a special THz spectrometer with **attenuated total reflection** (ATR) devices to measure accurately the response function in the THz frequency region including optical permittivity and conductivity. We intend to elucidate the dynamic properties of liquids, especially hydration effects in small molecules, proteins, and lipid layers.
4. Ultrafast dynamics in **meso-space**. We have developed a **time-resolved optical measurement** system with femtosecond time-resolution to monitor light-induced chemical reactions. Using this technique, we are preparing to elucidate how molecules in meso-space behave under light irradiation. Along these same lines, we are studying porous materials developed by the Kitagawa Lab.

* In the different units, 1THz=1ps=300μm=33cm^{-1}=4.1meV=47.6 K.

Selected Papers

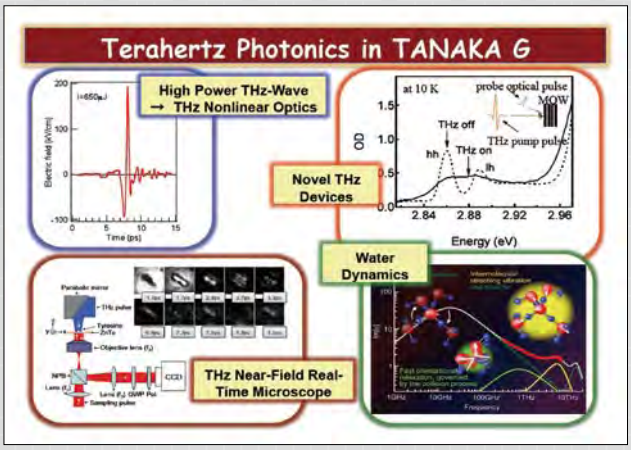
Hirori, H., Nagai, M. and Tanaka, K. Excitonic interactions with intense terahertz pulses in ZnSe/ZnMgSSe multiple quantum wells. *Phys. Rev. B* **81**, 081305 (2010).

Brefuel, N., Watanabe, H., Toupet, L., Come, J., Matsumoto, N., Collet, E., Tanaka, K. and Tuchagues, J.P. Concerted Spin Crossover and Symmetry Breaking Yield Three Thermally and One Light-Induced Crystallographic Phases of a Molecular Material. *Angew. Chem., Int. Ed.* **48**, 9304–9307 (2009).

Nagai, M., Jewariya, M., Ichikawa, Y., Ohtake, H., Sugiura, T., Uehara, Y. and Tanaka, K. Broadband and high power terahertz pulse generation beyond excitation bandwidth limitation via $\chi^{(2)}$ cascaded processes in $LiNbO_3$. *Opt. Express* **17**, 11543–11549 (2009).

Watanabe, H., Hirori, H., Molnar, G., Bousseksou, A. and K. Tanaka. Temporal decoupling of spin and crystallographic phase transitions in $Fe(PTZ)_6(BF_4)_2$. *Phys. Rev. B* **79**, 180405 (2009).

Bousseksou, A., Molnar, G., Real, J. A. and Tanaka, K. Spin crossover and photomagnetism in dinuclear iron(II) compounds. *Coord. Chem. Rev.* **251**, 1822–1833 (2007).



Kazumitsu Ueda Lab

Cellular Biochemistry

Faculty Members

Kazumitsu Ueda (Professor)

Research Overview

ABC (ATP-binding cassette) proteins comprise the largest membrane transporter family, which transports various compounds in an ATP-dependent manner. They play important physiological roles in almost all cells of all species from bacteria to humans. About 50 **ABC proteins** in humans function to defend our bodies against toxic compounds in the environment, circulate various metabolites, and maintain homeostasis of glucose, cholesterol, and other compounds. Functional defects in these proteins can lead to a variety of pathological conditions, including cardiovascular diseases, diabetes, senile blindness, respiratory failure of infants, skin diseases, and neuronal diseases. Our research on **ABC proteins** will contribute to human health by exploring the cause of such diseases and finding ways to prevent them.

At the iCeMS, we are carrying out the following cross-disciplinary research projects:

1. Analyzing the expression profile of **ABC proteins** in **ES and iPS cells**, and developing synthetic small molecules which can modulate the functions of **ABC proteins**. These compounds will facilitate the study of the physiological roles of **ABC proteins** in **ES and iPS cells** as well as finding ways to prevent various diseases. (In collaboration with the Nakatsuji, Yamanaka, and Uesugi Labs.)

2. ABCA1 and ABCG1 are key molecules for generating high-density lipoprotein (HDL), which is so-called “good cholesterol” and critical for cholesterol homeostasis. However, their functional mechanisms are still unclear. Furthermore, it is suggested that they reorganize some **meso-domains** on the plasma membrane and modulate immune and inflammation responses. We are trying to reveal the functions of these **ABC proteins** by visualizing them on the plasma membrane in collaboration with the Kusumi and Heuser Labs at the **CeMI** (Center for Meso-Bio Single-Molecule Imaging).

3. We are analyzing the **functional architectures** of **ABC proteins** using single molecule analysis and X-ray crystal structure analysis. We are trying to develop synthetic artificial transporters and channels, which can modulate cell functions and behaviors in response to chemical or physical stimuli, based on the knowledge of **functional architectures** of **ABC proteins**. (In collaboration with the Kitagawa and Imahori Labs.)

Selected Papers

Nagao, K., Kimura, Y., Matsuo, M. and Ueda, K. Lipid outward translocation by ABC proteins. *FEBS Lett.* **584**, 2717–2723 (2010).

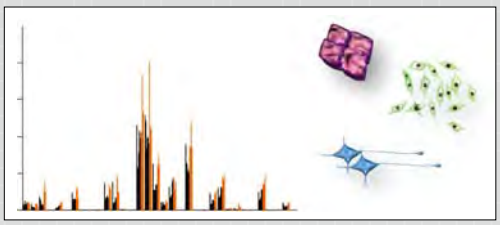
Hozoji, M., Kimura, Y., Kioka, N., and Ueda, K. Formation of two intramolecular disulfide bonds is necessary for apoA-I-dependent cholesterol efflux mediated by ABCA1. *J. Biol. Chem.* **284**, 11293–11300 (2009).

Hozoji, M., Munehira, Y., Ikeda, Y., Makishima, M., Matsuo, M., Kioka, N. and Ueda, K. Direct interaction of nuclear receptor LXRβ with ABCA1 modulates cholesterol efflux. *J. Biol. Chem.* **283**, 30057–30063 (2008).

