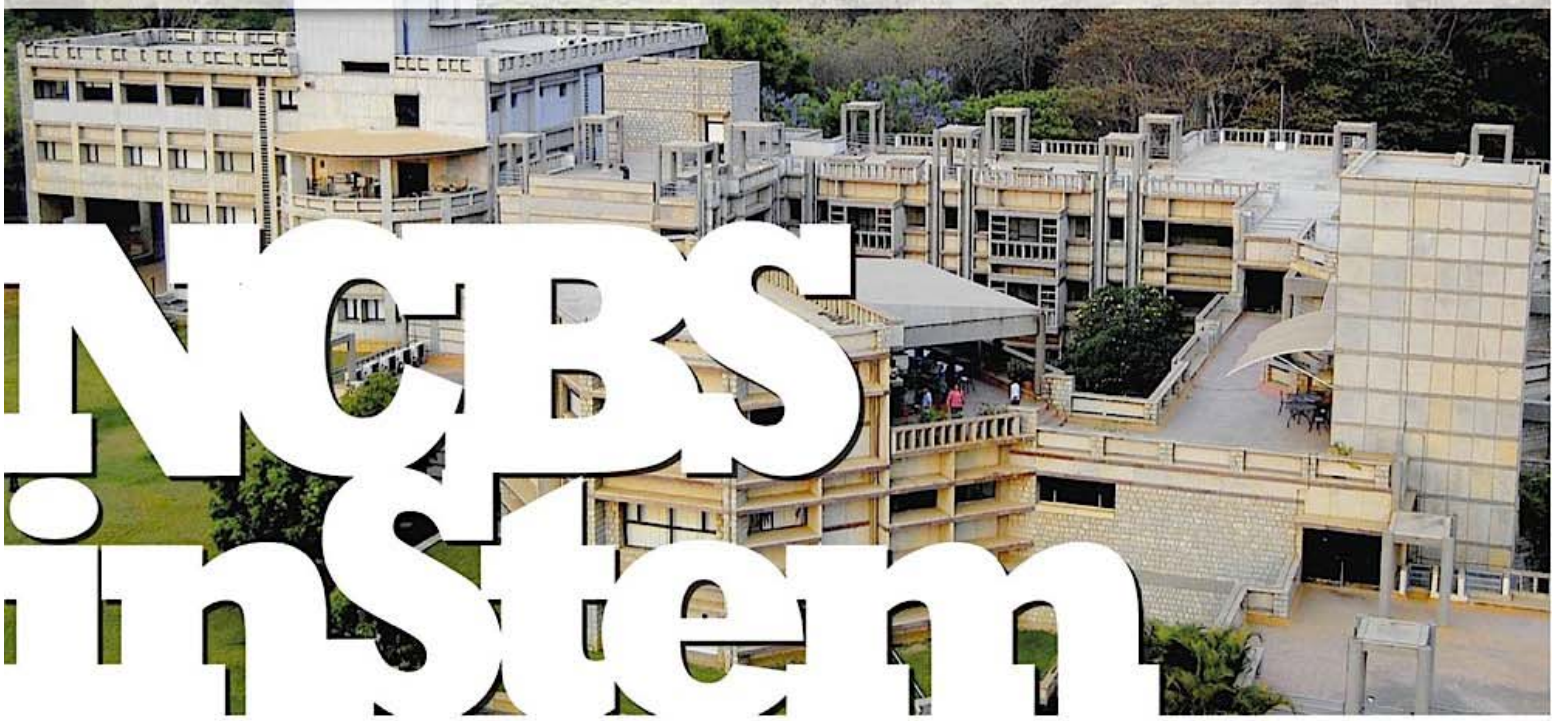
Commemorating the Opening of the NCBS-inStem Satellite at Kyoto University's iCeMS & the Second NCBS-inStem/iCeMS Joint Symposium



ncbs

inStem

iCeMS
KYOTO UNIVERSITY
WPI Research Center

KYOTO UNIVERSITY
FOUNDED 1897

Friday 17 Dec 2010

iCeMS Main Bldg • 2nd fl Smnr Rm

14:00—Satellite Opening Ceremony

15:00—Second Joint Symposium

Presentations include:

- *Eph/ephrin signaling sculpts form in an identified central neuron, with functional implications in courtship behaviour,* Prof K VijayRaghavan, NCBS Director
- *Multi-disciplinary research and application of pluripotent stem cells for disease mechanism research and drug discovery,* Prof Norio Nakatsuji, iCeMS Director

and others

Co-Hosts: Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University
National Centre for Biological Sciences (NCBS), India

From the Director

On behalf of all of my colleagues at Kyoto University's Institute for Integrated Cell-Material Sciences (iCeMS), it is my great pleasure to welcome you to the opening ceremony of the NCBS-inStem satellite at Kyoto University's iCeMS, and the second NCBS-inStem/iCeMS joint symposium.

