



Antibacterials Targeting *Yersinia pestis* Type III Secretion System

Keywords: Gram-negative, Inhibitor, Bacteria, *Yersinia pestis*, Secretion
US patent pending

Background

The predominant class of current antibacterials target bacterial protein & cell wall synthesis. With bacteria developing resistance to most existing antibiotics, there is an urgent need to find drugs with newer & novel mode of action. *Yersinia pestis* & other gram negative bacteria utilize a plasmid encoded **type III secretion system (T3SS)** to promote infection by delivering bacterial outer proteins into the cytosol of mammalian cells. This T3SS is absolutely necessary for *Yersinia* virulence, which makes T3SS an attractive target in the development of novel therapeutics for treatment of plague & harmful diseases.

Technology

UMass Medical School investigator Dr. Jon Goguen & colleagues have identified novel inhibitors that selectively target the *type III secretion system* utilized by a number of pathogenic gram negative bacteria to deliver virulence factors to mammalian cells. The cocktail of virulence factors delivered by this system prevents the host from generating a robust immune response to the infection. T3SS inhibitors block this transfer, thereby curtailing disease progression. Using a HTS method, developed in-house, compound sets from the US national screening laboratory were screened, yielding several potential candidates. When examined for their efficacy in secondary screens, four compounds showed great promise as leads for structure activity relationship studies. These compounds represent diverse groups, each having a unique chemical scaffold.

Applications

Anti-Bacterial for pathogenic gram negative bacteria such as *Yersinia pestis*

Salient Features and Competitive Advantages

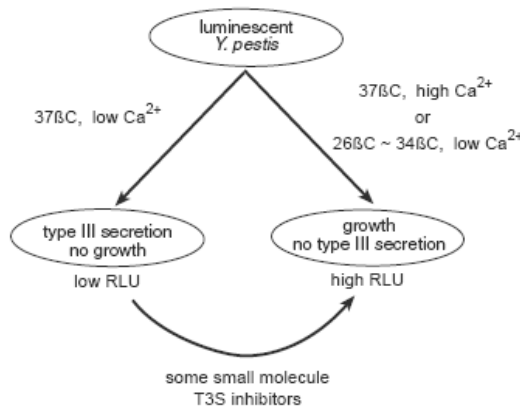
- **Novel Target:** Selectively inhibits the secretion system of gram negative bacteria, a novel target for potential antibacterial therapy.
- **Early Stage Inhibitors:** Unlike conventional antibiotics, these inhibitors have the ability to block transfer of virulence factors from pathogenic bacteria to mammalian cells, thereby blocking infection at its earliest stage and enabling the host to generate a robust innate and adaptive response against the pathogen.
- **Robust Activity:** Highly effective inhibition of virulence factors, YopH and YopM secretion
- **Safety:** Low cyto-toxicity to mammalian cells at inhibitory concentrations
- **Broad Applicability:** can be potentially utilized for treatment & prevention of disease caused by gram negative bacterial pathogens with similar type III secretion system
- **Market Potential:** The global antibacterial market was valued at \$25.5 billion in 2005.

Business Opportunity

UMass OTM is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology.

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