

## Inter-Regional Spreading Patterns of Contemporary PRRSV-2 in the U.S.: A Molecular Epidemiological Perspective

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### Key points:

- The majority of PRRSV-2 currently circulating within the U.S. (Lineage 1) originated in Canada in the late 1980s, indicating that it was initially introduced to the U.S. from Canada and subsequently replaced other wild-type viruses historically in the U.S in the 1990s.
- The Upper Midwest has consistently served as a major hotspot for the spread of PRRSV-2 since its establishment in the U.S. in the late 1990s, playing a pivotal role in its transmission to other regions.
- More recently, the Eastern U.S. has played a more prominent role in the spread of certain sub-populations of PRRSV-2, indicating a shift in the national-scale spreading pattern.

Porcine reproductive and respiratory syndrome (PRRS) usually ranks among the top list of pig diseases, posing a significant threat to the global industry. In the United States, swine producers have faced numerous waves of PRRS outbreaks caused by different well-known PRRSV-2 variants, including MN184 in the 2000s, the virulent 1-7-4 viruses in the early 2010s, and the novel L1C-1-4-4 variant in 2020. These variants belong to the same major sub-group of PRRSV-2 called lineage 1 (L1), responsible for over 60% of diagnostic cases today, while the other 40% of sequenced viruses are mostly vaccine-related (L5 and L8). Understanding the overall historical patterns of PRRSV-2 L1 spread is crucial for assessing previous disease mitigation efforts and providing guidance for better prevention in the future.

Genetic relationships amongst viruses can be used to estimate the virus's evolutionary dynamics and historical spread. To accomplish this, we utilized 19,395 ORF5 genetic sequences belonging to PRRSV-2 L1 collected between 1991 and 2021 in the United States and Canada. We curated and sub-sampled the data to minimize sampling bias before conducting the analysis known as "phylogeographic inference." This analysis aims to estimate the historical locations and migration routes of the virus based on its genealogical tree.

The results of the phylogeographic analysis consistently revealed the same history of the L1 virus over time and space (five U.S. regions plus Canada). First, the virus was inferred to have initially emerged in Canada in the late 1980s, which aligns with a previous study that referred to this virus as "Canada-like PRRSV" (Shi et al., 2013)<sup>1</sup>. In the late 1990s, the L1 virus became fully established in the Upper Midwestern United States, which subsequently became the primary hotspot for spreading the virus to other regions. Sub-lineage 1F, an early sub-lineage of L1 that included the infamous MN184 virus, played a significant role in L1 outbreaks during the 2000s and was primarily concentrated in the Upper Midwest. At the beginning of the 2010s, the predominant sub-lineage shifted from L1F to L1BG (including RFLP 1-18-2) and L1C (also known as NADC30-like viruses), with bidirectional spread observed between the Midwest and the East (specifically, North Carolina). Lastly, the most recent wave occurred in the mid-2010s when novel L1A viruses (including RFLP 1-7-4) emerged and likely spread from the hotspot in the East to the Midwest in a northwesterly direction (Figure 1). These dynamics suggest a gradual shift in virus spreading patterns and hotspots, likely influenced by the expansion of the U.S. swine industry, with long-distance pig-related transportation posing potential risks.

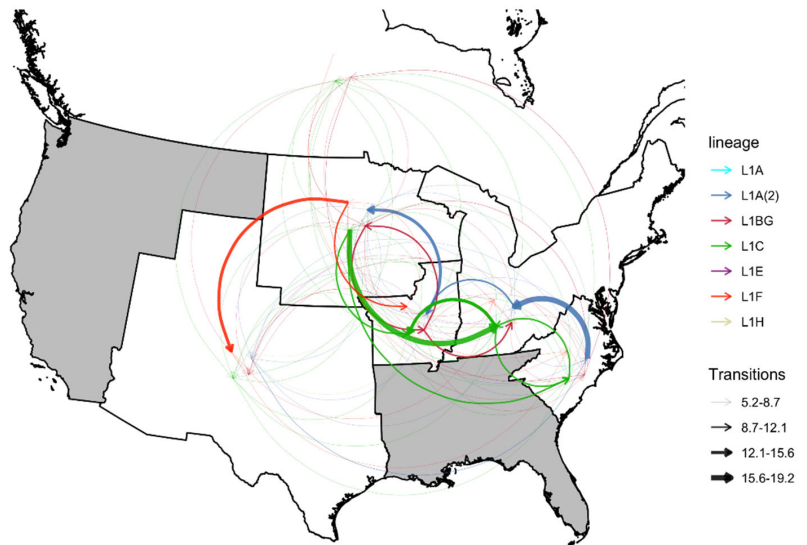


Figure 1. Inter-regional transitions of each L1 sub-lineage inferred by five phylogeographic analyses. The color of the arrow represents the sub-lineage, while the thickness of the arrow represents the number of transitions observed in the sub-samples.

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### Reference:

- <sup>1</sup> Shi, M.; Lemey, P.; Singh Brar, M.; Suchard, M.A.; Murtaugh, M.P.; Carman, S.; D'Allaire, S.; Delisle, B.; Lambert, M.E.; Gagnon, C.A.; et al. The spread of type 2 porcine reproductive and respiratory syndrome virus (prsv) in North America: A phylogeographic approach. *Virology* **2013**, *447*, 146–154.