Nagao, K., Takahashi, K., Hanada, K., Kioka, N., Matsuo, M. and Ueda, K. Enhanced apoA-I-dependent cholesterol efflux by ABCA1 from sphingomyelin-deficient CHO cells. *J Biol Chem.* **282**, 14868–74 (2007).

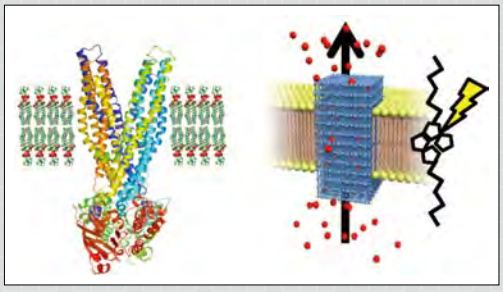
Morita, S.-y., Kobayashi, A., Takanezawa, Y., Kioka, N., Handa, T., Arai, H., Matsuo, M. and Ueda, K. Bile Salt-Dependent Efflux of Cellular Phospholipids Mediated by ATP Binding Cassette Protein B4. *Hepatology* **46**, 188–199 (2007).

hES cells

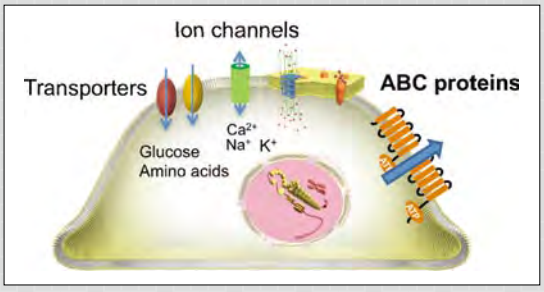


Physiological functions of ABC proteins in ES cells

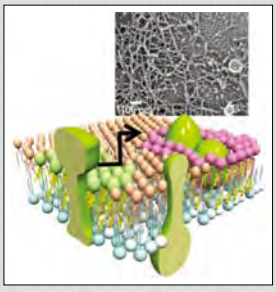
Development of activators and inhibitors of ABC proteins



Functional architectures



Transporters and channels



Membrane meso-domain formation

Motonari Uesugi Lab

Chemical Biology

Faculty Members
Motonari Uesugi (Professor)
Shinichi Sato (Assistant Professor)

Research Overview

Chemical biology is often defined as "chemistry-initiated biology," in which scientists start with chemistry and end up understanding biology by utilizing chemical tools. Our laboratory has been discovering or designing small-molecule tools that modulate fundamental processes in human cells. Such small organic molecules often serve as tools for basic cell biology and/or for cell therapy. Discovery or design of small molecules with unique biological activity permits small-molecule initiated exploration of complex cellular events, and may also contribute to the realization of cell therapy. Although our primary goal is to provide chemical tools for biological investigations, we also hope to open new avenues for small-molecule applications in a range of fields.

Below are a few examples of projects in our research group.

- Discovery and development of small-molecule fibronectin mimics. Cells in the human body form tissues and organs by attaching to the extracellular matrix. Cell attachment is mediated by the large protein, fibronectin. We have been designing small molecules that mimic this 440 KDa protein. "Small molecule fibronectins" may facilitate cost-effective culture, proliferation, and transplantation of human cells, and may be useful in both in basic cell biology and in cell therapy.
- Discovery and development of small molecule tools useful for cell therapy. One potential problem of cell therapy is high cost. Small molecule tools for cell therapy offer the advantage of cost-effective mass production. Thus, using small molecules in cell therapy will increase the affordability and accessibility of cell therapy worldwide. Most importantly, the use of stable and well-defined synthetic small molecules may compensate for ill-defined cell therapy.
- External control of transcription by small molecule transcription factors. Regulation of gene expression by transcription factors touches every process in eukaryotic biology. Our group previously showed that it is possible to create a functional transcription factor out of completely organic components. More precise mimics of naturally occurring transcription factors may serve as tools for cell biology and stem cell biology.

Selected Papers

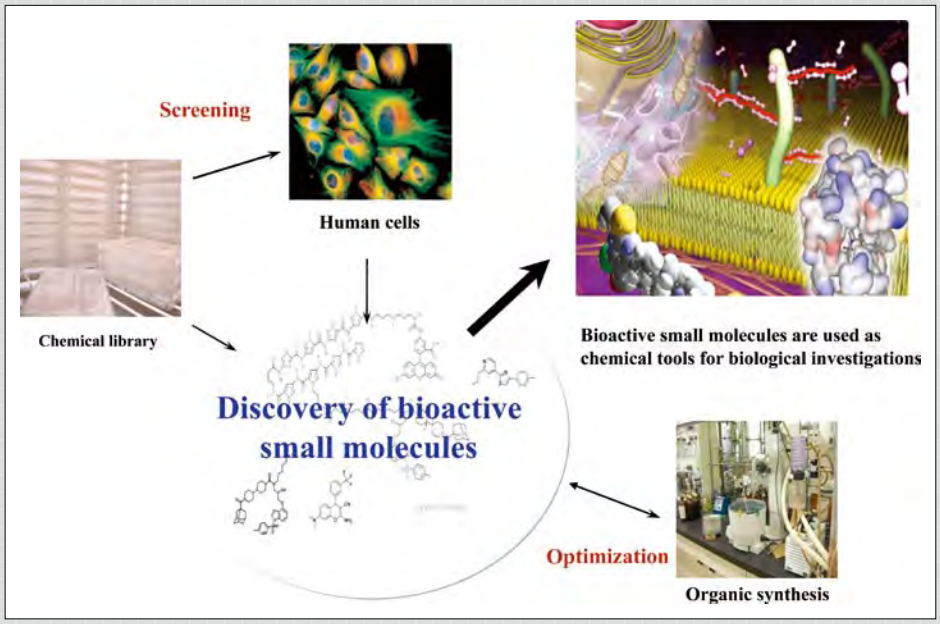
Hoshino, M., Tsujimoto, T., Yamazoe, S., Uesugi, M. and Terada, S. Adhesamine, a New Synthetic Molecule, Accelerates Differentiation and Prolongs Survival of Primary-Cultured Mouse Hippocampal Neurons. *Biochem. J.* **427**, 297–304 (2010).

