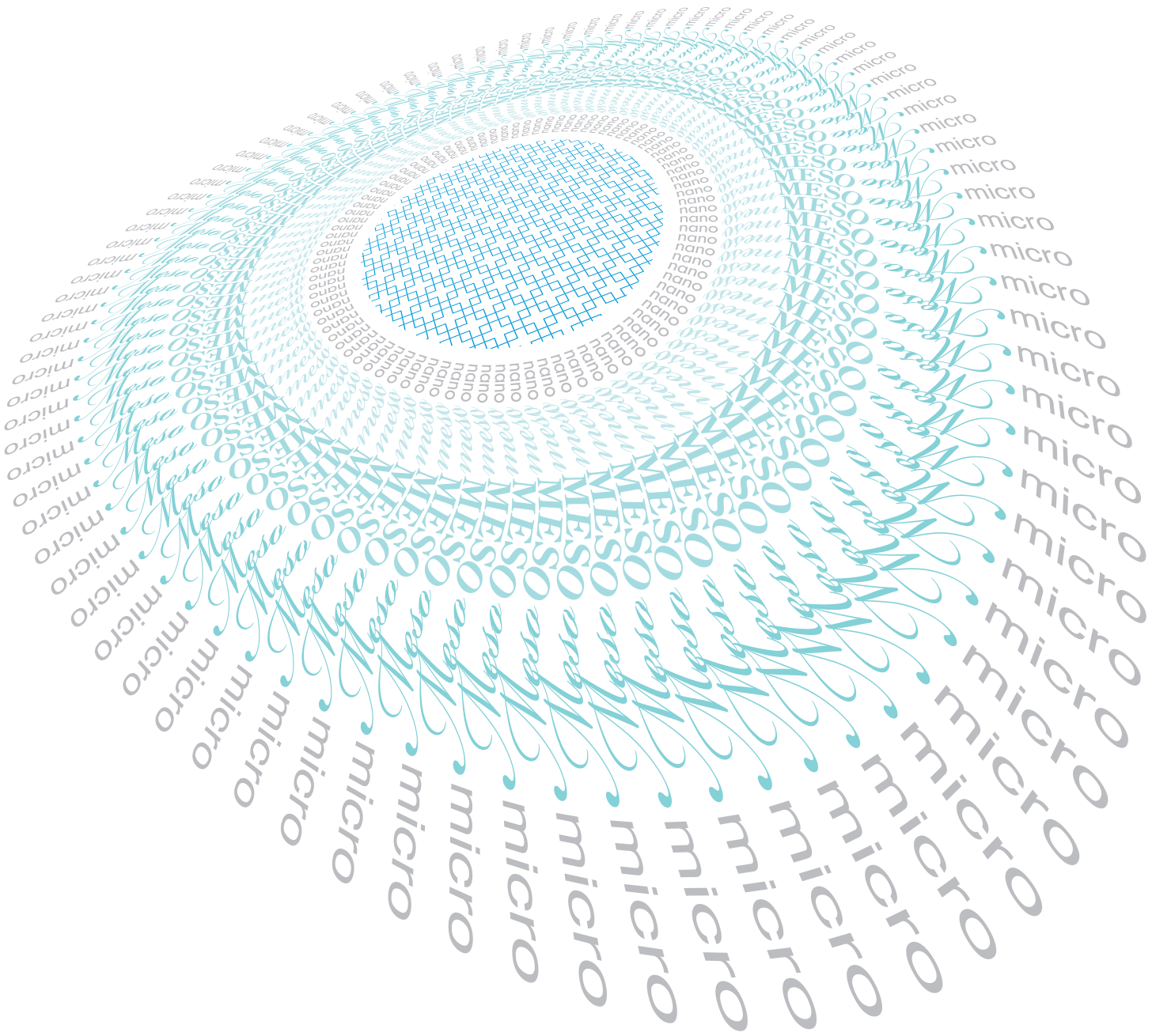

iCeMS
KYOTO UNIVERSITY
WPI Research Center

Institute for Integrated
Cell-Material Sciences

KYOTO UNIVERSITY
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President's Message: High Hopes for iCeMS and Mesoscopic Science

Hiroshi Matsumoto

President
Kyoto University

Founded in October 2007, Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS) was established as one of five original World Premier International Research Center Initiative (WPI) institutes throughout Japan. Led by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), the mission of this program is to create world-class, interdisciplinary research centers that break new ground in their global outlook and openness to management reform. In all these aspects, I am pleased to say that iCeMS has contributed significantly to making these goals a reality.

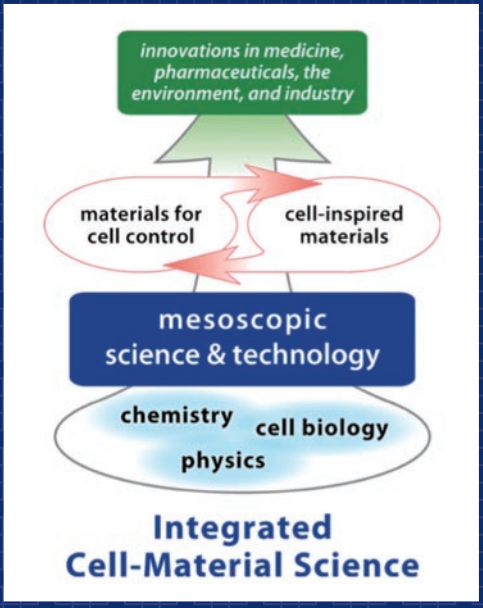
iCeMS has pioneered the new field of **mesoscopic science**, integrating materials and cells in the region between the nano and the micro. Numerous projects, such as the fabrication of chemical compounds to control processes within cells (e.g. stem cells), have been made possible because of the center's inherently interdisciplinary nature. Notably, iCeMS has played a prominent role in the founding and nurturing of the Center for iPS Cell Research and Application (CiRA), led by Professor Shinya Yamanaka, the renowned iPS cell researcher and 2012 Nobel Laureate in Physiology or Medicine. I am certain that iCeMS' environment will continue to prove ideal for fostering future "proto-sciences" with wide-ranging benefits for society.

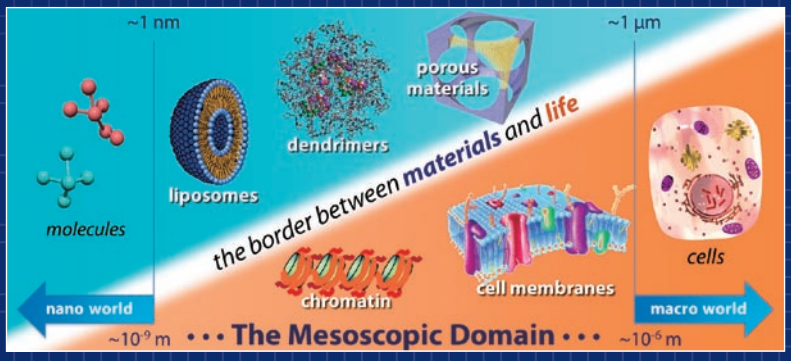
iCeMS also serves as a blueprint for planned university-wide management reforms, with globalization being a key component. Measures already being undertaken by the institute include: English as the official language; having at least 30 percent overseas researchers; active international efforts in public relations and overseas networking; streamlined executive decision making; and implementation of flexible employment practices and merit-based pay. I am confident that these initiatives pioneered by iCeMS will have a profound, university-wide impact, helping the entire institution attain a higher level of excellence.

Since iCeMS' inception, the tremendous efforts made by founding director and Professor Norio Nakatsuji have established a strong, cell biology-focused foundation for fusing the cell and materials sciences. But keeping pace with a rapidly evolving interdisciplinary research field requires an occasional change of leadership to inspire truly multidiscipline-minded young researchers and trigger new scientific breakthroughs. With this in mind, Professor Susumu Kitagawa succeeded the institute directorship in January 2013 to further accelerate integration from a material scientist's point of view. I fully expect this change to advance the fusion of cell-material sciences, such as in the development of "cell-inspired materials." I look forward to the advancement of iCeMS under the leadership of Director Kitagawa.

iCeMS is a world-class research institute for mesoscopic science, welcoming interdisciplinary scientists from across the globe. It is my strong desire that the center will continue serving as an international hub for these aspiring researchers, coming from numerous and diverse fields to join iCeMS and succeed in groundbreaking, collaborative work.

April 2013





Director's Vision for an Integrated Cell-Material Science

Susumu Kitagawa

Director
Institute for Integrated Cell-Material Sciences (iCeMS)
Kyoto University

All cellular processes can ultimately be comprehended as chemical events, and such a chemical understanding of cells should allow us to mimic cellular processes using chemical materials. Our institute seeks to illuminate precisely such a chemical basis of cells, **creating compounds to control processes in cells such as stem cells** (*materials for cell control*) in addition to **sparking cellular processes to create chemical materials** (*cell-inspired materials*). Combining Kyoto University's established strength in cell biology, chemistry, and physics to delve deeply into the mesoscale world lying at the boundary of materials and life, we are making a concerted effort, through interdisciplinary research, to ultimately create a new research field of **integrated cell-material science**.

Efforts to explain cell functions using chemistry are not new. Biochemistry, for instance, uses proteins as a starting point in attempting this at a molecular level, and molecular biology, while also focused on molecules, takes a DNA-based approach. And in their own ways, both methods have yielded significant innovations in pharmaceuticals and biotechnology.

Meanwhile, cell biology has also seen substantial success by considering the cell as a whole, most notably in research related to embryonic stem (ES) cells and induced pluripotent stem (iPS) cells, which are beginning to make an impact on the biomedical industry.

Our institute seeks a middle ground: between the large, whole-cell approach of cell biology, and the small, protein and DNA approaches of biochemistry and molecular biology. We call this the mesoscopic realm, lying between a few tens and a few hundreds of nanometers, on the border between materials and living matter. Investigating this boundary region, we strive to explain the material-chemical basis of cells' living functions, ultimately using materials to create facsimiles of these mechanisms.

A study of the melded boundary between cells and materials based on a fusion of cell biology, chemistry, and physics is our goal. We seek to be the best in the world, with the fruits of our international, interdisciplinary labors bringing nourishment and fresh ideas to research in industries as diverse as medicine and the environment. Our efforts are focused on examining the following two questions:

1. Can we describe mesoscopic cellular processes in terms of chemistry, and create materials to control them?

Cells sustain life through properties of self-assembly and cooperative interactions among nearly countless chemical materials, moving ceaselessly in space and time. Broadening our scope beyond the narrow confines of nanoscale molecular interactions, we find it necessary to take a wider, mesoscopic view of molecular complexes. To accomplish this, we are pursuing the development of advanced imaging technologies and modeling, and physical and chemical technologies to dissect complex cellular events. Based on this analysis, we seek to investigate ***materials for cell control***. Research areas in this context are as follows:

- **Gene Expression Control in Stem Cells**, such as a mesoscopic understanding of gene expression in cellular reprogramming and differentiation, and the development of materials to control such expression.

- **Organized Functions on the Cell Membrane**, such as a mesoscopic understanding of mechanisms controlling channels and transporters, and the development of materials to control such systems.

- **Biogas Control**, such as a mesoscopic understanding of mechanisms involving gases in living systems, and the development of porous materials for cellular control using such gases.

2. Can we reproduce mesoscopic cellular structures with materials, and manipulate them?

Renowned physicist Richard P. Feynman once wrote: "What I cannot create, I do not understand." In other words, only in the process of creation can we achieve true understanding.

In this spirit, our institute aims to replicate mesoscopic cellular functions with designed materials (***cell-inspired materials***). This should be possible once a full understanding of such cellular processes (as described above) has been achieved. We therefore simultaneously advance analysis and synthesis, applying the resulting higher level of knowledge to further research, such as in the proposed creation of the following chemical materials:

- **Materials for Cell Membrane Functions**, such as the development of materials based on a mesoscopic understanding of the complex balance and interaction of processes on the cell membrane.

- **Energy Storage in Cells**, such as the creation of mesoscopic materials mimicking living systems' abilities to sort and store energy bearing ions and molecules, and materials to unlock the energy storage potential of carbon dioxide and nitrogen gas.

January 2013

About WPI

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. The MEXT grants average ¥1.3–1.4 billion per center (up to ¥700 million each for centers selected in 2012) annually over 10–15 years, and interim evaluations are conducted at 5-year intervals. WPI centers are as follows (as of April 2013):

- Tohoku University Advanced Institute for Materials Research (AIMR) [selected 2007]
- The University of Tokyo Kavli Institute for the Physics and Mathematics of the Universe (Kavli IPMU) [selected 2007]
- Kyoto University Institute for Integrated Cell-Material Sciences (iCeMS) [selected 2007]
- Osaka University Immunology Frontier Research Center (IFReC) [selected 2007]
- National Institute for Materials Science International Center for Materials Nanoarchitectonics (MANA) [selected 2007]
- Kyushu University International Institute for Carbon-Neutral Energy Research (I²CNER) [selected 2010]
- University of Tsukuba International Institute for Integrative Sleep Medicine (IIIS) [selected 2012]
- Tokyo Institute of Technology Earth-Life Science Institute (ELSI) [selected 2012]
- Nagoya University Institute of Transformative Bio-Molecules (ITbM) [selected 2012]

wpi
World Premier International Research Center Initiative

www.jsps.go.jp/wpi

Timeline

2007	**Sep. 12**	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	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 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 iCeMS with Prof. Akihiro Kusumi as founding director.
	Apr. 28	iCeMS Main Building opening ceremony held.
	Jun. 26	iCeMS Gifu University Satellite opening ceremony held.
	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 sister institute to iCeMS with Prof. Shinya Yamanaka as founding director.
	Oct. 29	iCeMS Research Building is completed.
	Dec.17	India's Tata Institute for Fundamental Research's National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem) Satellite Laboratory opening ceremony held at the iCeMS.
2011	**Apr. 17**	iCeMS Satellite Laboratory opening ceremony held at the NCBS-inStem in Bangalore.
	Jul. 21–23	Heidelberg University Collaborative Research Center SFB 873-Kyoto University iCeMS joint symposium held in Heidelberg.
2012	**Apr. 1**	Peking University and Tsinghua University Center for Life Sciences (CLS)-Kyoto University iCeMS joint symposium held in Beijing.
	Oct. 8	Prof. Shinya Yamanaka wins the Nobel Prize in Physiology or Medicine.
	Dec. 3–5	iCeMS co-organizes the World Stem Cell Summit in Florida with the Karolinska Institutet and other leading institutions.
2013	**Jan.**	The first issue of *Biomaterials Science*, a joint venture between the Royal Society of Chemistry (RSC) and iCeMS, published.
	Jan. 1	Prof. Susumu Kitagawa succeeds Prof. Nakatsuji as director.
	Jan. 16	iCeMS directorship succession ceremony held.
	Mar. 18–19	RSC-iCeMS joint symposium held to commemorate the launch of *Biomaterials Science*.

Management

Adhering to the principles of the WPI program, iCeMS has implemented a new system of management which is unprecedented in a Japanese university.

Management Reform Initiatives

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

Initiatives Aimed at Meeting International Standards

- 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
- Establishment of the Internationalization Committee
- Active MoU and personnel exchange with many overseas partner institutions (see p 7 for more)
- Active overseas outreach via the Institutional Program for Young Researcher Overseas Visits (see p 7 for more)
- English-language workshops on obtaining competitive grants

Promoting Ground-Breaking, Interdisciplinary Research

- 18 world-class principal investigators (WPI PIs)
- iCeMS Kyoto Fellow (junior PI) and iCeMS Associate Kyoto Fellow positions
- Strategic Committee for Interdisciplinary Research (Kitagawa Task Force)
- Support for collaborative projects with other young Kyoto University researchers via the iCeMS Interdisciplinary Research Promotion Project (19 projects selected in FY 2010, 15 FY 2011, 15 FY 2012)
- iCeMS Accelerated Project Grants (launched in FY 2013) in the areas of primary importance for multidisciplinary research: 1) gene expression control in stem cells, 2) organized functions on the cell membrane, and 3) energy storage in cells
- Academic Advisory Committee consisting of leading scientists from across the globe
- Scientific Advisor position (held by Prof. Shinya Yamanaka)
- Facilities Management Committee and the implementation of open offices and shared laboratories
- Promotion of interdisciplinary research through the common use of large facilities, such as apparatuses in the Center for Meso-Bio Single-Molecule Imaging (CeMI)
- Hosting international symposia (approx. 3 annually)
- iCeMS Seminars regularly conducted by noted international researchers (approx. 30 seminars annually)
- Annual iCeMS Retreats to aid interaction between labs (74 faculty and staff attended in 2009, 115 in 2010, 152 in 2011, 164 in 2012)
- Young Scientists' Colloquia, a new interdisciplinary seminar series initiated by iCeMS Kyoto Fellows, inviting speakers, postdocs, and graduate students from across departments of the university (approx. 6 colloquia annually)

University-Industry-Government Collaboration

- Development of innovation management theory coupled with vigorous efforts to link the public and private sectors
- Strategic Committee for Open Innovation (Nakatsuji Task Force)
- Industrial Advisory Committee
- A research planning URA (university research administrator) hired to enhance intellectual property management at iCeMS, also building closer ties with the Kyoto University URA office (KURA)

Local and Global Outreach

- Development of science communication theory hand-in-hand with active outreach programs (e.g. science cafés, hands-on stem cell workshops for high school students)
- WPI joint outreach efforts both at home (e.g. symposia for high school students) and abroad (e.g. AAAS annual meetings)
- A public relations URA hired to extend iCeMS' global reach, also building closer ties with KURA

Organization Chart

As of July 2013

Executive Board


Susumu Kitagawa
Director


Ryoichiro Kageyama
Deputy Director


Motonari Uesugi
Deputy Director


Kazumitsu Ueda
Board of PIs Chairman


Shinji Tomita
Administrative Director

Scientific Advisor


Shinya Yamanaka
CiRA* Director

WPI Principal Investigators (PIs)


Yong Chen


Mitsuru Hashida


Hiroshi Imahori


Ryoichiro Kageyama


Mineko Kengaku


Makoto Kiso
Gifu Univ Satellite


Susumu Kitagawa


Norio Nakatsuji
Founding Director


Mitinori Saitou


Hiroshi Sugiyama


Motomu Tanaka


Kazumitsu Ueda

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


Yoshie Harada
CeMI Director


John Heuser


Akihiro Kusumi


Koichiro Tanaka


Motonari Uesugi


Shinya Yamanaka

iCeMS PIs


Mikio Takano


Easan Sivaniah

NCBS-inStem Satellite Lab


Kenichi Suzuki

Innovation Management


Shintaro Sengoku

Science Communication


Kazuto Kato

iCeMS Kyoto Fellows


Peter Carlton


Ziya Kalay


Franklin Kim


Tatsuya Murakami


Dan Ohtan Wang


Takuya Yamamoto

Administration

iCeMS

Admin Director Shinji Tomita Deputy Admin Director Takashi Kawahara

General Affairs & Planning	Research Planning	IT Strategy

Yoshida South Campus

Admin Director Haruhiko Uejo Deputy Admin Director Takashi Kawahara

General Affairs	Overseas Planning & Public Relations	Accounting

Adjunct Professors

- Kazunari Akiyoshi (Grad Sch Eng)
- Itaru Hamachi (Grad Sch Eng)
- Hiroshi Kageyama (Grad Sch Eng)
- Hiroshi Kitagawa (Grad Sch Sci)
- Hidetoshi Kotera (Grad Sch Eng)
- Michiyuki Matsuda (Grad Sch Bio/Med)
- Yasuo Mori (Grad Sch Global Env/Eng)
- Takashi Shinohara (Grad Sch Med)
- Masahiro Shirakawa (Grad Sch Eng)
- Ryosuke Takahashi (Grad Sch Med)
- Fumiko Toyoshima (Inst Virus Rsch)

