Tracing the evolutionary history of the novel PRRSV-2 L1C-1-4-4 variant

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Key Points:

- The L1C-1-4-4 variant has a L1C-like genomic backbone with evidence of recombination
- The variant diverged from other circulating PRRSV-2 viruses in late 2018 – 2019 with evidence of recombination at the nsp2 region with L1A-like viruses

Last year, the midwestern swine industry witnessed massive PRRS outbreaks caused by the novel PRRSV variant, L1C-1-4-4. Field isolates belonging to this variant were genetically highly similar (> 98%)[1] not only in ORF5, but also in the whole genome. Questions still remain on how this variant rapidly spread and led to atypical production losses. Previous studies demonstrate that virulence of PRRSV-2 is determined by several protein coding regions throughout the different genomic parts[2,3]. Thus, analyzing whole genome sequences (WGSs) of the L1C-1-4-4 variant is the first crucial step to understand how this virus differs from other circulating variants. Inferring a virus's evolutionary origin from whole genomes is complicated due to recombination, which is an evolutionary mechanism by which genomic portions are exchanged between viruses[4]. This contributes to the genetic diversity in the virus population and potentially leads to swift changes in virus characteristics.

To identify whether the novel variant is a recombinant virus or not, we performed recombination detection on a set of WGSs, including the recent outbreak L1C-1-4-4 variant (n=19) and publicly available isolates collected in the U.S. over the past two decades (n=232). Sequences were classified into lineages according to their ORF5 gene phylogeny. Three WGS fragments that exhibited low within-fragment recombination rates (partitioned according to recombination hotspots), were used to estimate the virus's evolutionary history and ancestral inter-(sub) lineage recombination via Bayesian phylodynamics with discrete trait analysis (DTA)[5].

Phylodynamic models confirmed that the novel variant was a recombinant virus with a L1C-like genomic backbone. The variant diverged in late 2018 to early 2019, acquiring a non-structural protein 2 coding region (a major part of ORF1a gene) from L1A like viruses through recombination. The closest relatives were two isolates belonging to L1C and L1A collected in 2018, both of which had a different recombination history than the novel variant (Figure 1). However, DTA suggests that inter-(sub)lineage recombination events resulting in widespread transmission (i.e., those that leave detectable numbers of progeny) were relatively uncommon (< 0.5 events/year).

Given these results, coupled with the field epidemiological situation, rapid exchange of genetic material through recombination between co-circulating PRRSV-2 strains may be a possible mechanism associated with variant emergence. While recombination may have contributed to the unprecedented epidemic caused by the current 2020-21 variant, recombination events that leave discernable traces on PRRSV-2 phylogenies appear somewhat rare. However, co-circulation of multiple, genetically-diverse lineages likely increases the chances that recombination will occasionally result in novel variants.

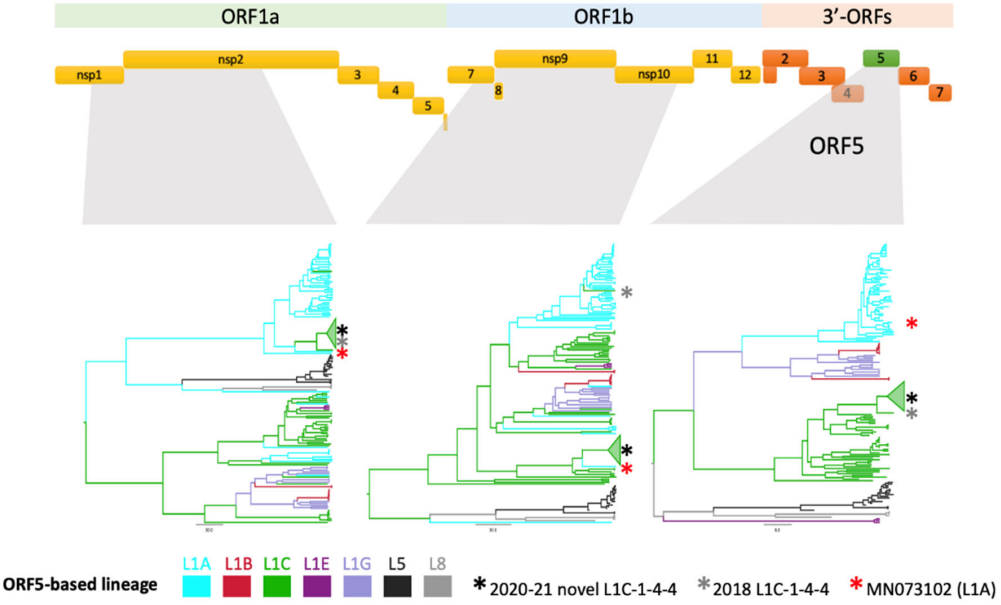

Figure 1. Phylogenetic trees presenting PRRSV-2 evolutionary history of each genomic portions colored by ancestral ORF5-based lineage or sub-lineage. Asterisks locate the phylogenetic position of taxa of interest

This research was funded by the Swine Health Information Center and USDA-NSF-NIH.

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