Small molecule antibiotic against A. baumannii without cross-resistance and potential new MoA

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The rise of drug-resistant pathogens is a ticking time bomb, threatening to set back decades of progress in global health. In the fight against these superbugs, carbapenem-resistant *Acinetobacter baumannii* emerges as one of the most critical bacteria, as classified by the World Health Organization.
In 2018, CDRI identified the thiourea derivative SRI-12742 as an antibiotic against AB (Chopra et al, Int. J. Antimicrob. Agents (2018) 22–27). The compound's MIC is 4 μg/mL against the MDR AB isolate BAA-1605 and activity for clinical strains was assessed (MICs 4 μg/mL to >64 μg/mL). SRI-12742 exhibited concentration-dependent bactericidal activity (1.6 log10 CFU/mL reduction at 10×MIC in 24h), comparable with minocycline. In a murine neutropenic thigh infection model of AB infection, SRI-12742 reduced CFU counts by ca. 0.9 log10 CFU, comparable to polymyxin B. In addition, SRI-12742 synergised with all classes of antibiotics tested.
In our work, the hit was expanded with over 150 synthetic derivatives. Highly active derivatives were identified with MICs down to 0.125-0.5 μg/mL against 25 clinical isolates. No cross-resistance has been observed, activities for target ID are ongoing and a novel mode-of-action has been suggested based on affinity proteomics.