Academic Advisory Committee

- Barbara Baird (Cornell University)
- Daniel Choquet (Université de Bordeaux 2)
- Mark Haw (The University of Strathclyde)
- Eng-Hin Lee (The University of Singapore)
- Laura Kiessling (University of Wisconsin-Madison)
- Keiji Morokuma (Kyoto University)
- Noriko Osumi (Tohoku University)
- Kenneth R. Poeppelmeier (Northwestern University)
- Ferdi Schüth (Max-Planck-Institut für Kohlenforschung)
- Fiona Watt (The University of Cambridge)

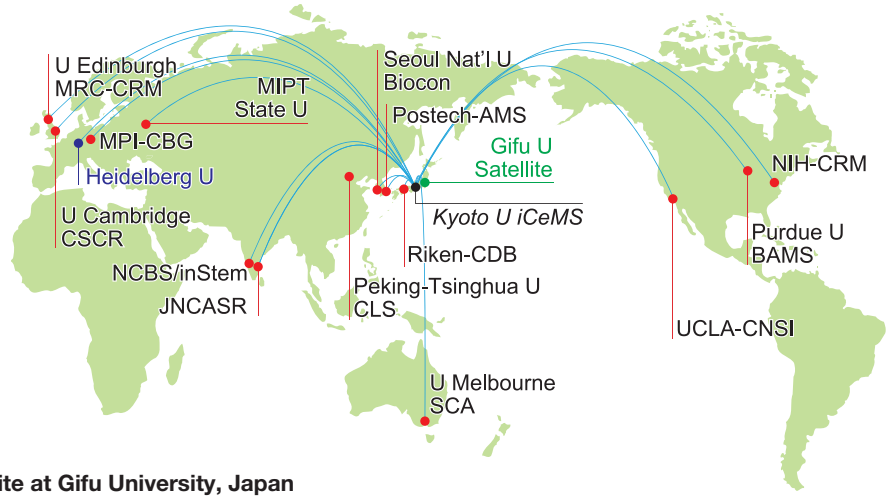
Industrial Advisory Committee

Members TBA

*Kyoto University Center for iPS Cell Research and Application

Partner Institutions & Satellite

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



- **iCeMS Satellite at Gifu University, Japan**
- **Heidelberg University, Germany (university-level MoU signed)**
- Institute for Stem Cell Biology and Regenerative Medicine (inStem), India*
- Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), India*
- Max Planck Institute of Molecular Cell Biology and Genetics (MPI CBG), Germany
- Moscow Institute of Physics and Technology (MIPT), Russia*
- NIH Center for Regenerative Medicine (NIH CRM), USA*
- Peking University and Tsinghua University Center for Life Sciences (CLS), China*
- Pohang University of Science and Technology Division of Advanced Materials Science (POSTECH AMS), South Korea*
- Purdue University Center for Basic and Applied Membrane Sciences (PUBAMS), USA
- Riken Center for Developmental Biology (CDB), Japan
- Seoul National University Medicinal Bioconvergence Research Center (Biocon), South Korea*
- Tata Institute of Fundamental Research National Centre for Biological Sciences (NCBS), India*
- The University of Edinburgh Medical Research Council Centre for Regenerative Medicine (MRC CRM), UK*
- The University of Melbourne Stem Cells Australia (SCA)
- UCLA California NanoSystems Institute (CNSI), USA*
- University of Cambridge Wellcome Trust Centre for Stem Cell Research (CSCR), UK

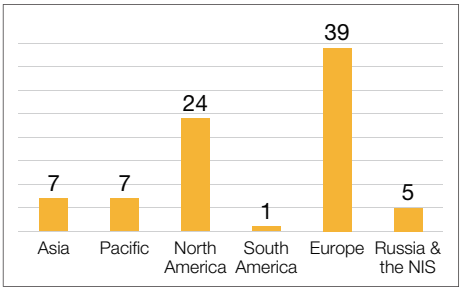
*MoU (memorandum of understanding) partners

iCeMS Overseas Visit Program for Young Researchers

The iCeMS-JSPS Overseas Visit Program for Young Researchers (also called Bon Voyage Program) has been successfully implemented from March 2010 to February 2013. Although JSPS support has ended, iCeMS continues the program using its own budget, making the most of the collective experiences and networks compiled to date. The main objective of this program is, as before, to provide young iCeMS researchers with opportunities to strengthen their international competitiveness, supporting overseas visits for around 1–3 weeks each. All young researchers are strongly encouraged to apply, and make the most of this opportunity to gain overseas research experience. Participants are also expected to act as evangelists for iCeMS.

cloud.icems.kyoto-u.ac.jp/bonvoyage

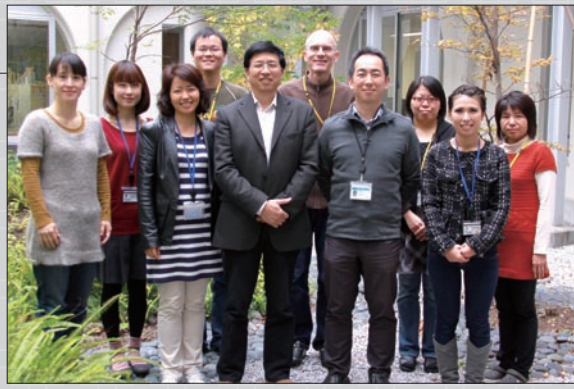
Number of past participants by region (March 2010–February 2013)



Yong Chen Lab

Nanobiotechnology, Microfluidics, Stem Cell Biology

Faculty Members
Yong Chen (Professor)
Ken-ichiro Kamei (Assistant Professor)
Li Liu (Assistant Professor)



Research Overview

Our main research interests are to develop new tools and methodologies for applications in cell biological studies based on **microfluidic** and **nanofabrication technologies**, which offer unique advantages over conventional biological experimental settings. In particular, the Chen group has focused on creating *in vitro* cellular microenvironments (or niche), which have been shown to play important roles in regulating cellular functions *in vivo* (i.e., **human pluripotent stem cells (hPSCs)**, neurons and cardiomyocytes). Indeed, the methods we developed allow establishing well-defined artificial regulatory cellular environments at nm~μm scales. By utilizing these artificial environments, we will be able to understand cellular environmental cues in detail and to more precisely control cellular functions. Such new methodological developments lead us to prepare stem cells for future applications in drug screening, cell-based therapy and regenerative medicine.

Our current research projects are listed below;

1. **Nanofabricated cellular scaffolds for maintaining hPSC self-renewal and inducing differentiation**. We are developing nanostructured substrates and nanofibers for culturing pluripotent stem cells at an undifferentiated status and inducing lineage-specific differentiation.
2. **Microfluidic platforms for high-throughput screening**. Microfluidics are based on microfabrication technologies and used for chemical synthesis, gene and cell analysis, and in vitro cancer diagnosis. Now, we are trying to develop new microfluidic platforms to screen drug candidates by using stem cells in a high-throughput fashion.
3. **Material assessment and optimziation for application in stem cell research**. As mentioned above, polymer-based microfabrication materials are very convenient for the purpose of creating 3D microenvironmental cues to control hPSC functions. However, before the device and technologies we developed can be used in real-world applications, we evaluate how the microfabrication materials affect hPSC behavior and functions.

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

1. Nano-substrates in conjunction with microfluidic platforms to perform hPSC culture and differentiation (Nakatsuji Lab).
2. Integration of meso-porous materials with nanoengineered substrates for controlling bioactive molecules in a spatial and temporal fashion (Kitagawa Lab).
3. Nanoinjectors to stimulate cells with high spatial resolution and imaging at subcellular level (Kusumi Lab).

Selected Papers

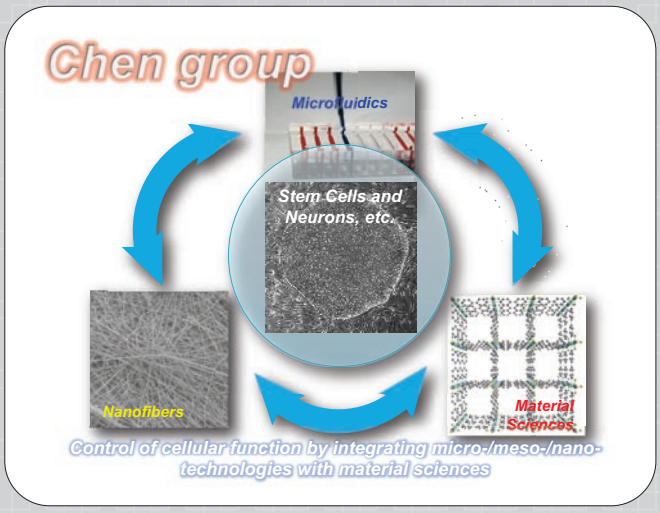
Kamei K., Hirai Y., Makino Y., Yoshioka M., Yuan Q., Nakajima M., Chen Y. and Tabata O. Phenotypic and transcriptional modulation of human pluripotent stem cells induced by nano/microfabrication materials. *Adv. Healthcare Mater.* **2**, 287-291 (2013).

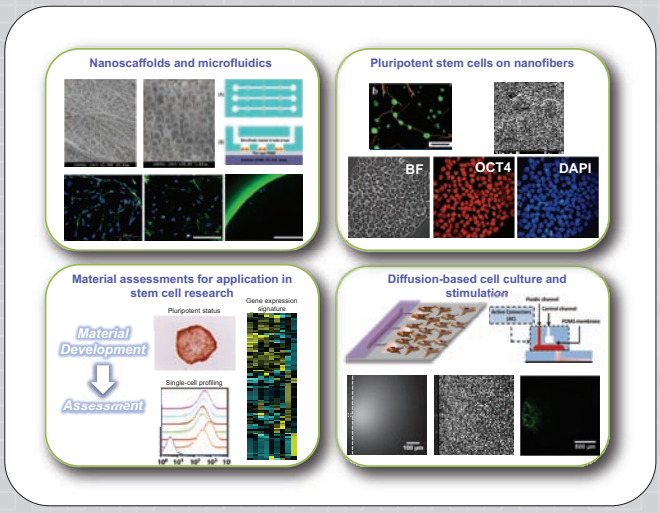
Liu L., Yuan Q., Shi J., Li X., Jung D., Yamauchi K., Nakatsuji N., Kamei K. and Chen Y. Chemically defined scaffolds created with electrospun synthetic nanofibers to maintain mouse embryonic stem cell culture under feeder-free conditions. *Biotechnol. Lett.* **34**, 1951-1957 (2012).

Li X., Liu L., Wang L., Kamei K., Yuan Q., Zhang F., Shi J., Kusumi A., Xie M., Zhao Z. and Chen Y. Integrated and diffusion-based micro-injectors for open access cell assays. *Lab Chip* **11**, 2612-2617 (2011).

Liu Y., Wang H., Kamei K., Yan M., Chen K.J., Yuan Q., Shi L., Lu Y., Tseng H.R. Delivery of intact transcription factor by using self-assembled supramolecular nanoparticles. *Angew. Chem. Int. Ed. Engl.* **50**, 3058-3062 (2011).

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. Microdev.* **12**, 505–511 (2010).





Yoshie Harada Lab

Single-Molecule Physiology, Biophysics

Faculty Members

Yoshie Harada (Professor)
Yohsuke Yoshinari (Associate Professor)
Mariko Ariyoshi (Associate Professor)
Yasuo Tsunaka (Senior Lecturer)
Yong-Woon Han (Assistant Professor)
Yasuko Osakada (Assistant Professor)
Takuma Sugi (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 are developing new imaging technologies and use these techniques to investigate the molecular mechanisms of biomolecules.

Three main research directions are as follows:
1. Development of a novel single-molecule imaging technique using fluorescent diamond nanoparticles
2. Analysis of biomolecular interactions with zero-mode waveguides
3. Analysis of dynamics of endogenous RNA in cells

Selected Papers

Yokota, H., Ayabe Chujo, Y and Harada, Y. Single-Molecule Imaging of the Oligomer Formation of the Nonhexameric Escherichia coli UvrD Helicase. *Biophysical Journal* **104**, 924–933 (2013).

Igarashi, R., Yoshinari, Y., Yokota, H., Sugi, T., Sugihara, F., Ikeda, K., Sumiya, H., Tsuji, S., Mori, I., Tochio, H., Harada, Y. and Shirakawa M. Real-Time Background-Free Selective Imaging of Fluorescent Nanodiamonds in Vivo. *Nano Letters* **12**, 5726–5732 (2012).

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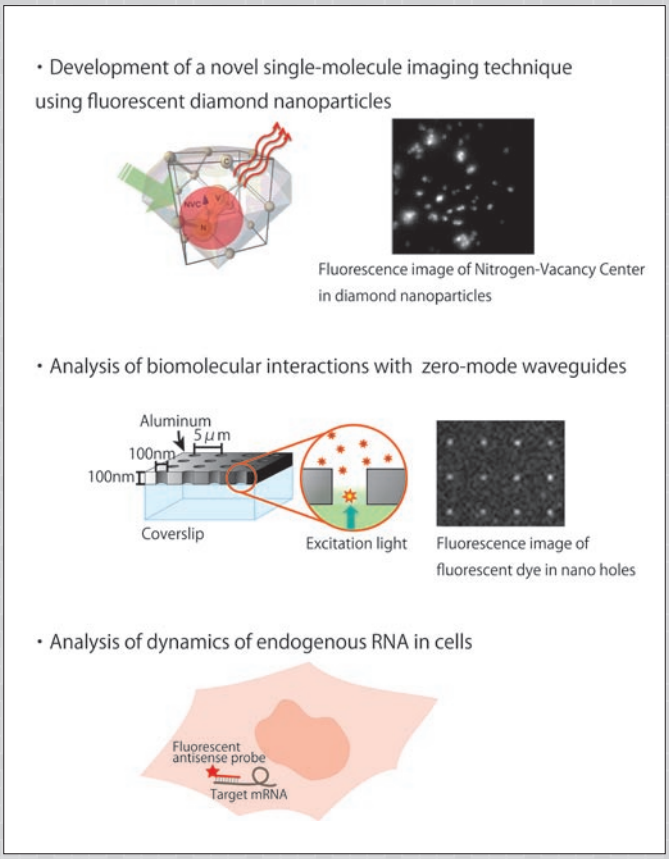
Endo, M., Tatsumi, K., Terushima, K., Katsuda, Y., Hidaka, K., Harada, Y. and Sugiyama H. Direct Visualization of the Movement of a Single T7 RNA Polymerase and Transcription on a DNA Nanostructure. *Angew. Chem. Int. Ed. Engl.* **51**, 8778-82 (2012).

Okabe, K., Inada, N., Gota, C., Harada, Y., Funatsu, T. and Uchiyama, S. Intracellular temperature mapping with a fluorescent polymeric thermometer and fluorescence lifetime imaging microscopy. *Nature Communications* **3**, 705 (2012).



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

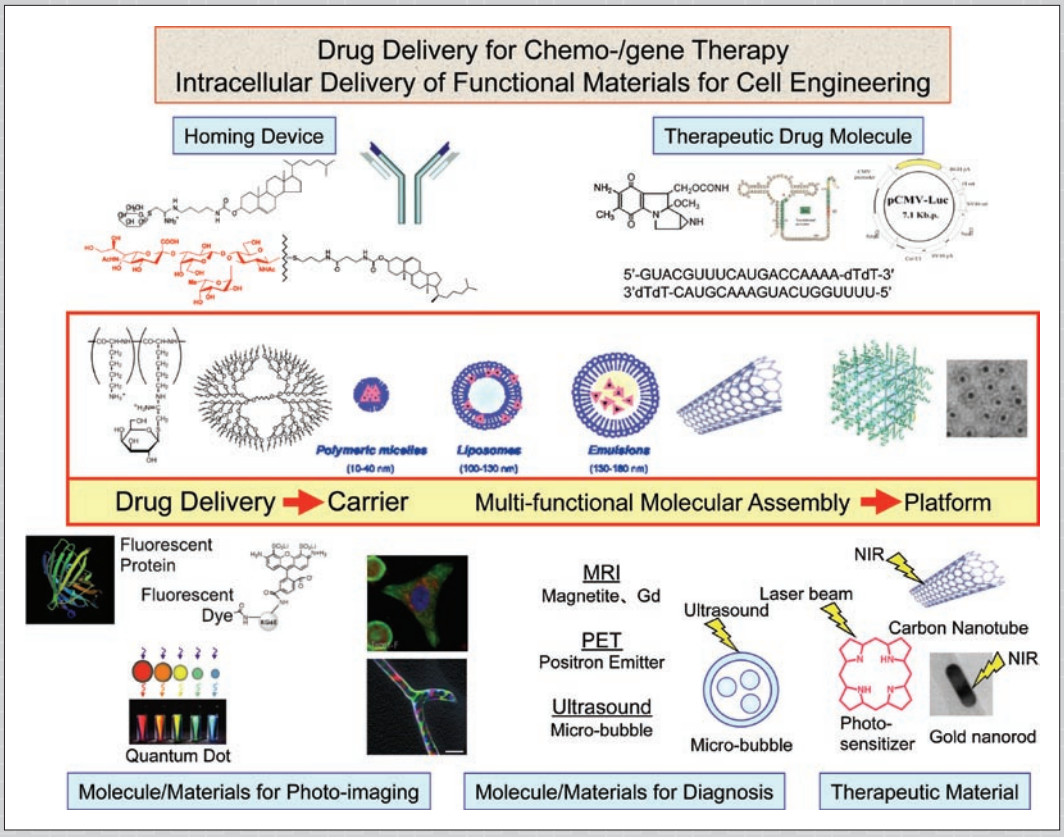
Selected Papers

Hashida, Y., Umeyama, T., Mihara, J., Imahori, H., Tsujimoto, M., Isoda, S., Takano, M. and Hashida, M. Development of a novel composite material with carbon nanotubes assisted by self-assembled peptides designed in conjunction with β-sheet formation. *J. Pharm. Sci.* **101**, 3398-412 (2012).

Un, K., Kawakami, S., Yoshida, M., Higuchi, Y., Suzuki, R., Maruyama, K., Yamashita, F. and Hashida, M. Efficient suppression of ICAM-1 using ultrasound-responsive and mannose-modified lipoplexes inhibits acute hepatic inflammation. *Hepatology* **56**, 259-69 (2012).

Yamashita, F., Feng, C., Yoshida, S., Itoh, T. and Hashida, M. Automated information extraction and structure-activity relationship analysis of cytochrome P450 substrates. *J. Chem. Inf. Modeling* **51**, 378-85 (2011).

Higuchi, Y., Wu, C., Chang, K. L., Irie, K., Kawakami, S., Yamashita, F. and Hashida, M. Polyamidoamine dendrimer-conjugated quantum dots for efficient labeling of primary cultured mesenchymal stem cells. *Biomaterials* **32**, 6676-82 (2011).



