iCeMS Focus
Institute for Integrated Cell-Material Sciences, Kyoto University
京 都 大 学
物質ー細胞統合システム拠点

In Commemoration of the Inaugural Issue: Welcome to Kyoto and to our Institute!

The concept of *meso science* may sound unfamiliar, but it is in this unique space that living cells perform all of the functions necessary to sustain life, and some artificial materials have functions controllable by external stimuli. The mesoscale is in fact so important, that we believe that interpreting, understanding, and eventually controlling this realm — fusing cell science with functional materials — will lead to unprecedented breakthroughs in fields ranging from medicine to industry.

The iCeMS is one of five institutes selected in 2007 to participate in the Japanese science ministry's World Premier International Research Center (WPI) Initiative. See pages 4–5, "iCeMS in Brief", for details. Join us as we explore the meso world, and design the future!

■ iCeMS Director, Norio Nakatsuji

Porous Crystal Found to Be Capable of Selective Sorption of Oxygen and Nitric Oxide

The discovery, published in *Nature Chemistry*, could lead to significant cost savings in gas separation technologies.

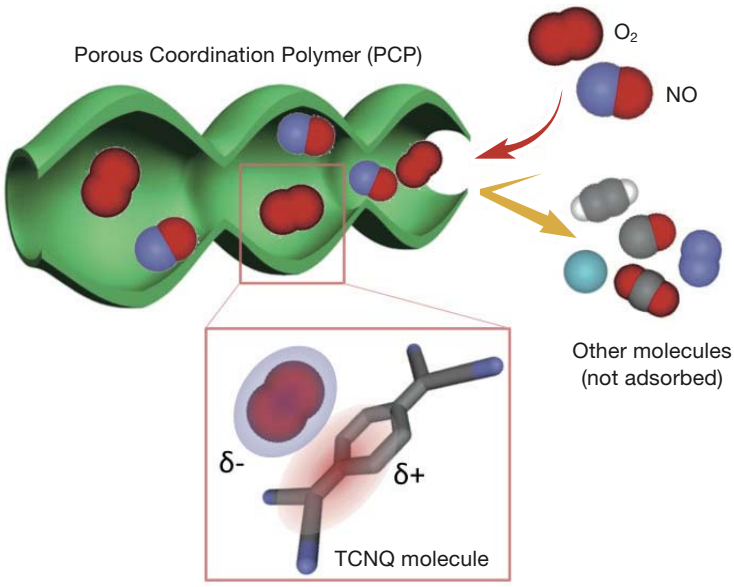

Diagram of a porous coordination polymer (PCP) selectively adsorbing O_2 and NO molecules. Inset shows the charge transfer between the PCP (in particular the TCNQ molecule) and the guest, as indicated by their relative electronegativity. (Courtesy Kitagawa Lab)

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Prof Ueda Wins 2010 JSBBA Award

Japan Society for Bioscience, Biotechnology, and Agrochemistry's top prize honors iCeMS PI's contributions to the study of ABC proteins.

Prof Kazumitsu Ueda of Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS) and the Graduate School of Agriculture has been selected as a recipient of the JSBBA's (Japan Society for Bioscience, Biotechnology, and Agrochemistry) top prize.

The award, presented at the society's annual meeting held in Tokyo in March, honored Prof Ueda's diligence in the field of ABC proteins, building on the first isolation of MDR1 from eukaryotes over 20 years ago. In accepting the prize, Prof Ueda delivered a talk at the meeting entitled "Understanding the Physiological Roles and Molecular Mechanisms of Human ABC Proteins".

"Compared to soluble proteins, working with membrane proteins is tedious and time consuming," explained Prof Ueda in an interview, adding "I'd like to devote another 10 years to basic research involving ABC proteins."

