

What are PRRS lineages?

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Last week we discussed how RFLPs are used to classify PRRSV type 2 (PRRSV2) viruses. We discussed how RFLP typing has distinct shortcomings, including an inability to represent genetic relationships between different RFLP types, the potential for distantly related viruses to share the same RFLP type, and the instability of RFLP types over few animal passages. Partially due to these issues in interpreting RFLP types, a complementary classification system based upon their genetic relatedness was proposed in 2010 [2,3]. Several ORF5 sequences from different countries were aligned and a phylogenetic tree was constructed. Based on the phylogenetic relationship between them, this classification system grouped PRRSV2 viruses into nine genetically related groups, called lineages (L). In terms of nucleotide identity, sequences of each lineage differ from sequences from other lineages on average 10-17% [3].

In the US, Lineage 1 (L1) has historically been the most prevalent since early 2000. Within L1, diversity and genetic substructures raised the need to further classify viruses into sublineages (SL), named L1A to L1H as described in 2019 and 2021 [1,4] (Figure 1A). The SL classification also takes into account the phylogenetic relationship in the ORF5 region. Based on nucleotide identity, sequences of each SL differ from other SLs by approximately 5-12%.

The L and SL classification of PRRSV2 tries to address some of the caveats present when evaluating PRRSV2 sequences based only on RFLP. For example, the L/SL classification **better tracks genetic relationship between sequences**. Sequences from different L/SL are unrelated or only very distantly related. **It is also more resistant to mutations in the ORF5 genome**. Because the natural accrual of mutations in the ORF5 does not change the L/SL of a sequence in the short term – the sequence won't "swap" between L/SL in different passages of a virus. As such, broader evolutionary patterns are better evaluated using L/SL. For example, the emergence of new sublineages is estimated to occur approximately every three years and different sub-lineages are more prevalent at different time points (Figure 1B). The rapid spread of emerging sublineages has been shown to be mostly driven by animal movements and local area spread [5,6]. Additionally, the L/SL terminology may be helpful in the quick identification of epidemic strains. In the recent L1C 1-4-4 variant emergence in the U.S. Midwest [7], a higher sensitivity and positive predictive value when identifying if sequences were part of that particular epidemic cluster was achieved when the L/SL and RFLP classification were taken into account simultaneously rather than alone. This demonstrates how L/SL classification may help identifying sequences relevant in a given context.

The L/SL classification still has shortcomings, for example, the extent of cross-immunity elicited by exposure to one L/SL when challenged to a second L/SL is unknown. In other words, **does the L/SL classification serve as a proxy to the immunological response pigs will develop?** While there are reasons to believe this may be true, this needs to be demonstrated rather than simply asserted. Another shortcoming is that even at the SL level within L1, **relationships between sequences may be too distant to aid in addressing questions that are often asked in the field**. While two L1A sequences are more closely related than an L1A and an L1B sequence, you cannot really evaluate if those two sequences are on the same transmission chain based upon L/SL classification alone. Lastly, similar to RFLPs (albeit in a much smaller scale), **new L/SL are expected to emerge after a few years**, and as such the PRRSV2 diversity from a L/SL perspective should be re-evaluated with a certain frequency.

The L/SL classification serves as a tool that can be helpful to address specific questions. While it **excels in evaluating broad evolutionary and region-wide spread of viruses**, it **may not be able to address all questions that arise at a farm-level**. It is also important to highlight that both L/SL and RFLP classifications are ORF5 based only, and it may be that more information can be obtained by investigating other portions of the genome. That said, the most adequate PRRSV2 classification tool to be used in a given scenario largely depends on the exact question being addressed.

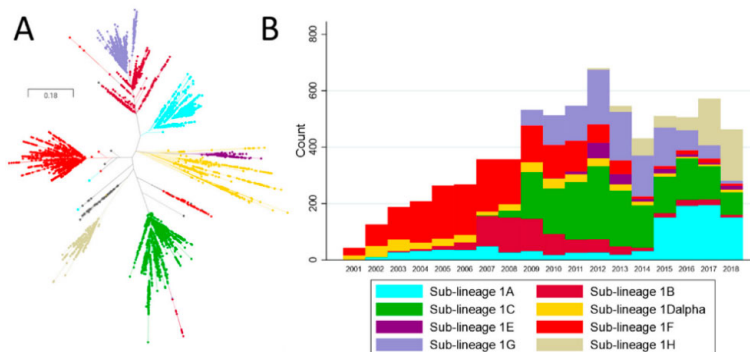


Figure 1A. Phylogenetic tree of the sub-lineages within Lineage 1 in the U.S. and **B.** Number of sequences per sub-lineage per year identified in the UMN VDL.

References

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