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

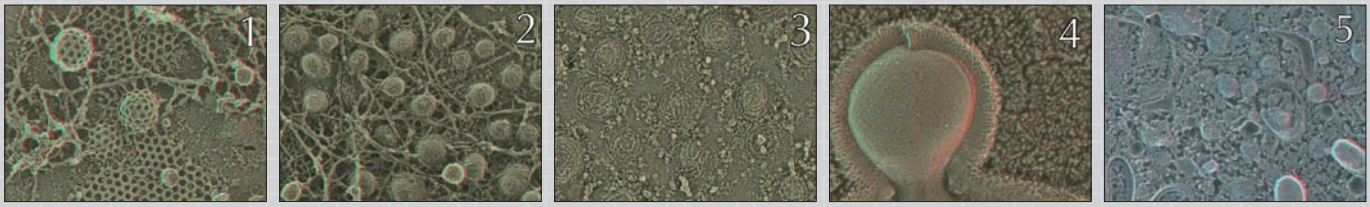
Hanson, P. I., Roth, R., Lin, Y. and Heuser, J. E. Plasma membrane deformation by circular arrays of ESCRT-III protein filaments. *J. Cell Biol.* **180**, 389–402 (2008).

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).

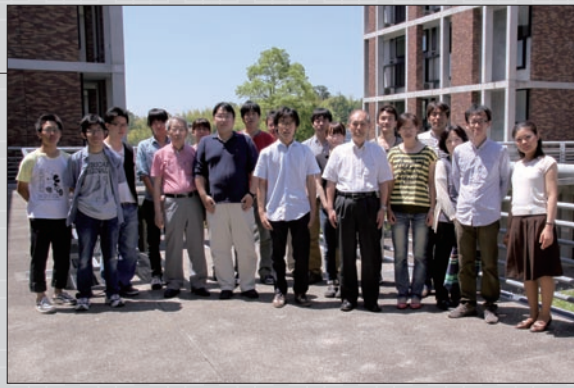
Heuser, J. Deep-etch EM reveals that the early poxvirus envelope is a single membrane bilayer stabilized by a geodetic "honeycomb" surface coat. *J. Cell Biol.* **169**, 269–283 (2005).



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

Hiroshi Imahori Lab

Organic Chemistry, Photochemistry, Drug Delivery Systems



Faculty Members

Hiroshi Imahori (Professor)
Yuta Takano (Assistant Professor)
Kei Kurotobi (Assistant Professor)

Research Overview

Our laboratory has been working on **artificial photosynthesis** and **solar energy conversion**. 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, durable 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 hybrid solar cells**. Currently, a power conversion efficiency of >9% has been achieved on our porphyrin-sensitized 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) **Light-harvesting meso-scale materials** for photodynamic and photothermal therapy (Murakami, Hashida, Takano labs)
2) **Light-emitting meso-scale materials** for cell imaging (Murakami, Hashida labs)
3) **Photoinduced charge separation meso-scale materials** for controlling cellular functions (Murakami, Mori, Heuser, Kengaku, Nakatsuji labs)

Selected Papers

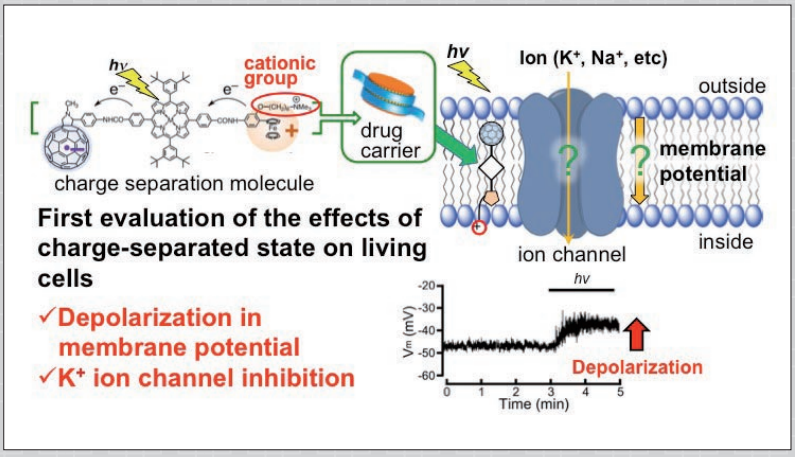
Numata, T., Murakami, T., Kawashima, F., Morone, N., Heuser, J. E., Takano, Y., Ohkubo, K., Fukuzumi, S., Mori, Y. and H. Imahori, Utilization of photoinduced charge-separated state of donor-acceptor linked molecules for regulation of cell membrane potential and ion transport. *J. Am. Chem. Soc.* **134**, 6092-6095 (2012).

Hayashi, H., Nihashi, W., Umeyama, T., Matano, Y., Seki, S., Shimizu, Y., and Imahori, H. Segregated donor-acceptor columns in liquid crystals that exhibit highly efficient ambipolar charge transport. *J. Am. Chem. Soc.* **133**, 10736-10739 (2011).

Umeyama, T., Tezuka, N., Kawashima, F., Seki, S., Matano, Y., Nakao, Y., Shishido, T., Nishi, M., Hirao, K., Lehtivuori, H., Tkachenko, N. V., Lemmetyinen, H. and Imahori, H. Carbon nanotube wiring of donor-acceptor nanograins by self-assembly and efficient charge transport. *Angew. Chem. Int. Ed.* **50**, 4615-4619 (2011).

Hayashi, H., Lightcap, I. V., Tsujimoto, M., Takano, M., Umeyama, T., Kamat, P. V. and Imahori, H. Electron transfer cascade by organic/inorganic ternary composites of porphyrin, zinc oxide nanoparticles, and reduced graphene oxide on a tin oxide electrode that exhibits efficient photocurrent generation. *J. Am. Chem. Soc.* **133**, 7684-7687 (2011).

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).



Ryoichiro Kageyama Lab

Developmental Biology, Neural Stem Cell Biology

Faculty Members
Ryoichiro Kageyama (Professor)
Hiromi Shimojo (Assistant Professor)

Research Overview

Neural stem cells are present not only in the embryonic but also in the adult brain and continuously produce new **neurons** although at different rates. Decrease in number or depletion of neural stem cells leads to severe damage in brain morphogenesis or impairment of higher brain functions such as learning and memory. We are investigating the molecular mechanisms of proliferation and differentiation of neural stem cells, aiming at controlling these cells at will. We have found several key genes that regulate proliferation of neural stem cells and differentiation of neurons and revealed that the **gene expression dynamics** are very important for their functions. For example, single genes exhibit different activities when their expression is steady or oscillatory. We are now characterizing the detailed mechanism of how these genes regulate each step differently when their expression dynamics are different. Although the same genes are responsible for regulation of both embryonic and adult neural stem cells, the former cells are active in proliferation and differentiation, while the latter cells are mostly dormant. We speculate that gene expression dynamics are different between these two cell types. It is expected that novel strategies using chemicals or biomaterials that control cell proliferation and differentiation will be developed with the acquisition of more detailed knowledge of the significance of gene expression dynamics. Such strategies will be useful for many medical purposes such as brain disease treatment and tissue regeneration.

Selected Papers

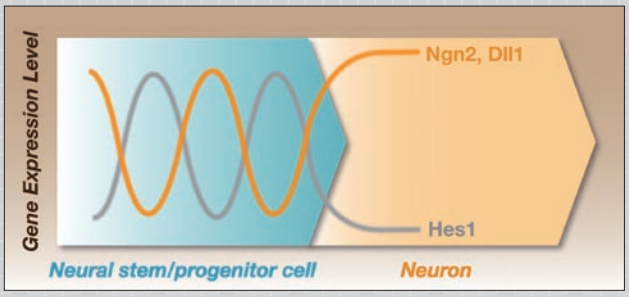
Harima, Y., Takashima, Y., Ueda, Y., Ohtsuka, T., and Kageyama, R. Accelerating the tempo of the segmentation clock by reducing the number of introns in the Hes7 gene. *Cell Reports* **3**, 1-7 (2013).

Niwa, Y., Shimojo, H., Isomura, A., González, A., Miyachi, H., and Kageyama, R. Different types of oscillations in Notch and Fgf signaling regulate the spatiotemporal periodicity of somitogenesis. *Genes Dev.* **25**, 1115-1120 (2011).

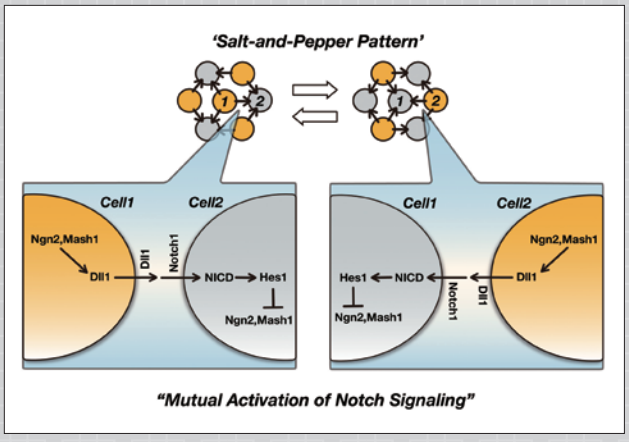
Kobayashi, T., Mizuno, H., Imayoshi, I., Furusawa, C., Shirahige, K., and Kageyama, R. The cyclic gene Hes1 contributes to diverse differentiation responses of embryonic stem cells. *Genes Dev.* **23**, 1870-1875 (2009).

Imayoshi, I., Sakamoto, M., Ohtsuka, T., Takao, K., Miyakawa, T., Yamaguchi, M., Mori, K., Ikeda, T., Itohara, S., and Kageyama, R. Roles of continuous neurogenesis in the structural and functional integrity of the adult forebrain. *Nature Neurosci.* **11**, 1153-1161 (2008).

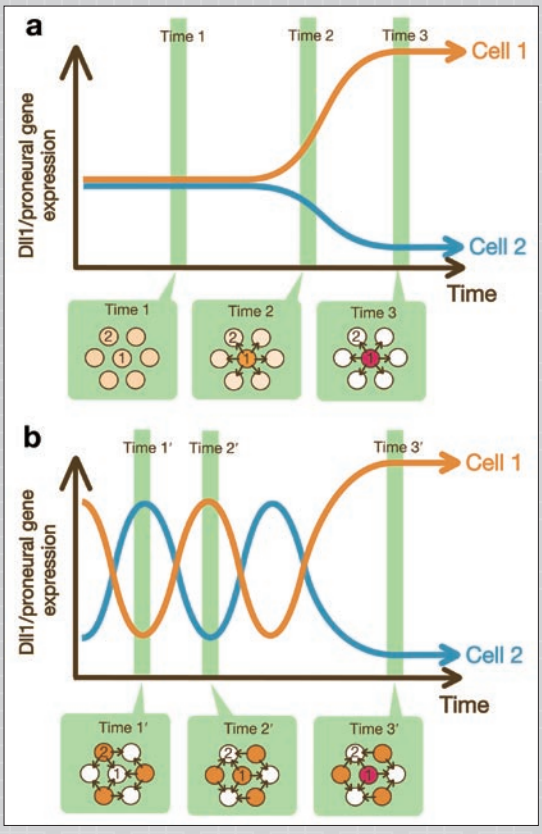
Shimojo, H., Ohtsuka, T., and Kageyama, R. Oscillations in Notch signaling regulate maintenance of neural progenitors. *Neuron* **58**, 52-64 (2008).



Gene expression dynamics in neural stem cells and differentiating neurons.



Mutual activation of Notch signaling in neural stem/progenitor cells.



Two models for a salt-and-pepper pattern mediated by Notch-dependent lateral inhibition.

Mineko Kengaku Lab

Developmental Neurobiology, Cell Biology

Faculty Members
Mineko Kengaku (Professor)
Kazuto Fujishima (Assistant 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

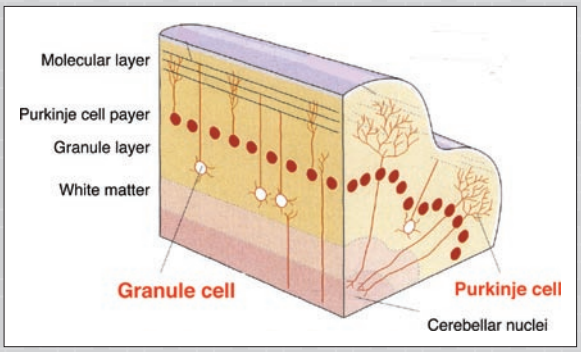
Umeshima, H. and Kengaku, M. Differential roles of cyclin-dependent kinase 5 in tangential and radial migration of cerebellar granule cells. *Mol Cell Neurosci.* **52**, 62-72 (2013).

Fujishima, K., Horie, R., Mochizuki, A. and Kengaku M. Principle branch dynamics governing shape characteristics of cerebellar Purkinje cell dendrites. *Development* **139**, 3456-3466 (2012).

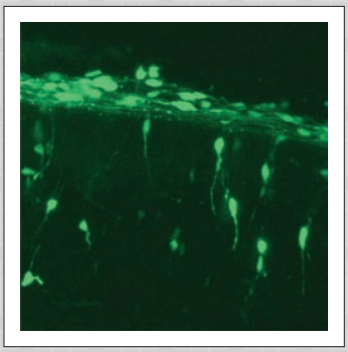
Kaneko, M., Yamaguchi, K., Eiraku, M., Sato, M., Takata, N., Kiyohara, Y., Mishina, M., Hirase, H., Hashikawa, T. and Kengaku, M. Remodeling of Monoplanar Purkinje Cell Dendrites during Cerebellar Circuit Formation. *PLoS ONE* **6**, e20108 (2011).

Sasaki, N., Kurisu, J. and Kengaku, M. Sonic hedgehog signaling regulates actin cytoskeleton via Tiam1-Rac1 cascade during spine formation. *Mol Cell Neurosci.* **45**, 335-344 (2010).

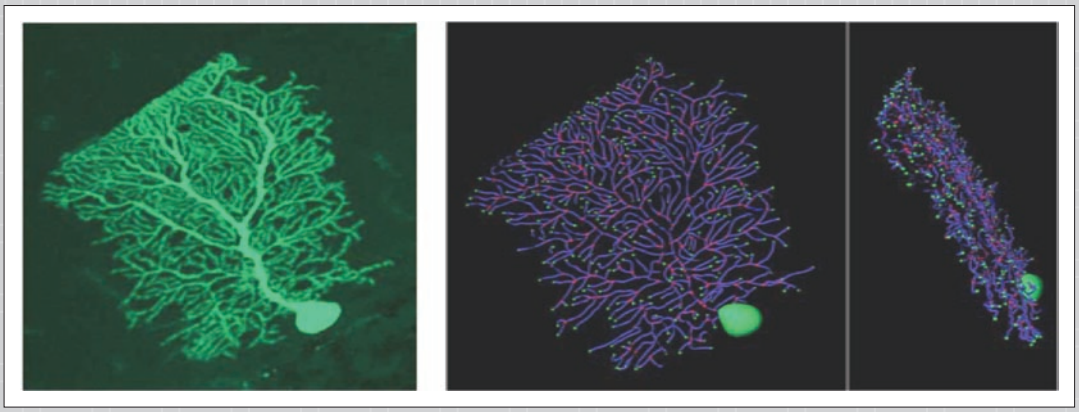
Kurisu, J., Fukuda, T., Yokoyama, S., Hirano, T. and Kengaku, M. Polarized targeting of DNER into dendritic plasma membrane in hippocampal neurons depends on endocytosis. *J. Neurochem.* **113**, 1598-1610 (2010).



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, Bio-active molecule chemistry

Faculty Members
Makoto Kiso (Professor)
Hiromune Ando (Associate Professor)

Research Overview

This satellite pursues the elucidation of the molecular basis underlying the multifunctions of carbohydrates (especially those called as "**glycans**") in various biological processes by chemical methods and its applications in medicine. Our research is focused on the development of versatile and powerful synthetic methodology of glycans, and the creation of the **Glycobank** possessing a wide spectrum of biologically-significant glycans and functionalized glycan probes. Utilizing the full entries of the Glycobank, we are going to conduct cross-disciplinary studies with molecular biology, developmental biology, structural biology, biophysics for the understanding and application of biological functions of glycans.

Our synthesized glycan have been utilized in diverse biological researches such as those on immune system, virus entry, cancer migration. At iCeMS, we have launched new cross-disciplinary projects using the entries of the Glycobank, which include:

1. Creation of the **glyco-director** system for stem cell engineering, which comprises of the arrays of homogenous synthetic glycans that (will) direct the differentiation, proliferation of stem cells (ES and iPS cells), by collaboration with the stem cell science (Nakatsuji G) and nanomaterial science (Kitagawa G).
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, by collaboration with single-molecule cell biophysics (Kusumi G, Suzuki G and Ueda G).
3. Innovation of **drug delivery system** (**DDS**) by creating new drug carrier using carbon nanotubes and liposomes functionalized with glycans by the collaboration with biopharmaceuticals (Hashida G).

Selected Papers

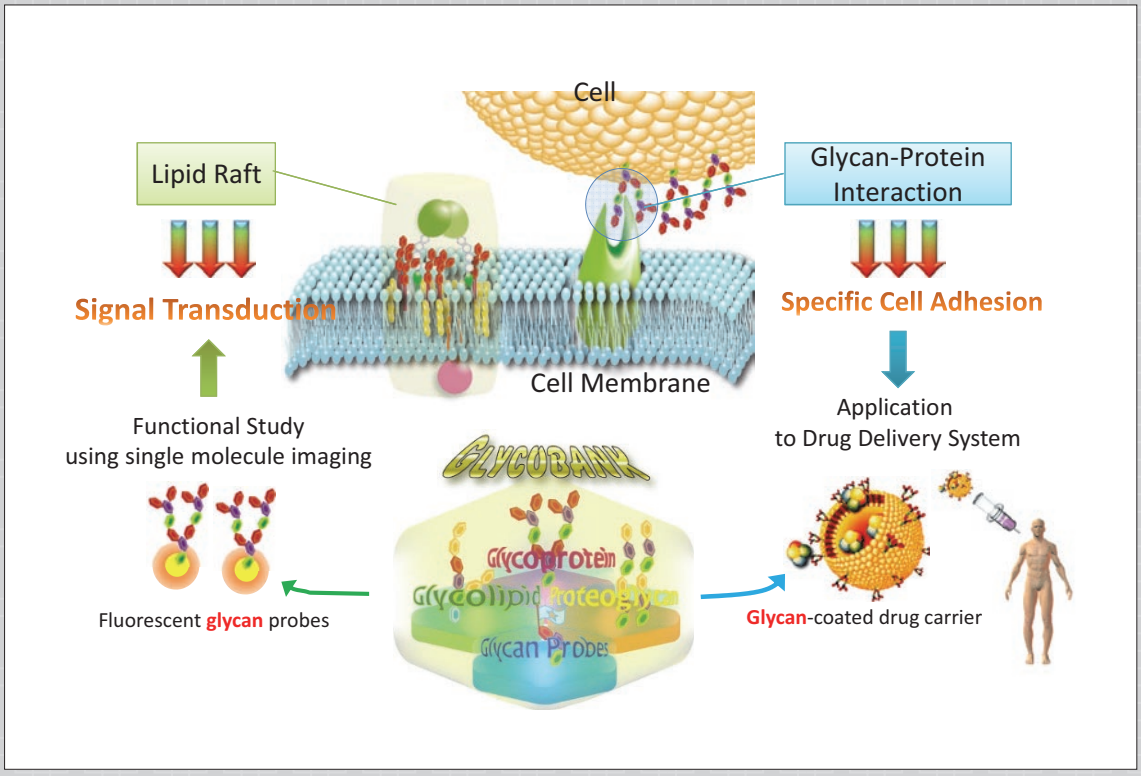
Nakashima, S., Ando, H., Saito, R., Tamai, H., Ishida, H. and Kiso, M.: Efficiently synthesizing lacto-ganglio-series gangliosides by using a glucosyl ceramide cassette approach: the total synthesis of ganglioside X2. *Chem. Asian J.* **7**, 1041-1051 (2012).

