REVITASTEM
UMBILICAL CORD STEM CELLS & PEPTIDES

Antimicrobial Peptides

LL-37

Antimicrobial Peptides (AMP) Overview

- AMPs serve as endogenous antibiotics that are able to rapidly kill an unusually broad range of bacteria, fungi, parasites and viruses.
- Direct effects involve selective disruption of prokaryotic cell membrane
- In addition to their direct antimicrobial activity, also have multiple modes of action, including immune modulating effects
- LL-37 boosts mesenchymal stem cell migratory behavior and immunomodulatory effects.
- Significant anti-biofilm activity at low levels
- The MIC of LL-37 is much lower in vivo than in-vitro due to its immune modulating effects.
- AMPs are synergistic with antibiotics and reduce the development of drug resistance.
- Effective against free borrelia spirochetes and cystic forms
- Even low doses block the bioactivity of endotoxins and neurotoxins
- Well-tolerated, very safe with little side effects and a large therapeutic window
- Caution with autoimmune disease at high doses, as with any immune modulator

AMP Mechanism of Action

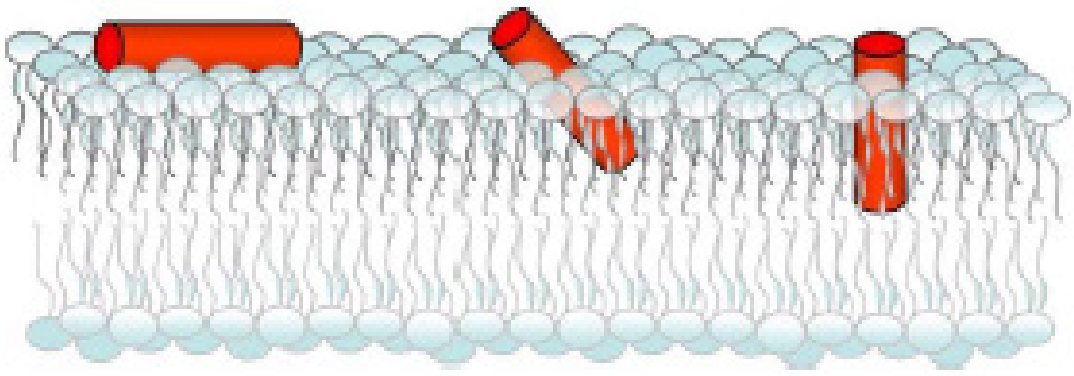


Fig. 2. Association of amphipathic α-helical peptides (cylinders) with a lipid bilayer can occur in three general orientations: parallel to the membrane surface, at an oblique angle, or perpendicular to the membrane surface (i.e., along the bilayer normal).

AMP Mechanism of Action (cont.)

