Detergent-like Membrane Disruption by Antimicrobial Peptides

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The rapid emergence of multi-resistant bacteria poses a global health problem and urges for the development of novel antibiotics [1]. The discovery of host defense peptides, which are frequently linear amphipathic cationic peptides, has opened new avenues for developing such drugs. These peptides kill bacteria within minutes, mostly by altering the permeability properties of membranes. The development of such peptides as novel antibiotics requires the understanding of the molecular mechanism(s) underlying their biological activity [2]. Microcalorimetric studies using membrane mimetic systems demonstrated that these peptides discriminate between host and target cells, i.e. mammalian and microbial cells that differ markedly in their membrane lipid composition. These and complementary results from X-ray and spectroscopic techniques indicated that affinity is mainly due to electrostatic interactions, while membrane perturbation is controlled by hydrophobic interactions. Distinctive different mechanisms of bacterial killing by antimicrobial peptides have been discussed. However, the amphipathic character of these peptides and their interactions with model membranes resemble in many ways the properties of detergent molecules. Thus we propose that the models such as pore formation or carpet mechanism, which have been suggested to explain the membrane disruption by antimicrobial peptides, might be special cases within complicated phase diagrams describing the morphological plasticity of peptide/lipid supramolecular assemblies [3].

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