RESEARCH ABSTRACT
SWINE HEALTH

Title: Global Gene Expression Profiling of PRRSV-infected Alveolar Macrophages - **NPB #06-122**

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Scientific Abstract:

Porcine reproductive and respiratory syndrome virus (PRRSV) is a major pathogen of swine worldwide and causes considerable economic loss. The primary target of infection is the porcine alveolar macrophage (PAM). Infection of PAMs by PRRSV causes significant changes in their function by mechanisms that are not understood. Serial Analysis of Gene Expression (SAGE) was used to examine the global expression of genes in PRRSV-infected PAM. Total cellular RNA was prepared from *in vitro* mock-infected and PRRSV strain VR-2332-infected PAMs at 0, 6, 12, 16 and 24 hours after infection. Each SAGE library was sequenced to obtain >95,000 tags per time point. The sequences were processed to account for sequencing error before generating tag:count databases. Examination of the SAGE data indicated that there were changes in gene expression occurring in the PRRSV-infected PAM over time post-infection. More than 400 unique tags with significantly altered expression levels were identified ($p<0.01$ with Bonferroni correction). The validity and kinetics of expression of genes identified by SAGE were confirmed using real-time RT-PCR. The most striking finding was that the expression of most of the genes identified in this study that are involved in the innate immune response (including IL-8, CCL4, TNF-α, and IL-1β, genes whose expression is known to be altered in response to other viral pathogens) showed little or no change or declined in transcript abundance following infection. Others showing little change or declined in transcript numbers included CCL3, macrophage inhibitory protein 3 (MIP3), and CXCL2. These data indicated that no innate immune response was initiated following infection. In addition, the enzyme arginase showed a significant, short-lived increase in transcript numbers at 6 hours PI. The increased expression of arginase indicated a possible inhibition of a pro-inflammatory response in the PAMs by inhibition of inducible nitric oxide synthase (iNOS) activity by competition for the common arginine substrate.