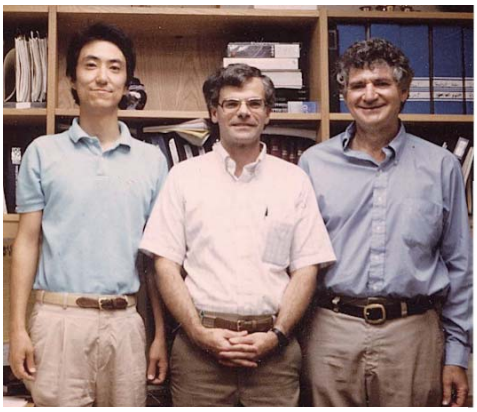

Photo courtesy Prof Ueda

At the US National Cancer Institute, where he conducted post-doctoral research from 1985 to 1987 (with Profs Michael Gottesman and Ira Pastan)

Photo iCeMS © 2010

Prof Ueda began his work in the field while conducting post-doctoral research from 1985–87 at the National Cancer Institute in the United States, where he was part of a project seeking to isolate genes related to multi-drug resistant cancers. Upon his return he joined Kyoto University's Faculty of Agricultural Chemistry, where in 1992 he was honored with the JSBBA's Award for the Encouragement of Young Scientists.

"I owe a large debt of thanks to friends overseas who have helped me mature as a scientist and a person," said Prof Ueda. "Interacting with researchers at conferences overseas and developing friendships with colleagues coming from completely different cultures and backgrounds has had a great influence on me. I get the feeling that younger Japanese today, raised in relative comfort, no longer have a strong desire to study abroad. It is my hope that my younger colleagues here at the iCeMS, while enjoying this research environment enlivened by many scientists from other countries, will also eagerly grasp opportunities to grow by spending time living overseas." ■

The iCeMS' Expanding Global Network

MoUs signed recently with the CNSI (USA) and NCBS (India).

The iCeMS global network of research partner institutions is expanding rapidly, with memoranda of understanding signed recently with the California NanoSystems Institute (CNSI) at UCLA, USA, and also with the National Centre for Biological Sciences (NCBS) in Bangalore, India.

While providing a framework for joint research projects, the MoUs also call for exchanges of researchers, joint hosting of symposia, possible satellite laboratories, and other cooperative efforts.

The iCeMS already has a satellite at Gifu University, headed by Prof Makoto Kiso. The list of ongoing partnerships includes the following institutions:

- California Nanosystems Institute (CNSI), UCLA, USA
- Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG), Germany
- National Centre for Biological Sciences (NCBS), Bangalore, India

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Researchers from Kyoto University have discovered a useful property of a type of **porous crystal** that may lead to the development of new environmental technologies capable of aiding in separating gasses.

The findings by Prof and Deputy Director Susumu Kitagawa and Assoc Prof Ryotato Matsuda of Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS) were published on June 6 in the online edition of *Nature Chemistry*.

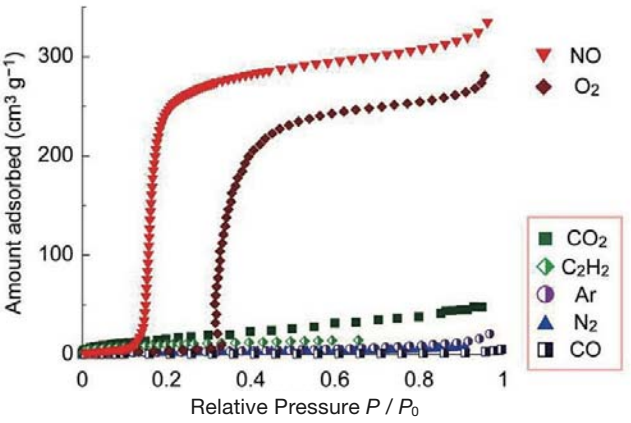
The flexible crystals, known as *porous coordination polymers* or *PCPs*, consist of metal ions linked with organic molecules: in this case, zinc ions linked by tetracyanoquinodimethane (TCNQ) molecules. This material combines the properties of being simultaneously crystalline and flexible, forming a regular yet dynamic porous domain.

The selective gas sorption properties of the material were found to depend on a charge transfer between TCNQ and the guest gas molecules, with a notable preference shown for oxygen (O_2) and nitric oxide (NO).

The researchers anticipate that industrial applications of this material will lead to significantly reduced costs for gas separation, and that the development of similar materials should make it possible to selectively adsorb other gases as well.

This research was conducted by the Kitagawa Integrated Pores Project, an Exploratory Research for Advanced Technology (ERATO) program funded by the Japan Science and Technology Agency (JST).

