Compositions and methods for treating gram-negative bacterial infection

Value Proposition

Antimicrobial resistance is considered to be one of the biggest crises facing modern medicine today. Without desperately needed intervention, it is estimated that by 2050 over 10 million deaths per year will be due to antibiotic-resistant infections. Gram-negative bacteria are particularly problematic and are noted as the most critical priority pathogens for R&D of new antibiotics by the World Health Organization. However, despite the clear need for novel targets and compounds, the last new class of antibiotics was developed over 30 years ago. Accordingly, rapid development of effective, widely applicable antibiotic compounds will be crucial to mitigate the global health risk and resulting economic fallout caused by increasing antimicrobial resistant pathogens.

Technology

Using multiple advanced structural methods, Duke inventors have developed rationally designed compounds that specifically inhibit enzymatic activity in an essential bacterial pathway. The inventors’ derivative compounds show potent antimicrobial effectiveness against multiple species known to acquire high levels of resistance to nearly all available antibiotics. Furthermore, inventors broadened the clinical applicability of their compounds by increasing their delivery to the target enzyme, rendering previously impervious bacterial strains susceptible to treatment with the novel antimicrobial compounds.

Advantages

- Inventors’ compounds inhibit a novel, essential, and conserved target
- Inventors’ rationally-designed derivatives exhibit potent antimicrobial activity against several bacterial species

Publications

- Structure-Activity Relationship of Sulfonyl Piperazine LpxH Inhibitors Analyzed by an LpxE-Coupled Malachite Green Assay (ACS Infectious Disease, 2019)