The iCeMS was founded in 2007 at the Japanese government's initiative, as one of five inaugural institutes in the World Premier International Research Center (WPI) program. This initiative aims to establish globally visible research centers in Japan, attracting world-class researchers from across the globe, in particular talented young scientists expected to become the world's future leading investigators.

At the iCeMS we strive to gain a fundamental understanding of and ability to control molecular complexes in the mesoscopic world, similar to techniques which living cells have developed through the course of evolution. Such methods, involving an understanding of molecular events in the meso-scale, are also key to the design and creation of various novel "smart materials". We consider these to be critical efforts in the creation of a new generation of science and technology. For this purpose, we are taking an international and cross-disciplinary approach to these new sciences focusing on functional architectures and stem cell systems.

In April this year, the iCeMS and the NCBS (National Centre for Biological Sciences, Bangalore, India) signed a Memorandum of Understanding to formalize the many years of fruitful exchanges and joint work that has taken place between individual scientists in both institutes. In August, our two institutions, along with inStem (the Institute for Stem Cell Biology and Regenerative Medicine, a newly established stem cell institute at the NCBS), held a joint symposium in Bangalore and agreed to establish mutual satellite laboratories in Bangalore and Kyoto. It is therefore our great pleasure to announce on this occasion the opening of the NCBS-inStem Satellite at the iCeMS.

We see this collaboration as having a multiplier effect for both organizations, as we strive to create a sustainable environment for cooperative research by boldly expanding the fields of mutual work. It is our intention to create opportunities for the brightest young researchers in Japan and India, as well as to make a significant contribution to bilateral ties through advances in science and technology.

Thank you very much for joining us to commemorate the opening of the NCBS-inStem satellite at Kyoto University's iCeMS, as well as for the second NCBS-inStem/iCeMS joint symposium.

Norio Nakatsuji, D.Sc.
iCeMS Director and Professor
Kyoto University

Opening Ceremony for the NCBS-inStem Satellite at iCeMS

Venue: iCeMS Main Building at Complex 1, 2nd floor Seminar Room
Chair: Dr. Shintaro Sengoku, iCeMS

Congratulatory Words from the Hosts

14:00–14:25 Prof. Norio Nakatsuji, iCeMS Director
Prof. K. VijayRaghavan, NCBS Director
Prof. Kiyoshi Yoshikawa,
Executive Vice-President for Research, Kyoto University

Congratulatory Words from the Guests

14:25–14:40 Dr. Toshio Kuroki, Deputy Director, Research Center for Science Systems,
Japan Society for the Promotion of Science and Program Director,
World Premier International Research Center (WPI) Initiative
Dr. Thadathil Pankajakshan, Science & Technology Counselor,
Embassy of India, Tokyo
Prof. Gautam Ray, Graduate School of Management, Kyoto University and
Indian Ministry of Finance

Commemorative Photograph

14:40–14:50 Commemorative photograph on stage

The Second NCBS-inStem/iCeMS Joint Symposium

Venue: iCeMS Main Building at Complex 1, 2nd floor Seminar Room
Chair: Prof. Akihiro Kusumi, iCeMS

Opening Remarks

15:00–15:10 Prof. Norio Nakatsuji, iCeMS

Presentations

15:10–15:40 **Prof. Norio Nakatsuji**
Multi-disciplinary research and application of pluripotent stem cells for disease mechanism research and drug discovery

15:40–16:10 **Prof. K. VijayRaghavan,** NCBS
Eph/ephrin signaling sculpts form in an identified central neuron, with functional implications in courtship behaviour

16:10–16:30 Break

16:30–17:00 **Dr. Kenichi Suzuki,** iCeMS
How does the meso-scale raft domain exist and transform to work?
—a single-molecule imaging study

17:00–17:30 **Prof. Satyajit Mayor,** NCBS
Local and regulated organization of membrane components during stem cell differentiation

Closing Remarks

17:30–17:35 Prof. K. VijayRaghavan

Reception

18:00–20:00 Venue: iCeMS Main Building 2nd floor Lounge

Abstracts

Multi-disciplinary research and application of pluripotent stem cells for disease mechanism research and drug discovery

Norio Nakatsuji
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Our research group has been working on development and differentiation of embryonic stem cells and germ cells in mammals. We have been carrying out various aspects of basic and application research using pluripotent stem cells. We are until recently the only group in Japan to have derived and distributed human ES cell lines to many biomedical researchers.

We have developed various methods of genetic modification in human pluripotent stem cell lines, including human ES cell lines with the insertion of *Cre/loxP* exchange cassette into the HPRT locus by homologous recombination, which enables reliable silencing-free integration of any transgenes into human ES/iPS cells. Recently, our group has been creating normal and disease model cells for disease mechanism research and drug discovery tools as an important application of pluripotent stem cell lines. It includes production of neurodegenerative disease model cells by introduction of mutated genes, toxicology studies using cardiomyocytes and chemical screening.