Kamisuki, S., Mao, Q., Abu-Elheiga, L., Gu, Z., Kugimiya, A., Kwon, Y., Shinohara, T., Kawazoe, Y., Sato, S., Asakura, K., Choo, H., Sakai, J., Wakil, S. J. and Uesugi, M. A Small Molecule that Blocks Fat Synthesis by Inhibiting the Activation of SREBP. *Chem. Biol.* **16**, 882–892 (2009).

Yamazoe, S., Shimogawa, H., Sato, S., Esko, J. D. and Uesugi, M. A Dumbbell-Shaped Small Molecule that Promotes Cell Adhesion and Growth. *Chem. Biol.* **16**, 773–782 (2009).

Jung, D., Shimogawa, H., Kwon, Y., Mao, Q., Sato, S., Kamisuki, S., Kigoshi, H. and Uesugi, M. Wrenchnolol Derivative Optimized for Gene Activation in Cells. *J. Am. Chem. Soc.* **131**, 4774–4782 (2009).

Sato, S., Kwon, Y., Kamisuki, S., Srivastava, N., Mao, Q., Kawazoe, Y. and Uesugi, M. Polyproline-rod approach to isolating protein targets of bioactive small molecules: Isolation of a new target of indomethacin. *J. Am. Chem. Soc.* **129**, 873–880 (2007).



Shinya Yamanaka Lab

Stem Cell Biology, Developmental Engineering

Faculty Members

Shinya Yamanaka (Professor)
Yasuhiro Yamada (Professor)
Yoshinori Yoshida (Senior Lecturer)
Akitsu Hotta (Assistant Professor)
Akira Watanabe (Assistant Professor)
Knut Woltjen (Assistant Professor)

Research Overview

Our research group is focused on stem cell biology and developmental engineering. In particular, we have established mouse and human induced pluripotent stem cells (**iPS cells**), and we are carrying out various aspects of basic and applied research using **iPS cell** technology.

iPS cells can be generated from a wide range of somatic cell types, and many different methods have been developed for their generation. It is believed, however, that iPS cells are not in fact completely identical with ES cells. Using cell biology methods, including in vitro differentiation induction, and molecular biology methods, we plan to evaluate the pluripotency and safety of these cell types. By expanding our understanding of the mechanisms that underlie **reprogramming** and pluripotency, we aim to generate and culture iPS cells compatible for use in clinical applications. We also seek to use patient-specific iPS cells to study disease mechanisms and applications in drug development.

Using the viral vector transgene delivery system which drives the undifferentiated pluripotent stem cell-specific expression of GFP and drug-resistance genes as a high-efficiency method of selecting human iPS cells, we have facilitated the derivation of various patient-specific iPS cell lines and investigated the intra-nuclear changes that accompany the **reprogramming** process. With this platform, we will develop techniques for the generation and selection of safer human iPS cells, aiming for a novel iPS-based gene therapy approach to the treatment of hemophilia and other genetic disorders.

We are also working to change the **epigenetic status** in cancer cells using **reprogramming** technology, thereby making differences between genetic abnormality and **epigenetic status** in cancer cells. Through the analysis of the biological behaviors of these reprogrammed cancer cells, we seek the significance of epigenetic abnormality in carcinogenesis. Our goal is to find out the original epigenetic abnormality which causes the cancer through an analysis of epigenetic changes in the reprogrammed cancer cells and to develop a new "epigenetic cancer therapy" which resets the epigenetic state in cancer cells.

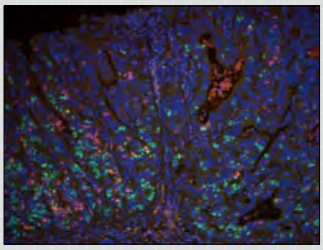
Selected Papers

Yamada, Y., Aoki, H., Kunisada T. and Hara, A. Rest promotes the early differentiation of mouse ESCs but is not required for their maintenance. *Cell stem cell* **6**, 10–15 (2010).

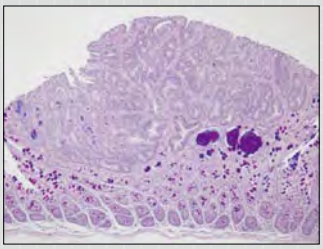
Hong, H., Takahashi, K., Ichisaka, T., Aoi, T., Kanagawa, O., Nakagawa, M., Okita, K. and Yamanaka, S. Suppression of induced pluripotent stem cell generation by the p53-p21 pathway. *Nature* **460**, 1132–1135 (2009).

Hotta, A., Cheung, A. Y., Farra, N., Vijayaragavan, K., Seguin, C. A., Draper, J. S., Pasceri, P., Maksakova, I. A., Mager, D. L., Rossant, J., Bhatia, M. and Ellis, J. Isolation of human iPS cells using EOS lentiviral vectors to select for pluripotency. *Nat. Methods* **6**, 370–376 (2009).

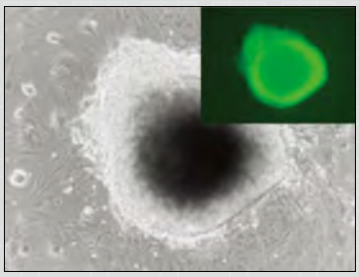
Yoshida, Y., Takahashi, K., Okita, K., Ichisaka, T. and Yamanaka, S. Hypoxia enhances the generation of induced pluripotent stem cells. *Cell Stem Cell* **5**, 237–241 (2009).