Additional details (including media coverage information) are available on the iCeMS website. ■

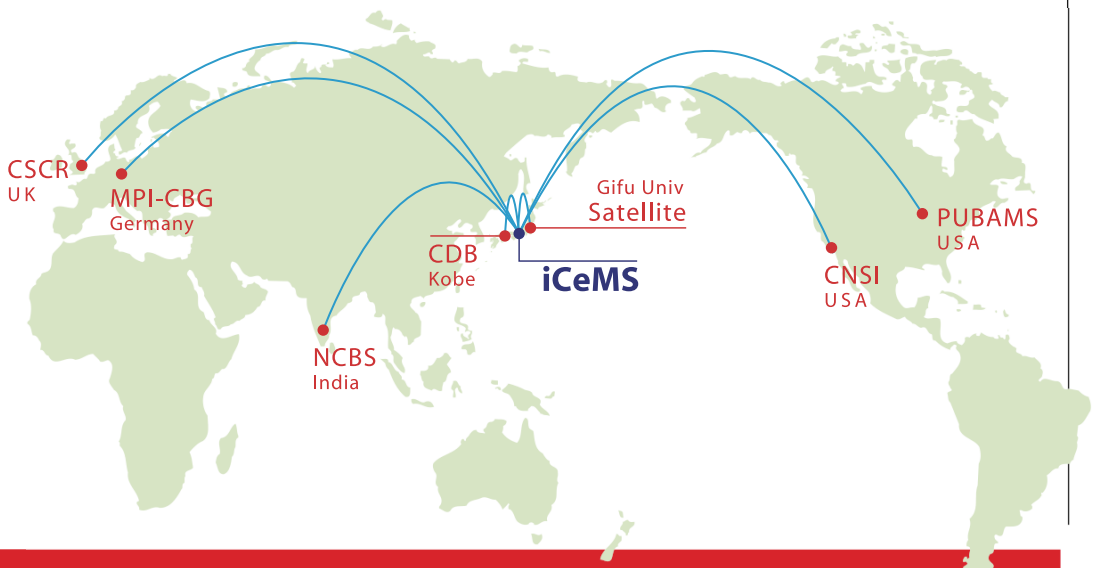


Graph of the porous coordination polymer selectively adsorbing O_2 and NO. Other guest molecules are scarcely adsorbed at all. (Courtesy Kitagawa Lab)

iCeMS Prof Susumu Kitagawa (left) and Assoc Prof Ryotaro Matsuda announcing their findings at a press briefing at Kyoto University.

Satoru Shimomura, Masakazu Higuchi, Ryotaro Matsuda, Ko Yoneda, Yuh Hijikata, Yoshiki Kubota, Yoshimi Mita, Jungeun Kim, Masaki Takata, and Susumu Kitagawa. **Selective sorption of oxygen and nitric oxide by an electron-donating flexible porous coordination polymer**. *Nature Chemistry*. Published online June 6, 2010. Doi 10.1038/nchem.684.

- Purdue University Center for Basic and Applied Membrane Sciences (PUBAMS), USA
- Riken Center for Developmental Biology (CDB), Kobe
- Wellcome Trust Centre for Stem Cell Research (CSCR), The University of Cambridge, UK ■



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

Mastering Meso Space: Functional Architectures and Stem Cell Systems

Why Meso Space?

Between the nanoscopic (the realm of atoms and simple molecules at most several nm in size) and the macroscopic (our everyday world, consisting of everything larger than 1μm) lies the mesoscopic*: a scale dominated by interactions among large molecules and within cells and cell systems.

Cells are in essence living factories of enzymes and molecules. Understanding these processes and ultimately learning to control or even mimic them promises to lead to breakthroughs in next generation (e.g. regenerative) medicine, targeted drug treatments, and green chemical technologies. Harnessing the power of cells — mastering meso space — is the key to solving many of the technological quandaries facing humanity today.

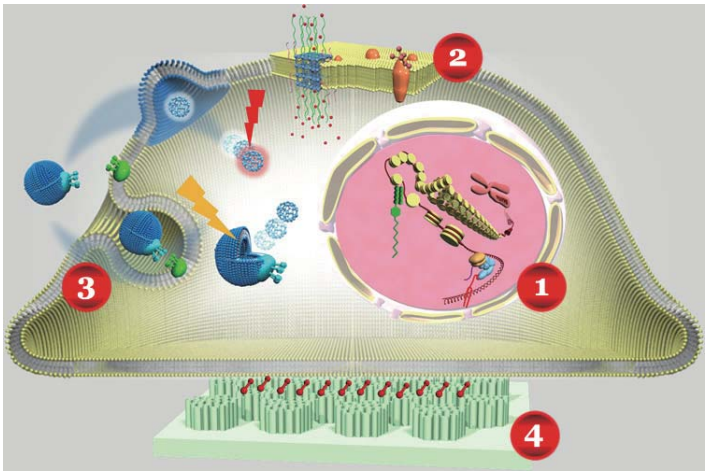
Meso-Control of Living Cells: Applications to Stem Cells

