TECHNOLOGY

Oral live-vector vaccine against Clostridium difficile-associated disease

OVERVIEW

UMB researchers have achieved significant clinical success with live vector vaccines based on attenuated Salmonella enterica serovar Typhi (proven safe in clinical trials). Adapting these typhoid vaccine strains for the delivery of foreign antigens offers exceptional flexibility for further vaccine development. Dr. Jim Galen's group devised multiple strategies to optimize such vaccines, including novel chromosal integration strategies (Ref. JG-2013-037), a non-antibiotic plasmid selection/stabilization system (Ref. JG-98-002) and protein export system (Ref. JG-2001-022 and JG-2008-080). These state-of-the-art strategies have been employed as the platform for an oral live vector vaccine against Clostridium difficile-associated disease. Synthetic genes for three important C. difficile virulence factors have been engineered for both genetic stability and efficient expression in an attenuated S. Typhi strain. The resulting live vector vaccine is currently being tested for its ability to elicit antigen-specific serum neutralizing antibodies and mucosal IgA response, and to protect against pathogen challenge in mice.

APPLICATIONS

Clostridium difficile is a type of bacteria which can infect the human intestinal tract. It's harbored by 3% of healthy adults without symptoms but can cause disease ranging from mild diarrhea to more severe and life-threatening pseudomembranous colitis, which, if left untreated leads to fulminant colitis and death. Transmission of C. difficile occurs primarily in healthcare facilities via fecal to oral transmission from contaminated surfaces and hand contact. At risk for C. difficile-associated disease (CDAD) are the elderly and patients being treated with a prolonged course of antibiotics. In the U.S., data suggest mortality rates due to CDAD increased from 5.7 per million population in 1999 to 23.7 per million in 2004. Estimates of the cost for treatment in the U.S. have soared from $1 billion in 2002 to $3.2 billion in 2007, due to a dramatic increase in the number of cases and increasing severity of the disease. An emerging more virulent strain has been associated with recent epidemics of CDAD in North America and Europe, with increased morbidity and mortality.

ADVANTAGES

Broad humoral and mucosal immunity is anticipated with this vaccine, and that may not be readily achieved using another approach based on a purified protein subunit vaccine.

STAGE OF DEVELOPMENT

UMB researchers have engineered the optimal multivalent, live vector C. difficile vaccine, and critical animal proof-of-concept experiments are underway.

R&D REQUIRED

Further pre-clinical development followed by clinical trials.

LICENSING POTENTIAL

UMB seeks partner to advance this technology into the healthcare field.

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PATENT STATUS

JG-2009-032 -US Patent 10,046,040 issued 08/14/2018 JG-2013-037- US CON 10,010,596 issued 07/03/2018, US CIP 9,446,113 issued 09/20/2016

CATEGORIES

- Vaccines

INVESTIGATOR(S)

James Galen

EXTERNAL RESOURCES

- Novel methods for expression of foreign antigens in live vector vaccines
- Salmonella enterica serovar Typhi live vector vaccines finally come of age
- A new generation of stable, nonantibiotic, low-copy-number plasmids improves immune responses to foreign antigens in Salmonella

JG-2009-032; JG-2013-037