Cholera Toxin Chimera and its use as a Staph Vaccine
U.S. Issued Patents 8,834,898 and 8,911,748
U.S. Patent Pending – 14/456,090
BSU File Reference #93 and 93B

Abstract

*Staphylococcus aureus* (*S. aureus*) is a common cause of hospital-acquired infection and represents an important public health threat. *S. aureus* can cause nosocomial (hospital) and community-acquired infections including impetigo, cellulitis, food poisoning, toxic shock syndrome, invasive necrotizing pneumonia, and endocarditis. *S. aureus* is also the most common species of staphylococci to cause staph infections. Currently, it is one of the top causes of infectious disease deaths in the United States. *S. aureus* also causes mastitis, which is a major problem in dairy cows with considerable economic implications.

Boise State University has developed a mucosal vaccine for the prevention of staph infections in humans and animals, which can be delivered through the nose, mouth, or skin. It is comprised of two physically linked protein segments: a nontoxic portion of the cholera toxin, and a surface protein (IsdA) from the *Staphylococcus aureus* bacterium. The attachment of cholera toxin to IsdA for vaccine delivery enhances the observed humoral and cellular immune response to staph bacteria, and has the potential to prevent both colonization and systemic infection. This vaccine can be used to inoculate humans to prevent diseases caused by the staph bacteria, the second leading cause of infectious disease deaths in the U.S. behind influenza. It also has the potential to prevent infections in dairy cows, inhibiting the development of mastitis, a contagious udder infection often requiring removal of the cow from the herd and subsequent economic loss.

Advantages

- There is currently no licensed vaccine against *S. aureus* for humans. There have been a number of potential vaccines that have entered clinical trials, but with limited immune response or protection.
- There are currently two vaccinations for cattle available; however they both lack efficacy and are widely unused.
- This vaccine induces the mucosal immunity that can potentially defend against colonization of *Staphylococcus aureus*, which is the major risk factor for systematic or invasive disease.
- This vaccine can be administered by the oral/nasal route, as opposed to using a needle or high-pressure air gun, which offers considerable economic cost cuts as well as logistical advantages.
- Multiple forms of vaccine are possible:
  - Different segments of the IsdA antigen, or alternative staph antigens
  - Different segments of the cholera toxin
  - Other bacterial enterotoxins substituted for cholera toxin

Stage of Development

- Immune responses studies have been conducted in both mice and cows.
- Induction of IsdA specific humoral immunity was observed. Significant increases in IsdA specific IgG (serum and milk) and IgA (mucosal) antibodies were observed.
- Vaccination resulted in significant increases in IsdA specific CD3+ T lymphocyte.
- Cytokine assays conducted were suggestive of a Th-2 response.
- Antibodies post vaccination successfully demonstrated an ability to significantly reduce binding of *S. aureus* to human epithelial cells.
- We are currently conducting challenge studies to evaluate colonization immunity and systemic infection immunity in mice models.
Figures 1A-1C show ribbon diagrams illustrating structures of cholera toxin, IsdA, and chimeric protein. Figure 1A shows a ribbon diagram of the cholera toxin crystal structure showing the CTA1 domain and connecting CTA2 domain, and the B subunit. Figure 1B shows a ribbon diagram of IsdA antigen that is replacing the toxigenic CTA1 domain to construct a chimeric protein that comprises an antigen and a non-toxigenic adjuvant. Figure 1C shows a ribbon diagram of one preferred chimeric protein, IsdA-CTA2/B.

The Inventor

Dr. Juliette Tinker is an Associate Professor and has been in the Department of Biological Sciences at Boise State University since 2005. She received her Ph.D. from the University of Iowa in Microbiology and worked as a Postdoctoral Fellow at the University of Colorado Health Sciences Center, where she began her work with cholera toxin. Her current research interests are focused on the development and characterization of bacterial enterotoxins as molecular tools and mucosal vaccine adjuvants. She has recently published her work on these topics, and has received several notable grants in relation to this research.

In October 2012, Dr. Tinker was awarded an Idaho Innovation Award for Early-Stage Innovation of the Year for her research surrounding this innovation. Tinker was one of three finalists in the Early-stage category. The Idaho Innovation Awards are presented by the Stoel Rives law firm, Kickstand and the Idaho Technology Council, and are supported by Idaho TechConnect and the Cooper Norman accounting firm.

Boise State is looking for a Licensee for this technology.

For more information contact:
Katy Ritter
Director and Technology Transfer Officer
Office of Technology Transfer
Boise State University
1910 University Drive
Boise, ID 83725-1135
208.426.5765
KatyRitter@boisestate.edu