

## Novel Antibiotic Agents

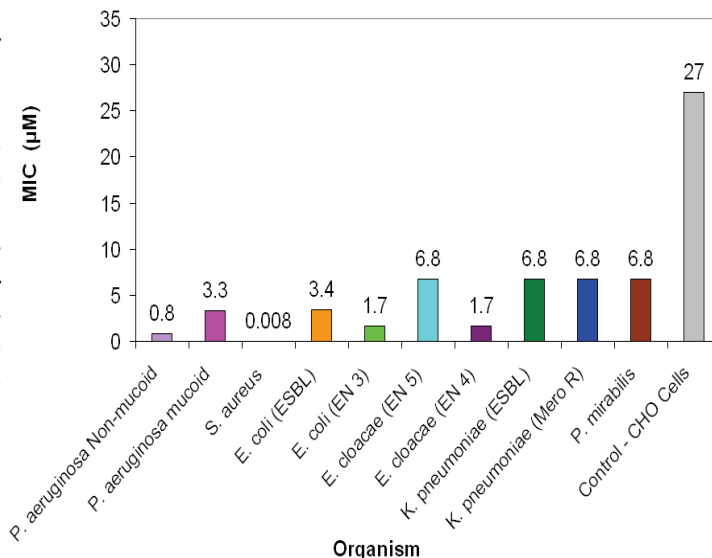
### Overview of Technology:

Rapid escalation of bacterial resistance has led to a significant decline in the number of effective therapeutics available to treat bacterial infections. Additionally, the current pipeline of new antibacterials in development is extremely thin—particularly for agents that target Gram-negative bacteria. In the United States alone there are 900,000 cases of bacterial sepsis annually resulting in 210,000 deaths.

Drs. Crandall and Szarek have developed a novel class of small molecules that can kill both Gram-negative and Gram-positive bacteria by selectively binding with lipopolysaccharide, an essential cell wall component in Gram-negative bacteria as well as with lipoteichoic acid, the equivalent molecule in Gram-positive bacteria. The novel mechanism of action and synthetic nature of the compounds suggests that pre-existing bacterial resistance mechanisms should not overcome these agents. Testing to date has shown these compound to be effective against highly drug-resistant strains of pathogenic bacteria. Additionally, these compounds may have a secondary capacity to bind and neutralize bacterial toxins.

For Gram-negative bacteria, compounds under development are active against all clinical isolates tested, including *Pseudomonas aeruginosa* (both mucoid and non-mucoid forms) and several species of *Enterobacteriaceae* including multidrug resistant (MDR) strains. For Gram-positive bacteria, the compounds are active against all clinical isolates tested including methicillin-resistant *Sataphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE), with minimum inhibitory concentrations (MIC) values in the low nanomolar range.

Comparative MIC values for mammalian cells are ~1 log higher than the bacterial values, giving a good therapeutic window. These compounds are excellent drug candidates since they have no chiral centers; can be synthesized rapidly and inexpensively; are stable; are soluble, and can easily cross membranes. Initial animal testing of this class of compounds has indicated that they are both bioavailable and well-tolerated.



MIC Values for a Developmental Lead Compound Against Various Clinical Isolate Bacterial Strains

### Inventors:

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