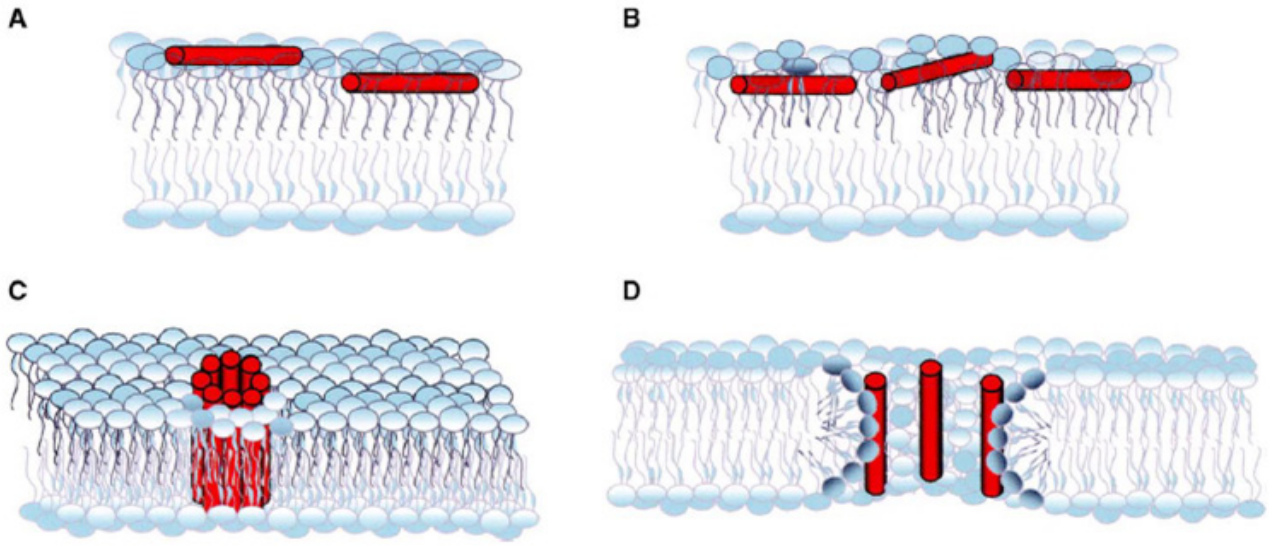
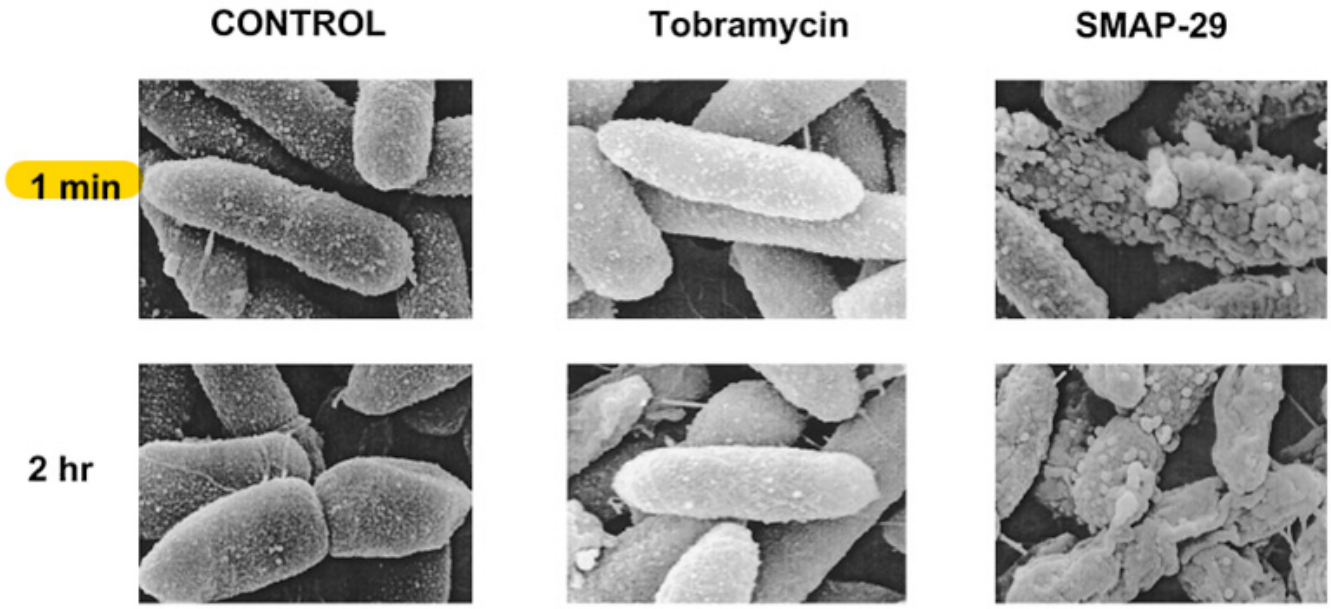


Fig. 8. Models of transmembrane channel formation. (A) Peptide α-helices (cylinders) initially associate parallel to the membrane surface, either superficially (left) or embedded just below the aqueous interface. (B) Peptides continue to accumulate at or near the bilayer surface, disrupting lipid packing and causing membrane thinning. This step may or may not involve peptide–peptide aggregation. Once a critical peptide/lipid ratio is reached, peptides either (C) insert into the membrane as a barrel-stave type pore, or (D) induce the localized formation of toroidal pores.

Sato H, Feix JB. Peptide–membrane interactions and mechanisms of membrane destruction by amphipathic a-helical antimicrobial peptides. Biochim Biophys Acta 2006;1758(9):1245-56.

AMP-Rapid Onset of Effect (1 minute)



AMP-Rapid Onset of Effect (1 minute) (cont.)

