RESEARCH ABSTRACT

SWINE HEALTH

Title: **Comparative genomic and virulence analysis of *Streptococcus suis* isolates - #17-084 – IPPA**

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Scientific Abstract: *Streptococcus suis* is a major swine pathogen responsible for significant economic losses to the swine industry worldwide. *S. suis* is capable of causing a wide variety of clinical diseases in pigs including pneumonia, meningitis, septicemia, and endocarditis. Additionally, *S. suis* is a zoonotic agent causing severe infections to people in close contact with infected pigs or pork-derived products. Despite the significant impact on swine health and public health implications, the strategies and mechanisms used by *S. suis* to colonize and cause disease remain unknown. More importantly, vaccines and/or intervention strategies that do not rely on broad spectrum antibiotics currently do not exist to mitigate *S. suis* disease burden. The overall goal of this project was to use an unbiased and comprehensive approach to identify genomic and/ or transcriptional differences responsible for the spectrum of virulent capacities that occur among *S. suis* strains. The specific objectives of this study were to 1) Obtain closed whole-genome sequences of *S. suis* isolates that are known to exhibit different pathogenic capacities to perform comparative genomic analyses. 2) Perform RNA sequencing of *S. suis* isolates to generate a more comprehensive assessment of the adaptive transcriptional response of these strains. 3) Use *in vitro* adherence, invasion, and biofilm assays to test the capacity of these strains to adhere, survive and/or persist within conditions that mimic various host microenvironments. Nine genetically diverse strains recently isolated within the U.S. were chosen and compared to a well-characterized highly virulent reference *S. suis* strain by whole genome sequence analysis and by virulence assessment following intranasal challenge. A spectrum of virulence phenotypes were observed among *S. suis* isolates following intranasal challenge of pigs. Whole genome sequencing followed by comparative genomic analyses revealed several notable regions of difference, including regions encoding secreted and membrane-associated factors, which likely contributed to the spectrum of clinical disease observed. These analyses revealed nucleotide diversity of genes encoding proposed virulence factors such as *codY*, *neuB*, and SSU0854 Hemolysin. Chromosomal gene content among all strains was analyzed and allowed for the determination of core genes (present in all strains), accessory genes (present in 2-9), and unique genes (present in 1). Transcriptome sequencing was performed on virulent and nonvirulent isolates following incubation in whole pig blood. Numerous laboratory assays were performed to test the capacity of these strains to adhere, survive, and/or persist within conditions that mimic various host microenvironments. However, no *in vitro* assay tested correlated with *in vivo* virulence phenotype observed following intranasal challenge of pigs. Collectively, these results provide a foundation for understanding the genomic attributes responsible for the spectrum of virulent phenotypes that exist among *S. suis* isolates. These results obtained should aid in the development of effective vaccines needed by the swine industry to mitigate *S. suis* disease and decrease public health concerns.