Fujikawa, K., Nakashima, S., Konishi, M., Fuse, T., Komura, N., Ando, T., Ando, H., Yuki, N., Ishida, H. and Kiso, M. The first total synthesis of ganglioside GalNAc-GD1a, a target molecule for autoantibodies in Guillain-Barré syndrome. *Chem. Eur. J.* **17**, 5641-5651 (2011).

Tamai, H., Ando, H., Tanaka, H., Hosoda-Yabe, R., Yabe, T., Ishida, H. and Kiso, M. The total synthesis of the neurogenic ganglioside LLG-3 isolated from the starfish Linckia laevigata. *Angew. Chem. Int. Ed.* **50**, 2330-2333 (2011).

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).



Susumu Kitagawa Lab

Coordination Chemistry, Porous Materials, Biomaterial Science

Faculty Members

Susumu Kitagawa (Professor)
Koji Tanaka (Professor)
Shuhei Furukawa (Associate Professor)
Ryotaro Matsuda (Associate Professor)
Stéphane Paul Diring (Assistant Professor)
Hiroshi Sato (Assistant Professor)
Julien Reboul (Assistant Professor)
Reiko Sakaguchi (Assistant Professor)
Masakazu Higuchi (Assistant Professor)
Katsuaki Kobayashi (Assistant Professor)
Maw Lin Foo (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 several nanometers to subnanometers 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**) or **Metal-Organic Frameworks** (**MOFs**). Moreover, we are interested in **mesoscopic** (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 (C2-C3) 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 monoixide (CO), nitric oxide (NO), hydrogen sulfide (H_2S) 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. Porous materials for energy conversion: In biological systems, cells efficiently convert exogenous energy to chemical energy. We are working on the development of artificial materials, which interconvert between light- or electro- energy and chemical energy.

Selected Papers

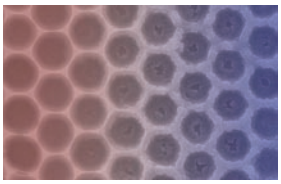
Reboul, J., Furukawa, S., Horike, N., Tsotsalas, M., Hirai, K., Uehara, H., Kondo, M., Louvain, N., Sakata, O., Kitagawa, S. Mesoscopic architectures of porous coordination polymers fabricated by pseudomorphic replication. *Nat. Mater.* **11**, 717-723 (2012).

Yanai, N., Kitayama, K., Hijikata, Y., Sato, H., Matsuda, R., Kubota, Y., Takata, M., Mizuno, M., Uemura, T., Kitagawa, S. Gas detection by structural variations of fluorescent guest molecules in a flexible porous coordination polymer. *Nat. Mater.* **10**, 787-793 (2011).

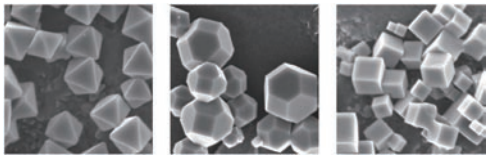
Takashima. Y., Martinez, M. V., Furukawa, S., Kondo, M., Shimomura, S., Uehara, H., Nakahama, M., Sugimoto, K., Kitagawa, S. Molecular decoding using luminescence from an entangled porous framework. *Nat. Commun.* **2**, 168 (2011), DOI: 10.1038/ncomms1170.

Sato, H., Matsuda, R., Sugimoto, K., Takata, M., Kitagawa, S. Photoactivation of a nanoporous crystal for on-demand guest trapping and conversion. *Nat. Mater.* **9**, 661-666 (2010).

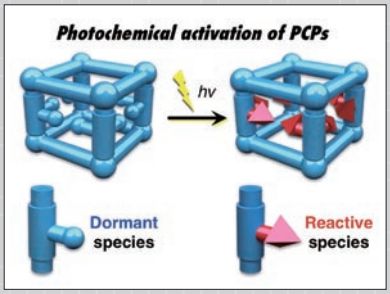
Horike, S., Shimomura, S., Kitagawa, S. Soft porous crystals. *Nat. Chem.* **1**, 695–704 (2009).



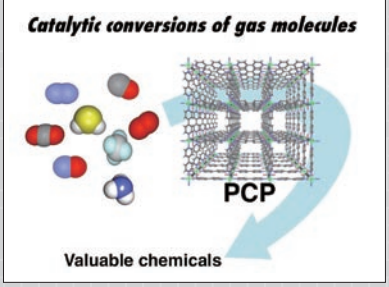
Mesoscopic architecture of porous coodination polymers fabricated by coordination replication



Mesoscopic crystals of porous coordination polymers with different Morphology



Photoactivation system embedded in porous coordination polymers

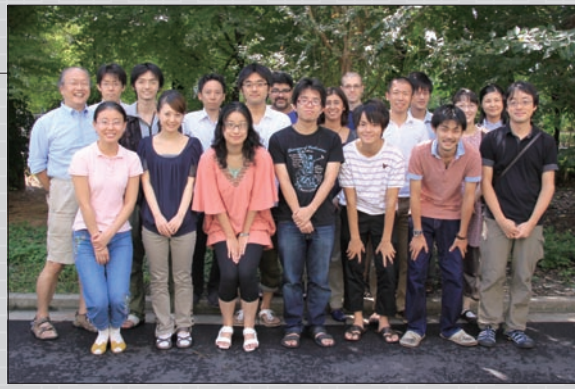


Catalytic conversions of gases by porous coordination polymers

Akihiro Kusumi Lab

Single-Molecule Cell Biophysics

Faculty Members
Akihiro Kusumi (Professor)



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

A. Kusumi, T. K. Fujiwara, R. Chadda, M. Xie, T. A. Tsunoyama, Z. Kalay, R. S. Kasai, and K. G. N. Suzuki. Organizing principles of the plasma membrane for signal transduction: Commemorating the fortieth anniversary of Singer and Nicolson's fluid-mosaic Model. *Ann. Rev. Cell Dev. Biol.* **28**, 215-250 (2012).

Suzuki, K. G. N., Kasai, R. S., Hirosawa, K. M., Nemoto, Y. L., Ishibashi, M., Miwa, Y., Fujiwara, T. K., and Kusumi, A. Transient GPI-anchored protein homodimers are units for raft organization and function. *Nat. Chem. Biol.* **8**, 774-783 (2012).

Kalay, Z., Fujiwara, T., and Kusumi, A. Confining domains lead to reaction bursts: reaction kinetics in the plasma membrane. *PLoS One* **7**, e32948 (2012).

Kasai, R. S., Suzuki, K. G. N., Prossnitz, E. R., Koyama-Honda, I., Nakada, C., Fujiwara, T. K., and Kusumi, A. Full characterization of GPCR monomer-dimer dynamic equilibrium by single molecule imaging. *J. Cell Biol.* **192**, 463-480 (2011).

Tanaka, K. A. K. , Suzuki, K. G. N., Shirai, Y. M., Shibutani, S. T., Miyahara, M. S. H., Tsuboi, H., Yahara, M., Yoshimura, A., Mayor, S., Fujiwara, T. K., and Kusumi, A. Membrane molecules mobile even after chemical fixation. *Nat. Meth.* **7**, 865-866 (2010).

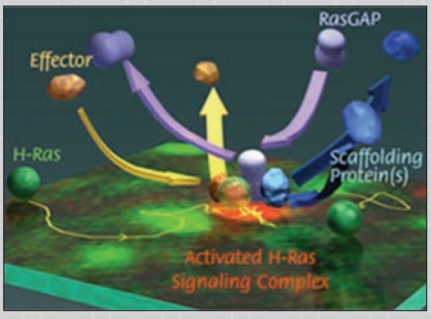


Fig. 2

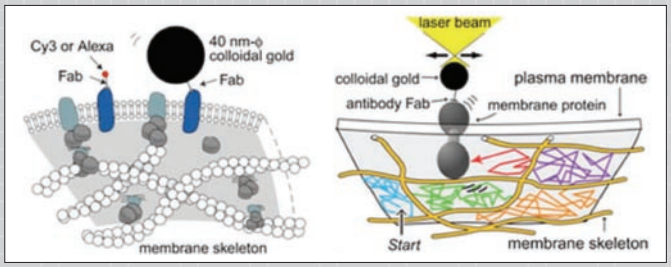


Fig. 1

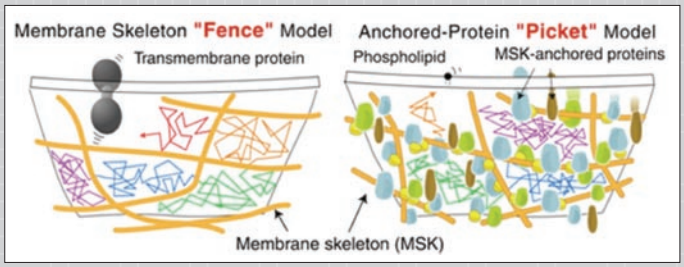


Fig. 3

Norio Nakatsuji Lab

Stem Cell Biology, Developmental Biology

Faculty Members
Norio Nakatsuji (Professor)
Kazuhiro Aiba (Associate Professor)
Itsunari Minami (Assistant Professor)

Research Overview

Our research group has been working on the 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**, **including human ES and iPS cells**.

We have developed 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.

1. Creation and analysis of model cells from human ES and iPS cell lines. They include **neurodegenerative disease model** cells, such as Alzheimer, ALS and Huntington disease models, which are 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 in the iCeMS.
2. Control of stem cells with **chemical compounds** and **nano/meso/micro-fabricated materials** for growth and differentiation of ES/iPS cells in collaboration with chemical biology groups (such as the Uesugi and Sugiyama Lab) and nano/meso/micro-engineering groups (such as the Chen Lab). For example, we have identified novel small molecules which can induce efficient and robust cardiomyocyte differentiation from many human ES and iPS cell lines in totally defined xeno-free conditions.
3. Development of novel technologies for large-scale production of high-quality human pluripotent stem cells using 3D culture system. It is a government-supported project for medical and pharmaceutical application of stem cells, and carried out by collaboration with several high-technology companies in addition to the collaboration with many academic research groups.

Selected Papers

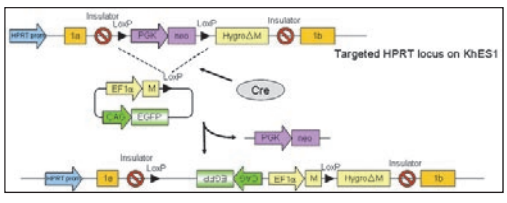
Minami, I., Yamada, K., Otsuji, T. G., Yamamoto, T., Shen, Y., Otsuka, S., Kadota, S., Morone, N., Barve, M., Asai, Y., Tenkova-Heuser, T., Heuser, J. E., Uesugi, M., Aiba, K. and Nakatsuji, N. A small molecule that promotes cardiac differentiation of human pluripotent stem cells under defined, cytokine- and xeno-free conditions. *Cell Rep.* **2**, 1448–1460 (2012).

Kadota, S., Minami, I., Morone, N., Heuser, J. E., Agladze, K. and Nakatsuji, N. Development of a reentrant arrhythmia model in human pluripotent stem cell-derived cardiac cell sheets. *Eur. Heart J.* DOI: 10.1093/eurheartj/ehs418 (2012).

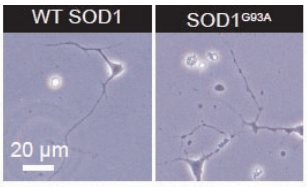
Miyazaki, T., Futaki, S., Suemori, H., Taniguchi, Y., Yamada, M., Kawasaki, M., Hayashi, M., Kumagai, H., Nakatsuji, N., Sekiguchi, K. and Kawase, E. Laminin E8 fragments support efficient adhesion and expansion of dissociated human pluripotent stem cells. *Nat. Commun.* **3**, DOI:10.1038/ncomms2231 (2012).

Wada, T., Goparaju, S. K., Tooi, N., Inoue, H. Takahashi, R., Nakatsuji, N. and Aiba, K. Amyotrophic lateral sclerosis model derived from human embryonic stem cells overexpressing mutant superoxide dismutase 1. *Stem Cells Transl. Med.* **1**, 396-402 (2012).

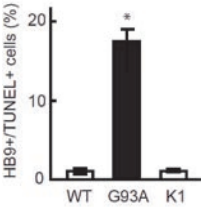
The International Stem Cell Initiative: Andrews, P. W. and others (incl. Miyazaki, T., Nakatsuji, N., Suemori, H., Takahashi, K., Yamanaka, S.) Screening ethnically diverse human embryonic stem cells identifies a chromosome 20 minimal amplicon conferring growth advantage. *Nat. Biotechnol.* **29**, 1132-1144 (2011).



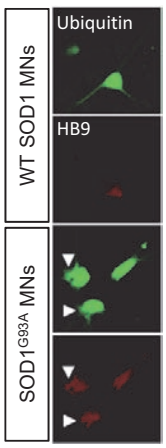
Cre/loxP mediated site-specific gene integration



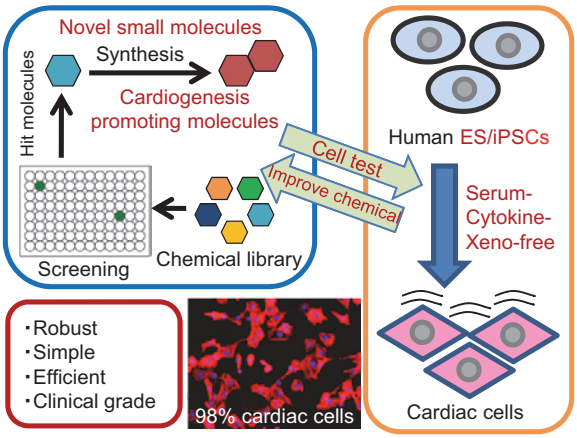
hESC-derived ALS models



Motor neuron-specific cell death



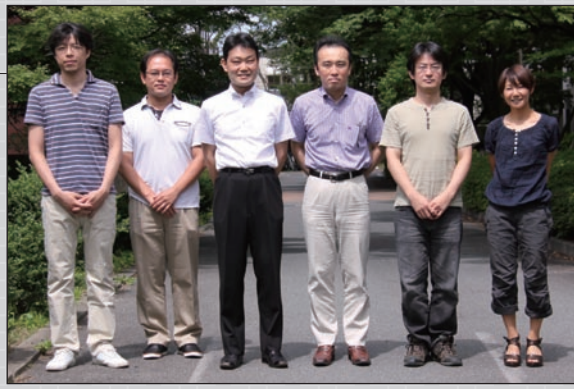
Abnormal ubiquitin inclusion formation



Small molecule-controlled cardiac differentiation

Mitinori Saitou Lab

Germ Cell Biology, Stem Cell Biology



Faculty Members
Mitinori Saitou (Professor)
Yoji Kojima (Assistant Professor)

Research Overview

The germ cell lineage ensures the creation of new individuals, thereby perpetuating and diversifying the genetic and epigenetic information across the generations. We have been investigating signaling, global transcription and epigenetic dynamics associated with germ cell specification and development in mice, and have proposed a concept that specification and development of **primordial germ cells (PGCs)**, precursors for the **spermatozoa** and the **oocytes**, involve an integration of three key events: repression of the somatic program, re-acquisition of potential pluripotency, and an ensuing genome-wide epigenetic reprogramming. Recently, using pluripotent stem cells [**embryonic stem cells (ESCs)** and **induced pluripotent stem cells (iPSCs)**], we have succeeded in precisely reconstituting the specification and development of PGCs in culture: ESCs/iPSCs are induced into epiblast-like cells (EpiLCs) and then into **PGC-like cells (PGCLCs)**, which contribute to sperm and oocytes with full developmental potential. This work will serve as a foundation for systems analysis of germ cell development, including the elucidation of key transcriptional network for germ cell development, the mechanism of genome-wide epigenetic reprogramming, and the mechanism of meiosis, as well as for the reconstitution of the entire germ-cell development process *in vitro*, not only in mice but also in other mammals, including humans.

Selected Papers

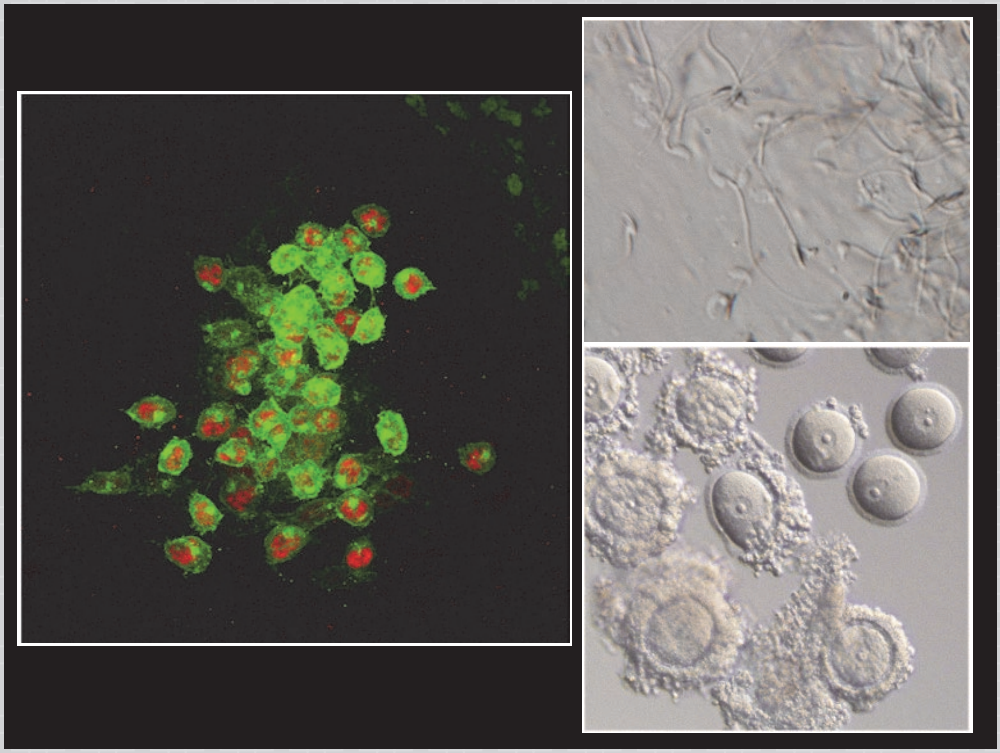
Yamaji, M., Ueda, J., Hayashi, K., Ohta, H., Yabuta, Y., Kurimoto, K., Nakato, R., Shirahige, K., and Saitou, M. PRDM14 ensures naïve pluripotency through dual regulation of signaling and epigenetic pathways in mouse embryonic stem cells. *Cell Stem Cell* **12**, 368-382 (2013).

Kagiwada, S., Kurimoto, K., Hirota, T., Yamaji, M., and Saitou, M. Replication-coupled passive DNA demethylation for the erasure of genome imprints in mice. *The EMBO Journal* **32**, 340-353 (2013).

Hayashi, K., Ogushi, S., Kurimoto, K., Shimamoto, S., Ohta, H., and Saitou, M. Offspring from oocytes derived from in vitro primordial germ cell-like cells in mice. *Science* **338**, 971-975 (2012).

Saitou, M., Kagiwada, S., and Kurimoto, K. Epigenetic reprogramming in mouse pre-implantation development and primordial germ cells. *Development* **139**, 15-31 (2012).

Hayashi, K., Ohta, H., Kurimoto, K., Aramaki, S., and Saitou, M. Reconstitution of the mouse germ cell specification pathway in culture by pluripotent stem cells. *Cell* **146**, 519-532 (2011).



