

Phylogenetic Structure and Sequential Dominance of Sub-Lineages of PRRSV Type-2 Lineage 1 in the United States

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- Lineage 1 PRRSV, the most prevalent PRRSV lineage in the U.S, can be sub-divided into eight sub-lineages
- We documented the cyclic emergence and turnover of different lineages and sub-lineages (about every 3 years) based on both sequence count data and estimated past viral population sizes inferred from genetic diversity through time.
- The eight sub-lineages differed in key GP5 amino acid sites that are thought to be involved in the immune response to the virus.

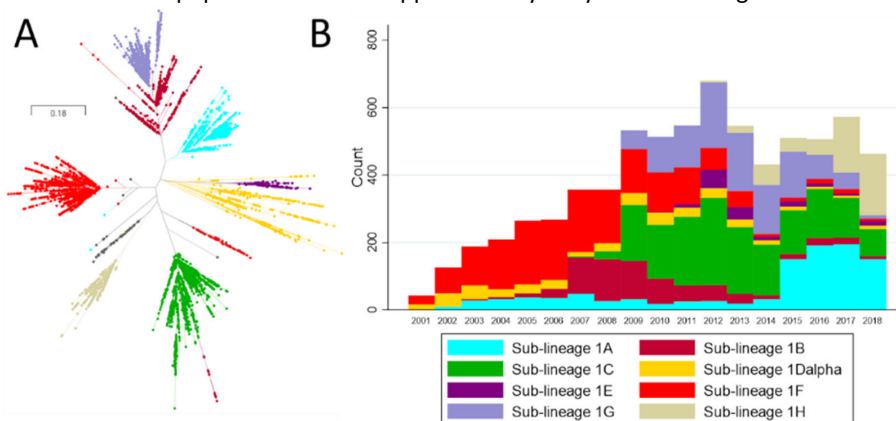
Immunity against PRRSV is characterized by varying cross-protection against homologous and heterologous challenges, and efforts to control PRRSV spread have had limited success and are further complicated by the emergence of new genetic variants. Although protection elicited by vaccination or intentional pre-exposure of animals to PRRSV may help mitigate clinical disease impact, current PRRS vaccines and pre-exposure procedures do not produce sterilizing immunity. This may unintentionally create conditions for immune-driven viral adaptation.

PRRSV type-2 viruses (those most common in North America) are commonly classified according to restriction fragment length polymorphisms (RFLP) in the open reading frame 5 gene (ORF5) portion of the viral genome. One limitation of RFLP typing is the inability to represent genetic relationships between different RFLP types, which limits interpretation of RFLP typing from an evolutionary standpoint. As such, an alternative classification system based upon phylogenetic lineages was proposed in 2010. This classification system grouped PRRSV type-2 viruses into nine lineages based on phylogenetic relationships in the ORF5 region. Of the Type-2 PRRS lineages, Lineage 1 is the most prevalent and diverse lineage within the U.S. swine industry; consequently, an updated and expanded sub-lineage classification system is needed to better track PRRSV Lineage 1 diversity in the U.S. and improve communication and coordination of control efforts.

Using the University of Minnesota Veterinary Diagnostic Laboratory PRRSV type-2 dataset, we delineated the phylogenetic structure within PRRSV Lineage 1, described past dynamics of different viral strains through quantifying viral population sizes across time, and identified antigenically relevant amino acid changes associated with each sub-lineage.

A total of 12,123 PRRSV sequences from the UMN VDL were classified into lineages. We further identified 8 sub-lineages within Lineage 1 (named Lineage 1A to 1H). Although sub-lineage 1C was the most prevalent overall, the relative population sizes of each sub-lineage fluctuated through time. For example, sub-lineage 1A (associated with RFLP 1-7-4 since 2014) was consistently detected across the early years of our data, but its prevalence sharply increased in 2015 and subsequently has been responsible for ~30 to 40% of all detected sequences. On average, we observed the emergence or re-emergence of a sub-lineage approximately every 1–4 years, and the time between sub-lineage emergence and its peak estimated viral population size was approximately 4.5 years on average.

At the amino acid level, ORF5 sequences belonging to different sub-lineages displayed unique patterns in the amino acids coding for N-glycosylation sites (sites 32–34) or epitopes (mainly in sites 58–59). This suggests that antigenic differences may be captured to some extent by phylogenetic classification based on ORF5. Viral infections by different sub-lineages within Lineage 1 may yield variable cross-protection, which could contribute to co-circulation of multiple PRRSV strains and the antigenic fitness of newly emerging variants in a given region, system, or farm. This lends further support to the hypothesis that immune-mediated competition or selection may drive the emergence of new sub-lineages within Lineage 1 in the U.S. Additionally, the interactions in the immune response elicited against these different sub-lineages warrants further investigation to provide insights into herd protection via vaccination, disease control, and viral evolution and different PRRSV strains/sub-lineages emergence.



(A) Phylogenetic tree of L1 sequences classified into sub-lineages according to discriminant analysis of principle components. (B) Absolute frequency of sequences per sub-lineage per year. Notice the relative dominance of different sublineages through time.