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# Poster abstract submission

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**Poster title**
Novel fragment-based antibiotics against Gram-negative WHO I pathogens

**Poster abstract**

Background
Currently, every 3rd bacterial infection worldwide is caused by resistant pathogens.
Still, the pipeline of novel antibacterials is insufficiently filled. Compounds with novel chemistry, novel Mode of Action and/or novel target are sparce.

Methods
We have chosen a fragment-based approach to identify novel antibacterial compound class(es) with direct antibiotic activity against WHO priority pathogens.

Results
Our novel (FTO confirmed), fully synthetic small molecule class shows direct antibacterial activity against A. baumannii, Enterobacteriales and Staphylococci, which is maintained in resistant clinical isolates of these pathogen species. Furthermore, compound activity in A. baumannii is synergistic with Polymyxin B. Slow killing suggests a specific Mode-of-Action, which is not accelerated when outer membrane integrity is impaired by PMBN. Confocal microscopy suggested a (primary) target in the inner membrane. Physico-chemical and in vitro ADME properties are promising. However, HepG2 cytotoxicity needs improvement.

Outlook
To prepare for a structure-based rational compound optimization, we are currently pursuing proteomics approaches and WGS analysis of induced resistant clones for target identification.

**Research topic** Small molecule therapeutics