Relationship between membrane disruption and cationic and hydrophobic content in synthetic antimicrobials

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Summary: Complementary x-ray and fluorescence techniques are used to systematically study the interaction of synthetic antimicrobials with model bacterial and eukaryotic cell membranes.

Membrane disruptive antimicrobial peptides (AMPs) are short (10-50 amino acids) amphipathic peptides with collective broad spectrum antimicrobial activity [1]. It is thought that AMPs disrupt membranes through a combination of electrostatic interactions of the cationic AMP with the anionic membrane followed by insertion of hydrophobic patches into the non-polar interior of the bilayer. A detailed understanding how AMP cationicity and hydrophobicity contribute to disruption and loss of barrier function in cell membranes has been elusive.

Synthetic AMP analogues have been constructed that demonstrate in vitro broad antimicrobial activities with low cytotoxicities against mammalian cells [2]. Like AMPs they are cationic and amphipathic. One advantage of synthetic antimicrobials is that their features can be tuned to allow a systematic investigation of how their electrostatic and hydrophobic interactions lead to selective membrane disruption. We investigate the membrane association behavior of synthetic AMP mimics with model bacterial and eukaryotic cell membranes at multiple length scales, using the complementary experimental techniques of small angle xray scattering, confocal microscopy, and fluorimetry. From our results, we will discuss the how an antimicrobial's hydrophobicity and cationicity affects its membrane disruption ability.