Novel Antimicrobial Drug Targets: Genetic Screens for Intein Function

Summary:

Our invention provides a novel approach to drug screening by adopting inteins as a drug target and testing the efficacy of agents which inhibit intein function in microbial pathogens. Inteins are naturally occurring protein elements that catalyze their own excision from within a larger protein together with the ligation of their flanking "extein" sequences which allow normal protein processing to occur. If the inteins are not removed, protein function will be interrupted and the viability of the cell may be compromised. Inteins are widespread, occurring in microbial pathogens such as *Mycobacterium* and *Cryptococcus*. This invention is directed at screening novel drugs to determine which have application for administration as intein-blockers or intein-inhibitors.

Our system of drug targeting against intein function provides a new approach to prevent the growth of organisms in critical genes by inhibiting inteins. Of additional benefit is that, while inteins are widespread, >400 inteins have been found in >35 different types of proteins, they are absent in mammalian genes. This is a positive indication for toxicity concerns which surround the development, approval and use of drugs. Our method provides a simple and targeted drug screening application for a new line of antimicrobial drugs. Crucial to pathogen survival, yet absent from all human proteins, the intein is a promising new drug target to overcome the drug resistance problem.

Applications:

- Identification of drugs that inhibit intein function to be useful as antimicrobial agents for a broad spectrum of pathogens
- Testing & monitoring the efficacy of antimicrobial agents that inhibit intein function
- A novel method of monitoring of intein function of *Mycobacterium tuberculosis*
Advantages:

- Unique ability to interrupt genetic sequences containing inteins and retard the growth of the organisms
- Overcoming drug resistance of traditional drugs via intein-blocking
- Ability to screen drugs against novel molecular targets within microbial pathogens

State of Development:

Empirical assay for screening chemical agents is available for use. Assay is available for development for specific fields of use.

Patents:

USPTO # 5,795,731

Licensing Potential:

HRI is seeking commercial partners for development

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