Aberrant cell proliferation of carcinoma cells in the large intestine

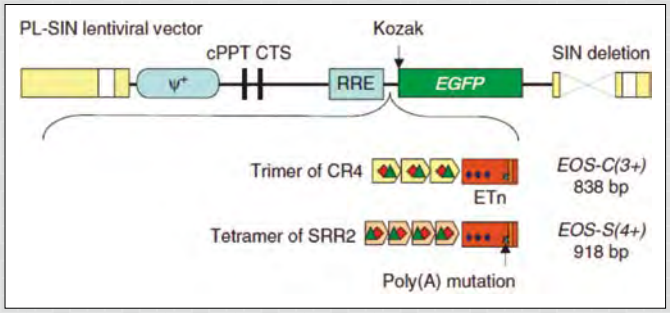


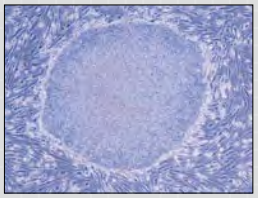
Aberrant differentiation of carcinoma cells in the large intestine



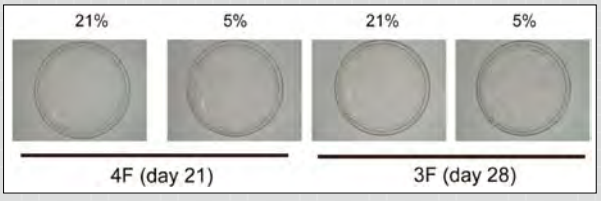
Mouse iPS cells

Progeny of chimeric mice derived from Nanog-iPS cells

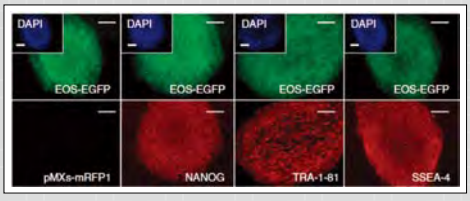




Human iPS cells



Hypoxic enhancement of reprogramming efficiency



EOS lentiviral vector selection system for human iPS cells

Shintaro Sengoku (Innovation Management Group)

Innovation Management, Science & Technology Management

Faculty Members

Shintaro Sengoku (Associate Professor)

Research Overview

In addition to being institutions for advanced learning and research, present day universities are increasingly expected to provide knowledge applicable to society. Consequently, an institutional effort must be undertaken to manage the mindsets of university personnel in order to realize for society the promises of their leading edge inventions and discoveries.

Our group explores a novel **innovation management** model which aims to achieve true innovation by exploring and developing three research domains: **transaction-based knowledge management** (Fig. 1), the management science of **scientific integration** and **cross-disciplinary research** (Fig. 2), and the management science of international collaboration between **academia and the public and private sectors**.

Selected Papers

Sengoku, S., Sumikura, K. and Oki, T. The uptake and diffusion of innovations: a case of stem cell technology. *Proceedings of the XXII International Society for Professional Innovation Management (ISPIM) Conference* (2010).

Sengoku, S., Yoda, T. and Seki, A. Fresh look at the valuation of drug R&D. *Diamond Harvard Business Review* 137–139 (April 2010).

Sengoku, S., Takahashi, K. and Kimura, H. Transaction process redesign in the pharmaceutical industry: an institutional approach to realize open innovation. *Journal of Intellectual Property Association of Japan* **5**, 48–64 (2009).

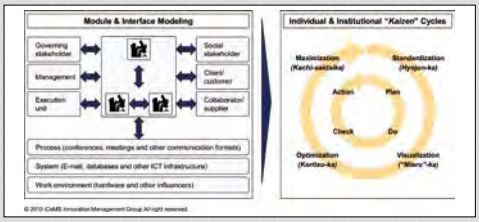


Fig. 1
Schematic diagram of the transaction-based management approach

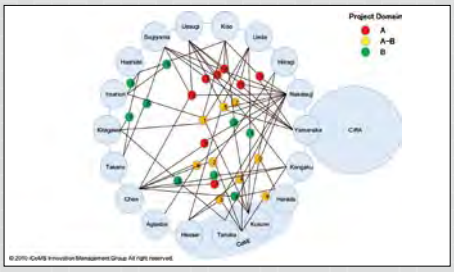


Fig. 2
Example network analysis of scientific integration and cross-disciplinary collaboration in the iCeMS (preliminary version)

Kazuto Kato (Science Communication Group)

Science Communication

Faculty Members

Kazuto Kato (Adjunct Associate Professor) Kei Kano (Assistant Professor)

Research Overview

Science's rapid development and ever growing influence on society make it imperative that researchers recognize the social impact and meaning of their research, as well as actively engage with the general public.

Our group has been developing and evaluating three kinds of science communication activities, which we call the 3Cs (see figure). Through these, we aim to develop a **teaching program for researchers to enhance science communication skills** in a bid to build stronger mutual relations among researchers in different fields and between scientific communities and society.

Selected Papers

Kato, K., Kano, K. and Shirai, T. Science Communication: Significance for Genome-Based Personalized Medicine – A View from the Asia-Pacific. *Curr. Pharmacogenomics Pers. Med.* **8**, 92–96 (2010).

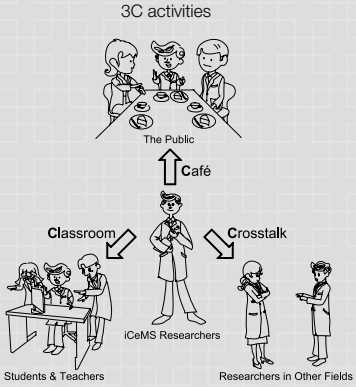
Zarzeczny, A., Scott, C., Hyun, I., Bennett, J., Chandler, J., Chargé, S., Heine, H., Isasi, R., Kato, K., Lovell-Badge, R., McNagny, K., Pei, D., Rossant, J., Surani, A., Taylor, P. L., Ogbogu, U. and Caulfield, T. iPS Cells: Mapping the Policy Issues. *Cell* **139**, 1032–1037 (2009).

Kano, K., Yahata, S., Muroi, K., Kawakami, M., Tomoda, M., Miyaki, K., Nakayama, T., Kosugi, S. and Kato, K. Multimedia presentations on the human genome: Implementation and assessment of a teaching program for the introduction to genome science using a poster and animations. *Biochem. Mol. Biol. Educ.* **36**, 395–401 (2008).

Cafés: As in "science cafés". iCeMS principal investigators (PIs) and colleagues engage in conversations with the public over tea and coffee in a relaxed, friendly atmosphere.

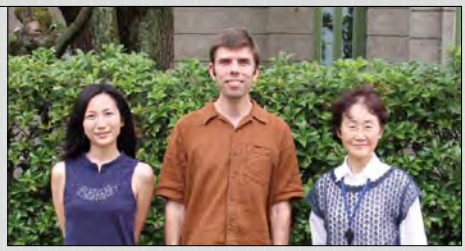
Crosstalks: A young researcher of the iCeMS speaks with one of the iCeMS PIs of his or her choice on the PI's thoughts about research and science.

Classrooms: Young iCeMS researchers collaborate with school teachers on cutting-edge educational programs. These hands-on research seminars include both laboratory work as well as extensive group discussions.



