Guiding membrane proteins to the ER: chaperone cascades, ATPase tangos, and protean clamps

Presented by Shu-ou Shan, California Institute of Technology

Proper functioning of cells requires all newly synthesized membrane proteins to be delivered to and inserted into the appropriate cellular membrane. The biogenesis of membrane proteins, however, poses multiple fundamental challenges to the cell. How are these hydrophobic proteins effectively protected as they traverse the aqueous cytosol? Given the multiple membranes in a eukaryotic cell, how are nascent proteins sorted to their correct cellular destinations? What provides the energetic driving force, and what ensures the fidelity of these pathways? The Guided Entry of Tail-anchored protein (GET) pathway has emerged as a paradigm to address these questions. I will discuss our recent biochemical and biophysical work that elucidates how a chaperone cascade and conserved ATPase in this pathway overcome these mechanistic challenges, and thus effect efficient delivery of an essential class of tail-anchored proteins to the endoplasmic reticulum.

Shu-ou Shan completed her undergraduate degree in Chemistry and Biochemistry at the University of Maryland, and the doctorate at Stanford University in 2000, with a combination of training in biochemistry, enzymology, and physico-organic chemistry. After her post-doctoral training in cell biology and biophysics at UC San Francisco, she joined the California Institute of Technology as an assistant professor in 2005 and became full professor in 2011.

Work in the Shan lab aims to understand the mechanism of cellular machines in protein biogenesis and homeostasis, by integrating quantitative approaches in biochemistry, biophysics and mechanistic enzymology with structural and molecular cell biology. Unique to the research in the Shan lab is an attempt to understand these complex cellular processes at the level of physical and chemical principles, and to establish models that have accurate, quantitative predictive power. Her current work focuses on the mechanism of co-translational protein targeting by the Signal Recognition Particle (SRP), the mechanism of post-translational membrane protein targeting by the Guided-Entry-of-Tail-Anchored Proteins (GET) pathway, the roles and mechanisms of molecular chaperones dedicated to membrane proteins, and the principles of molecular recognition and regulation by a large, growing class of dimerization-activated nucleotide hydrolases.