NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

# VIRTUAL BIOLOGY COLLOQUIUM

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Hosted by A/P Lu Gan

## Control of cellular cholesterol homeostasis via GRAMD1 lipid transfer proteins


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Cells maintain optimal levels of cholesterol in their membranes. Such control is important since improper cholesterol levels can lead to health problems, including heart attacks and dementia. Up to 90% of cellular cholesterol is enriched in the plasma membrane (PM). However, the regulatory network that controls its biosynthesis and uptake is located in the endoplasmic reticulum (ER). Thus, cells monitor how much cholesterol is in their PM and tell the ER to adjust cholesterol production/uptake. Such crosstalk between the PM and the ER is mediated, at least in part, through regulated transport of biochemically defined pool of cholesterol, termed accessible cholesterol, but the molecular mechanisms responsible for this process remain elusive. In my presentation, I will describe our recent characterization of evolutionarily conserved and ER-anchored sterol transfer proteins, GRAMD1s (Lam/Ltc proteins in yeast). We found that GRAMD1s sense a transient increase of accessible cholesterol in the PM and facilitate its non-vesicular transport to the ER at ER-PM contact sites. In the absence of GRAMD1s, cells exhibit striking expansion of the accessible pool of PM cholesterol and dysregulation of cholesterol metabolism. Thus, our study provides deeper insights into the molecular mechanisms of intracellular cholesterol transport and their importance for cholesterol homeostasis.


***About the Speaker***

*Yasunori Saheki is a Nanyang Assistant Professor at Lee Kong Chian School of Medicine (LKCMedicine), Nanyang Technological University, Singapore. He obtained his M.D. from Okayama University Medical School, Japan, in 2005 and his Ph.D. from The Rockefeller University, USA, in 2010 under the mentorship of Dr. Cori Bargmann. After finishing his postdoctoral training with Dr. Pietro De Camilli at Yale University, USA, he joined the faculty at LKCMedicine in 2016. He is also a Visiting Associate Professor at the Institute of Resource Development and Analysis, Kumamoto University, Japan. In 2020, he was selected as a European Molecular Biology Organization (EMBO) Global Investigator. His laboratory employs mammalian cell biology and C. elegans genetics to tackle fundamental questions in cellular lipid regulation as well as the mechanisms that underlie neurological disorders.*

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