



## TECHNOLOGY READINESS LEVEL

1-3

### Seeking

Investment | Licensing | Research

### Keywords

- Antibacterial Resistance
- Gram-Negative Bacteria
- Antibiotic
- Novel Therapeutic Inhibitors

### Researchers

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## Technology Summary

Gram-negative bacteria are formidable pathogens because their cell envelope presents an adaptable barrier to environmental and host-mediated challenges. The stress response pathway, controlled by the alternative sigma factor  $\sigma^E$ , is critical for maintenance of the cell envelope. Because  $\sigma^E$  is required for the virulence or viability of several Gram-negative pathogens, including Enterobacteriaceae, it may represent a novel target for antibiotic development. No known antibiotics target the  $\sigma^E$  pathway. Using a patented high-throughput screening system, Penn State Inventors created and defined a novel suite of  $\sigma^E$  inhibitors that exhibit antibiotic activity and drug-like physical properties. Structure-activity relationship (SAR) studies assessed the importance of different functional groups for approximately 50 analogs. Compounds from the lead series show MIC levels of 1-3  $\mu\text{g/mL}$  in *E. coli*. No cytotoxicity or CYP450 inhibition was observed. Drugs that emerge from these compounds have the potential to be used as stand-alone treatments or as supplements to traditional antibiotics. Inhibition of this pathway is novel.

## Application & Market Utility

There is a critical need for new drugs to treat infections of gram-negative antibiotic-resistant bacteria. The problem is especially urgent in hospital settings where resistance to multiple antibiotics is found in approximately 20% of infections caused by gram-negative Enterobacteriaceae. Gram-negative bacilli are the most common cause of hospital-acquired infection and the most common causes of infection in the ICU. To reduce the incidence of hospital-associated infections caused by antibiotic-resistant bacteria, novel drugs that inhibit pathways not currently targeted by existing antibiotics are needed.

## Next Steps

Seeking industry collaboration and licensing opportunities to drive forward clinical validation and use.



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