Therapy for Septic Shock

Tech ID: 19482 / UC Case 2004-263-0

BACKGROUND

Bacterial sepsis remains a major challenge for modern medicine. Septic shock is the most severe form of sepsis, in which perfusion of the liver, kidney, and other vital organs are compromised. This syndrome, which can be caused by both gram-negative and gram-positive bacteria, has a mortality rate of 30-60 percent. Systemic infection is a complication of many types of medical therapy, such as surgery, immuno-suppression for transplant, or cancer chemotherapy. There are currently no effective treatments for sepsis and the number of patients in the U.S. and Europe is large and will likely increase as intensive medical therapy becomes more widespread.

A key component of the mammalian innate immune system that acts as a first line of defense against pathogens is a family of toll like receptors (TLRs). Lipopolysaccharide (LPS), a major component of gram-negative bacteria, activates a variety of cells to produce inflammatory cytokines leading to septic shock in humans. MD2 is a pattern recognition receptor that binds LPS with a high affinity and without the need for LPS binding protein to catalyze the reaction. It is an extracellular protein that is co-expressed with TLR4, and necessary for TLR4 LPS receptor function. Truncation of MD2 leads to LPS non-responsiveness, and a monoclonal antibody that recognizes the MD2/TLR4 complex, blocks LPS activation of cells.

TECHNOLOGY DESCRIPTION

Scientists at the UC San Diego have developed a possible treatment for sepsis caused by infectious diseases (both bacterial and fungal) by providing methods and compositions for decreasing the levels of LPS in the circulation of an individual with sepsis. The invention provides variant MD-2 polypeptides and methods of using them as bacteria-targeting agents. The invention is also directed to chimeric proteins comprising these mutant MD-2 polypeptides and an opsinizing agent, e.g., antibody Fc domains, or equivalent. These chimeric proteins can be used as bacteria-targeting agents to deliver compositions, including other protein moieties, to treat sepsis or any gram-negative bacterial infection. The mutant proteins could also be further modified to improve their therapeutic capabilities and they provide a promising new approach to the treatment of septic shock.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,821,884	09/02/2014	2004-263

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Monoclonal Antibodies to Soluble Human MD-2

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OTHER INFORMATION

CATEGORIZED AS

- **Medical**
  - Disease: Infectious Diseases
  - Other

RELATED CASES

2004-263-0