At iCeMS, we are developing multidisciplinary research projects using ES and iPS cell lines by collaboration with other research groups of iCeMS. They include (a) creation and analysis of neurodegenerative disease model cells produced by genetic modification of ES/iPS cells and differentiation into relevant cells in each disease. (b) Control of stem cells by screening of synthetic small molecules to control differentiation of ES/iPS cells.

Recent Publications:

(1) T. Sumi et al., Development 135, 2969-2979 (2008).
(2) K. Suzuki et al., Proc. Nat. Acad. Sci. USA 105, 13781-13786 (2008).
(3) T. Wada et al., PLoS ONE 4, e6722 (2009).
(4) M. Shoji et al., Developmental Cell 17; 775-787 (2009).
(5) K. Sakurai et al., Nucleic Acids Research 2010; doi: 10.1093/nar/gkp1234.
(6) T. G. Otsuji et al., Stem Cell Research 4, 201-213 (2010)

Eph/ephrin signaling sculpts form in an identified central neuron, with functional implications in courtship behaviour

Ajeet Pratap Singh, Rudra Nayan Das, Veronica Rodrigues and K. VijayRaghavan
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Targeting and confinement of neuronal arbors within appropriate target field is a prerequisite for partner-specific connectivity in the brain. Mechanisms that regulate neuronal branch positioning and confinement within the target field are likely to involve interactions between incoming neurites and cellular substrates in the target field mediated by cell-surface signaling molecules and other target-derived cues. Using the *Drosophila* antennal lobe as a genetically tractable and anatomically well-defined model neuronal circuit, we demonstrate that Eph/ephrin signaling plays instructive role in confining the arbors of central neurons within the boundary of their target field and in regulating targeting of neuronal arbors within specific sub-domains of the target field. We find that Eph/ephrin signaling regulates glomeruli-specific innervations of an identified central neuron in the antennal lobe. We relate this data to the function of specific glomeruli involved in courtship behaviour.

How does the meso-scale raft domain exist and transform to work? −a single-molecule imaging study

Kenichi G. N. Suzuki[1,2], Rinshi S. Kasai[2], Koichiro M. Hirosawa[2], Munenori Ishibashi[2], Yoshihiro Miwa[3], Takahiro K. Fujiwara[2], and Akihiro Kusumi[2]
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Raft domains in nonstimulated cells remain elusive. Using advanced single fluorescent-molecule imaging (high-speed, FRET, bimolecular fluorescence complementation), we found that GPI-anchored proteins (GPI-APs), putative raft-associated proteins with a phospholipid anchoring chain, continually convert back and forth between transient (140-300-ms lifetime) mobile homodimers (and not heterodimers) and monomers in the plasma membrane. Such short-lived homodimers are prevalent even (1) at their lower physiological expression levels of 1000 - 5000 copies/cell and (2) in the presence of large numbers of other GPI-APs. The homodimer formation of GPI-APs was found with CD59, DAF, and GFP-GPI, and to be based on specific ectodomain protein interactions, stabilized by cholesterol- and GPI-anchor-dependent lipid interactions (Fig. 1). Therefore, these short-lived complexes of GPI-AR homodimers and cholesterol would unequivocally represent a class of raft domains existing in steady-state cells. These transient homodimer-rafts further formed transient greater complexes based on raft-lipid interactions, consistent with the results by the Mayor group.

Upon ligation, engaged CD59 (but not CD59TM or after cholesterol depletion) molecules were found to create stable rafts, probably because engaged CD59 formed more stable homodimers. Such ligand-induced stable rafts recruited various raftophilic signaling molecules, triggering intracellular signals, leading to intracellular Ca^{2+} responses.

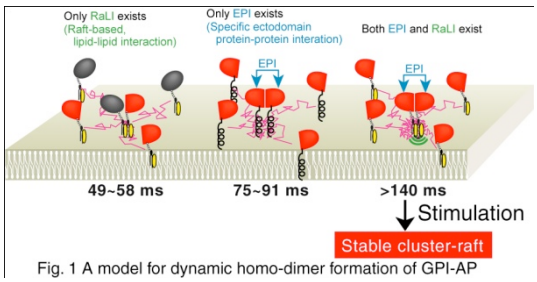

Fig. 1 A model for dynamic homo-dimer formation of GPI-AP

Local and regulated organization of membrane components during stem cell differentiation

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The membrane of living cells, a two dimensional fluid-mosaic, is the primary interface that delineates cells from their surroundings. At the same time it is this interface that must reproducibly interpret and respond to a particular niche or microenvironment to transmit information to the cell interior, to maintain a consistent cell-state or trigger a reproducible response to cellular differentiation cues. Recent data from our laboratory suggest that the membrane of a living cell is not a well mixed fluid, instead is actively organized at multiple scales. These observations pose fundamental questions regarding the mechanism of regulated organization of membranes components in cell membranes. In my talk I will put forth new ideas regarding how living cells may regulate the organization of membrane lipids and proteins, and discuss how these principles may influence our understanding of stem cell differentiation.