Generation of Non-Toxic Mutants of Pathogenic Gram Negative Bacteria

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Technology description

Technology Summary

Researchers at the University of Iowa have developed a potential vaccine with efficacy across various pathogenic gram negative bacteria. The vaccine is based upon a conserved portion of an LOS, known as conLOS, fromNeisseria meningitidis. This element, GlcNAc-Hep2phosphoethanolamine-KDO2-LipidA, is common across a broad range of gram negative bacteria. Hence, the vaccine can elicit an immune response against bacteria such as:Neisseria meningitides, Neisseria gonorrhoeae, Haemophilus influenza, Chlamydia trachomatis, Pseudomonas aeruginosa, Bordetella pertussis, Vibrio cholera, among others. The endotoxin-based form of the vaccine can be used alone or in combination with a protein carrier (and other elements), and delivered as a vaccine. In an alternate vaccine format, the specific gram negative bacteria with a mutated htrB gene (which produces the mutant LOS) can be used as a live cell vaccine that is specific for each of the gram negative bacteria listed above.

Background Information

Gram-negative bacteria have an outer membrane comprised of proteins, lipoproteins, phospholipids and glycolipids. The glycolipids are consisted primarily of endotoxin-lipopolysaccharides (LPS) or lipooligosaccharides (LOS), depending on the bacteria. LPS and LOS are considered as bacterial components which have potential vaccine applications because of the antigenic determinants in their structures. However, the chemical nature of LPS and LOS prevents the use of these molecules in vaccine formulations – active immunization with LPS or LOS is unacceptable due to the inherent toxicity of the lipid A portion. The negative health effects induced by lipid A of LPS or LOS include fever, leucopenia, abortion, and in larger doses, shock and death. Accordingly, there are no currently available vaccines which induce antibody responses to LPS or LOS.

Advantages

Multiple Formats

Vaccine can take any of three formats: Live cells with attenuated htrB gene; Mutated endotoxin; Mutated endotoxin conjugated to a carrier protein

Broad Spectrum Gram Negative Target

Vaccine takes advantage of an endotoxin or gene that is common across various gram negative bacteria

Potential for Use in Combination

Vaccine preparation could be combined with others and used to increase the efficacy and/or coverage of desired bacterial targets

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