Washington University in St. Louis
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TARGET AND SMALL MOLECULE DRUGS TO SELECTIVELY NEUTRALIZE BACTERIA IN URINARY TRACT INFECTIONS

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Technology Description

Researchers in Prof. Jeffrey Henderson's laboratory have discovered a drug target and a class of small molecule candidates that could be used to selectively prevent pathogenic enterobacteria from causing diseases such as urinary tract infections (UTIs).

Currently, UTI's are treated with broad-spectrum antibiotics that can lead to bacterial resistance and "off-target" damage to "good" microbiome bacteria. To avoid these problems, this new antimicrobial therapy employs an approach that is mechanistically distinct from typical antibiotics. Instead of killing bacteria, this method of treatment is designed to specifically block a pathway that synthesizes virulence factors in enterobacteria (the most dangerous uropathogens). Because the antivirulence target is not present in "good" bacteria or humans, this therapy is expected to narrowly prevent the pathogenic effects from the enterobacteria while sparing healthy microbes. Beyond UTI's, the treatment could potentially be used for enterobacterial infections more broadly.

Related technology

The Henderson lab has also identified a biomarker that could be used as a theranostic to identify infections that are susceptible to drugs targeting this virulence pathway (WUSTL Technology T-011741).

Stage of Research

- **Target validation** – the inventors validated that the target/pathway is associated virulence in a mouse model of infection
- **Lead identification in vitro** – the inventors identified a known small molecule compound that inhibits biosynthesis from the virulence pathway

Applications

- **Anti-microbial drug** – small molecule compounds to treat or prevent diseases caused by enterobacteria (e.g., urinary tract infections, hospital associated infections, *Yersinia* infections, veterinary diseases)
- **Drug development target** to screen for anti-microbial drugs that prevent virulence

Key Advantages

- **Selective to avoid "off-target" damage:**
  - **target is only present in pathogenic bacteria (not in "good" microbiome bacteria or in**

humans)
    - expected to reduce risk of yeast or *Clostridium difficile* infections which can be caused by using traditional broad-spectrum antibiotics
    - may protect against future infections (recent studies have suggested that using conventional antibiotics increases UTI recurrence)
- **First in class –** unique mechanism prevents bacterial virulence unlike traditional antibiotics which kill the pathogenic bacteria
- **Active against multidrug resistant (MDR) bacteria –** drug target is strongly associated with clinical MDR isolates.

Publications - Robinson, A.E., Heffernan, J., Henderson, J.P. The iron hand of uropathogenic *E. coli*: the role of transition metal control in virulence". *Future Microbiology*, 13: 745-756. 2018. PMID: 29870278

Patents - Provisional U.S. Patent Application Filed

Website - Henderson Lab