

## PRRSV 1-7-4 ORF5 diversity over time

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### Key Points:

- PRRSV ORF5 sequence monitoring over time contributes to the understanding of pathogen evolution.
- Range of PRRSV 1-7-4 percent divergence has decreased over the last 16 years between 2003 and 2019, which is consistent with lineage turnover previously described.
- PRRSV 1-7-4 can belong to a specific lineage or sublineage, 1A being the most common currently.

The Morrison Swine Health Monitoring Project (MSHMP) has been monitoring restriction fragment length polymorphisms (RFLP) of PRRS outbreaks in participating herds. One of the most common RFLPs is the 1-7-4 cut pattern which is currently a source of concern especially in herds undergoing wild-type elimination procedures. Although the virus has been successfully eliminated from sow herds, it has also challenged some systems as it has been a difficult one to eliminate<sup>1</sup>. Additionally, 1-7-4 RFLP-type has been described as one of the most virulent strains causing important economic losses<sup>2</sup>. As reported in a previous science page, the frequency of detection of this virus has had a decreasing trend. Here we examined the diversity within the 1-7-4 group of ORF5 MSHMP participant sequences in order to investigate whether there has been a pattern over time that could help explain occurrence and persistence.

All 1762 unique ORF5 1-7-4 PRRSV sequences from 2003 to 2019 shared by MSHMP participants were analyzed and aligned to the dataset's oldest 1-7-4 virus as a reference. Each sequence was compared to the reference and both the percent identity (percent of nucleotides that match exactly), and its complement (percent nucleotide difference), were calculated. The resulting percent difference was graphed over time, as shown in Figure 1, according to each unique sequence's first appearance in the dataset.

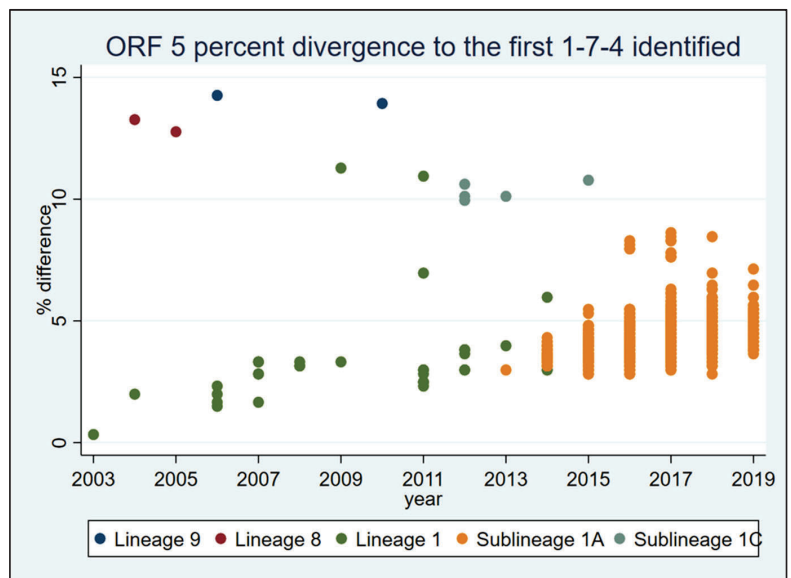
Over time the range difference has had a decreasing trend. In the early 2000's, the few ORF5 sequences available had an approximate 13% range difference. The range decreased over time to approximately 3.5%. PRRSV is clearly a pathogen that evolves through time. The changes in range of this subset of sequences could exemplify a situation in which diversity decreases as a consequence of the disappearance of certain strains, or as the result of the evolution of a specific strain that became widespread in a short period of time.

While it can be a valuable tool to assess viral diversity in specific scenarios, we need to highlight an important limitation on RFLP interpretation. Since the enzymes cut the genome only where there is a complete nucleotide match, even a small number of mutations have the potential to change whether or not the enzyme will provide a cut or even the location of the cut, changing the RFLP pattern completely. Thus, RFLP does not directly correlate to genetic distance, which we are discussing here. For example, in terms of genetic lineage, RFLP 1-7-4s within our dataset can be classified as lineage 1, but it can also be classified as lineage 8 or lineage 9 according to the Shi et al.<sup>3</sup> lineage classification system. If we look in terms of sublineages as described by Paploski et al.<sup>4</sup>, this decrease in divergence range likely illustrates changes in lineage/sublineage frequency over time, which is consistent with PRRSV lineage turnover described in their paper. They showed an increase of lineage 9 PRRSV in the early 2010's and the emergence of a different lineage 1 subtype. The remaining lineage 1 sequences that were not classified into sublineages shown here likely represent a different sublineage not described by Paploski et al.

It is important to note, however, that both RFLP-type and lineage determination lack evidence of their correlation to immunogenicity. Still, we should keep in mind that ORF5 represents a small portion of the virus genome, and 1-7-4 RFLPs might represent very different viruses in terms of genetic similarity, especially prior to 2014 within our studied population. Furthermore, this dataset represents those cases from which we have obtained sequences which leads to some level of bias. ORF5 sequence monitoring over time provides important information from a pathogen evolution standpoint and allows the industry to build a database of these type of viruses that can contribute to understand the ever-changing nature of PRRSV.

### References

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- 2- van Geelen AGM, Anderson TK, Lager KM, et al. Porcine reproductive and respiratory disease virus: Evolution and recombination yields distinct ORF5 RFLP 1T7T4 viruses with individual pathogenicity. *Virology* 2018; 513: 168–79.
- 3- Shi M, Lam TT-Y, Hon C-C, Hui RK-H, et al. Molecular epidemiology of PRRSV: A phylogenetic perspective. *Virus Research* 2010; 154(1-2): 7-17.
- 4- Paploski IAD, Corzo C, Rovira A, Murtaugh MP, Sanhueza JM, Vilalta C, Schroeder DC, VanderWaal K. Temporal dynamics of co-circulating lineages of porcine reproductive and respiratory syndrome virus. *Front. Microbiol.* 2019; DOI: 10.3389/fmicb.2019.02486.



**Figure 1.** MSHMP ORF5 PRRSV 1-7-4 sequences percent difference when compared to the reference virus.