RESEARCH ABSTRACT

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SWINE HEALTH

**Title:** Characteristics of Unusually Virulent Contemporary PRRSV Isolates, **NPB 17-171**

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**Scientific Abstract:**

In the majority of cases involving new PRRSV isolates, outbreak severity initially is tremendous, then decreases over time as herd immunity and biosecurity is managed to reduce and prevent disease. Challenge studies have shown that commercial vaccines significantly improve outcomes compared to infection of naïve animals. PRRS viruses that break in solidly immune, vaccinated herds as if they were naïve are very difficult to manage and threaten economic swine production. In January 2014, a new family of aggressive viruses appeared and within 15 months was linked to severe outbreaks in well managed herds. These viruses are markedly different from other contemporary field viruses in their ability to spread rapidly and cause severe disease in immune (endemic) herds, suggesting immunity due vaccine or field virus exposure is not cross-protective. This research examined the cross-protective immunity to these new viruses as well as genetic features that may be responsible for its unusual virulence and immune insensitivity, and point to a need for new directions and better ways to characterize and diagnose severe PRRS.

The results of this study identified differences in the highly virulent contemporary isolates as compared to historical isolates. Viral neutralization of serum from animals vaccinated or infected with different isolates identified a lack of neutralization of contemporary viruses by animals that had only seen vaccine or a historical isolate. Animals that had seen other different contemporary isolates were able to neutralize the 1-7-4 RFLP contemporary isolate. This suggests that the 1-7-4 isolate was sufficiently antigenically distinct from vaccine that it evaded vaccine-induced antibodies. Even though vaccine was unable to protect against 1-7-4 challenge, previous infection with other contemporary viruses was able to induce cross-protective neutralizing antibodies against 1-7-4, suggesting a new contemporary viral vaccine may be needed. Besides neutralization, another method for the 1-7-4 RFLP viruses to evade protection would be if they were able to grow more quickly or to higher titers making it more difficult to control infection. A comparison of growth characteristics in vitro were examined between the contemporary and historical isolates identifying similar growth rates, thus viral growth does not explain the high virulence of this 1-7-4 virus. Next, genome sequences from 19 viruses were examined to determine if a unique virulence feature or putative protein could be identified to explain highly virulent strains. Interestingly, 6 conserved features were observed in both contemporary and historic isolates, including a putative ORF7a protein, and although these do not seem to be virulence targets, it is interesting to note that we continue to identify novel putative proteins for this virus. However, we did identify 3 putative virulence targets in the genome that differ between low or non-virulent strains and virulent viruses that need to be further investigated to determine if they can be exploited for vaccine development. Finally, a variety of clustering methods were examined and compared to RFLP typing in an effort to obtain a better method for identifying

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highly virulent strains. Examination of phylogenetic trees created from ORF5 or whole genome sequences, clustered PRRSV isolates similar to that of RFLP typing, but identified the difference between virulent 1-4-2 virus and historical non-virulent 1-4-2 virus, which are not differentiated by RFLP typing. However, these phylogenetic trees were not any more successful at identifying highly virulent strains than that of RFLP typing. Use of ORF5 clustering in conjunction with neutralizing antibody assays to determine cross-neutralization between viral strains or clusters of strains, would allow for identification of new viral clusters able to evade vaccine-induced protection. This would identify when new vaccines need to be developed and hopefully use of the 3 putative vaccine targets identified in this study will allow for development of quicker, more effective vaccines.