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Mechanism and Regulation of a Membrane Protein Chaperone

Shu Ou Shan[1]*, Fu-Cheng Liang[1], Camille Mc Avoy[1], Chris Chi[1], Gerard J. Kroon[2] and **Peter Wright[2]**
[1]California Institute of Technology, USA
[2]The Scripps Research Institute, USA

Molecular chaperones play key roles in maintaining protein homeostasis within cells. Membrane protein chaperones face particular challenges, as they not only protect highly aggregation-prone membrane protein substrates, but also need to achieve tight spatiotemporal coordination of their chaperone cycle. I will describe our biochemical and biophysical work that define the chaperone cycle for cpSRP43, which protects the largest family of membrane proteins, the Light Harvesting Chlorophyll a/b-binding Proteins (LHCPs), during their delivery to the thylakoid. Our study revealed that cpSRP43's substrate binding domain samples at least three distinct conformations. This enables it to be readily switched 'on' by positive regulators in the soluble phase to ensure tight substrate binding, and be switched 'off' by the translocase at the membrane to ensure facile and productive substrate release. Our work demonstrates how the intrinsic conformational dynamics of a chaperone enables spatially coordinated substrate capture and release and suggests how leveraging the activitiesand properties of cpSRP43 provides opportunities for bioengineering efforts.

Biography:

Shu Ou 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 Dr. Shan's research is an attempt to understand complex cellular processes at the level of quantitative models that provide accurate predictive power. Her current work focuses on the mechanism of post-translational protein targeting pathways, the roles and mechanisms of molecular chaperones dedicated to membrane the principles of molecular recognition and regulation by a large, growing class of dimerization-activated nucleotide hydrolases.