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

BIOLOGY COLLOQUIUM

Friday, 25 Jan 2019 | 4pm | DBS Conference Room 1

Hosted by A/P Low Boon Chuan

Dynamics of Signaling and Protein Interaction Networks: Billion Years and Present

*Chris graduated from NUS with a BSc and a MSc from the Department of Biological Sciences and School of Computing respectively, before embarking his PhD training at the University of Toronto (Canada) with the late Tony Pawson. There, he made key revelations on the evolution of phosphorylation-based signaling network related to organismal complexity and human diseases (Tan et al., Science 2009; Tan et al., Science Signaling 2009). He moved to the Center of Molecular Medicine (CeMM) in Vienna, Austria where he was exposed academic drug discovery, further advanced our understanding of phosphoproteomics data (Tan et al., Nature Method 2012) and contributed to a drug target deconvolution technology (Huber et al., Nature Method). He joined the laboratory of Pär Nordlund in the Institute of Molecular & Cell Biology (A*STAR, Singapore) in 2015 as a senior research fellow and invented arguably the first proteome-wide approach for studying the dynamic of protein complexes directly from intact cells and tissues (Tan et al., Science 2018). Since April 2018, Chris leads an interdisciplinary research group as a joint independent fellow in IMCB and BII (A*STAR). Armed with strong analytical skills and unique tools (experimental and computational) in chemical and network biology for elucidating mechanism-of-action of drugs and chemicals, he is an advocate of phenotypic drug discovery for uncovering novel therapeutic approaches and new biology.*

By **Chris Tan Soon Heng**

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Cellular activities are orchestrated through a myriad of physical interactions occurring among proteins with metabolites, nucleic acids and lipids that are regulated in time and space. We are interested in understanding how the biomolecular interaction networks underlying various cellular phenotypes had changed during evolution and in human diseases. I will first present a comparative genomics approach that we used to dissect the evolutionary dynamics of phosphotyrosine signaling networks. We identified genome-wide features co-occurring with the expansion of tyrosine kinase and phosphotyrosine-binding SH2 domain in the metazoan lineage that likely contributed to fidelity in the phosphotyrosine signaling system. Moving to network dynamics of a much shorter timeframe, I will present our most recent work adapting a drug target deconvolution technology for arguably the first and only technique currently for intracellular and proteome-wide profiling of protein complex dynamics. The technique exploits an intracellular biophysics phenomenon termed Thermal Proximity Co-Aggregation (TPCA) to monitor the assembly and disassembly of multiple protein complexes simultaneously with protein mass spectrometry. Proof-of-concept experiments validated that TPCA profiling can identify known modulated protein complexes that occurred in the absence of protein expression changes as well as identifying protein-protein interactions that are cell-type specific. As the technique is proteome-wide, rapid, requires neither antibody nor genetic engineering (for protein tagging), applicable on primary cells and tissues, it is posed to be a powerful tool for comparing the dynamics of protein complexes and interactions across cell types, physiological states and disease conditions.

Artwork by Ann Nee, DBS, NUS