Leading the world in the exploration of meso space is Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS), founded in 2007. As one of only five research centers selected by Japan's education and science ministry under its World Premier International Research Center (WPI) Initiative, the institute aims to advance the integration of cell and material sciences — both traditionally strong fields for the university — by creating a uniquely innovative global research environment.

The iCeMS seeks to integrate the biosciences, chemistry, material science, and physics to capture the potential power of meso-control of functional architectures and stem cells. Cells in living organisms have acquired these tools to control the mesoscale realm through the course of evolution, thereby realizing clean chemical reactions in ambient environments to perform functions such as energy conversion, cell growth, and differentiation.

Research falls into the following four broad categories: 1) Chromatin architecture/function and meso-control; gene expression control with bio-functional chemicals/materials, 2) Cell membrane architecture/function and meso-control; ion channel/transporter/receptor with bio-functional chemicals/materials, 3) Intracellular delivery of bio-functional materials; control by external signals, 4) Cellular environment architecture/function and meso-control; nano/meso/micro-engineered materials with bio-functional molecules.

*For an examination of the mesoscopic realm, see Mark Haw's *Middle World: The Restless Heart of Matter and Life* (Palgrave Macmillan, 2006).



The Goal: Meso-control of cellular functions through the integration of cell and material sciences. Diagram © iCeMS.

Embryonic stem (ES) and induced pluripotent stem (iPS) cells are at the heart of this research. Ultimately realizing their full potential, by applying artificial meso-control strategies to ES/iPS cells, could result in unprecedented abilities to shape the course of future technology development.

Globally Visible, Truly Open and International

The iCeMS aims to make such breakthroughs possible by bringing together the world's top scientists in a premier research environment. Open office space and common laboratories equipped with state-of-the-art research instruments encourage interaction and an increased exchange of ideas.

A ground-breaking shared use imaging lab, including Profs **Akihiro Kusumi** and **John Heuser**, is available even to non-institute researchers. This Center for Meso-Bio Single-Molecule Imaging (CeMI) also serves as a development platform for emerging imaging technologies such as terahertz optics.

All of this exists in an open environment supportive of new ideas and young as well as female scientists. Institute management has been streamlined to allow for quick decision-making and budget approvals. English is the official language. An active global recruitment effort aims to put the institute at the center of career development plans for the world's brightest junior investigators.

In addition, the institute has launched the iCeMS Kyoto Fellow program, targeted toward attracting the best new scientists in the

From left: Kyoto University Clock Tower, Director Norio Nakatsuji, garden in the iCeMS main building. Photos © Kyoto University, iCeMS.

Join us in Kyoto to master meso space — and design the future.

field. These 5-year positions include start-up and operating budgets to cover the fellows' own research groups and other related expenses.

Solid Science, Steeped in Tradition

This vigorous work takes place in one of Japan's premier national universities, against the backdrop of Kyoto, a city steeped in traditions dating back well over a millennium. And in spite of its relatively recent establishment, the iCeMS has already produced a notable catalog of scientific achievements (see www.icems.kyoto-u.ac.jp for details on all 18 PIs and their research groups).

Institute Director Prof **Norio Nakatsuji**'s lab carries out cross-disciplinary research on ES/iPS cells focusing on control of pluripotency and differentiation, and also on the germ cell lineage. His group is still the only to have succeeded in establishing human ES cell lines in Japan. Recent publications: *Dev Cell* **17**, 775 (2009); *Development* **135**, 2969 (2008); *Nat Biotechnol* **26**, 739 (2008).

