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.

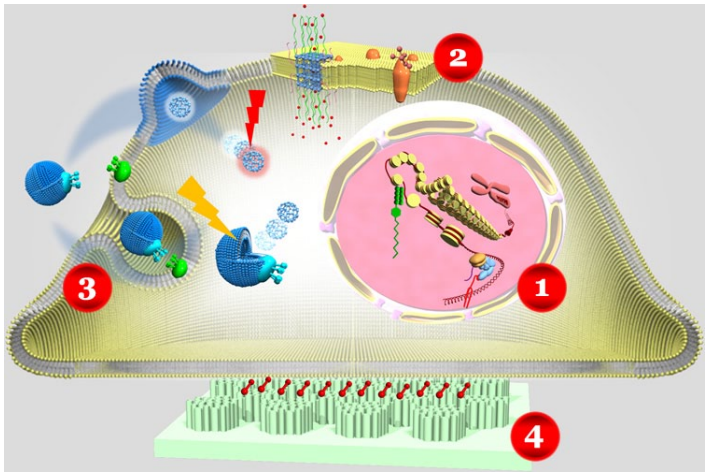
Meso-Control of Living Cells: Applications to Stem Cells

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

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

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 inculde:

Konstantin Agladze (Biophysics, Non-linear Science), **Yong Chen** (Nano-biotechnology), **Yoshie Harada** (Single-Molecule Physiology), **Mitsuru Hashida** (Biopharmaceuticals), **Takashi Hiiragi** (Developmental Biology), **Hiroshi Imahori** (Photochemistry), **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)

info@icems.kyoto-u.ac.jp
www.icems.kyoto-u.ac.jp

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