Peter Carlton

Meiosis, Chromosome Biology, Optical Microscopy



Faculty Members

Peter Carlton (Assistant Professor / iCeMS Kyoto Fellow)

Research Overview

Our research group studies how the structure and dynamic behavior of **chromosomes** in **meiosis** control pairing, recombination, and the correct transmission of the genome. Errors in meiosis cause many human health problems, from infertility to birth defects. We use the nematode Caenorhabditis elegans as a model system for its excellent genetic and cytological qualities. A main focus of the lab is the use of **superresolution** techniques such as **3D structured illumination** and **single-molecule composition microscopy** to assess chromosome structure at the mesoscale. We aim to find the mechanisms underlying the recognition of chromatin as paired or unpaired, and understand why **meiotic** recombination occurs between homologs rather than sister chromatids. An additional area of interest is the study of dynamic processes such as **chromosome** movement with fast three-dimensional multiwavelength fluorescence imaging under conditions that preserve full viability. Collaborative efforts within iCeMS will apply advanced optical microscopy to questions of nuclear organization in mammalian stem cells, meiosis in mammalian systems, and neural development.

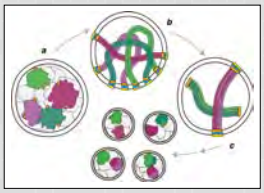
Selected Papers

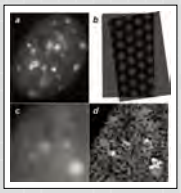
Wang, C. J. R.*, Carlton P. M.*, Golubovskaya, I. and Cande, W. Z. Interlock formation and coiling of meiotic chromosome axes during synapsis. *Genetics* **183**, 905–915 (2009).

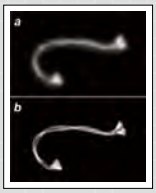
Schermelleh, L.*, Carlton, P. M.*, Haase, S., Shao, L., Winoto, L., Kner, P., Burke, B., Cardoso, M. C., Agard, D. A., Gustafsson, M. G., Leonhardt, H. and Sedat, J. W. Subdiffraction multicolor imaging of the nuclear periphery with 3D structured illumination microscopy. *Science* **320**, 1332–1336 (2008).

Carlton, P. M. Three dimensional structured illumination microscopy and its application to chromosome structure. *Chromosome Res.* **16**, 351–365 (2008).

*co-first authors

1 

2 

3 

1. Meiosis creates haploid gametes from diploid precursor cells by an intricately coordinated reorganization of chromosomes. Chromosomes elongate (*a*) and attach their ends to the nuclear envelope. The ends undergo dynamic movement thought to contribute to the pairing process. Paired chromsomes (*b*) undergo recombination, exchanging genetic material. After two cell divisions (*c*), newly arranged chromosomes are contained in haploid gametes.

2. 3D Structured Illumination Microscopy (3D-SIM) has twice the resolution of optical microscopy. A striped pattern of light (*a*) interacts with the sample, allowing detection of fine details due to the moiré effect (*b*). Two views of mouse interphase chromatin at the nuclear periphery demonstrate increased resolution: (*c*), a conventional image, and (*d*), the same region with 3D-SIM. The exclusion of chromatin from the nuclear pore complexes appears as holes less than 150nm in diameter. (See Schermelleh, et al. 2008)

3. Conventional (*a*) and 3D-SIM (*b*) immunofluorescence images of a mouse meiotic chromosome synaptonemal complex (α-Sycp3 immunostaining). The separation and twisting of the synaptonemal complex can only be seen in the 3D-SIM image. Material provided by Dr. Shinichiro Chuma, Institute for Frontier Medical Sciences, Kyoto University.

Ziya Kalay

Statistical Physics

Faculty Members

Ziya Kalay (Research Associate / iCeMS Kyoto Fellow)

Research Overview

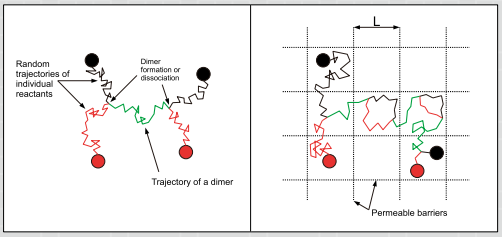
In predicting the state of a system in the future, system size and the number of constituents often determine the way we proceed. For just a few atoms, we can use quantum mechanics. For a collection involving multiples of Avogadro's number of them, we have statistical theories at our disposal. In between, there are many meso-scale systems of interest, for which well-established theories are not available. We are mainly interested in filling this gap by finding answers to questions such as the following: Can **mesoscopic structures** found in biological systems make use of thermal fluctuations to perform their functions? If so, how? How does **confinement** of membrane molecules **in mesoscale** (30–300 nm) **compartments** modify their reaction rate? This is one of the many questions we would like to answer to understand the hierarchical organization of the plasma membrane of live cells that spans the nano-meso-micron scales. In many cases, biological systems can be modeled by a collection of coupled oscillators, e.g. a network of neurons. To what extent can we predict the **response** of a collection of **coupled oscillators** to varying stimuli?

Selected Papers

Kenkre, V. M., Kalay, Z. and Parris, P. E. Extensions of effective-medium theory of transport in disordered systems. *Phys. Rev. E* **79**, 011114 (2009).

Kalay, Z., Parris, P. E. and Kenkre, V. M. Effects of disorder in location and size of fence barriers on molecular motion in cell membranes. *J. Phys.: Condens. Matter* **20**, 245105 (2008).

Kenkre, V. M., Giuggioli, L. and Kalay, Z. Molecular motion in cell membranes: analytic study of fence-hindered random walks. *Phys. Rev. E* **77**, 051907 (2008).



Schematic illustration of the kinetics of dimer formation involving two diffusing reactants in free space (left), and in the presence of an array of partially permeable barriers (right). Partial confinement can enhance reaction efficiency by increasing the chances of collision after dissociation. In the plasma membrane of various live cells, lipids and proteins are observed to be partially confined in regions with L ~ 30-300 nm (Kusumi et al., Annu. Rev. Biophys. Biomol. Struct. 34 (2005), 351).

