RESEARCH ABSTRACT

SWINE HEALTH

Title Development of novel foot and mouth disease virus with multiple mutations for evaluation as live attenuated DIVA vaccine candidates – **NPB #12-206**

revised

Investigator: Teresa de los Santos Ph.D. and Elizabeth Rieder Ph.D.

Institution: Plum Island Animal Disease Center, North Atlantic Area, Agricultural Research Service, United States Department of Agriculture, Orient Point, NY, 11957

Date Submitted: June 10th, 2014

Scientific Abstract: Foot-and-mouth disease virus (FMDV) leader proteinase (L^{pro}) is a virulence factor. Viruses with deletions of L^{pro} coding region (leaderless) are viable and display an attenuated phenotype in vivo in swine and cattle. Attempts to use the leaderless virus as a vaccine have shown promising results but with limitations. In some instances the virus was virulent and in others adaptive immunity fell short of inducing protection against challenge. Recently, we have found that viruses with mutations in L^{pro} SAP domain (SAP mutant) are viable and can mount a strong adaptive immunity in swine. Remarkably, SAP mutant virus inoculated animals developed a strong neutralizing antibody response and were completely protected against challenge with WT FMDV as early as 2 and for at least 21 days post inoculation. However, in rare occasions, SAP mutant virus reverted to virulence. We have also reported that mutations to create negative antigenic markers in the 3D polymerase (3Dpol) and 3B nonstructural proteins generated slightly attenuated mutant viruses. Here we have evaluated the possibility of combining mutations in L^{pro} and other non structural viral protein coding regions to increase stability and safety as well as to be able to differentiate between vaccinated and infected animals (DIVA). We observed that mutation of the SAP domain in A24 FMDV L^{pro} was maintained in vivo but virus was only mildly attenuated. Attenuation increased when SAP mutations were combined with mutations in 3B and 3D that conferred DIVA properties, however mild clinical signs of disease were detected. These results suggest that the level of attenuation could be further manipulated to obtain FMDV strains with potential for live attenuated vaccine development as a novel strategy to control FMD.