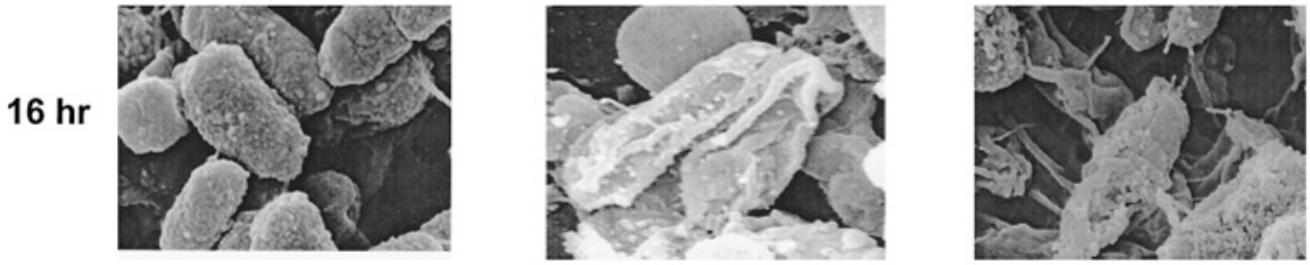
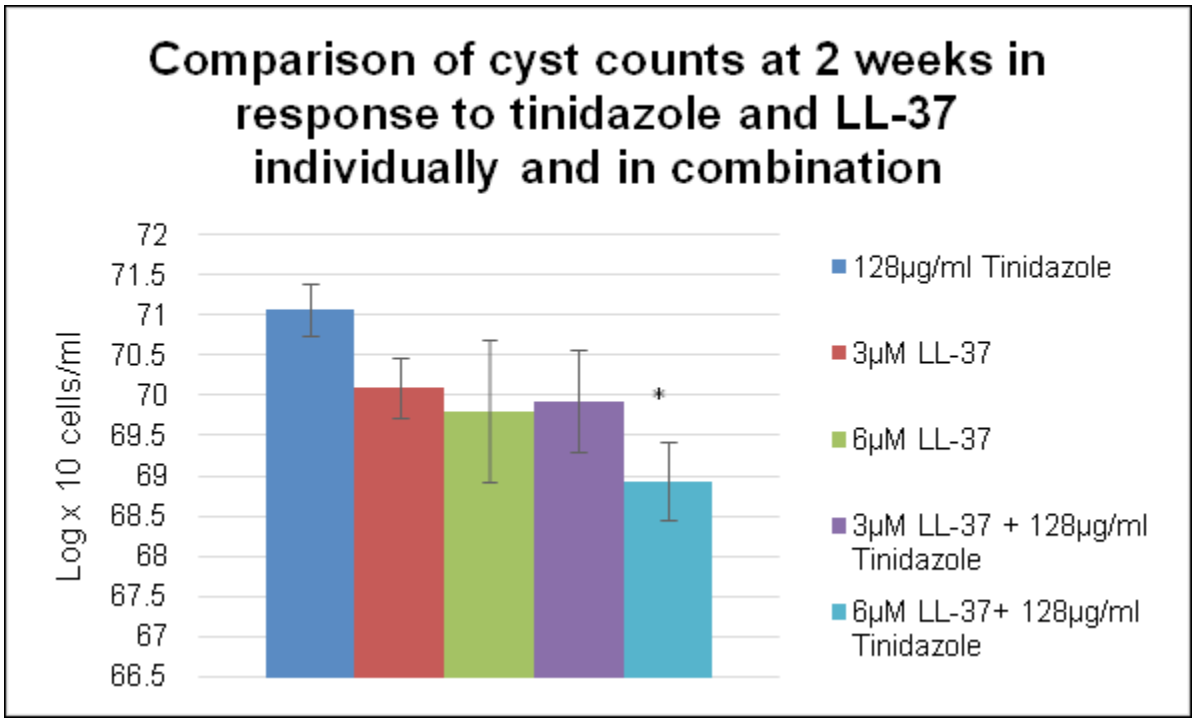


FIG. 3. Effects of SMAP29 or tobramycin treatment on the morphology of *P. aeruginosa* PAO1 evaluated by scanning electron microcopy. PAO1 was treated with media alone, tobramycin (5 μg/ml), or SMAP29 (0.5 μg/ml). At 1 min, 2 h, and 16 h the bacteria were processed for scanning electron microscopy. Within one minute, treatment with SMAP29 resulted in blebbing or blistering of the outer cell wall. The effects of tobramycin were much slower in their onset.

Sato H, Feix JB. Peptide–membrane interactions and mechanisms of membrane destruction by amphipathic a-helical antimicrobial peptides. Biochim Biophys Acta 2006;1758(9):1245-56.

LL-37 for Lyme Disease (cystic form)



"Combining antimicrobial peptides with commonly prescribed antibiotics to treat Lyme disease may provide a new approach to the treatment of chronic infections due to the significant synergistic effect of a combination"

Eckard A, Wood S. In-Vitro Susceptibility of Different Morphological Forms of Borrelia burgdorferi to Common Lyme Antibiotics in Combination with Antimicrobial Peptides. J Microb Exp 2016;3(4):1-19