Tatsuya Murakami

Cell Engineering, Protein Engineering

Faculty Members

Tatsuya Murakami (Assistant Professor / iCeMS Kyoto Fellow)

Research Overview

Recent progress in the field of nanotechnology has enabled the creation of various nanostructures, including nanoparticles, nanodiscs, nanocubes, nanorods, and nanofibers. Some of these can be made responsive to **external stimuli**, and used, for instance, to kill cancer cells. When size-controlled at the mesoscale, they have potential as vehicles for cellular uptake and allow prolonged blood circulation, the latter being an essential function in drug delivery systems. To utilize these properties, however, it is necessary to refine the surface of the nanostructures to make them biocompatible and give them useful functions.

We have developed methods for modifying the surface of carbon nanomaterials for use in double **photodynamic and photothermal** cancer chemotherapy. We have also published papers on strategies for size control of protein-lipid nanodiscs at the **mesoscale**, and on a biocompatible carrier for **intracellular delivery** of various materials.

In the interests of making further progress based on these experiences, we have now started multidisciplinary research projects on biological applications of functionalized nanostructures in collaboration with other research groups in- and outside the iCeMS:

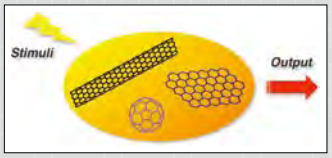
1. Development of **biocompatible dispersants** using protein engineering approaches
2. **Manipulation of cell function and fate** with external stimuli-responsive nanostructures
3. **Spatiotemporal regulation of drug therapy** with external stimuli-responsive nanostructures

Selected Papers

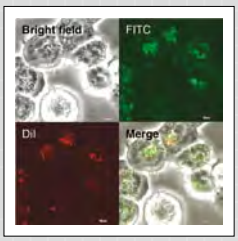
Murakami, T., Wijagkanalan, W., Hashida, M. and Tsuchida, K. Intracellular drug delivery by genetically engineered high density lipoprotein nanoparticles. *Nanomed* in press (2010).

Murakami, T., Tsuchida, K., Hashida, M. and Imahori, H. Size control of lipid-based drug carriers by drug loading. *Mol. BioSyst.* **6**, 789–791 (2010).

Zhang, M., Murakami, T., Ajima, K., Tsuchida, K., Sandanayaka, A. S., Ito, O., Iijima, S. and Yudasaka, M. Fabrication of ZnPc/protein nanohorns for double photodynamic and hyperthermic cancer phototherapy. *Proc. Natl. Acad. Sci. U.S.A.* **105**, 14773–14778 (2008).



Carbon nanomaterials



Confocal images of cells treated with cell-penetrating nanodisc

Takuya Yamamoto

Molecular Biology, Bioinformatics

Faculty Members

Takuya Yamamoto (Assistant Professor / iCeMS Kyoto Fellow)

Research Overview

Elucidation of the molecular mechanisms of iPS cell induction processes is an important step toward applications of iPS cells for regenerative medicine. Analytical techniques (dry), such as bioinformatics, as well as molecular- and cell-biological experimental techniques (wet) are essential to extract biologically meaningful information from the enormous amounts of data acquired by such analytical devices as **microarrays and the next-generation sequencers**.

Our primary objective is to perform exhaustive analysis of the entire genome through multilateral approaches, fuse the dry and wet techniques by feedback, and elucidate the molecular mechanisms during iPS cell induction in an integrative way. Through our research, we would like to improve the efficiency and shorten the time needed to generate iPS cells.

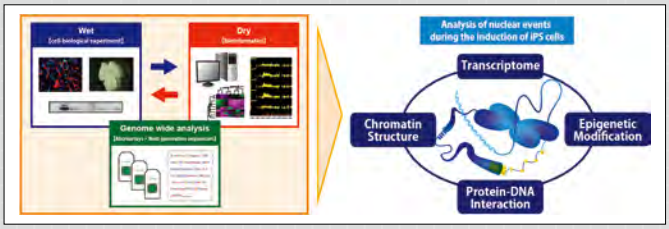
1. By using microarrays and next generation sequencers, we will perform **whole-transcriptome analysis** in iPS and ES cells to clarify the overall picture for gene expression controlling pluripotency.
2. By using next generation sequencers, we will perform **genome-wide analysis of epigenetic modifications, chromatin structures, and protein-DNA interaction** to shed light on the regulatory mechanisms in the nuclei of pluripotent stem cells.

Selected Papers

Honjoh, S., Yamamoto, T., Uno, M. and Nishida, E. Signalling through Rheb mediates intermittent fasting-induced longevity in C. elegans. *Nature* **457**, 726–730 (2009).

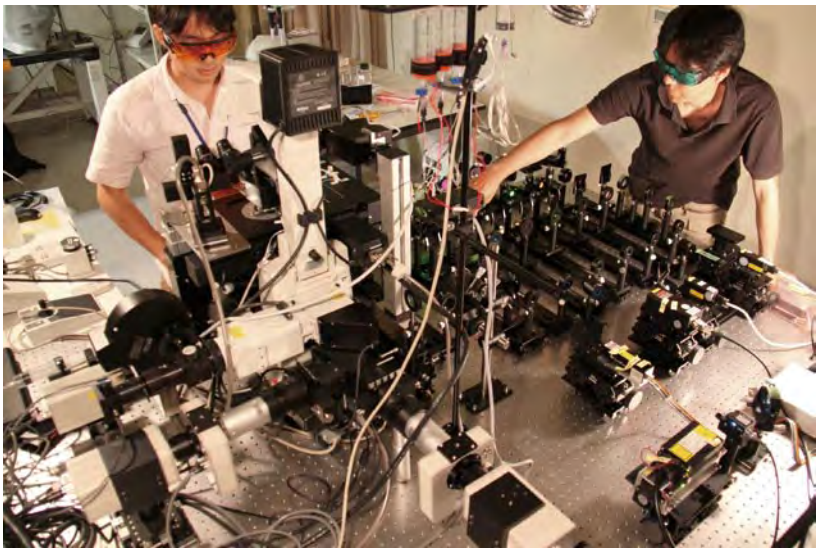
Ebisuya, M., Yamamoto, T., Nakajima, M. and Nishida, E. Ripples from neighbouring transcription. *Nat. Cell Biol.* **10**, 1106–1113 (2008).

Yamamoto T., Ebisuya M., Ashida F., Okamoto K., Yonehara S. and Nishida E. Continuous ERK activation downregulates antiproliferative genes throughout G1 phase to allow cell-cycle progression. *Curr. Biol.* **16**, 1171–1182 (2006).