(left) PGCs in mouse embryo at embryonic day 7.5. Green: Blimp1-mVenus, Red: AP2γ.
(right, top) Spermatozoa from PGCLCs from ESCs.
(right bottom) Oocytes from PGCLCs from ESCs.

Hiroshi Sugiyama Lab

Chemical Biology

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

Research Overview

The Sugiyama group's research interests involve the chemical biology of nucleic acids. Using the tools of organic synthesis and molecular biology, the Sugiyama group is defining the chemical principles underlying the recognition, reactivity, and structure of nucleic acids. The group utilizes a chemical approach in following areas: design of highly efficient sequence-specific DNA acting agents, design of unnatural nucleic acid for understanding of nucleic acid structure and function, design of DNA nanostructures for control and observation of the single molecular dynamic and single reaction, and development of a general method probing DNA local conformation in vivo. The 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 for cell biology. Using the 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, the research focuses on the following points: (1) Programmed assembly and functionalization of 2D and 3D DNA nanostructures; (2) Regulation of biomolecule reactions in designed nanostructures; (3) Biophysical analysis of the single molecule behavior in nanostructures. (4) Design and construction of controllable dynamic molecular system in nanostructures. Real-time AFM imaging system is employed for analysis of the single molecular dynamics and single reaction in the designed nano-space.

Selected Papers

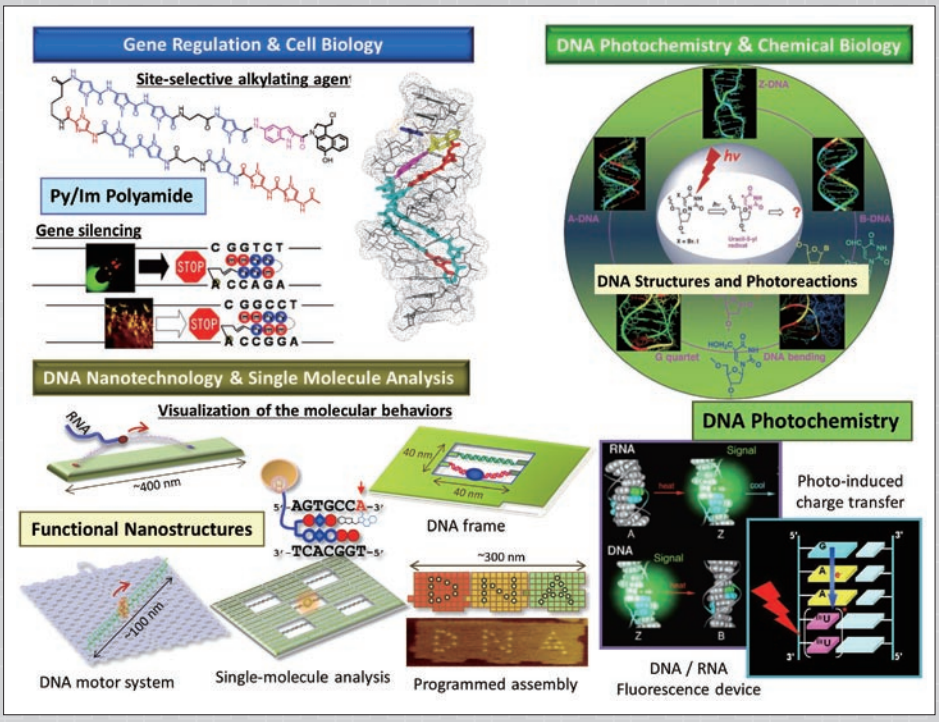
Endo, M., Yang, Y., Suzuki, Y., Hidaka, K., Sugiyama, H. Single-molecule observation of hybridization and dissociation of photoresponsive oligonucleotides and their reversible mechanical behavior in the designed DNA nanostructure. *Angew.Chem. Int. Ed.* **51**, 10518-10522 (2012).

Endo, M., Tatsumi, K., Terushima, K., Katsuda, Y., Hidaka, K., Harada, Y., Sugiyama, H. Direct Visualization of the Movement of a Single T7 RNA Polymerase and Transcription on a DNA Nanostructure. *Angew.Chem. Int. Ed.* **51**, 8778-8782 (2012).

Endo, M., Miyazaki, R., Emura, T., Hidaka, K., Sugiyama, H. Transcription Regulation System Mediated by Mechanical Operation of DNA Nanostructure. *J. Am. Chem. Soc.***134**, 2852-2855 (2012).

Wickham, S. F. J., Bath, J., Katsuda, Y., Endo, M., Hidaka, K., Sugiyama, H. Turberfield, A. J. A DNA-based molecular motor that can navigate a network of tracks. *Nat. Nanotechnol.* **7**, 169-173 (2012).

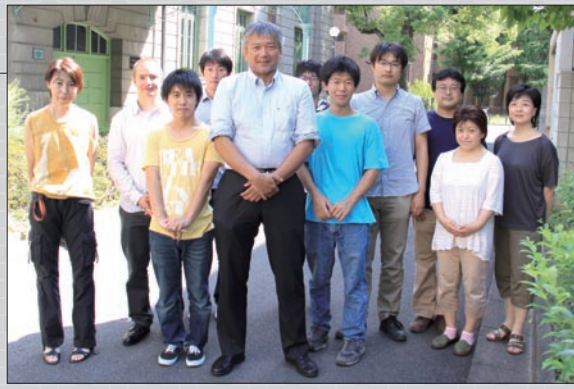
Wickham, S. F. J., Endo, M., Katsuda, Y. Hidaka, K. Bath, J., Sugiyama, H., Turberfield, A. J. Direct observation of stepwise movement of a synthetic molecular transporter. *Nat. Nanotechnol.* **6**, 166-169 (2011).



Koichiro Tanaka Lab

Teraherz Optical Science

Faculty Members
Koichiro Tanaka (Professor)
Hideki Hirori (Assistant Professor)



Research Overview

Terahertz (THz) wave, 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 (3mJ/pulse). This has allowed us to generate an intense THz wave over 1 MV/cm in the electric field with the repetition rate of 1 KHz. Recently, our group has been exploring **non-linear optical responses** of semiconductors and mesoscopic 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-wave, the microscope will work at video rates. Biological applications are now possible and will be conducted in collaboration with Kusumi, Kitagawa, and Kengaku groups.

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

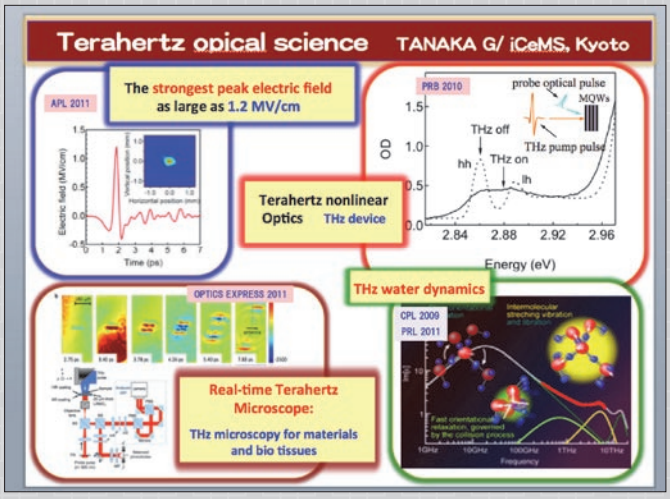
Tani, S., Blanchard, F., and Tanaka, K. Ultrafast Carrier Dynamics Under high electric field in grapheme. *Phys. Rev. Lett.* **109**, 166603 (2012).

Blanchard, F., Ooi, K., Tanaka, T., Doi, A., and Tanaka, K. Terahertz spectroscopy of the reactive and radiative near-field zones of split ring resonator. *Optics Express* **20**, 19395-19403 (2012).

Hishida, M., and Tanaka, K. Long-range hydration effect of lipid membrane studied by terahertz time-domain spectroscopy. *Phys. Rev. Lett.* **106**, 158102 (2011).

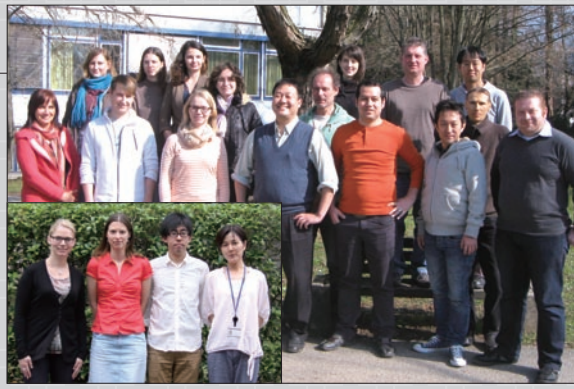
Hirori, H., Shinokita, K., Shirai, M., Tani, S., Kadoya, Y., and Tanaka, K. Extraordinary Carrier Multiplication Gated by a Picosecond Electric Field Pulse. *Nature Communications* **2**, 594 (2011).

Tanaka, K., Hirori, H., and Nagai, M. THz Nonlinear Spectroscopy of Solids. *IEEE Transactions on Terahertz Science and Technology* **1**, 301-312 (2011).



Motomu Tanaka Lab

Biological Physics, Interface Science, Non-Equilibrium Soft Matter



Faculty Members

Motomu Tanaka (Professor)

Fernanda Rossetti (Senior Lecturer)

Research Overview

The Tanaka Laboratory is cultivating a new research field "**Physics of Cells and Tissues**" by the combination of (1) **tailor-made biointerface models** (such as "supported membranes", Tanaka and Sackmann, Nature, 437, 656 (2005)) and (2) **quantitative physical tools** both in real space (e.g. live-cell imaging and analysis) and reciprocal space (advanced X-ray and neutron scattering, diffraction imaging).

One of our focuses in the iCeMS is to shed light on the **interfaces**, "*where cells meet materials*". The reactions at soft, biological interfaces cannot be described only as a sum of individual molecular elements, which has been a common strategy in the past decades. In order to deal with *dynamic, stochastic processes out of equilibrium*, such as **diseases and development**, we must consider the cooperativity and fluctuation in *mesoscopic reaction spaces*. Thus, the introduction of concepts in statistical physics is a powerful strategy to extract **spatio-temporal correlations**. In addition to the development of new "*in house*" physical techniques to quantify the strength of cell-material interactions, we intensively perform cutting-edge research at synchrotron and neutron facilities to gain hierarchical-structures at soft interfaces over different length scales.

Our laboratory is a highly interdisciplinary, international team that consists of people with training backgrounds in physics, chemistry, and biology. The principal investigator (Prof. Motomu Tanaka) has developed his scientific career in Europe (Germany), serving as a full professor in chemistry and physics at the University of Heidelberg. Within the framework of Japanese-German University Partnership Program (HeKKSaGOn Alliance), he got a cross-appointment as the "First HeKKSaGOn Professor" at Kyoto University since April 2013. Our global challenge is to establish a new scientific discipline in iCeMS through tight collaboration with our main lab in the University of Heidelberg (Germany) and many collaborating partners in Europe and Japan.

Selected Papers

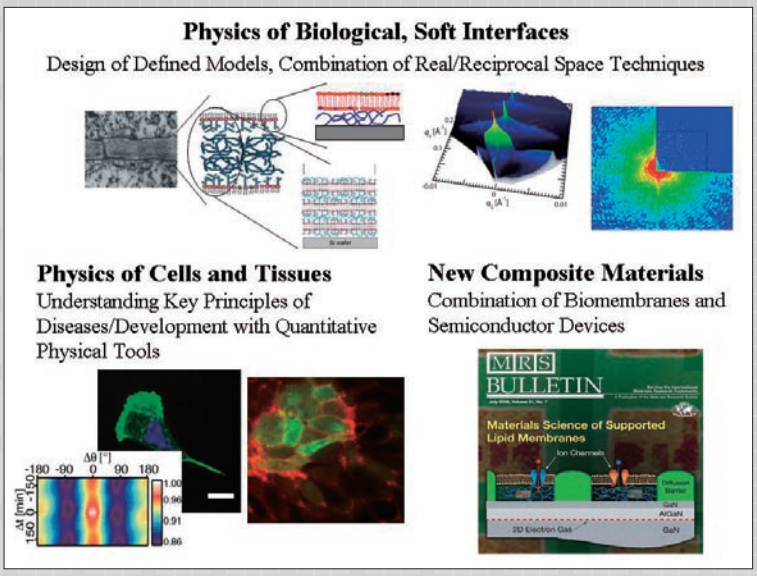
E. Schneck, T. Schubert, O.V. Konovalov, B.E. Quinn, T. Gutsmann, K. Brandenburg, R.G. Oliveira, D.A. Pink, M. Tanaka, Quantitative Determination of Ion Distributions in Bacterial Lipopolysaccharide Membranes by Grazing-Incidence X-ray Fluorescence. *Proc. Natl. Acad. Sci. USA* **107**, 9147 (2010).

R.G. Oliveira, E. Schneck, B.E. Quinn, O.V. Konovalov, K. Brandenburg, T. Gutsmann, T. Gill, C.B. Hanna, D.A. Pink, M. Tanaka, Crucial roles of charged saccharide moieties in survival of gram negative bacteria against protamine revealed by combination of grazing incidence x-ray structural characterizations and Monte Carlo simulations. *Phys. Rev. E.* **81**, 041901 (2010).

H. Y. Yoshikawa, F. F. Rossetti, S. Kaufmann, T. Kaindl, J. Madsen, U. Engel, A. L. Lewis, S. P. Armes, M. Tanaka, Quantitative Evaluation of Mechanosensing of Cells on Dynamically Tunable Hydrogels. *J. Am. Chem. Soc.* **133**, 1367 (2011).

T. Kaindl, H. Rieger, L. Kaschel, U. Engel, A. Schmaus, J. Sleeman, M. Tanaka, Spatio-Temporal Patterns of Pancreatic Cancer Cells Expressing CD44 Isoforms on Supported Membranes Displaying Hyaluronic Acid Oligomers Arrays. *PLoS One* **7**, e42911 (2012).

A. Koerner, C. Deichmann, F.F. Rossetti, A. Koehler, O. Konovalov, D. Wedlich, M. Tanaka, Cell Differentiation of Pluripotent Tissue Sheets Immobilized on Supported Membranes Displaying Cadherin-11. *PLoS One* **8**, e54749 (2013).



Kazumitsu Ueda Lab

Cellular Biochemistry

Faculty Members
Kazumitsu Ueda (Professor)
Atsushi Kodan (Assistant Professor)
Koh Nagata (Assistant Professor)

Research Overview

Humans are made of **materials**, such as amino acids, carbohydrates and lipids. These **materials** are absorbed and circulated in the body via transporter proteins. ABC (ATP-binding cassette) proteins are membrane proteins, which mainly transport various lipids. **ABC proteins** work in the forefront of the interaction between cells and lipophilic materials and also generate physiologically important materials in the body, such as "good cholesterol". 48 **ABC proteins** in humans play physiologically important roles and their functional defects can lead to a variety of pathological conditions, including cardiovascular diseases, respiratory failure of infants, skin diseases, neuronal diseases, senile blindness, diabetes, and gout. Our research on **ABC proteins** will establish the basis for **Cell-Material interactions** and 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. We are revealing the physiological roles of **ABC proteins** in pluripotent **ES and iPS cells**, and developing small-molecule fluorescent probes specific for **ES and iPS cells**. These compounds can be used to identify pluripotent E**S and iPS cells** and will be a useful tool for basic cell biology research and stem cell therapy. (In collaboration with the Nakatsuji, Yamanaka, and Uesugi Labs.)
2. We are revealing the **functional architectures** of **ABC proteins** using single molecule analysis and X-ray crystal structure analysis, which will facilitate our understanding of the mechanism of **Material** recognition by **ABC proteins**.
3. ABCA1 and ABCG1 are key molecules for generating plasma **meso-particle** high-density lipoprotein (HDL), which is so-called "good cholesterol" and critical for cholesterol homeostasis. Furthermore, it is suggested that they reorganize some **meso-domains** on the plasma membrane and modulate immune and inflammation responses. We succeeded for the first time in visualizing ABC proteins in function on the plasma membrane in collaboration with the Kusumi and Heuser Labs at the **CeMI** (Center for Meso-Bio Single-Molecule Imaging). We are revealing the mechanism of HDL formation, which is important to prevent atherosclerosis.
4. In collaboration with the Kengaku Lab and other Labs, we are revealing the role of **ABC proteins** in **meso-domain** formation in neuronal cells and other tissues, such as skin.
5. The microenvironment surrounding cells is a critical factor for determining the fate of cells, including proliferation and differentiation. We are elucidating the mechanism by which cells sense their microenvironment through associations made with the extracellular matrix, which ultimately determines their fate.

Selected Papers

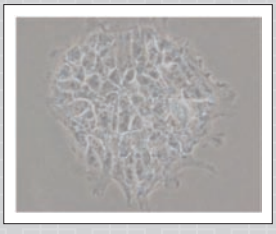
Nagata, K., O., Nakada, C.,, Kasai, R. S., Kusumi, A. and Ueda, K. ABCA1 dimer-monomer interconversion during HDL generation revealed by single-molecule imaging. *Proc. Natl. Acad. Sci. USA* (2013) in press.

Hirayama, H., Kimura, Y., Kioka, N., Matsuo, M. and Ueda, K. ATPase activity of human ABCG1 is stimulated by cholesterol and sphingomyelin. *J. Lipid Res.* **54**, 496-502 (2013).

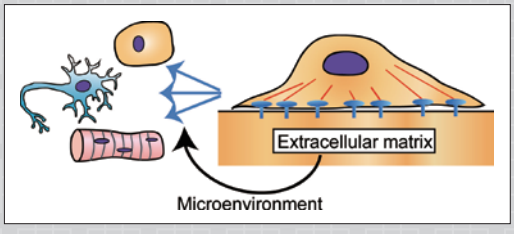
Ichikawa T, Matsuo M, Ueda K, and Kioka N. Role of Dlg5/lp-dlg, a Membrane-Associated Guanylate Kinase Family Protein, in Epithelial-Mesenchymal Transition in LLc-PK1 Renal Epithelial Cells. *PLoS One* **7**, e35519 (2012).

Nagao, K., Takahashi, K., Azuma, Y., Takada, M., Kimura, Y., Matsuo, M., Kioka, N. and Ueda, K. ATP hydrolysis-dependent conformational changes in the extracellular domain of ABCA1 are associated with apoA-I binding. *J. Lipid Res.* **53**, 126-136 (2012).

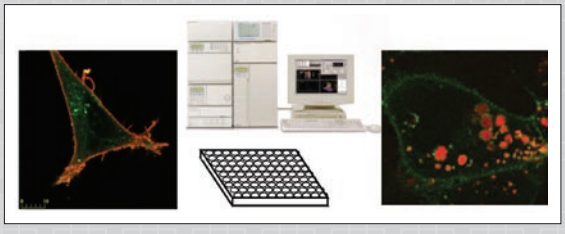
Hozoji-Inada, M., Munehira, Y., Nagao, K., Kioka, N., and Ueda, K. LXR directly interacts with ABCA1 to promote HDL formation during acute cholesterol accumulation. *J. Biol. Chem.* **286**, 20117-24 (2011).



