

Translocon-Assisted Folding of Membrane Proteins: New Insights into Lipid-Protein Interactions

S. White

*Department of Physiology and Biophysics, University of California at
Irvine, Irvine, California, United States*

Recent studies of the translocon-assisted folding of membrane proteins have revealed two unexpected findings about the insertion of transmembrane helices across the endoplasmic reticulum membrane. First, the so-called S4 voltage-sensor helix of potassium channels, comprised of hydrophobic residues and four arginine residues, can be inserted. Second, poly-leucine helices as short as 10 residues are readily inserted. Exploration of these observations using physical studies of synthetic peptides in model membranes and molecular dynamics simulations provide new insights into lipid-protein interactions. They reveal that the lipid bilayer is far more complex ——— and interesting ——— than its usual lollypop cartoon suggests. The biological, physical, and molecular dynamics data to be presented demonstrate the extreme adaptability of phospholipids that arises from the privileged relationship between their phosphate groups and lysine and arginine residues. This adaptability makes possible the transmembrane insertion of very short helices and the independent stability of potassium channel voltage-sensor domains in membranes. [Research supported by the National Institute of General Medical Sciences and the National Center for Research Resources.]

**Proceedings of The Joint 2nd Pacific Rim International
Conference on Protein Science and 4th Asian-Oceania
Human Proteome Organization, Cairns- Australia, 22-26
June 2008**