Research on the elucidation of iPS cell induction by comprehensive genome-wide analysis

Center for Meso-Bio Single-Molecule Imaging (CeMI)



The CeMI was established on March 3, 2009, as the iCeMS' imaging innovation center for **cellular meso-science**. Its key missions are:

- develop new, powerful technologies for imaging the *restless* nano- to meso-scale universe of biomolecular complexes in living cells, at the spatiotemporal resolutions of functioning single molecules, and
- make these technologies available quickly to the scientific community worldwide for the further advancement of cellular meso-science.

The center places special emphasis on **single-molecule imaging** and **tracking**, and on **terahertz spectroscopy and microscopy**.

The following CeMI-built stations are currently in operation: four, single fluorescent-molecule tracking (SFMT) stations, each with various specific capabilities, including simultaneous three-color SFMT (unique in the world; see photo above), photoactivation, and the world's fastest frame-rate at 10 kHz (all operable for live cells at 37 ˚C in 5% CO_2 atmosphere); and a one terahertz microscope with the world's fastest image acquisition rate (10 Hz). Other advanced, commercial confocal/time-lapse fluorescence microscopes are also available.

The center has the following four specific areas of activity:

1. **Core Research**: Technology development and initial applications. These are conducted both in the laboratories of the core PIs as well as in the CeMI.
2. **Collaborative Research**: Following the development of new, pilot technologies and instruments by CeMI's core members, the first instruments for practical applications will be installed at the CeMI and then made available to all interested parties on a collaborative research basis. New, broad applications are expected to lead to further ground-breaking technologies and instruments. In addition, selected new technologies developed elsewhere will be implemented at the CeMI so that important advances can be incorporated as soon as possible.
3. **Education and Training**: The center will hold symposia, seminars, workshops, and hands-on training sessions, open to the scientific community worldwide.
4. **Services**: On a limited basis, CeMI personnel are available to obtain data for interested users, but only when the users are physically present. Commercial instruments, including those with both standard and advanced capabilities, are available to iCeMS scientists as well as to researchers outside of the iCeMS wishing to use the instruments for collaborative studies with iCeMS scientists.

The CeMI's aim is to become a world hub, where scientists from across the globe can gather to engage in **meso-bio**, **single-molecule imaging**, and to develop the meso-science of cells.

Core Members

Participating PIs: Peter Carlton, Yoshie Harada, John Heuser, Ziya Kalay, Akihiro Kusumi (CeMI Director), and Koichiro Tanaka
Scientific Manager: Takahiro Fujiwara (Senior Lecturer)
Imaging Technologists: Hiroko Hijikata and Hisae Tsuboi

Industry Partners Carl Zeiss Microimaging Co., Ltd., Hamamatsu Photonics K.K., JEOL Ltd., Leica Microsystems Japan Co., Ltd., Nikon Instech Co., Ltd., Nikon Instruments Co., Ltd., Olympus Corp., Photron Ltd.

Dr. Fujiwara (center) and the CeMI staff

People

As of May 1, 2010

Professor	18
Associate Professor	9
Senior Lecturer	7
Assistant Professor	13
Research Associate	58
iCeMS Kyoto Fellow	4
Adjunct Faculty	7
Visiting Faculty	29
Research Support Staff	54
Administrative Staff	27
Total	**226**

Finance

As of May 1, 2010
US $1 = 100 yen

WPI Grant	1 million USD / 100 million yen
FY 2007	**6.8**
FY 2008	**15.6**
FY 2009	**13.5**

Competitive Research Grant	
FY 2007	**6.4**
External Research Funding	4.8
MEXT/JSPS Grant-in-Aid for Scientific Research	1.5
Donations	0.1
FY 2008	**35.6**
External Research Funding	23.6
MEXT/JSPS Grant-in-Aid for Scientific Research	5.6
Donations	6.3
FY 2009	**56.4**
External Research Funding	46.1
MEXT/JSPS Grant-in-Aid for Scientific Research	9.7
Donations	0.6

MEXT: Ministry of Education, Culture, Sports, Science and Technology
JSPS: Japan Society for the Promotion of Science (a non-profit, independent administrative institution under the auspices of the MEXT)

Awards

Month/Year	Award/Prize	Awardee
Mar. 2010	Japan Bioscience, Biotechnology and Agrochemistry Society Award	Kazumitsu Ueda
Mar. 2010	ABC2010 Young Investigator Award	Koh Nagata
Mar. 2010	Imperial and Japan Academy Prizes	Shinya Yamanaka
Jan. 2010	March of Dimes Prize in Developmental Biology	Shinya Yamanaka
Nov. 2009	Lectureship Award of Frontiers in Chemical Research, Texas A & M University	Susumu Kitagawa
Nov. 2009	Award for the Best Research Paper (Asian Association for Biology Education)	Kei Kano
Sep. 2009	Albert Lasker Basic Medical Research Award	Shinya Yamanaka
Jun. 2009	Kurita Water Research Prize	Hideki Koyanaka
Apr. 2009	Canada Gairdner International Award	Shinya Yamanaka
Mar. 2009	The Chemical Society of Japan (CSJ) Lectureship Award	Shuhei Furukawa
Jan. 2009	The Chemical Society of Japan Award	Susumu Kitagawa
Nov. 2008	Medal of Honor with Purple Ribbon 2008	Shinya Yamanaka
Jul. 2008	Incentive Award for Young Scientist (by Tokai branch of The Society of Synthetic Organic Chemistry)	Hiromune Ando
Apr. 2008	Humboldt Research Award	Susumu Kitagawa
Apr. 2008	Special Prize for Science and Technology by the Japanese Minister of Education, Culture, Sports, Science and Technology	Shinya Yamanaka
Feb. 2008	Robert Koch Prize 2008	Shinya Yamanaka
Jan. 2008	Asahi Award 2007	Shinya Yamanaka
Dec. 2007	2007 NISTEP Prize (by the National Institute of Science and Technology Policy of the Japanese Ministry of Education, Culture, Sports, Science and Technology)	Hiroshi Imahori
Nov. 2007	Award for the best theoretical model (European Powder Metallugy Association, PM Thesis Competition 2006)	Mitsuru Hashida
Nov. 2007	The 25th Osaka Science Prize	Hiroshi Imahori

Facilities

As of May 1, 2010

Main Building:
Located at the Higashiyama-Higashiichijo intersection,
across from the university headquarters

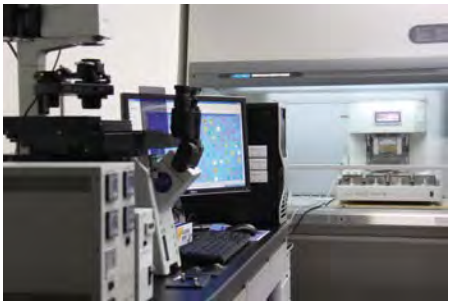
iCeMS Complex 1

Approx. 5,000 m² of floor space

- Main Building | Completed in March 2009
- West Wing | Completed in September 2008

iCeMS Complex 1 serves as the headquarters and consists of two buildings. In addition to ample shared laboratory space, the main building includes a seminar hall, a lounge for informal researcher get-togethers, and an exhibition room that doubles as a meeting space.

