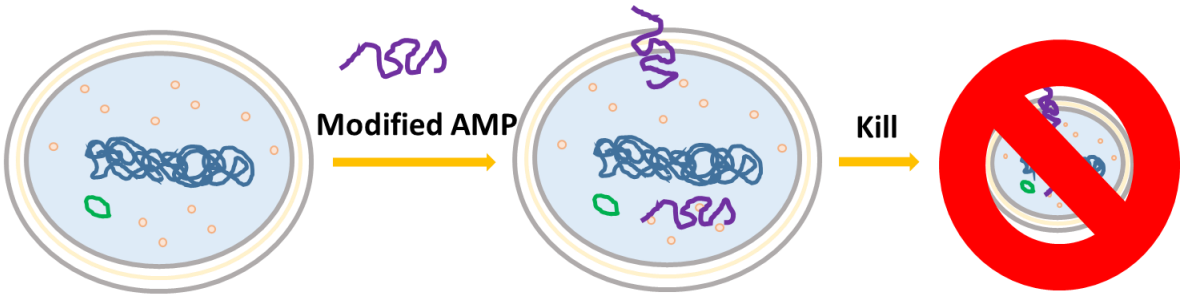
THE TECH TRANSFER OFFICE
UNIVERSITY OF COPENHAGEN

First-in-class treatment of Gram-negative infections

Enhanced antimicrobial peptides (AMPs) with high potency, low toxicity and low risk of resistance



Resistant Gram-negative bacteria

Efficient uptake and kill

For further information, please contact Commercial Officer Liv Thomsen
liv.thomsen@adm.ku.dk, +45 2057 0297 (Mobile)
Case number: 521-0704

Background

The continuous emergence and worldwide rapid spreading of multidrug-resistant (MDR) Gram-negative bacteria constitute a serious threat to human health. Gram-negative bacteria cause a large fraction of hospital-acquired infections, and even pan-resistant pathogenic bacterial strains are now appearing. Thus, there is an urgent unmet need for new treatment options for patients suffering from such infections.

Antibacterial agents based on antimicrobial peptides (AMPs) constitute a promising compound class as it appears to be less prone to inducing rapid development of antimicrobial resistance. Polymyxins (e.g., colistin) and daptomycin are examples of marketed AMP-based antibiotics. Most AMPs act via membrane-disruptive mechanisms, which may give rise to toxicological side effects. In contrast, modification of intracellularly acting AMPs with our uptake-enhancing constructs provides a unique class of novel AMPs as a source of drug leads with a favourable ratio between efficacy and general toxicological side effects.

The invention

Our uptake-enhancing constructs increase the potency of the conjugated AMP substantially (up to 32-fold). Also, modification essentially abolishes undesired effects of the resulting conjugates on the viability of mammalian cells (even at 4000-fold higher concentrations). This improves the possibility for a successful translation of such AMPs into new therapeutics. Due to different mode of actions our modified AMPs overcome pre-existing resistance to e.g. colistin, which is the most important last-resort antibiotic for Gram-negative MDR infections.

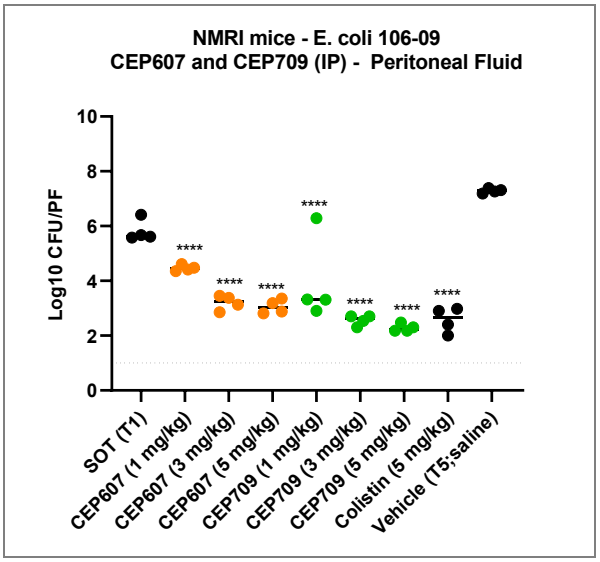


Figure 1. *In vivo*; *E. coli* mouse peritonitis model: our lead compounds CEP-607 and CEP-709 exhibit potent activity at low doses.

Key features

- Potent activity against:
  - Gram-negative pathogens (e.g. *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii*)
  - MDR strains and clinical isolates
- Low frequency of resistance
- Low toxicity to mammalian cells
- High stability in biological matrices
- *In vivo* proof of concept in animal models

Development status

We have proof of concept *in vivo* (TRL 3). Early data on compound properties, antimicrobial activity and early stability and toxicological assessment are available for lead compounds. Determination of further antimicrobial spectrum, safety profile and structure-activity optimisation is ongoing.

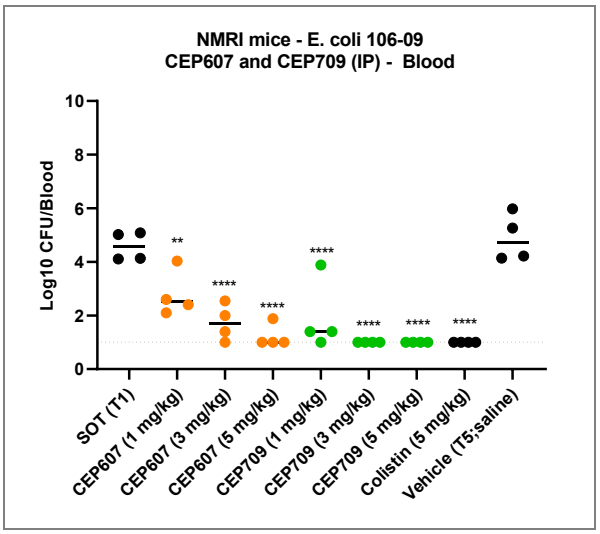


Figure 2. *In vivo*; *E. coli* mouse peritonitis model, our lead compounds CEP-607 and CEP-709 prevent the infection spreading to the blood.

Intellectual property rights

PCT application filed, claiming priority from our European patent application filed on 16 Sep 2020.