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Hierarchy of Specific Lipid-Peptide Interactions Produces the Activity of Cell-penetrating and Cell-permeating Peptides MATTHEW DAVIS, DANIEL PARENTE, VERNITA GORDON, ABHIJIT MISHRA, NATHAN SCHMIDT, LIHUA YANG, ROBERT CORIDAN, ABHIGYAN SOM, GREGORY TEW, GERARD WONG, University of Illinois, Urbana-Champaign —
Protein transduction domains can cross cell membranes with high efficiency, even when carrying a variety of cargos, and thus has strong biotechnological potential. The molecular mechanism of entry, however, is not well understood. We use small-angle x-ray scattering (SAXS) and confocal microscopy to systematically study the interaction of the TAT and ANTP PTD with model membranes of variable composition. Their membrane transduction activity requires the presence of both PE and PS lipids in the membrane. Antimicrobial peptides (AMP's) are cationic amphiphiles that comprise a key component of innate immunity. Synthetic analogs of AMP's, such as the family of phenylene ethynylene antimicrobial oligomers (AMO's), recently demonstrated broad-spectrum antimicrobial activity, but the underlying molecular mechanism is unknown. PE lipid greatly enhances permeating activity of AMO in these membranes, showing the importance of specific lipid composition for the activity of cell-permeating peptides. Since bacterial cell membranes are richer in PE lipids than are eukaryotic cell membranes, this may indicate a mechanism for antimicrobial specificity.

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