

Pilot Project Abstract

The role of sIgA B memory cells in mucosal mechanisms of protection in *Shigella* challenge studies.

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Shigella is one of the top enteric killers of children worldwide. An intracellular Gram-negative bacillus causing diarrhea and dysentery in an estimated 165 million people per year, *Shigella* kills over 1 million, mostly children less than 5 years of age in the developing world. Natural immunity does occur, but typically only after a serious and life threatening battle with this disease. Promising candidate vaccines are being developed, but the mechanisms of immune protection are not completely understood. Currently, the process of selecting the *Shigella* vaccine candidates that advance in clinical development is based on trial and error. To date, immune markers that have been described include serum anti-lipopolysaccharide (LPS) IgG as well as peripheral blood anti-LPS sIgA antibody secreting cell (ASC), neither of which accounts for protection completely. Furthermore, low anti-LPS sIgA ASCs post challenge have been the strongest predictor of protection, suggesting that cells producing sIgA appear in the periphery post vaccination, home to the gut mucosa, and do not need to be elevated in peripheral blood after challenge in those that are protected. The objective of this project is to test the **hypothesis that antigen-specific sIgA B memory (B_M) cells contribute to mucosal mechanisms of protection in *Shigella* infection.** Specific Aim: Quantify sIgA B_M cells specific to antigens that include LPS and Invasion plasmid antigen (Ipa) B in existing specimens from *Shigella* challenge studies that have a clinical outcome. The B_M cell assay is an exciting new assay that has been applied by our group as well as others in vaccination and natural infection. **This project will, for the first time, apply this assay to challenge specimens and determine the role of antigen-specific sIgA B_M cells in protection.** Defining optimal immune correlates and surrogates of protection early in vaccine development will expedite *Shigella* vaccine development and prevention.