

PUBLIC HEALTHWORKER SAFETY

Title: *Salmonella* DIVA vaccine for cross-protection against *Salmonella* serovar I 4,[5],12:i:- minimizing antibiotic usage and protecting swine and public health - #16-113 IPPA

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Scientific Abstract: In 2015, a multistate outbreak of *Salmonella* serovar I 4,[5],12:i:- was associated with pork products from Washington state and resulted in 188 illnesses including 30 individuals being hospitalized. The *Salmonella* isolates associated with the outbreak were determined to be multidrug-resistant (resistant to ≥ 3 antimicrobials) and ~523,380 pounds of pork products were recalled. *Salmonella* serovar I 4,[5],12:i:- has increased globally over the last 10-15 years and as of 2015 serovar I 4,[5],12:i:- was the 4th most common *Salmonella* serovar associated with human illness in the U.S. We investigated 33 *Salmonella* serovar I 4,[5],12:i:- strains that were isolated by the USDA, Food Safety and Inspection Service (FSIS) during 2015-2016 from pork products in 15 states. Thirty of the serovar I 4,[5],12:i:- isolates were multidrug-resistant including all 11 isolates from WA that were associated with the 2015 *Salmonella* outbreak. Nineteen serovar I 4,[5],12:i:- isolates had the same primary PFGE pattern (JPXX01.1314) including all of the outbreak-associated strains from WA state but also isolates from CA, IL, KY, MI, NY, SD, and TX. This data indicates that serovar I 4,[5],12:i:- isolates that are closely related to the 2015 outbreak-associated strains are present in numerous states across the U.S. We analyzed the genome sequence for *Salmonella* serovar I 4,[5],12:i:- isolate FSIS1503788 associated with the 2015 pork outbreak. Two unique genomic insertions were identified in serovar I 4,[5],12:i:- isolate FSIS1503788 compared to closely related *Salmonella enterica* serovar Typhimurium. FSIS1503788 has an ~28 kb module encoding resistance to the metal mercury and the antimicrobials ampicillin, streptomycin, sulfisoxazole, and tetracycline (R-type ASSuT). The second insertion is *Salmonella* Genomic Island 4 (SGI-4) an ~80 kb DNA island that contains multiple genetic operons encoding potential resistance to copper, arsenic, and zinc. We created a derivative of serovar I 4,[5],12:i:- isolate FSIS1503788 that does not contain SGI-4 and therefore does not contain potential metal resistance genes for copper, arsenic, and zinc. A phenotypic assay was performed comparing FSIS1503788 and the SGI-4 mutant. The wildtype strain grew better in the presence of copper and arsenic compounds compared to the SGI-4 mutant indicating that genes for resistance to copper and arsenic are present on SGI-4 and enhance growth of FSIS1503788 in the presence of these metals. A pathogenesis trial was performed in swine with serovar I 4,[5],12:i:- isolate FSIS1503788 challenge. The pathogenesis of serovar I 4,[5],12:i:- was similar to other swine pathogenesis trials that have been performed with *Salmonella* Typhimurium. A transmission trial of serovar I 4,[5],12:i:- was conducted in vaccinated and mock-vaccinated swine that shared a pen with directly inoculated pigs. The colonization of serovar I 4,[5],12:i:- isolate FSIS1503788 was significantly reduced in the cecal contents of vaccinated swine compared to mock-vaccinated pigs following 14 days of exposure to donor pigs. Vaccination against *Salmonella* may provide a swine management tool to assist in reducing *Salmonella* serovar I 4,[5],12:i:- carriage in pigs. The *Salmonella* serovar I 4,[5],12:i:- strains associated with the 2015 pork outbreak are similar to serovar I 4,[5],12:i:- strains that are distributed across the U.S. and globally. These serovar I 4,[5],12:i:- strains have 2 unique genomic insertions that encode metal and antimicrobial resistance genes. The use of metal compounds as alternatives to antimicrobials in swine may select for *Salmonella* serovar I 4,[5],12:i:- isolates that contain metal resistance genes.

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