TECHNOLOGY

Vaccines Against ETEC with Isolation and Characterization of the csa Operon (ETEC-CS4 Pili)

OVERVIEW

Enterotoxigenic Escherichia coli (ETEC) is a major cause of diarrhea in infants and young children in developing countries, accounting for a high rate of infantile morbidity and mortality, and is also a major cause of traveler's diarrhea. Following ingestion of contaminated food or water containing ETEC, the bacteria can attach to the small intestine by means of proteinaceous hair-like fimbriae. These fimbriae serve as colonization factors that allow ETEC to evade the body's defense mechanism. The attached bacteria produce toxins which cause the watery diarrhea characteristic of ETEC disease. Considerable evidence supports the contention that immunity to ETEC is mediated by anti-fimbrial antibodies capable of inhibiting colonization. The most common fimbrial types found on human ETEC strains include CFA/I and CS1 through CS6. All seven of these fimbrial types are considered essential for inclusion in an ETEC vaccine to elicit broad-spectrum protection against the disease. Researchers at UMB's Center for Vaccine Development have cloned and sequenced the fimbrial antigen CS4 and expressed this and other ETEC antigens in attenuated strains of Shigella flexneri, including strain CVD 1204 and CVD 1208. Guinea pigs vaccinated with these strains showed high-titer immune responses against CS4 and other ETEC antigens and against the Shigella vector itself.

APPLICATIONS

-Vaccine against diarrheal disease caused by ETEC. -Efficient multivalent Shigella-based oral vaccine against both Shigella and ETEC.

ADVANTAGES

-Significant advance to the field of ETEC vaccines with first-time sequence information for one of the critical antigens, CS4. -Offers a much improved strategy for clinical development of a vaccine against disease caused by ETEC.

STAGE OF DEVELOPMENT

-Proven immunogenic in animal studies and an efficient strategy for clinical development of a combination vaccine against Shigella and ETEC. - Human phase studies are planned. -UMB has developed attenuated Shigella strains clinically proven in Phase 1 and pending Phase 2 Trials (see technology under UMB docket numbers AF-94-028 and ML-95-053) -UMB has also developed novel technologies for enabling live vector vaccines, such as stabilized expression plasmids which are not dependent on antibiotic resistance markers for selection (see under "Vaccine Enabling Technologies").

R&D REQUIRED

Phase 1 Clinical Trial is planned for a live Shigella vaccine expressing multivalent ETEC antigens.

LICENSING POTENTIAL

UMB seeks development partner for advanced clinical development.

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PATENT STATUS

Issued patents in U.S. U.S. Patent No. 6.902,736, issued June 7, 2005. U.S. Patent No. 7,399,474, issued July 15, 2008.

CATEGORIES

- Therapeutics
- Vaccines

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ATTACHMENTS

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