Protein Inhibitors of TcdB for Prevention or Treatment of Clostridium Difficile Infection

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Technology description

Overview

Clostridium difficile infection (CDI) is the leading cause of hospital acquired infectious diarrhea resulting in morbidity and mortality. A significant percentage (7%) of patients acquire CDI after hospitalization. It claims lives of ~30,000 people annually and results in >$6 billion in treatment associated costs. The pathology of CDI is caused by the two C. difficile secreted exotoxins – toxin A (TcdA) and toxin B (TcdB).

CDI can be treated using antibiotics, but in 20-25% of the cases it relapses due to infection by antibiotic-resistance or so-called hypervirulent strains. CDIs occur frequently in people who have illness or conditions requiring prolonged use of antibiotics, and the elderly because their capacity to fight infections is diminished. The antibiotics administered to these individuals eliminate their normal gastrointestinal microflora thereby rendering their intestines vulnerable to opportunistic colonization by C. difficile organisms which display an innate resistance to many conventional antimicrobial agents. CDI can also be treated using antibody proteins. The relapse rate following treatment with antibodies is lower than that of the antibiotics, however, it still remains high at 15-17%. Manufacturing of antibodies is expensive, costing as much as $3,000/dose. Also, antibody treatment must be administered through intravenous (I.V.) channels.

Technology

Inventors at Texas A&M University have engineered an anti-toxin TcdB DARPin (designed ankyrin repeat protein) as a potential therapy for CDI. The DARPin a small non-antibody protein which neutralizes TcdB. The molecule was engineered using phage-panning and high-throughput in vitro functional screening techniques. DARPins do not require manufacturing in mammalian cells, but rather can be manufactured in E. coli on a large scale and at a low cost. Ease of production and high stability makes it potentially possible to formulate the anti-toxin DARPin into an oral therapy.

Research Interests

Protein Therapeutics

Virology

Infectious Disease

Publications

R. Simeon, Z. Chen Z. **"In vitro-engineered non-antibody protein therapeutics."** Protein & Cell. 2018.

R. Simeon, M. Jiang, A.M. Chamoun-Emanuelli, H. Yu, R. Meng, J. Jakana, J. Zhang, H. Feng, Z. Chen **"Novel Designed Ankyrin Repeat Proteins as Potent Inhibitors of Clostridium difficile Toxin B."** Manuscript in revision by Nature Communication.

TECHNOLOGY COMMERCIALIZATION

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