

Leveraging Biophysical and Biochemical Methods to Investigate the Interplay of Host-Defense Mechanisms at Biological Membranes

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Host-produced antimicrobial peptides are multifunctional molecules that perform vital roles to prevent and fight infections. Not only can they directly eradicate bacteria by disrupting their membranes or targeting intracellular processes but they can also display immunomodulatory effects. The multiple functions of peptides in the piscidin family, the first antimicrobial peptides to be discovered in mast cells, encompass antibacterial, antiviral, antifungal, anticancer, and anti-inflammatory activities. In our research, we perform biochemical and biophysical experiments to investigate piscidin's molecular targets and mechanisms of action in bacterial and cancer cells, and their respective mimics. Using an array of tools that include high-resolution solid-state NMR, neutron diffraction, oriented circular dichroism, permeabilization assays, biological-activity testing, confocal microscopy, and molecular dynamics, we contribute to the efforts of mapping at the molecular and atomic levels the landscape of intrinsic structural features and environmental conditions that allow a peptide and its synergistic agents (e.g. copper ions; glycolipids) to unleash a multiplicity of functions in support of host defense.