The Singapore Bioimaging Consortium (SBIC)
presents a seminar

on

"Physiological Functions of Synucleins"

Speaker: **Dr Sreeganga Chandra**
Associate Professor
School of Medicine
Yale University
Host : **Dr Han Weiping**
Date : **Tuesday, 1 December 2015**
Time : **11.00am – 12.00pm**
Venue : **SBIC Seminar Room**
11 Biopolis Way
Level 2, Helios Building, Singapore 138667
(Please enter via Level 1)

Abstract

α-Synuclein is a member of a family of three abundant, presynaptic proteins that includes β- and γ-synuclein. To delineate the physiological functions of synucleins, we have taken a loss-of-function approach and have generated αβγ--synuclein triple KO mice. Our analysis revealed that deletion of synucleins results in age-dependent neuronal dysfunction. This suggests that synucleins are important for long-term neuronal health and has major implications for the development of α-synuclein targeted therapeutics for PD. To obtain insight into the molecular functions of synucleins, we implemented several parallel approaches. We have compared the entire synaptic proteome of wildtype and synuclein null mice. These experiments showed a select upregulation of proteins that bend membranes such as endophilin A1. We then tested if synucleins also share this property and found for the first time that all synucleins can robustly generate membrane curvature. Since our original publication, several groups have shown that synucleins can sense and generate membrane curvature. These properties suggests that synucleins function either at the exo- or endocytic steps of the synaptic vesicle (SV) cycle, two steps that require membrane bending. We monitored SV cycling in wildtype and αβγ-Syn$^{-/-}$ neuronal cultures using pHlourin imaging, and observed a striking endocytic phenotype in αβγ-synuclein in triple KO neurons. We confirmed our result showing slowed endocytosis αβγ-Syn$^{-/-}$ neurons using electron microscopy and slice electrophysiology. We are presently using *in vitro* endocytic reconstitution assays to precisely define the endocytic step where synucleins act. Our progress has established that synucleins regulate the kinetics of SV endocytosis by acting at early during membrane bending

and cargo selection. This is the first description of a conserved function for the synuclein protein family, since the discovery of these proteins over two decades ago.

About the Speaker

Dr Sreeganga Chandra is an Associate Professor at Yale University. After completing her undergraduate degree in India, she received her PhD from Purdue University. She did her postdoctoral studies in the lab of Dr Thomas Südhof, then at UT Southwestern Medical Center at Dallas, where she characterized the structure and function of α-synuclein. In 2007, she started her independent lab at Yale University. The central theme of her research is synaptic dysfunction in neurodegenerative diseases, with a focus on Parkinson's disease and lysosomal storage diseases.

--- Admission is free and all are welcome ---