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

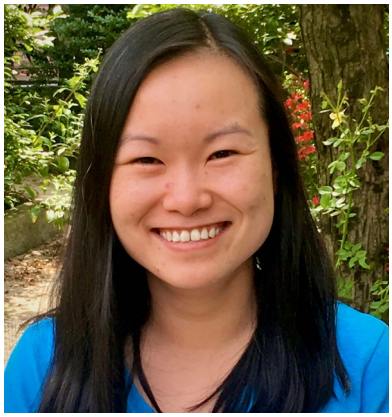
VIRTUAL BIOLOGY COLLOQUIUM

Friday, 26 Aug 2022 | 10 am | Online Zoom Session

Hosted by Dr Lin Zhewang

Mechanisms of membrane protein quality control

By **Susan Shao**
Harvard University



The biosynthesis of thousands of proteins requires insertion of a signal sequence or transmembrane segment (TM) into the endoplasmic reticulum (ER) membrane. Diverse hydrophobic α-helices such as TMs and signal sequences must localize to the appropriate cellular membrane and integrate in the correct topology to maintain cellular homeostasis. We recently showed that the P5A-ATPase (Spf1 in yeast, ATP13A1 in humans) dislocates mislocalized mitochondrial tail-anchored (TA) membrane proteins containing a single C-terminal TM from the ER, which provides TA proteins with additional opportunities to correctly localize to mitochondria. Here, we show that the P5A-ATPase is also required for the topogenesis of a subset of N-terminal type II TMDs and signal sequences that should integrate into the ER membrane with their N terminus facing the cytosol. Cells lacking P5A-ATPase activity accumulate type II proteins in the incorrect topology that undergo ER-associated degradation (ERAD). Thus, the P5A-ATPase plays a fundamental role in corrective quality control to prevent wasteful degradation of otherwise well-folded proteins.

About the Speaker

Susan trained with Manu Hegde, first as a PhD student in the Johns Hopkins - NIH partnerships program, and then as a postdoc at the MRC Laboratory of Molecular Biology. In 2016, she started her lab in the Department of Cell Biology at Harvard Medical School, where she is currently an associate professor. Her lab uses biochemistry, cell biology, and structural biology approaches to dissect molecular mechanisms required for protein and cellular homeostasis.

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