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TEMASEK LIFESCIENCES LABORATORY

10 May 2016 (Tuesday), 4pm
The Auditorium (Level 1)
Hosted by: Dr Fumio MOTEGI

Cross-talk between the endoplasmic reticulum and the plasma membrane mediated by the extended synaptotagmins

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Yasunori attended Okayama University Medical School in Okayama, Japan, obtaining his MD in 2005. He then pursued his graduate studies at the Rockefeller University in New York, USA. Working in the laboratory of Dr. Cori Bargmann, he investigated the mechanisms of ion channel localization at the nerve terminals using *C. elegans*. After receiving his PhD in Neurobiology in 2010, Yasunori moved to the Department of Cell Biology at the Yale University School of Medicine in New Haven, where he worked as a postdoctoral fellow in the laboratory of Dr. Pietro De Camilli. Using a combination of genome editing, biochemistry, quantitative cellular imaging, and optogenetics, he studied the regulatory mechanisms that govern cellular lipid homeostasis. Yasunori joined the faculty at Lee Kong Chian School of Medicine, Nanyang Technological University as a Nanyang Assistant Professor in March, 2016. His laboratory employs the combination of *C. elegans* genetics and mammalian cell biology to tackle fundamental questions in cellular lipid regulation as well as the mechanisms that underlie neurological disorders.

Lipid homeostasis plays a central role in membrane dynamics and integrity, as well as in cell viability in all eukaryotic cells. Transfer of lipids from one cellular compartment to another plays a key role in these processes. However, our knowledge of the mechanisms underlying this transfer remains limited. The majority of membrane lipids are synthesized in the endoplasmic reticulum (ER). Their transfer from the ER to other membranous organelles and to the plasma membrane has primarily been studied in the context of vesicular transport, which relies on membrane budding and fusion reactions. Accumulating evidence, however, suggests that "membrane contact sites", the sites of close physical proximity between intracellular membranes, play important roles in lipid exchange without membrane fusion.

In my seminar, I will describe the characterization of the extended synaptotagmins (E-Syt1, E-Syt2, and E-Syt3) as evolutionary conserved tethers between the ER and the plasma membrane. Lipid-harboring modules present in all the three E-Syts and their ability to transfer glycerolipids will also be described. Finally, I will discuss our recent characterization of genome-edited cells lacking E-Syts, which suggest their roles in the control of plasma membrane lipid homeostasis. Using E-Syts as an entry point, our lab aims to elucidate important, yet unknown, mechanisms of lipid homeostasis, focusing on the role of non-vesicular transport at membrane contact sites.

Recent Publications:

1. **Saheki Y**, Bian X*, Schauder CM*, Sawaki Y, Surma MA, Klose C, Pincet F, Reinisch KM, and De Camilli P. Control of plasma membrane lipid homeostasis by the extended synaptotagmins. Nat Cell Biol. 2016 Apr 11. doi: 10.1038/ncb3339
2. Schauder CM, Wu X*, **Saheki Y***, Narayanaswamy P, Torta F, Wenk MR, De Camilli P, and Reinisch KM. (2014). Structure of a lipid-bound extended-synaptotagmin indicates a role in lipid transfer. Nature. 510, 552-5 *Equal contribution
3. Giordano F*, **Saheki Y***, Idevall-Hagren O, Colombo S, Pirruccello M, Milosevic I, Gracheva EO, Sviatoslav BN, Borgese N, and De Camilli P (2013). PI(4,5)P2 dependent and Ca2+-regulated ER-plasma membrane interactions mediated by the Extended Synaptotagmins. Cell. 153, 1494-509 *Co-first authors