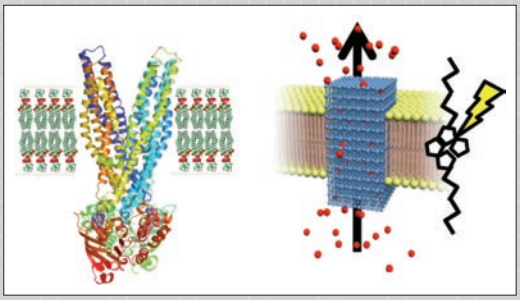
hES cells



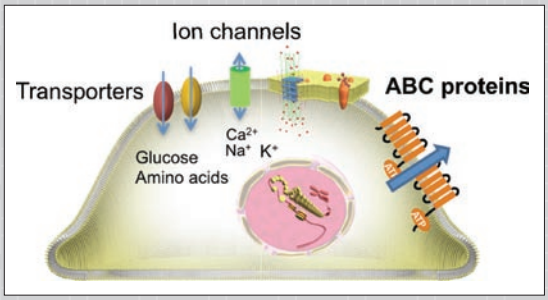
Microenvironment determines cell's fate



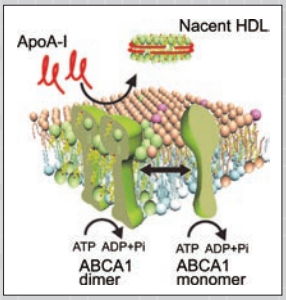
Development of activators and inhibitors of ABC proteins



Functional architectures



Transporters and channels



Mechanism of HDL formation by ABCA1

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 molecules 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 the ill-defined cell therapy.

Selected Papers

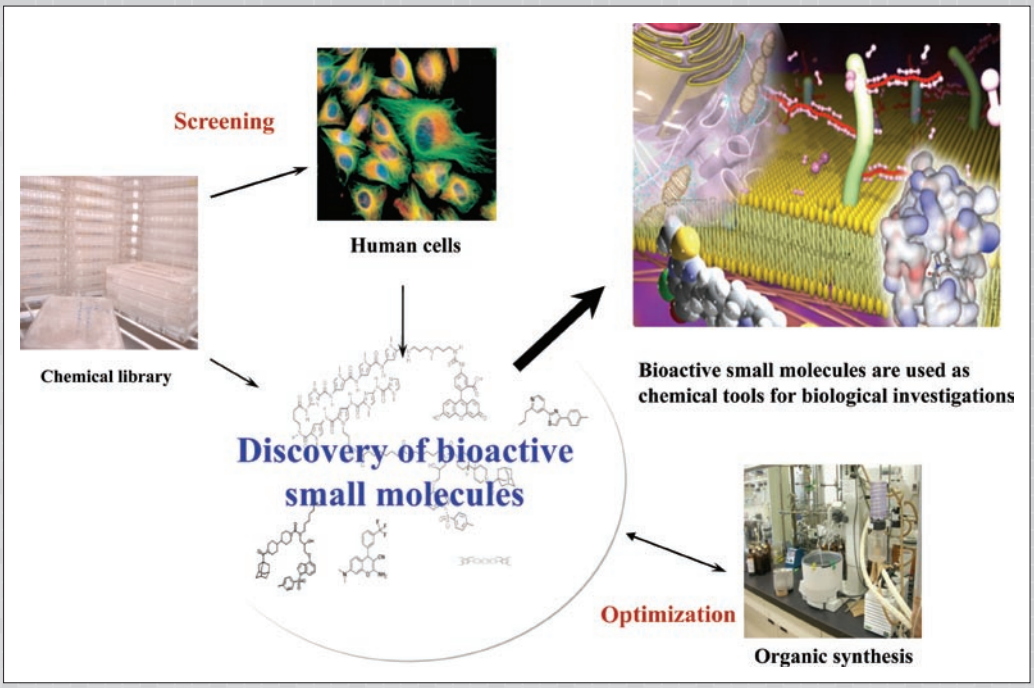
Kamisuki, S., Shirakawa, T., Kugimiya, A., Abu-Elheiga, L., Choo, H., Yamada, K., Shimogawa, H., Wakil, SJ., Uesugi, M. Synthesis and evaluation of diarylthiazole derivatives that inhibit activation of sterol regulatory element-binding proteins. *J. Med. Chem.* **54**, 4923-4927 (2011).

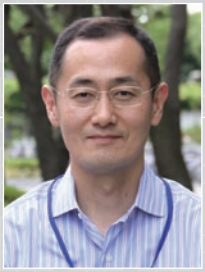
Kawazoe, Y., Shimogawa, H., Sato, A., Uesugi, M. A mitochondrial surface-specific fluorescent probe activated by bioconversion. *Angew. Chem. Int. Ed.* **50**, 5478-81 (2011).

Sato,S., Murata, A., Orihara, T., Shirakawa, T., Suenaga, K., Kigoshi, H., Uesugi, M. Marine natural product Aurilide activates the OPA1-mediated apoptosis by binding to prohibitin. *Chem. Biol.* **18**, 131-139 (2011).

Yamazoe, S., Shimogawa, H., Sato, S., Esko, J. D., Uesugi, M. A dumbbell-shaped small molecule that promotes cell adhesion and growth. *Chem. Biol.* **16**, 773-782 (2009).

Sato, S., Kwon, Y., Kamisuki, S., Srivastava, N., Mao, Q., Kawazoe, Y., 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)
Akitsu Hotta (Assistant Professor)
Akira Watanabe (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. However, it remains controversial whether iPS cells are distinguishable from 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 to achieve iPS cell-mediated cell transplantation therapy.

Using a drug-regulated transgenic mouse system, we are examining the role of iPS cell reprogramming factors in various somatic cells. Prematurely terminated reprogramming reverts cells back towards their original state, suggesting retention of an epigenetic memory. We are examining the chromatin changes induced by transcription factors leading to repression of key differentiation genes and stabilization of pluripotency. Understanding this mechanism may help to enhance reprogramming efficiencies and generate higher quality iPS cells. Also we have developed transposons as non-viral transgene delivery vectors for iPS cell reprogramming. Now, we are applying modifications of transposon technology to address genetic modification, gene discovery (functional annotation) and disease modeling in human iPS cells.

In order to apply iPS cells in a clinical setting, the risk of tumorigenesis from iPS cell-derived cells is to be eliminated. We are now trying to understand the mechanisms how tumor cells arise from iPS cell-derived cells to develop the safer methods of clinical application of iPS cells. We also expand the iPS cell research to understand the cancer biology, by applying the technology for inducing iPS cells to cancer cells in order to change the epigenetic status of cancer cells. Such epigenetically modified cancer cells may be useful to uncover the role of epigenetic control in cancer development.

Selected Papers

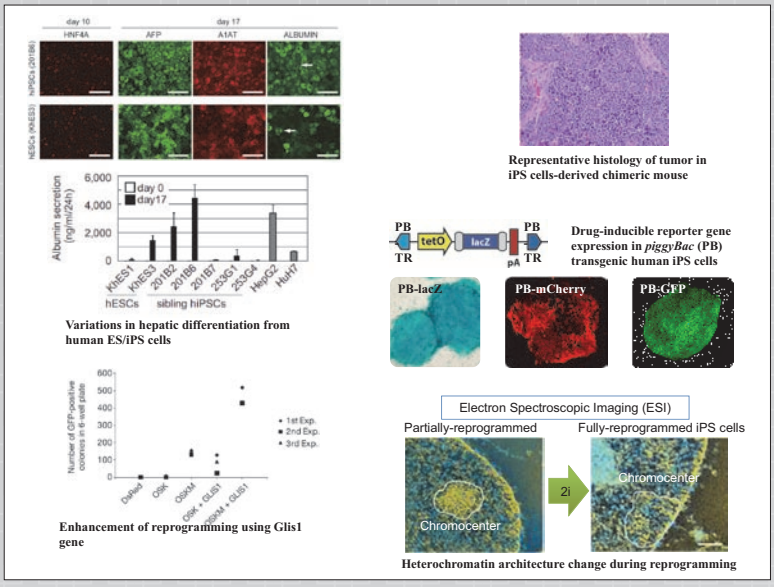
Okita K, Yamakawa T, Matsumura Y, Sato Y, Amano N, Watanabe A, Goshima N, Yamanaka S. *Stem Cells* **3**, 458-66 (2013).

Maekawa, M., Yamaguchi, K., Nakamura, T., Shibukawa, R., Kodanaka, I., Ichisaka, T., Kawamura, Y., Mochizuki, H., Goshima, N. and Yamanaka, S. Direct reprogramming of somatic cells is promoted by maternal transcription factor Glis1. *Nature* **474**, 225–229 (2011).

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).

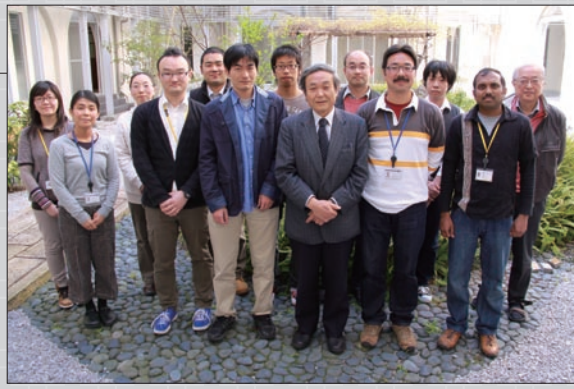
Hotta, A., Cheung, A.Y., Farra, N., Vijayaragavan, K., Seguin, C.A., Draper, J.S., Pasceri, P., Maksakova, I.A., Mager, D.L., Rossant, J., Bhatia, M. and Ellis, J. Isolation of human iPS cells using EOS lentiviral vectors to select for pluripotency. *Nat. Methods* **6**, 370–376 (2009).

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).



Mikio Takano Lab

Solid State Chemistry



Faculty Members

Mikio Takano (Professor)
Seiji Isoda (Visiting Professor)
Shinpei Yamamoto (Assistant Professor)
Naoaki Hayashi (Assistant Professor)

Research Overview

We are carrying out **solid state chemistry** (synthesis, structural analysis, and clarification of physical and chemical properties) on materials containing **3d transition metals** such as titanium (Ti), manganese (Mn), iron (Fe), and nickel (Ni). 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 their superior functionalities 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, $LiFePO_4$, $LiCoO_2$), etc. Using various artificial synthetic techniques, we recently succeeded in preparing $BaFeO_3$ which is the very first ferromagnetic iron oxide and also $BaTiO_{2.4}(H^-)_{0.6}$ which is the very first titanium oxide containing hydride ions. On the other hand, natural iron oxides produced by aquatic bacteria have attracted us very much. Their compositional, structural, and morphological features, which are somewhat beyond our imaginings, are suggestive of unique functionalities (collaboration with Prof. J. Takada's group, Okayama Univ.).

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 Chen and Harada 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 nano-sized particles of strong magnets like the iron metal (**α-Fe**) and an iron nitride, **$Fe_{16}N_2$**, coated with organic layers providing biocompatibility and bio-functionality (see Fig. 1). We note here that this nitride, being made of ubiquitously available elements only, is the most promising candidate for the next generation, resource conflict-free magnet.
2. **Analysis of composition, structure, and morphology**
   Functionality of a material essentially depends upon its chemical composition, arrangement of constituent atoms (structure) and morphology. While there are many tools to analyze them, electron microscopy is employed extensively for analyses of nano- to meso-scale materials developing in Takano group as well as in collaborative groups such as the Imahori, Hashida, and Kitagawa Labs. Studies are being conducted on magnetic nanoparticles, materials modified with light sensitive molecules or proteins, and also products of nano-space reactions.

Selected Papers

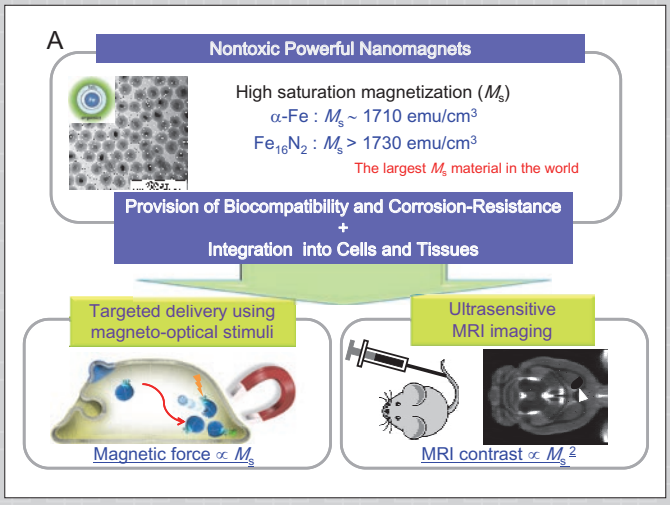
Kobayashi, Y., Hernandez, Olivier J., Sakaguchi, T., Yajima, T., Roisnel, T., Tsujimoto, Y., Morita, M., Noda, Y., Mogami, Y., Kitada, A., Ohkura, M., Hosokawa, S., Li, Z., Hayashi, K., Kusano, Y., Kim, J. e., Tsuji, N., Fujiwara, A., Matsushita, Y., Yoshimura, K., Takegoshi, K., Inoue, M., Takano, M., and Kageyama, H., An oxyhydride of $BaTiO_3$ exhibiting hydride exchange and electronic conductivity. *Nature Materials* **11**, 507-511 (2012).

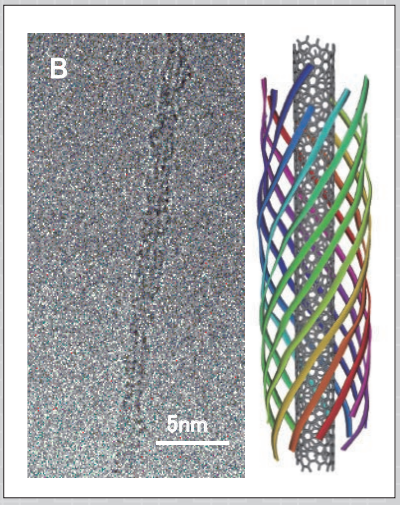
Hayashi, N., Yamamoto, T., Kageyama, H., Nishi, M., YWatanabe, Y., Kawakami, T., Matsushita, Y., Fujimori, A., and Takano, M., $BaFeO_3$: A Ferromagnetic Iron Oxide. *Angew. Chem. Int. Ed.* **43**, 12547-12550 (2011).

Yamada, I., Tsuchida, K., Ohgushi, K., Hayashi, N., Kim, J., Tsuji, N., Takahashi, R., Matsushita, M., Nishiyama, N., Inoue, T., Irifune, T., Kato, K., Takata, M., and Takano, M., Giant Negative Thermal Expansion in the Iron Perovskite $SrCu_3Fe_4O_{12}$. *Angew. Chem. Int. Ed.* **50**, 6579-6582 (2011).

Yamamoto, S., Gallage, R., Tamada, Y., Kohara, K., Kusano, Y., Sasano, T., Ohno, K., Tsujii, Y., Kageyama, H., Ono, T., and Takano, M., Transformation of Nano- to Mesosized Iron Oxide Cores to α-Fe within Organic Shells Preserved Intact. *Chem. Mater.* **23**, 1564-1569 (2011).

Kawakami, T., Tsujimoto, Y., Kageyama, H., Chen Xing-Qiu, 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. & Takano, M., Spin transition in a four-coordinate iron oxide. *Nature Chemistry* **1**, 371-376 (2009).





A: Nontoxic powerful nanomagnets prepared in our group, which are being employed for progressive applications such as spatiotemporally controlled intracellular release of physiologically active substances and ultrasensitive MRI imaging.

B: Real TEM image and a schematic model of a single-walled carbon nanotube (SWCNT) partially wrapped with peptide molecules. It is clearly seen that the peptide molecules are spirally adsorbed on the SWNT.

Easan Sivaniah

Polymer Science, Bionanotechnology

Faculty Members

Easan Sivaniah (Associate Professor)

Research Overview

The Sivaniah group manipulates materials with synthetic and biological approaches whilst seeking to establish a viable interface between the two.

In recent years we have delivered notable biomaterials research papers on intelligent scaffolds to interrogate the factors that influence cell migration. One example is well-defined scaffolds to determine the role of 3-D architectures on cell migration (*Biomaterials* **31**, 2201–2208, 2010). Another example is the controlled generation of spatially variant stiffness in 2D gels to interrogate cell mechanotaxis (*Advanced Materials* **24**, 6059–6064, 2012). Moreover our group studies the generation of bioplastics using bacterial and enzymatic tools.. Through such works, we will channel our experiences to develop practical principles that can support our vision of a grand challenge of generating industrially relevant processes via bionanotechnology.

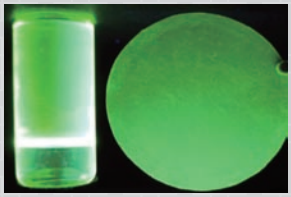
Although soft-matter bionanotechnology forms one key part of our research, our approach is to mix both synthetic and biosynthetic methods of materials development (with a current primary focus in achieving energy efficiency and environmental targets in separation technology). Examples include the report of a transformative platform technology for generating nanoporous materials (*Nature Materials* **11**, 53–57, 2012) and high performance microporous membranes for the separation of important environmental gases.

Selected Papers

Song, Q., Cao, C., Lu, L., Zavala-Rivera, P., Li, W., Shuai, Z., Cheetham A. K., Al-Muhtaseb S. A., Sivaniah E. Photo-oxidative enhancement of polymeric molecular sieve membranes. *Nat. Commun.* **4**, DOI:10.1038/ncomms 2942 (2013).

Sangiambut, S., Channon, K., Thomson, N., Sato, S., Tsuge, T., Doi, Y., Sivaniah, E. A robust route to enzymatically functional, hierarchically self-assembled peptide frameworks. *Adv. Mat.* **25**, 2661–2665 (2013).

Zavala-Rivera, P., K. Channon, V. Nyugen, Nataraj S. K., Kabra D., Friend R. H. and Al-Muhtaseb S. A., Hexemer, A., Calvo, M. E., Miguez, M., Sivaniah, E. Collective osmotic shock in ordered materials. *Nat. Mat.* **11**, 53–57 (2012).



Green light for green membrane technology

The photo shows fluorescence of solution (left) and membrane (right) made of a polymer of intrinsic microporosity (PIM-1) under irradiation of ultraviolet light. The ultraviolet irradiation induces oxidation and surface densification of the polymeric molecular sieve membranes. These highly permeable and selective membranes would make gas separation process more energy efficient and environmental friendly.

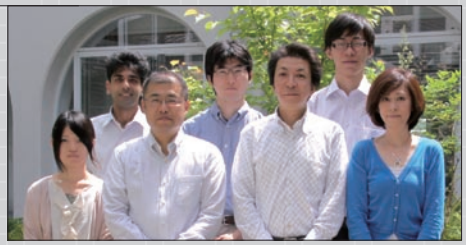
NCBS-inStem Satellite Lab Group

Kenichi Suzuki

Single molecule Cell Biophysics, Membrane Biology

Kouichi Hasegawa

Stem cell Biology, Developmental Biology



Faculty Members Kenichi G. N. Suzuki (Associate Professor) Kouichi Hasegawa (Senior Lecturer)

Research Overview

Our group's primary mission is to strengthen the international relationship among the iCeMS in Kyoto and the Tata Institute for Fundamental Research (TIFR), National Centre for Biological Sciences (NCBS) and the Institute for Stem Cell Biology and Regenerative Medicine (inStem) in Bangalore, India. This partnership includes not only research collaboration, but also joint symposia, researcher exchanges, and management of satellite facility and laboratories at both the iCeMS and at NCBS-inStem.

