Pharmacological Mitigation of Late-Stage Toxemia

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BACKGROUND

Anthrax disease, caused by Bacillus anthracis, is a highly lethal infection with patient fatality rate between 45-85% during fulminant, toxemia-related late-stages of infection. Systemic release of anthrax edema toxin during late-stage infection induces vascular collapse through endothelial barrier disruption, culminating in fatal hypovolemic shock, a hallmark of systemic anthrax infection. Existing therapeutic strategies to mitigate the effects of anthrax infections only target early-stage infection vis-à-vis bacterial clearance (antibiotics) and toxin-host cell interactions (anti-toxin antibodies), but are ineffective in preventing toxemic-shock which is induced even after pathogen clearance. In fact, patients with fulminant infection require aggressive, continuous fluid drainage and assisted breathing, and no effective therapeutic interventions exist currently for this critical stage of infection. Pathogen induced cell-cell barrier disruption (anthrax, cholera, traveler's diarrhea, gastroenteritis, pertussis, pneumonia) account for significant socio-economic impacts each year. Stand-alone antitoxin therapies such as those mentioned here can fulfill the unmet medical need for measures that significantly improve the survival rate of patients with severe infections, and lower the risk for development of antibiotic resistance.

High fatality rate of anthrax infections, despite intense antibiotic and supportive therapies, are primarily due to the continuing activities of anthrax exotoxins (ET and LT) released in the patient's circulatory system. Edema toxin or ET, a highly active adenylate cyclase that induces uncontrolled, pathological elevation in cellular levels of the second messenger cAMP is a major virulence protein of Bacillus anthracis and mediates significant lethality during fulminant stages of infection. ET induces rapid disruption of the endothelial barrier, resulting in irreversible tissue damage and lethality due massive fluid loss resulting in cardiovascular collapse and hypovolemic shock. It is therefore imperative that new therapeutic measures be developed that effectively blocks the intracellular function of ET (i.e. cellular proteins/pathways co-opted to induce barrier instability), to reduce fatalities associated with anthrax toxemia.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have an invention and method that provides a treatment wherein the condition is caused by anthrax, cholera, traveler's diarrhea, gastroenteritis, pertussis, or pneumonia.

APPLICATIONS

The application would include the administration of an inhibitor(s) which would treat the cell-cell barrier disruption-associated condition.

STATE OF DEVELOPMENT

In vivo experiments have been conducted in mice.

INTELLECTUAL PROPERTY INFO

The invention is patent pending and available for licensing.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Anthrax, antitoxin, asthma, cholera, inflammatory bowel disease, late-stage inhibitor, small molecule therapeutics

CATEGORIZED AS

- **Medical**
  - Disease: Infectious Diseases
  - Therapeutics

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