Chemical Screening Center (Main Building, 2nd floor)
Established in November 2009
Including an automated screening system, cell culture equipment, and a chemical library of over 20,000 compounds, this center serves as a core facility for discovering novel small organic molecules that modulate fundamental characteristics in mammalian cells, including stem cells and iPS cells.



Research Building 3 (artist's rendering):
Located at the Hyakumanben intersection,
about 200 meters away from the iCeMS Complex 1

iCeMS Complex 2

Approx. 6,000 m² of floor space

- Research Building 1 (Project Lab) | Completed in September 2008
- Research Building 2 | Completed in July 2009
- Research Building 3 | To be completed in November 2010

Open offices in both complexes (conceptual drawings):
Designed to be shared by research groups from various fields in order to facilitate active daily exchanges

iCeMS Complex 2 consists of three buildings. Researchers from different groups collaborate with each other in extensive shared laboratory and office spaces to advance cross-disciplinary research.

Directions

Yoshida Campus, Kyoto University

iCeMS Complex 1

- Main Building
- West Wing

Yoshida Ushinomiya-cho, Sakyo-ku, Kyoto
One-minute walk from “Kyodai Seimon-mae” Stop
(Kyoto City Bus)

iCeMS Complex 2

- Research Building 1
- Research Building 2
- Research Building 3

Yoshida Honmachi, Sakyo-ku, Kyoto
One-minute walk from “Hyakumanben” Stop
(Kyoto City Bus)

Center for iPS Cell Research and Application (CiRA)

53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto
Five-minute walk from Jingu-Marutamachi Station
(Keihan Railway)

Katsura Campus, Kyoto University

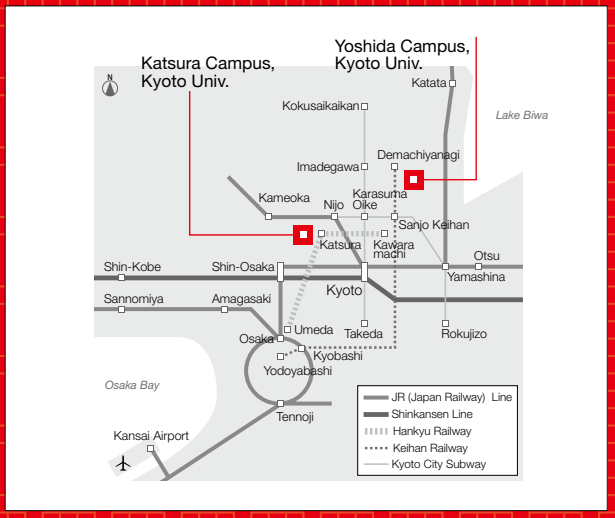
iCeMS Katsura Laboratory for Meso-Control of Functional Architectures

Kyoto University Katsura, Nishikyo-ku, Kyoto
Three-minute walk from “Kyodai Katsura Campus-mae”
Stop (Kyoto City Bus / Keihan Kyoto Kotsu Bus)

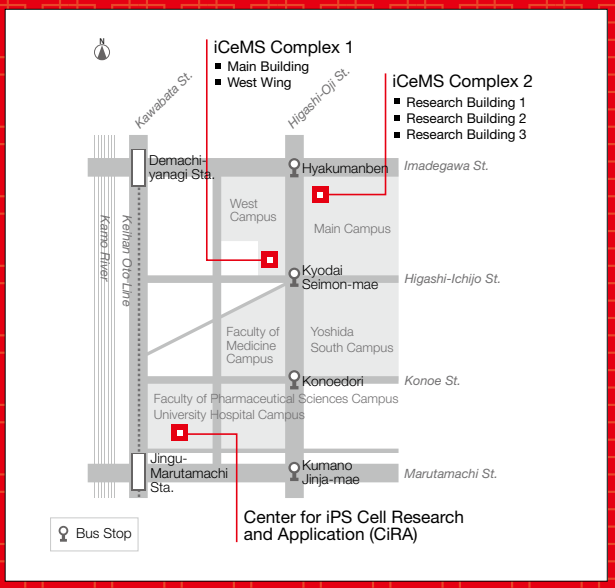
iCeMS Brochure | Issued: July 2010

Faculty member information is current as of May 1, 2010.

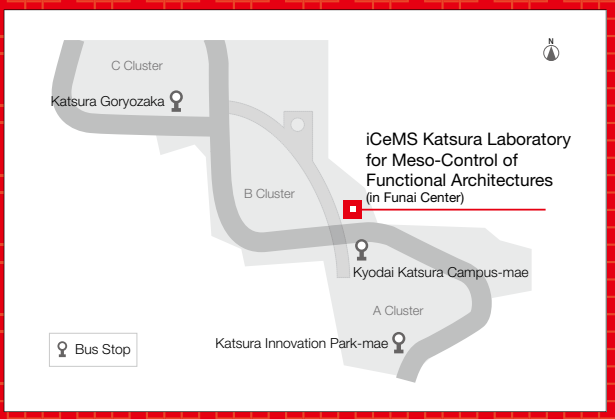
Email: info@icems.kyoto-u.ac.jp
Phone: 81-75-753-9753 (Int'l) / 075-753-9753 (Domestic)
Fax: 81-75-753-9759 (Int'l) / 075-753-9759 (Domestic)
Address: Yoshida Ushinomiya-cho, Sakyo-ku, Kyoto 606-8501, Japan
URL: www.icems.kyoto-u.ac.jp



Directions to iCeMS, Kyoto University



Yoshida Campus, Kyoto University



Katsura Campus, Kyoto University