Our research is focused on **understanding how signal transductions regulate cell proliferation, migration, differentiation, and functions**. We are pursuing this primary goal using a variety of biological processes and samples including many types of cultured cells (such as human ES/iPS cells) as well as using laboratory mice. We are also employing various conventional and advanced tools in biophysics, chemistry, single molecule imaging, developmental biology, and cell and molecular biology. Our main projects are listed below:

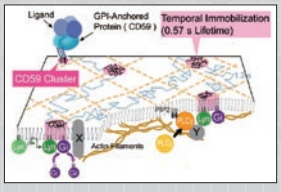
1. **Understanding dynamic mechanisms in cellular systems** using high-resolution and multicolor **single molecule imaging** of receptors and signaling molecules in living cells (Suzuki)
2. **Elucidation of molecular mechanisms in cell plasma membranes** using **single molecule imaging** with high temporal resolution (Suzuki)
3. Understanding how **signaling cascades regulate the pluripotent transcriptional network** and epigenetic reprogramming (Hasegawa)
4. Investigating **molecular mechanisms involved in cell fate determination** in early embryonic development and pluripotent stem cell differentiation (Hasegawa)

Selected Papers

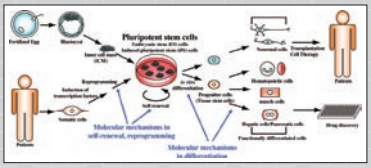
Suzuki, K.G.N., Kasai, R.S., Hirosawa, K.M., Nemoto, Y.L. Ishibashi, M., Miwa, Y., Fujiwara, T.K. and Kusumi, A. Transient GPI-anchored protein homodimers are units for raft organization and function. *Nature Chem. Biol.* **8**, 774-783 (2012).

Hasegawa, K., Yasuda, S., Teo, J.L., Nguyen, C., McMillan, M., Hsieh, C.L., Suemori, H., Nakatsuji, N., Yamamoto, M., Miyabayashi, T., Lutzko, C., Pera, M.F. and Kahn, M. Wnt signaling orchestration with a small molecule DYRK inhibitor provides long-term xeno-free human pluripotent cell expansion. *Stem Cells Translational Medicine* **1**, 18-28 (2012).

Tanaka, K.A.K*, Suzuki, K.G.N* (*equal contribution), Shirai, Y.M., Shibutani, S.T., Miyahara, M. S., Tsuboi, H., Yahara, M., Yoshimura, A., Mayor, S., Fujiwara, T.K. and Kusumi, A. Membrane molecules mobile even after chemical fixation. *Nature Methods* **7**, 865-866 (2010).



Single molecule observation enabled us to propose a working model showing how liganded CD59 clusters may function as a transient platform to transduce the extracellular signal to the intracellular signal.



Research objective in regenerative medicine

Shintaro Sengoku (Innovation Management Group)

Management of Science and Technology

Faculty Members

Shintaro Sengoku (Associate Professor)

Research Overview

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

The Innovation Management Group (IMG) **explores a novel managerial model which aims to achieve true innovation** by exploring and developing three research domains:

1. **Organisation dynamics in scientific interdisciplinary research** for organisational development, human resource management and strategic management
2. **Integrative innovation management research, human resources development, and support for commercialisation in the stem cell science and technology sphere** (funded by CSTP-JSPS NEXT Program, FY2010-2013)
3. **Innovative collaboration systems across the academic, private and public sectors and practice** (in collaboration with Kyoto SMI, a satellite non-profit organisation)

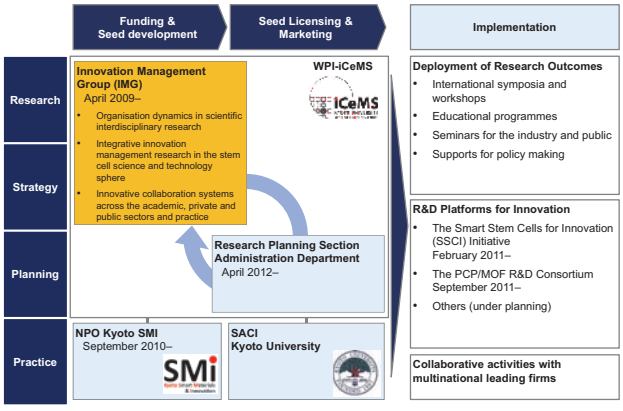
Selected Papers

Sengoku, S., Sumikura, K., Oki, T., Nakatsuji, N. Redefining the Concept of Standardization for Pluripotent Stem Cells. *Stem Cell Reviews and Reports* **7**, 221-226 (2011).

Anzai, T., Kusama, R., Kodama, H., Sengoku, S. Holistic observation and monitoring of the impact of interdisciplinary academic research projects: An empirical assessment in Japan. *Technovation* **32**, 345-57 (2012).

Kodama, H., Watatani, K., Sengoku, S. Competency-based Assessment of Academic Interdisciplinary Research and Implication to University Management, *Research Evaluation* **22**, 93-104 (2013).

The Overview of Activities at IMG

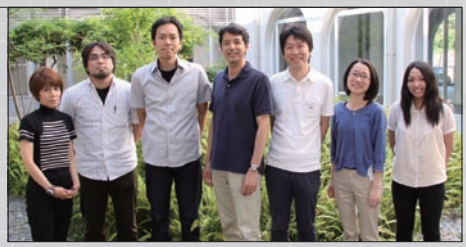


Kazuto Kato (Science Communication Group)

Science Communication

Faculty Members

Kazuto Kato (Professor) Kei Kano (Senior Lecturer)



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. Since the Great East Japan Earthquake on 11 March, 2011, the influence of science communities on society has received attention, on the contrary, the influence of society on science communities has been growing.

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 dialogue skills** in a bid to build stronger mutual relations among researchers in different fields and between scientific communities, public, and policy makers. We also conduct research and development on "Science of Science, Technology and Innovation Policy".

Selected Papers

Mizumachi, E., Matsuda, K., Kano, K., Kawakami, M., and Kato, K. Scientists' attitudes toward a dialogue with the public: a study using "science cafes", *J. Science Communication* **10**, A02 (2011).

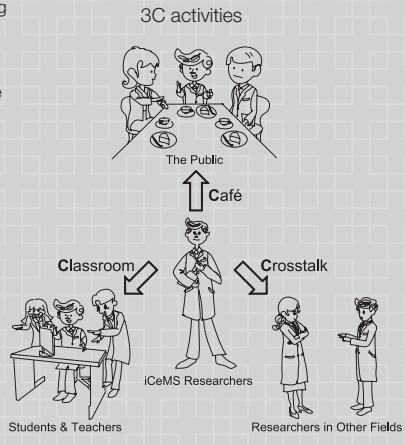
Kato, K., Kano, K. and Shirai, T. Science Communication: Significance for Genome-Based Personalized Medicine – A View from the Asia-Pacific. *Curr. Pharmacogenomics Pers. Med.* **8**, 92-96 (2010).

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).

Cafés: As in "science cafés". Young iCeMS researchers engage in conversations with the public over tea and coffee in a relaxed, friendly atmosphere. The science cafés are designed to improve young researchers in dialogue skills.

Crosstalks: "How to challenge a new field?" "How should we collaborate with researchers in different fields or policy makers?" A young researcher of the iCeMS speaks with experts in various disciplines on their thoughts about research and science.

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



Peter Carlton

Meiosis, Chromosome Biology, Superresolution Optical Microscopy

Faculty Members

Peter Mark 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 homology, 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 apply advanced optical microscopy to questions of nuclear organization in pluripotent stem cells, meiosis in mammalian systems, and neural development.

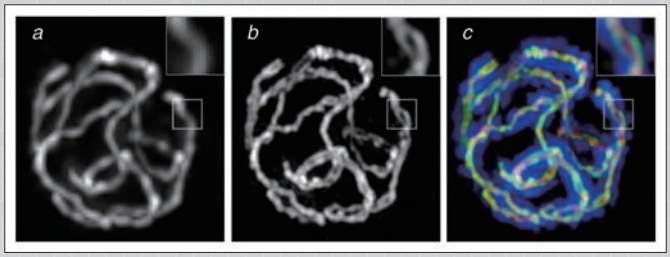
Selected Papers

Zhang W., Miley N., Zastrow M. S., Macqueen A. J., Sato A., Nabeshima K., Martinez-Perez E., Mlynarczyk-Evans S., Carlton P. M., Villeneuve A. M. HAL-2 promotes homologous pairing during Caenorhabditis elegans meiosis by antagonizing inhibitory effects of synaptonemal complex precursors. *PLOS Genet.* **8**, e1002880 (2012).

Carlton P. M., Boulanger J., Kervrann C., Sibarita J. B., Salamero J., Gordon-Messer S., Bressan D., Haber J. E., Haase S., Shao L., Winoto L., Matsuda A., Kner P., Uzawa S., Gustafsson M., Kam Z., Agard D. A., Sedat J. W. Fast live simultaneous multiwavelength four-dimensional optical microscopy. *Proc. Natl. Acad. Sci. USA* **107**, 16016-22 (2010).

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).

*co-first authors

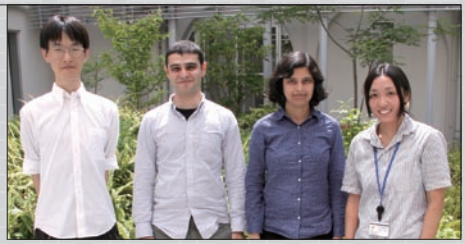


3D-SIM superresolution imaging reveals the dual-axis nature of the meiotic synaptonemal complex.

a, Conventional deconvolution image of a C. elegans meiotic nucleus immunostained for axis component HTP-3; axes appear as single strands due to their separation (c. 150nm) being smaller than the diffraction limit. ***b***, reconstructed 3D-SIM image, displaying the separation between strands. ***c***, combined 3D-SIM image of HTP-3 (green), DNA stained with DAPI (blue), and SC central element SYP-1 (red).

Ziya Kalay

Statistical Physics, Quantitative Biology



Faculty Members

Ziya Kalay (Assistant Professor / iCeMS Kyoto Fellow)

Research Overview

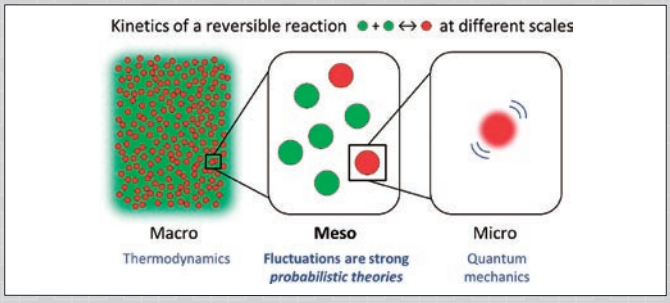
Although science has made remarkable progress in observing and predicting phenomena at the level of a single isolated molecule and a collection of Avogadro's number of molecules, our understanding of the intermediate, **mesoscopic systems** is disproportionately underdeveloped. The main reason for this is that mesoscopic systems usually have a small number of components and are strongly coupled to their noisy environment, making their behavior **stochastic**. Remarkably, most of the components of a biological cell are mesoscopic systems, as the number of functional molecules such as proteins and the size of functional complexes like organelles are small, and fluctuate. Our group is interested in developing a **quantitative understanding** of biological processes at the subcellular level by collaborating with experimental biophysicists and cell biologists at iCeMS. Our background is in theoretical physics and we use/develop statistical mechanics to study the physics of molecular interactions and **chemical reactions** at the mesoscale. We focus on the **effects of a complex environment** and intrinsic/extrinsic **fluctuations**, which are both relevant in cell biology. Some of the specific questions that we have been addressing are: How does the hierarchical organization of the plasma membrane affect **dimerization kinetics** of membrane molecules and downstream signaling? How does the stochastic binding kinetics of transcription factors affect the temporal pattern of mRNA synthesis?

Selected Papers

Kalay Z., Fujiwara T. K. and Kusumi A. Confining domains lead to reaction bursts: reaction kinetics in the plasma membrane. *PLoS ONE* **7**, e32948 (2012).

Kalay, Z. Reaction kinetics in the plasma membrane. *Biotechnology Journal* **7**, 745–752 (2012).

Kalay, Z. Fundamental and functional aspects of mesoscopic architectures with examples in physics, cell biology, and chemistry. *Critical Reviews in Biochemistry and Molecular Biology* **46**, 310–326 (2011).

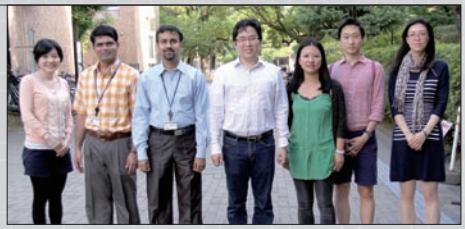


Franklin Kim

Synthetic Nano-/Meso-Chemistry, Self-Assembly

Faculty Members

Franklin Kim (Assistant Professor / iCeMS Kyoto Fellow)



Research Overview

Our group is interested in using various **nanomaterials as building blocks** for **constructing novel functional nano/mesoscale structures**, either through chemical synthesis or self-assembly. We focus on developing strategies which will allow precise control over the property of the produced structures, with emphasis in applications for cell-biological studies. Not only are we interested in using such materials for applications such as sensing and drug delivery, but also in gaining fundamental understanding on how they interact within the biological system in the molecular level. The multidisciplinary and strong collaborative environment of iCeMS makes it an excellent place to pursue such research that intersects materials science and biology.

We are currently exploring the following topics.

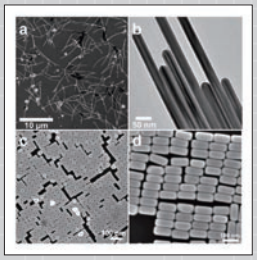
1. **Gold nanoparticles & nanowires**
   Due to their strong optical responses and biocompatibility, gold nanoparticles are used in a wide range of biological studies. Through precise control over the particle morphology and surface modification, we aim to develop structures that can be used for bio-sensing and therapeutics.
2. **Graphene-based composites**
   Graphene has gained much recent interest due to their high surface area, impressive electrical and mechanical properties, and chemical stability. We aim to utilize these sheets as a substrate for loading functional materials such as biomolecules and nanoparticles, which can then be integrated into cells.
3. **Self-assembly using Langmuir-Blodgett technique**
   Langmuir-Blodgett is a powerful method for preparing well-controlled two-dimensional assembly of nanoscale building blocks. Through assembly of biomolecules such as DNA, we plan to develop platforms for studying cell growth and proliferation.

Selected Papers

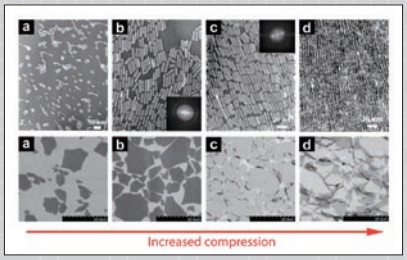
Zou, J., Kim, F. Self-assembly of two-dimensional nanosheets induced by interfacial polyionic complexation. *ACS Nano* **6**, 10606 (2012).

Tsotsalas, M., Umemura, A., Kim, F., Sakata, Y., Reboul, J., Kitagawa, S., Furukawa, S., Crystal morphology-directed framework orientation in porous coordination polymer films and freestanding membranes via Langmuir–Blodgettry. *J. Mater. Chem.* **22**, 10159 (2012).

Kim, F., Cote, L., and Huang, J. Graphene oxide: surface activity and two-dimensional assembly. *Adv. Mater.* **22**, 1954 (2010).



Shape controlled synthesis of gold nanoparticles (a and b: nanowire, c: nanocube, d: square cuboid)



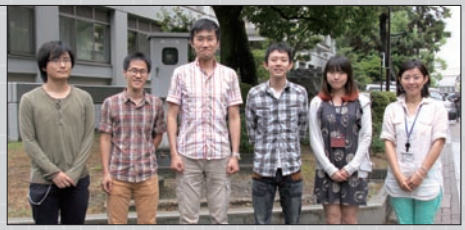
Two-dimensional (2D) assemblies of nanoscale building blocks prepared by Langmuir-Blodgett technique (top: $BaCrO_3$ nanorods, bottom: graphene oxide nanosheets)

Tatsuya Murakami

Protein Engineering, Cell Engineering

Faculty Members

Tatsuya Murakami (Assistant Professor / iCeMS Kyoto Fellow)



Research Overview

The Murakami group is aiming at developing novel cell engineering technologies for therapy and drug delivery systems against intractable diseases by **external stimuli–responsive nanomaterials**. In both cases, how the nanomaterials are delivered to a specific site of interest is one of the most important challenges. This is because their output, e.g., heat, can be cytotoxic and cause adverse effects on our body unless spatially controlled. Furthermore, such nanomaterials themselves must be stable under physiological conditions and biocompatible. We are trying to overcome these challenges with **naturally occurring nanomaterials in our body** for biocompatible carriers / dispersants. In particular, the biocompatible nanomaterials are genetically and chemically engineered so that external stimuli–responsive nanomaterials are easily incorporated into them and targeted to a specific site *in vitro* and *in vivo*.
The followings are ongoing cross–disciplinary research projects in collaboration with several domestic and international labs.

1. Development of surface biocompatibilization and functionalization technologies for external stimuli–responsive nanomaterials
2. Precise localization of photoreactive nanomaterials in cells and photoregulation of cell functions
3. Precise localization of photreactive nanomaterials in our body and phototherapy against intractable diseases
4. Development of ***in vivo*** **gene carrier systems** with naturally occurring nanomaterials

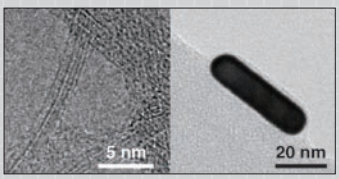
Selected Papers

Murakami, T., Nakatsuji, H., Inada, M., Matoba, Y., Umeyama, T., Tsujimoto, M., Isoda, S., Hashida, M., Imahori, H. Photodynamic and photothermal effects of semiconducting and metallic-enriched single-walled carbon nanotubes. *J. Am. Chem. Soc.* **134**, 17862-17865 (2012).

Kasai, H., Murakami, T., Ikuta, Y., Koseki, Y., Baba, K., Oikawa, H., Nakanishi, H., Okada, M., Shoji, M., Ueda, M., Imahori, H., Hashida, M. Creation of pure nanodrugs and their anticancer properties. *Angew. Chem. Int. Ed.* **51**, 10315-10318 (2012).

Numata, T., Murakami, T., Kawashima, F., Morone, N., Heuser, J. E., Takano, Y., Ohkubo, K., Fukuzumi, S., Mori, Y., Imahori, H. Utilization of photoinduced charge-separated state of donor-acceptor-linked molecules for regulation of cell membrane potential and ion transport. *J. Am. Chem. Soc.* **134**, 6092-6095 (2012).

1



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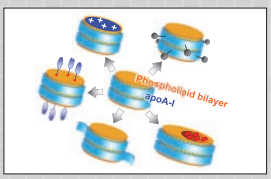


1. Electron microscopy images of photoresponsive nanomaterials. Carbon nanotubes (left) and gold nanorods (right).
2. Schematic illustration of HDL and its engineering: The protein moiety, apoA-I, offers suitable sites for chemical modification, and can also be genetically fused with functional peptides and proteins. The surface charge of the lipid bilayer is controllable by using anionic and cationic lipids, and functional molecules with a hydrophobic domain are membrane-anchored. A phospholipid nanodisc reveals various hydrodynamic diameters dependent on the amount of the drug incorporated.

