The broad goal of my laboratory’s work on membrane-active peptides has been to describe the general principles of the interactions of peptides with lipid bilayer membranes. What have we learned after thirty years of work? I will highlight some key ideas that have emerged that guide our current thinking, including the structure of fluid lipid bilayers, how to describe the partitioning of peptides into bilayers, experiment-based-hydrophobicity scales, the induction of secondary structure by lipid bilayers, and the additivity of hydrophobic and electrostatic interactions. Where are we now? To answer that question, I will discuss how our knowledge of principles of peptide-lipid interactions have helped us understand how SecY/Sec61 translocons identify transmembrane helices during membrane protein assembly. I am pleased to acknowledge the research support of the National Institute of General Medical Science and the National Institute of Neurological Disorders and Stroke.