RESEARCH ABSTRACT
SWINE HEALTH

Title: PRRS host genetics consortium (PHGC): a proposal to continue consortium work to study the role of host genetics and resistance to PRRSV – **NPB #12-061**

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Scientific Abstract:

Despite extensive efforts to eliminate PRRS from US production facilities, it remains a key disease issue and poses a continued economic threat to the industry, particularly in pig dense areas. A major factor that complicates PRRS control is viral persistence. Viral survival is maintained because a proportion of the herd has persistent virus which is shed occasionally (due likely to other diseases or stress). This shed virus then infects the remaining herd pigs which are naïve and thus susceptible. This project proposed to identify pigs which have persistent PRRSV infections and to determine if there are immune or genetic correlates of PRRSV persistence.

Currently there is no good technology to accurately identify PRRSV carrier pigs. This proposal determined the frequency of pigs with persistent PRRSV using viral RNA levels in tonsil as a surrogate measure of persistence. To perform this we took advantage of the repository of samples that were collected through the NPB funded PRRS Host Genetics Consortium (PHGC). Each PHGC pig, provided at weaning from current commercial breeding stocks, was infected with PRRSV isolate (NVSL 97-7985) and followed for 42 days post infection (dpi). Every pig that survived to 42 dpi had tonsil tissue archived. Moreover the PHGC database (www.animalgenome.org/lunney/index.php) contains extensive data on each PHGC pig, including its pedigree, response to PRRSV infection (viral levels and weight gain data), and extensive genotypic information (60K SNP chip). As part of this grant the PHGC database has been updated and expanded to include capacity to archive gene expression data from microarrays and next generation sequencing data as well as manuscripts and slide presentations.

For PHGC trials 3 and 5 RNA was carefully extracted from tonsil of every pig that survived to 42 dpi. That RNA was then tested for viral RNA using a sensitive TaqMan assay. The resulting data clearly show that there is high variability in tonsil viral levels at 42 dpi with PRRSV isolate (NVSL 97-7985) in nursery pigs. Testing for tonsil viral RNA levels is not an ideal persistence measure since studies of long-term persistent virus have identified tissues with detectable viral RNA levels but which cannot transmit to naïve pigs. However, using this surrogate persistence measure, especially with sets of similarly PRRSV challenged pigs that have great variation in both serum and tonsil viral RNA levels, provides us with testable hypotheses to query controls of persistence. Since sera from persistently infected pigs frequently are virus and antibody negative, these results and the PHGC data archive provided substantial means to affirm if there are any tissue or serological correlates of PRRSV persistence.

Our results affirmed that there is no correlation between tonsil viral RNA levels of pigs and 1) serum viral level at 42 dpi; 2) early serum viral levels (0-21 dpi); 3) weight gain changes (0-42dpi); or 4) immune gene expression in tonsil (limited survey). These results, while disappointing, were not unexpected given data accumulated from previous experiments.

These results set the stage for more detailed analyses. The wide variability of tonsil viral RNA levels opened up new avenues for querying factors that might be involved in tonsil virus persistence. Our new NPB grant (#14-223) will use sophisticated genome mapping techniques to determine whether there are genomic regions and host genes that regulate tonsil virus persistence. We will probe for mechanisms controlling tonsil PRRS viral levels using deep sequencing techniques of tonsil RNA based on gene expression and statistical analyses. Comparing data from pigs with high versus low tonsil PRRS viral levels, and using bioinformatic tools, we hope to identify molecular pathways and genes involved in anti-persistence responses. With this knowledge, efforts can be planned to selectively breed for these pigs or, preferably, to identify means of stimulating these responses in pigs with high persistent PRRS viral RNA.