INVITED LECTURE T2

How do cell penetrating peptides and antimicrobials restructure heterogeneous membranes?

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Antimicrobial peptides comprise a key component of innate immunity, and have been proposed as potential drugs against multi-antibiotic resistant bacteria. There are a number of proposed models for how such antimicrobial peptides permeate bacterial membranes, but the detailed molecular mechanism remains unclear. The same is true for cell penetrating peptides, such as TAT from the HIV-1 virus and ANTP from the fruit fly, which can cross cell membranes with high efficiency, but without killing the target cell. In both cases, cationic peptides interact and self-assemble with heterogeneous biological membranes composed of lipids with different charge and intrinsic curvature. Using synchrotron x-ray scattering, confocal microscopy, and genetic engineering, we investigate how such heterogeneous membranes are restructured by cell penetrating peptides, antimicrobials, as well as engineered peptides and sugars with different presentation of cationic, H-bonding, and hydrophobic groups, and correlate these results with cell-based studies. Homologies as well as differences between antimicrobials and cell penetrating peptides will be compared.