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Bacterial Histidine Kinase Inhibitor

Technology No. 20170232

IP Status: Pending US Patent; **Application #:** 16/615,585

Novel antibacterial drug targets

New compounds inhibit activity of multiple bacterial histidine kinases (HKs) and hold potential as therapeutics or antibiotics. These scaffolds could provide valuable starting points for designing broadly effective HK inhibitors, globally reducing bacterial signaling, and ultimately, developing a class of antibiotics with a new mechanism of action. HKs are one part of the bacterial two-component systems (TCSs), the primary signaling pathways bacteria use to respond to their environment. The new antibacterial compounds attenuate these signaling pathways by broadly targeting the histidine kinase family—they focus on the highly conserved ATP-binding domains in TCSs. Because HKs are very specific to bacteria, their inhibitors can target multiple types of bacteria while minimizing the possibility of human toxicity. Multi-targeted therapy may also hinder drug resistance since concurrent mutation of several drug target-encoding genes is unlikely.

New antibiotics for treating infectious disease

Bacteria have developed resistance to known antibiotics; therefore, novel therapeutics are needed to treat infections stemming from such antibiotic-resistant bacteria. New therapeutics would ideally aim for novel targets in such a way that antibiotic resistance does not rapidly develop. These new compounds circumvent bacterial resistance by targeting bacterial histidine kinases, a class of proteins not currently targeted with known drugs.

Phase of Development

- In vitro assessment. In vitro data in whole-cell assays.

Benefits

- Decreased chance for resistance to develop
- Decreases possibility of human toxicity

- Targets multiple types of bacteria

Features

- Potential therapeutics/antibiotics
- Targets highly conserved ATP-binding domains in bacteria
- Targets a new class of proteins not targeted with known drugs

Applications

- Antibiotics (specifically for drug resistant bacteria)
- Developing a new class of antibiotics
- Agricultural applications for treating antibiotic-resistant bacteria
- May re-sensitize resistant bacteria to existing drugs

Researchers

Erin Carlson, PhD
Associate Professor, Chemistry
External Link (carlson.chem.umn.edu)

Publications

Inactivation of Multiple Bacterial Histidine Kinases by Targeting the ATP-Binding Domain
ACS Chem. Biol. , 2015, 10 (1), pp 328–335
Rational Design of Selective Adenine-Based Scaffolds for Inactivation of Bacterial Histidine Kinases
J. Med. Chem. , 2017, 60, 19, 8170-8182

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