Dan Ohtan Wang

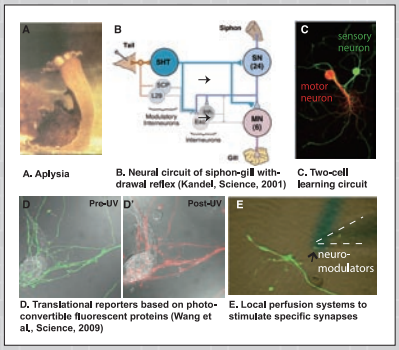
Neuroscience, RNA Biology, Photochemistry

Faculty Members

Dan Ohtan Wang (Assistant Professor / iCeMS Kyoto Fellow)

Research Overview

Our group studies the molecular and cell biological mechanisms of learning-related **neuronal plasticity**, a process in which the strength and number of synaptic connections between neurons are altered by experience. Such structural and functional changes in our brain occur in an activity-dependent manner and are **mediated by highly orchestrated gene networks**. We are particularly interested in understanding how gene expression in the neural circuits is regulated in **space and time** during long-term neuronal plasticity, a critical molecular aspect of the formation and storage of lasting memories. To detect changes in gene expression in situ with high spatiotemporal resolution, we are developing imaging methods to sensitively and quantitatively study **RNA dynamics** in living cells by exploiting gene-specific hybridization-sensitive fluorescent probes.



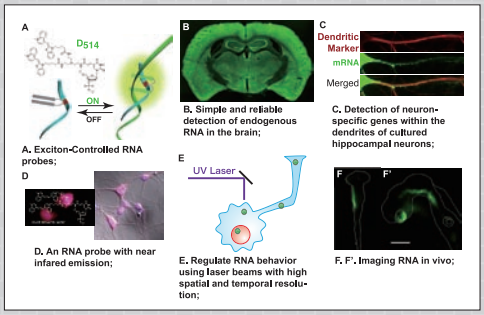
Imaging local protein synthesis at sensory-motor neuron synapses in Aplysia

Selected Papers

Wang DO*, Hitomi Matsuno, Shuji Ikeda, Hiroyuki Yanagisawa, Yasunori Hayashi, and Akimitsu Okamoto*. A quick and simple FISH protocol with hybridization-sensitive fluorescent linear oligodeoxynucleotide probes. *RNA* **18**, 166-75 (2012).

Wang DO, Martin KC, and Zukin RS. Spatially restricting gene expression by local translation at synapses. *Trends Neurosci.* **33**, 173-82 (2010).

Wang DO, Kim SM, Zhao Y, Hwang HG, Miura SK, Sossin WS, and Martin KC. Synapse- and stimulus-specific local translation during long-term neuronal plasticity. *Science* **324**, 1536-40 (2009).



Visualizing endogenous RNA in highly sensitive and quantitative manner in living neuronal circuits.

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.

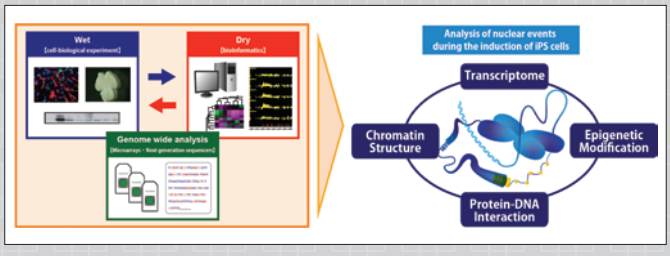
2. By using next generation sequencers, we will perform **genome-wide analysis of epigenetic modifications, chromatin structures, and protein-DNA interaction** to shed light on the regulatory mechanisms in the nuclei of pluripotent stem cells.

Selected Papers

Matsumura, S., Hamasaki, M., Yamamoto, T., Ebisuya, M., Sato, M., Nishida, E., and Toyoshima, F. ABL1 regulates spindle orientation in adherent cells and mammalian skin. *Nature Communications* **3**, 626 (2012).

Sunadome, K., Yamamoto, T., Ebisuya, M., Kondoh, K., Sehara-Fujisawa, A., and Nishida, E. ERK5 Regulates Muscle Cell Fusion through Klf Transcription Factors. *Dev. Cell* **20**, 192-205 (2011).

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).

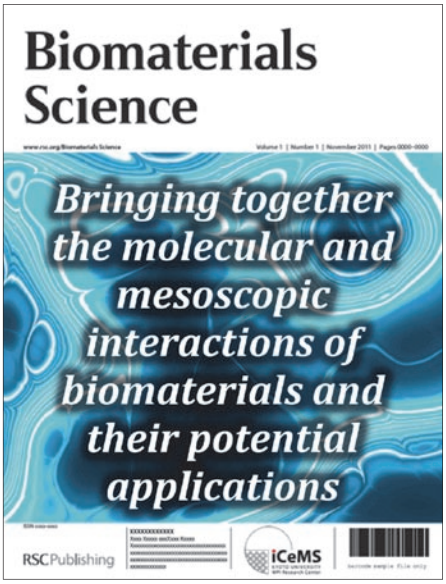


Research on the elucidation of iPS cell induction by comprehensive genome-wide analysis

RSC-iCeMS New Journal *Biomaterials Science*

In January 2013 the Royal Society of Chemistry (RSC) published the first issue of *Biomaterials Science*, a new multi-disciplinary journal launched in collaboration with iCeMS. Its founding director Norio Nakatsuji and Prof. Hiroshi Sugiyama serve as co-editor-in-chief and associate editor respectively. The broad scope of the journal ranges from the fundamental science of biomaterials to their biomedical applications. Main research areas include (but are not limited to):

- Mesoscopic science of cells and materials
- Molecular design of biomaterials
- Materials for nanomedicine and drug delivery systems
- Materials for stem cell research
- Tissue engineering and regenerative medicine
- Nanomaterials at the biointerface
- Biologically inspired and biomimetic materials
- Interfacial phenomena in biomineralization



www.rsc.org/biomaterialsscience

Collaboration with CiRA

In November 2007 Prof. Shinya Yamanaka, an iCeMS principal investigator (PI), reported that his team had successfully generated induced pluripotent stem cells (iPS cells) from human skin cells. In January 2008 then iCeMS Director Norio Nakatsuji appointed Prof. Yamanaka as founding director of the Center for iPS Cell Research and Application (CiRA), which was established under the auspices of iCeMS in order to advance iPS cell research. In April 2010 Kyoto University re-established CiRA as a full-fledged university research institute, with Prof. Yamanaka as its founding director.

Since that time, both institutes have continued to collaborate closely as sister institutes, with iCeMS aiming to integrate the cell and material sciences, contributing to the advancement of stem cell research such as with ES and iPS cells, and CiRA continuing its pioneering work in the areas of regenerative medicine and drug discovery using iPS cells.

CiRA

www.cira.kyoto-u.ac.jp

Yamanaka Wins Nobel Prize

Prof. Shinya Yamanaka, CiRA director and iCeMS PI, and Prof. Sir John Gurdon of the University of Cambridge shared the Nobel Prize in Physiology or Medicine 2012 for their discovery that mature cells can be reprogrammed to become pluripotent.

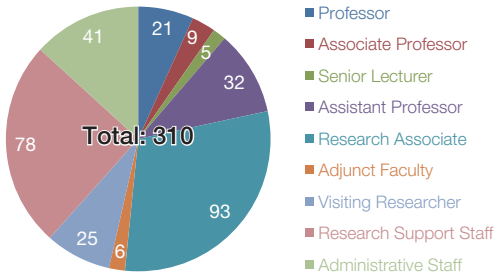
Sir John Gurdon (left) speaking at an iCeMS Seminar with Prof. Shinya Yamanaka (right) in the audience (November 2010, iCeMS)

Honors and Awards

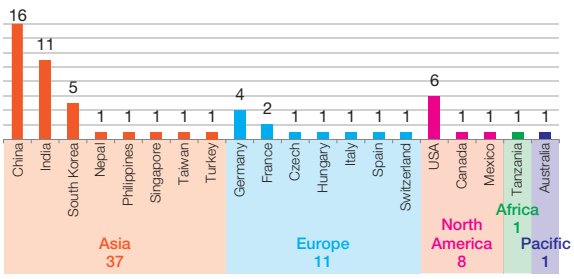
Month/Year	Award/Prize	Awardees
May 2013	RSC de Gennes Prize	Susumu Kitagawa
Jan 2013	Quadrant Award First Prize	Nobuhiro Yanai
Nov 2012	Order of Culture	Shinya Yamanaka
Nov 2012	Life-time Achievement Award (Journal of Drug Targeting)	Mitsuru Hashida
Oct 2012	Nobel Prize in Physiology or Medicine	Shinya Yamanaka
Oct 2012	The 7th Young Scientist Award of the Physical Society of Japan	Hideki Hirori
Aug 2012	Poster Award Grand Prize (Information Education Symposium 2012)	Yoshitaka Morimura, Kei Kano, Eri Mizumachi
Mar 2012	Japan Society for Bioscience, Biotechnology, and Agrochemistry Award	Hiromune Ando
Jan 2012	Japanese Society of Carbohydrate Research Annual Meeting Poster Award	Naoko Komura
Dec 2011	Wakayama Prefecture Culture Award	Norio Nakatsuji
Nov 2011	AAAS Days of Molecular Medicine Young Investigator Award	Ganesh N. Pandian
Nov 2011	Kyoto Newspaper Grand Prize	Susumu Kitagawa
Oct 2011	Member of the Science Council of Japan	Susumu Kitagawa
Aug 2011	Best Lecture Award for the 4th Chemical Society of Japan Kanto Competition	Yuta Takano
Jun 2011	Medal of Honor with Purple Ribbon 2011	Susumu Kitagawa
May 2011	Member of National Academy of Sciences	John Heuser, Shinya Yamanaka
Mar 2011	German Innovation Award Gottfried Wagener Prize (1st Prize)	Motonari Uesugi
Mar 2011	Hot Topics Award at Annual Meeting of Japan Society for Bioscience, Biotechnology, and Agrochemistry 2011	Koh Nagata
Feb 2011	Wolf Foundation Prize in Medicine	Shinya Yamanaka
Sep 2010	2010 Thomson Reuters Citation Laureates	Susumu Kitagawa, Shinya Yamanaka
Jun 2010	2010 Kyoto Prize in Advanced Technology	Shinya Yamanaka
Mar 2010	Imperial and Japan Academy Prizes	Shinya Yamanaka
Mar 2010	ABC2010 Young Investigator Award	Koh Nagata
Mar 2010	Japan Bioscience, Biotechnology and Agrochemistry Society Award	Kazumitsu Ueda
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
Apr 2009	Canada Gairdner International Award	Shinya Yamanaka
Mar 2009	The Chemical Society of Japan Lectureship Award	Shuhei Furukawa
Jan 2009	The Chemical Society of Japan Award	Susumu Kitagawa
Jul 2008	Incentive Award for Young Scientist, Tokai branch of The Society of Synthetic Organic Chemistry, Japan, 2008	Hiromune Ando
Apr 2008	Young Scientists' Prize for Science and Technology by the Japanese Minister of Education, Culture, Sports, Science and Technology	Takafumi Ueno
Apr 2008	Humboldt Research Award	Susumu Kitagawa
Feb 2008	Robert Koch Prize 2008	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	The 25th Osaka Science Prize	Hiroshi Imahori
Nov 2007	American Association of Pharmaceutical Scientists, Research Achievement Award in Pharmaceutics and Drug Delivery	Mitsuru Hashida

Facts and Figures

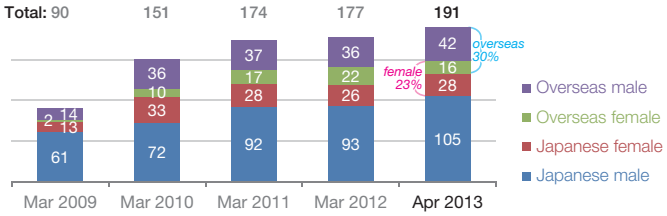
All staff (April 2013)



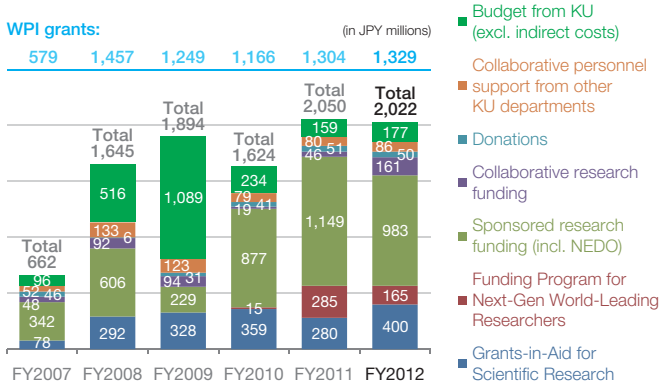
Researchers from overseas (April 2013)



Researchers (April 2013)



Finance (March 2012)



Center for Meso-Bio Single-Molecule Imaging

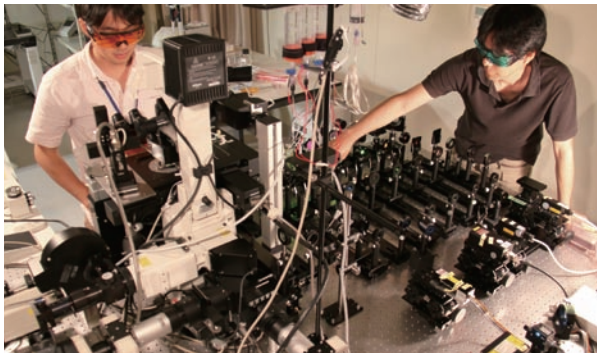
Director Yoshie Harada | **Deputy Director** Takahiro Fujiwara

CeMI iCeMS Imaging Center

www.cemi.icems.kyoto-u.ac.jp

The CeMI was established on March 3, 2009, as the iCeMS' imaging innovation center for **cellular mesoscopic science**. Its key missions are: 1) 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 2) make these technologies available quickly to the scientific community worldwide for the further advancement of cellular mesoscopic 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); a terahertz near-field microscope with the world's fastest image acquisition rate (500Hz) and highest spatial resolution (λ/30); and other

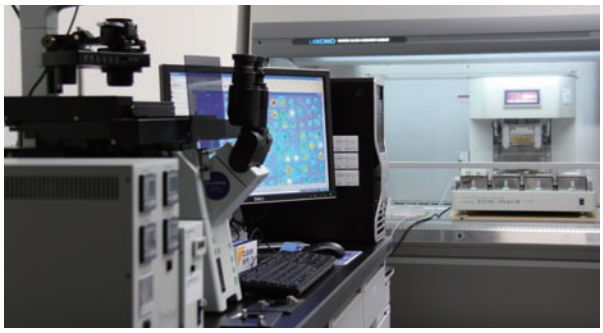


advanced, commercial confocal/time- lapse fluorescence microscopes. The center will also hold symposia, seminars, workshops, and hands-on training sessions, open to the scientific community worldwide.

Industry Partners (alphabetical order): Carl Zeiss Microscopy Co., Ltd., Hamamatsu Photonics K.K., JEOL Ltd., Leica Microsystems K.K., Nikon Instech Co., Ltd., Nikon Instruments Co., Ltd., Olympus Corp., Photron Ltd.

iCeMS Chemical Screening Center

Including an automated screening system, cell culture equipment, and a chemical library of up to 70,000 compounds, this center in the iCeMS main building serves as a core facility for discovering small organic molecules that modulate fundamental characteristics in mammalian cells, including ES/iPS cells. These resources are available to all iCeMS scientists, as well as to non-iCeMS researchers working in collaboration with iCeMS scientists.



The Chemical Screening Center in the iCeMS main building

iCeMS Katsura Laboratory

A 220 m^2 shared-use laboratory on Kyoto University's Katsura campus, with collaboration by four professors of the university's Graduate School of Engineering at its core. Research includes work on smart polymers whose phase transition (gel to solution) can be triggered by external stimuli. Such polymers can be combined, for example, with porous coordination polymers (PCPs) to enhance their functionality and compatibility with living cells.

iCeMS Katsura Lab Adjunct Professors (from left): Kazunari Akiyoshi (Department of Polymer Chemistry), Itaru Hamachi (Department of Synthetic Chemistry and Biological Chemistry), Yasuo Mori (Department of Synthetic Chemistry and Biological Chemistry), Masahiro Shirakawa (Department of Molecular Engineering)

Facilities

As of May 1, 2012

iCeMS Main Building | Completed in March 2009

iCeMS West Building | Completed in September 2008

Approx. 5,000 m² of floor space

The iCeMS Main Building serves as the headquarters. In addition to ample shared laboratory space, it includes a seminar hall, a lounge for informal researcher get-togethers, and an exhibition room that doubles as a meeting space.

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

iCeMS Research Building | Completed in October 2010

Research Building No.1/Project Lab | Completed in September 2008

Research Building No.1 Annex | Completed in July 2009

Approx. 6,000 m² of floor space

Researchers from different groups collaborate with each other in extensive shared laboratory and office spaces to advance cross-disciplinary research.

iCeMS Research Building:
Located at the "Hyakumanben" intersection, about 200 meters from the iCeMS Main Building

Shared laboratories and open offices:
Designed to be shared by research groups from various fields in order to promote cross-disciplinary research

Directions

Yoshida Campus, Kyoto University

iCeMS Main Building

iCeMS West Building

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

iCeMS Research Building

Research Building No.1/Project Lab
Research Building No.1 Annex

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

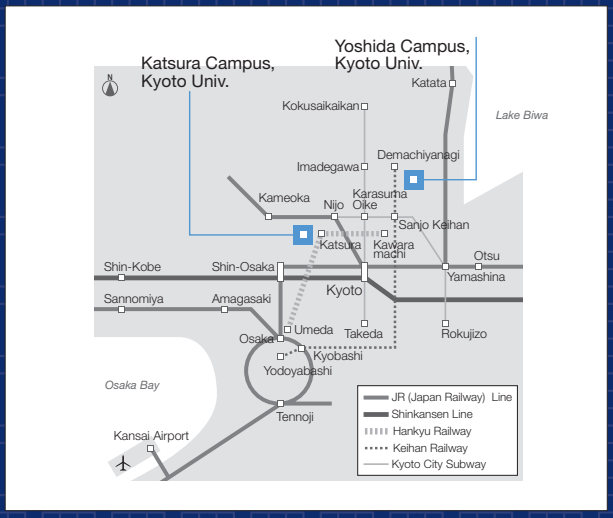
Kyoto University Center for iPS Cell Research and Application (CiRA)

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

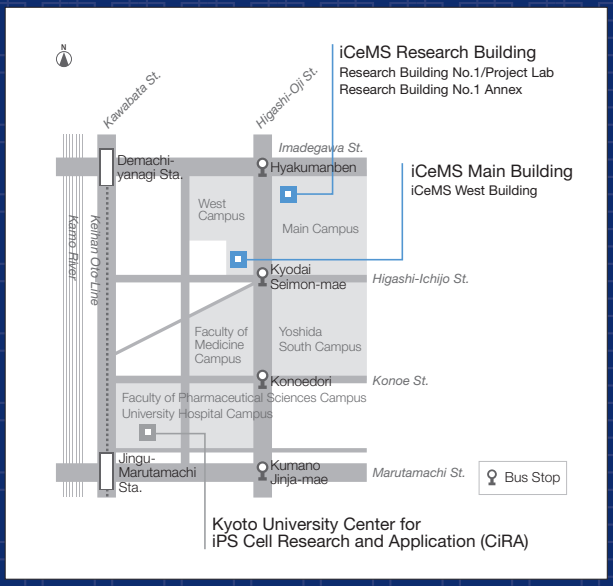
Katsura Campus, Kyoto University

iCeMS Katsura Laboratory

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



Directions to iCeMS, Kyoto University



Yoshida Campus, Kyoto University

Katsura Campus, Kyoto University

iCeMS Brochure | Issued: April 2013 Revised: July 2013

Lab group information is current as of July 1, 2013.

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