RESEARCH ABSTRACT

SWINE HEALTH

Title: Identifying PRRSV structural components that activate regulatory T cells and diminish protective immunity - **NPB #08-193**

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Scientific Abstract

Porcine reproductive and respiratory syndrome virus (PRRSV) accounts US swine industry losses of up to $600 million each year. Protective immunity is delayed and weak because of virus-mediated immune-modulation, leading to virus persistence and severe secondary respiratory infections. Infection and vaccination with PRRSV induces a rapid, non-neutralizing antibody response, and an early, weak non-specific gamma interferon (IFN-γ) response. A PRRSV-specific T cell IFN-γ response does not appear until at least 2 weeks after infection, gradually increases and then plateaus at 6 months postinfection, and is associated with a slow increase in neutralizing antibody. Protective immunity requires both an IFN-γ and neutralizing antibody response; however, peak viremia and shedding occur before development of neutralizing antibody and IFN-γ. Current commercial vaccines provide good homologous protection; however, heterologous protection is often incomplete. The virus activates regulatory T cells (T_{regs}) and delays IFN-γ production leading to immune suppression. Vaccines that induce IFN-γ rather than IL-10 confer better heterologous protection. The objective of this study was to test the **hypothesis** that **certain structural components of PRRSV drive the activation of regulatory T cells.** Stimulating these T cells would thereby diminish the protective immune response. Our long term goal is to design improved vaccines containing the necessary components for producing protective immunity rather than immune suppression. Since some investigators have shown that cross protection depends more on the ability of a vaccine to induce IFN-γ than on virus homology, these vaccines should provide cross protection as well. To test this hypothesis, we expressed structural proteins GP2-5, M, and N in *E. coli* and used them in an *in vitro* T_{reg}-activation assay. Our results show that both GP4 and GP5 are capable of activating Tregs. We are currently using synthetic peptides to fine-map the T_{reg}-epitopes to determine which epitopes should be mutated for development of a more efficacious vaccine that does not activate T_{regs} and provides heterologous protection.