MSE-Colloquium@NTU

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Synthetic Molecular Evolution of Membrane-Active Peptides

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About the Talk

Membrane-active peptides have potential utility in many areas, including cellular delivery of polar compounds, cancer therapy, biosensor design, and in antibacterial, antiviral and antifungal therapies. Yet, despite decades of research on thousands of known examples, useful sequence-structure-function relationships are essentially unknown. Because peptide-membrane interactions within the highly fluid bilayer are dynamic and heterogeneous, accounts of mechanism are necessarily vague and descriptive, with little predictive power. This creates a significant roadblock to advances in the field. We are bypassing this roadblock with a synthetic molecular evolution: iterative peptide library design and orthogonal high-throughput screening. We start with template sequences that have at least some useful activity, and create small, focused libraries using structural and biophysical principles to design the sequence space around the template. Orthogonal high-throughput screening is used to identify gain-of-function peptides by simultaneously selecting for several different properties (e.g. solubility, activity and toxicity). Multiple generations of iterative library design and screening have enabled identification of membrane-active sequences with heretofore unknown properties, including spontaneous membrane translocation, as well as clinically relevant, broad-spectrum activity against drug-resistant bacteria and enveloped viruses.

About the Speaker

Professor Wimley received his B.S. in Biophysics from the University of Connecticut in 1985 and his Ph.D. in Biochemistry from the University of Virginia in 1990. He joined the Tulane faculty in 1998 as an Assistant Professor in the Department of Biochemistry at the Health Sciences Center. Since 2011, he is a Professor in the Department of Biochemistry, Tulane University School of Medicine. The primary theme of Professor Wimley's research is the structure, folding and design of proteins in membranes. Much of his research utilizes peptide models of membrane proteins. His laboratory has developed a unique understanding of the structure and mechanism of action of membrane-active peptides. At the same time, they have pioneered synthetic molecular evolution of membrane-active peptides, including antimicrobial peptides, by iterative library design and orthogonal screening. These lines of research have led us to our current focus on translational research toward peptide drugs.