TECHNOLOGY

Plasmid maintenance system for antigen delivery

OVERVIEW

For live bacterial vaccines, various plasmid-based expression technologies may be utilized to express foreign antigens from the host bacteria. Keys to success using such systems include the need to achieve adequate antigen production to generate a good immune response, while reducing toxicity that may be associated with the foreign protein, and ensuring stable maintenance of the expression plasmids. Plasmids may be lost over time, making it critical to select for the host cells containing plasmid in order to maintain immunogenicity of the live vaccine. The UMB inventor engineered a novel stabilized plasmid expression system incorporating these genetic features: (1) an origin of replication to limit the number of plasmid copies per cell; (2) a partitioning function for stable inheritance of plasmid; and (3) a post-segregational killing function, to remove bacteria in which proper inheritance of plasmids has not occurred. A preferred method employs deletion of the ssb gene from the live vector chromosome combined with a plasmid encoding the SSB protein (which plays an essential role in DNA replication and repair), so that cells will not survive following plasmid loss. UMB researchers studied a mouse model of anthrax infection with an attenuated S. Typhi live vector and SSB-stabilized expression plasmids, and demonstrated the utility of this system in comparison to a more conventional system (same live vector without ssb deletion, using plasmid with antibiotic resistance marker). Lowering the copy number of SSB-stabilized plasmids in the ssb-deleted S. Typhi vector resulted in a 10-fold higher serum IgG response compared to the conventional system. This enhanced immunogenicity is thought to be the result of reduced metabolic burden on the host cell.

APPLICATIONS

The use of antibiotic-based plasmid selection systems is currently discouraged by vaccine regulatory agencies due to the potential to spread antibiotic resistance amongst bacteria, so that alternative approaches are required. This technology addresses the current regulatory requirements and offers enhanced immunogenicity over more conventional approaches, thus promising to enable the successful development of multiple live vector vaccines.

ADVANTAGES

Efficient plasmid selection with no reliance on antibiotic resistance markers.
Offers enhanced immunogenicity over conventional approaches.
Cassette technology allows modifications without compromising resident stabilization functions.
May be widely employed for expression in any strain.

STAGE OF DEVELOPMENT

Tests in animal models of anthrax infection show considerable promise for this approach to live vector vaccines, and further studies are underway in animal models of other clinically important infectious diseases.

R&D REQUIRED

Implementation for specific clinical application.

LICENSING POTENTIAL

UMB seeks a development partner in multiple fields.

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PATENT STATUS

Multiple Issued U.S. Patents and pending applications, including: U.S. Patent No. 6,413,768, issued July 2, 2002. U.S. Patent No. 6,703,233, issued March 9, 2004. U.S. Patent No. 6,969,513, issued November 29, 2005. U.S. Patent No. 6,977,176, issued December 20, 2005. U.S. Patent No. 7,125,720, issued October 24, 2006. U.S. Patent No. 7,138,112, issued November 21, 2006. U.S. Patent No. 7,141,408, issued November 28, 2006.

CATEGORIES

- Therapeutics
- Vaccines

INVESTIGATOR(S)

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ATTACHMENTS

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