Granulytics: Antimicrobial protein-lipid complexes derived from the human immune peptides to tackle Antimicrobial resistance

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Antimicrobial resistance is one of the biggest threats to public health, with millions of deaths every year. To develop new antimicrobial drugs which can tackle bacteria resistant to conventional antibiotics, we took advantage of our immune system and identified promising natural antimicrobial peptides. These human antimicrobial peptides (AMP) are involved in the immune response and can compromise the bacterial cell membranes, leading to bacterial death.. However, their poor stability is a major drawback for pharmaceutical applications.

Our technology stabilizes the AMP to retain its antimicrobial activity. This system is a pH-responsive dispersed lipid self-assembly that act as a nanocarrier for the AMP. This unique pH-triggered structural transitions allowed encapsulation of the AMP at pH 7.0 and caused drastic changes in size and zeta potential at lower pH releasing the AMP. Biological *in vitro* assays showed high antimicrobial 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 successfully translated into *in vivo* surgical infections caused by *S. aureus* in the mice skin model.

The ability to switch their biological activity "on" and "off" in response to changes in pH has the potential to focus the antimicrobial peptides' action on areas of specific pH in the body. The delivery of the AMP to the bacterial membrane presents a promising strategy against various multi drug resistant bacteria while eliminating adverse effects.

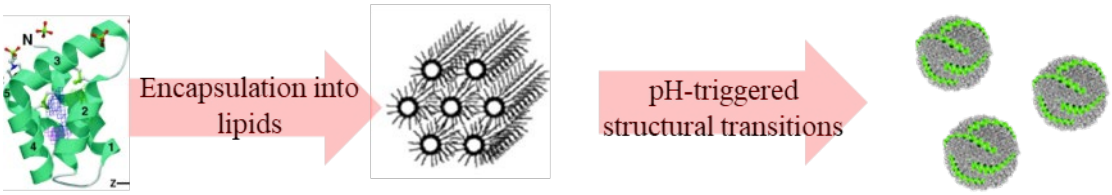

Figure: Protein-lipid self-assemblies and the release of antimicrobial peptide with pH-triggered structural transitions at the site of infection.