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# Poster abstract submission

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**Poster title**

Beta-clamp targeting peptides (BTPs); antibacterial peptides with a new target and a new mode of action

## Poster abstract

Beta-clamp targeting peptides (BTPs) constitute a novel antibiotic class with a unique target and mechanism of action. These peptides exhibit rapid, broad-spectrum bactericidal activity, show no cross-resistance with existing antibiotics, and possess potent antibiofilm properties. By binding to the beta-clamp, BTPs inhibit DNA replication and, at sub-MIC concentrations, suppress translesion synthesis (TLS) and mutagenesis, thereby significantly reducing the likelihood of resistance development. Multi-omics analyses further reveal that BTPs activate the envelope stress response and inhibit protein translation, underscoring their multifaceted antibacterial effects. Additionally, BTPs demonstrate additive activity when combined with multiple antibiotics and have shown in vivo efficacy in murine wound infection models [1–5]. Importantly, BTPs exhibit no nephrotoxicity in rats following daily infusions for seven consecutive days.

Given their broad-spectrum activity, BTPs are effective against WHO priority pathogens. For clinical development, we have selected Pseudomonas aeruginosa and Acinetobacter baumannii lung infections as lead indications, with intravenous administration (i.v.) as the preferred route. Supporting this choice, pilot data from a murine lung infection model (Streptococcus pneumoniae) indicated reduced pulmonary CFU following BTP intravenous injection, confirming lung distribution.

From over 60 candidates, we recently identified two frontrunners with antibacterial activity comparable to early versions of BTPs, but with improved safety profiles (lower infusion-related toxicity and higher MTD after i.v. bolus injection), enabling new IP opportunities. Both frontrunners exhibit potent MIC values against multiple A. baumannii and P. aeruginosa strains. Notably, their stability is enhanced, and MIC values decrease up to 10-fold in the presence of fractionated plasma. Ongoing analyses aim to identify plasma components responsible for this/these effect(s), which is also observed for other antibacterial peptides and antibiotics.

1. Nedal et al, 2020. Nucleic Acids Research, doi: 10.1093/nar/gkaa278
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3. Nepal et al, 2021. Frontiers in Microbiology, doi: 10.3389/fmicb.2021.764451
4. Singleton, et al, 2023. Frontiers in Microbiology, doi: 10.3389/fmicb.2023.126012
5. Singleton, et al, 2025. mSphere, doi: 10.1128/msphere.00068-25

## Research topic

Biological therapeutics