RESEARCH ABSTRACT

SWINE HEALTH

Title: Development of a Broadly Protective PRRS Vaccine – **NPB #05-205**

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Abstract

Current PRRS vaccines provide limited protection against heterologous strains of viruses. The sub-optimum level of protection is likely caused by 1) a high degree of sequence variation in structural proteins and 2) deceptive imprinting due to the presence of immunodominant non-protective epitopes (IDNPEs). We hypothesize that variable IDNPEs act as decoys to mislead the host from mounting humoral or cellular immune responses against more highly conserved epitopes that may otherwise induce cross-strain protection. We have proposed to apply immune refocusing technology to the development of a broadly protective PRRS vaccine. Our review of available sequence databases, epitope discovery data, and published literature has led us to focus on the design of new vaccines containing immune refocused GP5 glycoproteins. We have identified two GP5 domains that appear to contain IDNPEs. By site-directed mutagenesis, we have introduced a series of mutations in the N-terminal ectodomain and the C-terminal endodomain of GP5 for expression in recombinant vaccinia virus vectors. A subset of the GP5 mutants have been co-expressed with the viral M protein to determine whether the formation of GP5-M heterodimers result in improved immunity. A preliminary antigenicity study in mice has been completed. Serum samples have been analyzed for neutralization of PRRS virus using a newly developed microneutralization assay. Results indicate that some GP5 mutants induced sera with reduced neutralization activity (as compared to wild-type GP5): these mutants are helpful in mapping important viral epitopes. The results also indicate that some of the mutants induced sera with increased neutralizing activity: these mutants appear to refocus the immune system to recognize protective viral epitopes and will be the focus of future studies. Taken together, the results from the current work suggest that several of the mutants represent enhanced vaccine candidates. In a future study, we propose to incorporate these immune refocused GP5 genes into molecular clones of vaccine strains for immunogenicity and protection studies in swine.