Prof **Shinya Yamanaka**'s lab, renowned for its success in generating iPS cells from adult fibroblasts, aims to 1) understand molecular mechanisms underlying iPS cell induction, 2) develop new methods for iPS cell induction to increase their safety, and 3) screen for novel factors involved in iPS cell induction. Prof Yamanaka is also director of Kyoto University's Center for iPS Cell Research and Application (CiRA). Recent publications: *Nature* **460**, 1132 (2009); *Science* **322**, 949 (2008); *Cell* **131**, 861 (2007). Recent honors: Albert Lasker Basic Medical Research Award (2009), Gairdner International Award (2009).

Prof **Akihiro Kusumi**'s lab has developed the world's fastest single-molecule tracking technique and applied the method to the study of the plasma membrane in living cells, allowing for a number of unprecedented observations and fostering a new basic understanding of molecular diffusion, interaction, and signal transduction in the plasma membrane. Prof Kusumi is also the CeMI director. Recent publications: *Biophys J* **95**, 435 (2008); *J Cell Biol* **177**, 717 (2007).

Prof **John Heuser** is the pioneering world leader in quick-freeze, deep-etch 3-D electron microscopy. His techniques allow for examinations of meso architectures such as cell membranes at unprecedented high resolution. Recent publications: *Nat Cell Biol* **11**, 219 (2009); *Science* **320**, 382 (2008).

Prof **Motonari Uesugi**'s lab has discovered various small organic molecules, modulating gene expression or cellular signaling, for use as chemical tools to control stem cells (e.g. “fatostatin” that blocks fat synthesis in cells, a finding that received wide international press coverage: *Chem Biol* **16**, 882; 28 Aug 2009). Recent publication: *J Am Chem Soc* **131**, 4774 (2009).

Deputy Director Prof **Susumu Kitagawa**'s lab is creating novel porous coordination polymers for application in a pioneering cross-disciplinary field combining cell membranes and porous materials to examine and control cell functions. Recent publications: *Nat Chem* **1**, 695 (2009); *Nat Mater* **8**, 831, (2009); *Nat Mater* **6**, 142 (2007). Recent honors: Thomson Reuters Moving Fronts for his highly influential paper (2009), Humboldt Research Award (2008).

Principal Investigators also include:

Konstantin Agladze (Biophysics, Non-linear Science), **Yong Chen** (Nanobiotechnology), **Yoshie Harada** (Single-Molecule Physiology), **Mitsuru Hashida** (Drug Delivery Systems), **Takashi Hiiragi** (Developmental Biology), **Hiroshi Imahori** (Organic Chemistry, Photochemistry, Drug Delivery Systems), **Mineko Kengaku** (Developmental Neurobiology, Cell Biology), **Makoto Kiso** (Glycotechnology), **Hiroshi Sugiyama** (Chemical Biology), **Mikio Takano** (Solid State Chemistry), **Koichiro Tanaka** (Teraherz Optical Science), **Kazumitsu Ueda** (Cellular Biochemistry)

iCeMS Kyoto Fellows (junior PIs)

Peter Carlton (Meiosis, Chromosome Biology, Optical Microscopy), **Ziya Kalay** (Statistical Physics), **Tatsuya Murakami** (Cell Engineering, Protein Engineering), **Takuya Yamamoto** (Molecular Biology, Bioinformatics)

Other research groups

Shintaro Sengoku (Innovation Management), **Kazuto Kato** (Science Communication)

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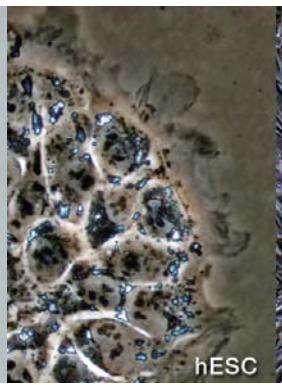
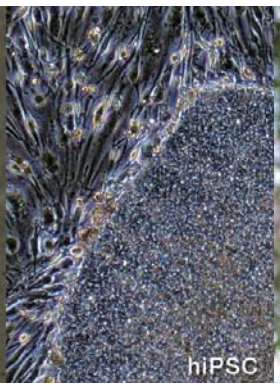
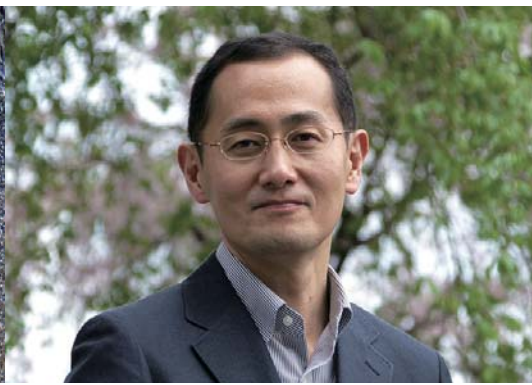
WPI Research Center

From left: Deputy Director Susumu Kitagawa, human ES/iPS cells, Prof Shinya Yamanaka (CiRA Director). Photos © iCeMS, CiRA.







