EFFICACY OF WRSD1 SHIGELLA DYSENTERIAE-1 VACCINE IN A Rhesus Monkey Model of Shigellosis

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Background: Shigellosis, “bacillary dysentery,” is a worldwide disease affecting both humans and primates. Shigella dysenteriae type 1, also known as the Shiga bacillus, is the most virulent of the four serogroups of Shigella and is the only cause of epidemic dysentery. WRSD1 is a live attenuated S. dysenteriae-1 vaccine candidate strain.

Objectives: This study determines the safety and efficacy after immunization with WRSD1 by challenging immunized monkeys with S. dysenteriae-1 1617 strain (parent strain of WRSD1).

Methods: A total of 10 monkeys, (2 groups of 5 each) were randomly assigned to one of the two groups. The immunization group (Group 1) of 5 monkeys is immunized by intragastric administration of a WRSD1 vaccine dose of 2 x 10^10 WRSD1 on study days 0, 3 and 6. The control group (Group 2) will likewise receive a placebo (20 ml sterile PBS) at the same route and schedule as the Group 1. At 30 days after last immunization or placebo, all monkeys are challenged with the wild-type S. dysenteriae-1 1617 strain at 2 x 10^10 cfu dose.

Results: One monkey had anorexia after multiple immunization doses. After challenge with a dose of 2x10^10 CFU of S. dysenteriae-1 1617 strain all 5 control monkeys were severely sick, had loose stool with mucus and blood and severe vomiting. One of the control monkeys died the day after challenge with acute necrotizing and hemorrhagic colitis, jejunitis and gastritis. One of the immunized monkeys also died 3 days after challenge with a three day history of anorexia. The 4 remaining immunized monkeys had anorexia only.

After immunization, plasma IgA and IgG responses against S. dysenteriae-1 LPS is 20 fold and 48 fold respectively compared to base line level. When these monkeys challenged, plasma antibody levels boosted, IgA 30 fold increase and IgG 165 fold increase.

Conclusion: This study suggests that WRSD1 is safe in monkeys and protects 80% of monkeys against a large challenge dose of S. dysenteriae.