



TECHNOLOGY READINESS LEVEL

1-3

Seeking

Investment | Licensing | Research

Keywords

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

Researchers

Kenneth Keiler, PhD

Associate Department Head for Graduate Education and Professor of Biochemistry and Molecular Biology
[Online Bio](#)

Originating College

Eberly College of Science

Office of Technology Management Contact

Long, Melissa
 mkl137@psu.edu
 814-865-5730

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 sE, is critical for maintenance of the cell envelope. Because sE 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 sE pathway. Using a patented high-throughput screening system, Penn State Inventors created and defined a novel suite of sE 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 µg/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.



Invent Penn State is a Commonwealth-wide initiative to spur economic development, job creation, and student career success. Invent Penn State blends entrepreneurship-focused academic programs, business startup training and incubation, funding for commercialization, and university-community collaborations to facilitate the challenging process of turning research discoveries into valuable products and services that can benefit Pennsylvanians and humankind. Learn more at invent.psu.edu.

Penn State is an equal opportunity, affirmative action employer, and is committed to providing employment opportunities to all qualified applicants without regard to race, color, religion, age, sex, sexual orientation, gender identity, national origin, disability or protected veteran status.