Design of antimicrobial protein-lipid complexes: From purification to delivery of human immune peptides against antibiotic resistance

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There is an urgent need to develop new antimicrobial materials to outsmart bacteria that are increasingly becoming resistant to conventional antibiotics. Natural antimicrobial peptides involved in the human immune response can compromise the barrier function of bacterial cell membranes providing a promising alternative to the conventional antibiotics. However, their poor stability in biological media is a major drawback for pharmaceutical application.

This presentation demonstrates the design of pH-responsive dispersed lipid self-assemblies as functional nanocarriers for antimicrobial peptides. The nanocarriers were characterized at different composition and pH values using small angle X-ray scattering, dynamic light scattering, zeta potential and their biological activity in vitro and in vivo.

The pH-triggered structural transitions allowed encapsulation of the peptides showing change in size and zeta potential at pH 7. Biological in vitro assays showed high activity against colistin resistant Escherichia coli and methicillin-resistant S. aureus with the positively charged nanocarriers at pH 5.0, while negligible antimicrobial activity was observed at pH 7.0 for the negatively charged nanocarriers. This was translated into in vivo surgical infections caused by S. aureus, revealing their activity in the skin model in mice.

The ability to switch their biological activity “on” and “off” in response to changes in pH has potential to focus the antimicrobial peptides’ action to areas of specific pH in the body [1]. The delivery of the antimicrobial peptide to the bacterial membrane presents a promising strategy against various multi drug resistant bacteria while protecting the beneficial microbiome in the body and eliminating adverse effects [2].

Figure 1. Protein-lipid self-assemblies and the release of antimicrobial peptide with pH-triggered structural transitions at the site of infection.