

Title: Identifying the Genetic Profile of the *Salmonella*-carrier Pig to Improve Food Safety and Decrease Pre-Harvest Disease – NPB #05-176

Investigator: Shawn Michele Dunkin Bearson

Institution: USDA, Agricultural Research Service, National Animal Disease Center

Co-Investigators: Uthe, Jolita J., Wang, Yanfang, Qu, Long, Dekkers, Jack, Nettleton, Dan, Tuggle, Christopher

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Abstract

Salmonella shed from colonized swine can contaminate: slaughter plants and pork products during meat processing, edible crops when swine manure is used as a fertilizer, water supplies if manure used as crop fertilizer runs off into streams and waterways, and neighboring pigs resulting in a continuous food safety problem and animal health issue. Therefore, pre-harvest control of *Salmonella* in swine is an essential step in controlling animal disease, protecting the environment and preventing foodborne illness with *Salmonella*. A major focus of our collaborative research program is to investigate the porcine response to infection with *Salmonella* to 1) identify porcine genes differentially regulated during infection and 2) identify and associate genetic polymorphisms within these genes with infection status across swine populations. The goal of the research program is to provide molecular insight into the host gene expression responses that lead to the undesirable carrier state of *Salmonella* in pigs in order to identify approaches to control the re-emergence of *Salmonella* during transportation and marketing stress.

In the current study, 40 crossbred pigs were intranasally inoculated with *Salmonella enterica* serovar Typhimurium and monitored for *Salmonella* fecal shedding and blood immune parameters at 2, 7, 14 and 20 days post-inoculation (dpi). Using a multivariate permutation test, a positive correlation was observed between *Salmonella* shedding and interferon-gamma (IFNG) levels at 2 and 7 dpi ($p < 0.05$), with a greater number of *Salmonella* shedding in the animals with higher IFNG levels. In addition, a positive correlation was observed of the IFNG levels with the number of circulating neutrophils at 7 and 14 dpi, mature banded neutrophils at 2 dpi, monocytes at 7 dpi and white blood cells (WBCs) at 7, 14 and 20 dpi. We have further performed association studies of immune response parameters or shedding status of the *Salmonella*-infected pigs with single nucleotide polymorphisms (SNPs) in 11 genes: VCP, CCT7, LCP1, CD47, SCARB2, SDCBP, CD163, CCR1, NCF2, IL8 and TYROBP. Expression of these genes was identified by our group as differentially-regulated during *Salmonella* infection, and assays for these SNPs have been developed in our laboratories. A

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For more information contact:

National Pork Board, P.O. Box 9114, Des Moines, Iowa USA

800-456-7675, Fax: 515-223-2646, E-Mail: porkboard@porkboard.org, Web: <http://www.porkboard.org/>

positive association of SNP genotype A/G at nucleotide 1026 (relative to start codon) of the CCT7 gene was observed with circulating neutrophils and WBCs ($p < 0.05$) as well as *Salmonella* shedding ($p = 0.0012$) at 7 dpi compared to the G/G heterozygote genotype. CCT7 encodes a molecular chaperone involved in tubulin folding and protection, and our work is the first report of its response to *Salmonella* infection. Thus, our analyses are linking the porcine immune response to *Salmonella* infection with specific genes and genetic polymorphisms, thereby providing potential markers for carrier pigs as well as targets for disease diagnosis, intervention and prevention.