New Center for iPS Cell Research and Application (CiRA) Opens

Kyoto University institute becomes sibling to the iCeMS. iCeMS Prof Yamanaka named first CiRA Director.

First established in 2008 as a part of the iCeMS, the Center for iPS Cell Research and Application (CiRA) was reorganized as an independent institute within Kyoto University on April 1, 2010, with iCeMS Prof Shinya Yamanaka as its inaugural director.

The new institute will maintain close ties to the iCeMS, sharing basic research and some faculty.

For more details, see the CiRA website at:

www.cira.kyoto-u.ac.jp ■

Prof Yamanaka (fourth from left) joined by Prof Nakatsuji (far left), MEXT Administrative Vice Minister Toichi Sakata (center), Kyoto University President Hiroshi Matsumoto (fourth from right), and other dignitaries for a gala opening ceremony of the new CiRA building on May 8. (Courtesy CiRA)

New iCeMS Brochures Published

The iCeMS has just published updated, comprehensive brochures describing all of the institute's laboratory groups and state-of-the-art research facilities.

"These brochures will help scientific colleagues across the globe better understand the importance of meso science," explains iCeMS Administrative Director Prof Shinji Tomita, adding, "we look forward to working with researchers from many countries and from many scientific disciplines."

The new brochures, in both English and in Japanese, may be downloaded from the institute's website. Printed copies are available upon request. ■

iCeMS Scientists Enliven S&T Festival

Young researchers play host to several hundred area students and residents drawn to the iCeMS' "play hard" booths at event.

On June 5, 2010 the Japanese Cabinet Office spearheaded the organization of the first "Science and Technology Festa in Kyoto", part of a campaign to increase public awareness of the government's commitment to science and its investments in technology development. A total of over 5,000 students, local residents, and private and public sector representatives attended the event.

Nearly two dozen young iCeMS scientists participated in an exhibition related to the WPI program. They demonstrated concepts central to the iCeMS's cutting-edge research using educational materials and hands-on activities. The iCeMS "play hard" booths alone counted 700 visitor interactions.

For details, please see the iCeMS website. ■

Observing ES and iPS cells (Nakatsuji Lab).

Making microfibers with a candy machine (Chen Lab).

DNA origami via puzzle making (Sugiyama Lab).

Making molecule houses (Kitagawa Lab).

Cross-Disciplinary Grant Opportunities Open to Non-iCeMS Researchers

The following grant programs have been established at the iCeMS to promote cross-disciplinary research.

iCeMS Cross-Disciplinary Research Promotion Project

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

iCeMS Exploratory Grants for Junior Investigators

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

More information about these and other opportunities is available by contacting: *oap@icems.kyoto-u.ac.jp*

We are also actively sending our researchers on overseas visits, so if you meet one of our staff somewhere, please say hello! ■

iCeMS*Focus*

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The WPI program was founded in 2007 at the initiative of Japan's Ministry of Education, Culture, Sports, Science and Technology (MEXT) with the aim of establishing and operating a network of world-class scientific research centers.

Kyoto University's iCeMS is one of five founding institutes in this program.

World Premier International Research Center Initiative

See: www.mext.go.jp/english/wpi/
www.jsps.go.jp/english/e-toplevel/

upcoming events

8th iCeMS Int'l Symposium

Meso-Control of Functional Architectures

9–11 November 2010

Venue: Kyoto University Shiran Kaikan
Organizers: iCeMS Kitagawa and Sugiyama Labs
Contact: (075) 753-4002, *kitagawa-g@icems.kyoto-u.ac.jp*

9th iCeMS Int'l Symposium

Mesoscale Control and Engineering of Self-Organized and Excitable Systems in Biology and Chemistry

2–3 December 2010

Venue: iCeMS Main Building
Organizer: iCeMS Agladze Lab
Contact: (075) 753-9835, *agladze-g@icems.kyoto-u.ac.jp*