



A *Salmonella*-based oral vaccine for Anthrax

The Challenge: Anthrax is caused by the spore-forming bacterium, *Bacillus anthracis*, and is classified as a potential bioterrorism threat. The current anthrax vaccine is based on Protective Antigen (PA) from an avirulent, non-encapsulated strain of *B. anthracis*. It requires six subcutaneous injections over an 18-month period and annual boosters to be effective. Others have investigated alternative delivery methods for PA, including use of the *Salmonella*-based vaccine currently approved by the FDA as a live oral vaccine for typhoid. However, these attempts have proved unsuccessful in that they are unable to express PA from *Salmonella* with sufficient immunogenicity such that a single dose oral vaccine would be feasible.

UMBI Solution: A UMBI scientist has improved the immunogenicity of the *Salmonella*-based oral vaccine for anthrax by developing strains of *Salmonella* capable of expressing both the anthrax PA and a biologically inactive Lethal Factor (LF) simultaneously. The “A” sub-unit of anthrax Lethal Toxin has been shown in animal studies to be capable of conferring immunity to anthrax. UMBI’s anthrax vaccine is delivered orally by means of live *Salmonella*, stimulating the generation of high affinity antibodies. Simultaneous expression of domains of PA and LF significantly enhance the magnitude and breadth of the resulting immune response leading to more rapid protection with fewer doses.

UMBI plans to expand the development of the *Salmonella*-based platform to serve as a vehicle for the expression of vaccine targets for a range of bio-defense organisms.

Commercial Applications:

- Anthrax vaccine - Single, oral-dose vaccine.
- Protection from bioterrorism – Appropriate for mass vaccination in response to a bio-threat.
- Platform technology – Platform for developing multivalent vaccines against a wide range of agents.

Advantages:

- Non-invasive delivery method through oral dosing.
- Can be stored and shipped at room temperature.
- Uses a *Salmonella* strain currently approved by the FDA for use in humans.
- Uses components of the currently approved injectable vaccine.
- May be used in combination with current vaccine to provide boost in immune response and shorten timeframe for effectiveness.
- Single dose decreases alum exposure.
- May be combined with other antigens for multivalent vaccines.

Stage of Development: Preclinical. Tested in murine and Guinea Pig *Salmonella* model systems. Ready for production of GMP quality material and phase I clinical trials.

Patent Status: Pending US and PCT applications

Licensing Potential: UMBI is seeking exclusive or non-exclusive licensees to part or all of this technology portfolio. The UMBI Inventor would welcome the opportunity to collaborate with any licensee to further refine this invention or extend its capabilities.

Inventor & UMBI Reference: Baillie, 04-019

Relevant Publications:

1. Albrecht MT, Li H, Williamson ED, Lebutt CS, Flick-Smith HC, Quinn CP, Westra H, Galloway D, Mateczun A, Goldman S, Groen H, Baillie LW. 2007. Human monoclonal antibodies against anthrax lethal factor and protective antigen act independently to protect against *Bacillus anthracis* infection and enhance endogenous immunity to anthrax. *Infect Immun.* 75(11):5425-33.
2. Stokes MG, Titball RW, Neeson BN, Galen JE, Walker NJ, Stagg AJ, Jenner DC, Thwaite JE, Nataro JP, Baillie LW, Atkins HS. 2007. Oral administration of a *Salmonella enterica*-based vaccine expressing *Bacillus anthracis* protective antigen confers protection against aerosolized *B. anthracis*. *Infect Immun.* 75(4):1827-34.
3. Baillie LW. Past, imminent and future human medical countermeasures for anthrax. 2006. *J Appl Microbiol.* 101(3):594-606. Review.
4. Hepburn MJ, Hugh Dyson E, Simpson AJ, Brennehan KE, Bailey N, Wilkinson L, Hornby R, Mateczun AJ, Bell MG, Baillie LW. 2007. Immune response to two different dosing schedules of the anthrax vaccine precipitated (AVP) vaccine. *Vaccine.* 25(32):6089-97.

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