The virus

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Highlights

PPRSV1 and PRRSV2 -the former European and North American PRRS viruses- are now recognized as two different species with the new Genus Poraterivirus.

Non-structural proteins are only expressed during the replication cycle but are not present in the virion. However, they have a very important role in the inhibition of the innate immune response of the host.

Structural proteins form the virion. Several of the structural proteins are glycosylated and are involved in the attachment and entry of the virus in the target cell. Also, several structural proteins induce neutralizing antibodies in the pig.

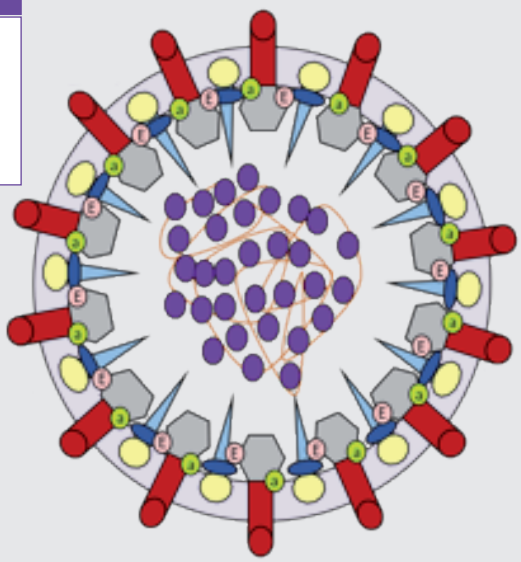
PRRS virus (PRRSV) was first discovered by Dutch researchers in 1991 and soon thereafter it was isolated in the United States. Further studies indicated that PRRSV was a single-stranded positive-sense enveloped RNA virus and based on its characteristics it was classified in the Family *Arteriviridae* within the Order *Nidovirales*. Comparison of the genome of European and North American isolates suggested that two distinct genotypes existed that were named 1 and 2, respectively. More recently, the analysis of the available data for different arteriviruses led to a revision of the Family *Arteriviridae*. At present, two different PRRSV species are recognized within the new genus *Poraterivirus*, PRRSV1 and PRRSV2, which correspond to the former European and North American genotypes 1 and 2. At least 4 subtypes of PRRSV1 have been identified so far while for PRRSV2 only one subtype is accepted although several phylogentic clades have been identified as well.

PRRSV genome is about 15,000 nucleotides in length that encode for both structural and nonstructural proteins (nsp); namely, proteins present in the virion and proteins that are only expressed during the replication cycle but not in the complete viral particle, respectively. Nsps are encoded in two open reading frames (ORF) -ORF1a and ORF1b- that are located in the 5' end of the genome. Translation of each of those ORFs results in a polyprotein (PP1a and PP1b) that after further enzymatic cleavage produce the nsp. At present, at least 16 nsp are known, 14 resulting from PP1a and PP1b -1α, 1β, 2, 3, 4, 5, 6, 7a, 7b, 8, 9, 10, 11, 12- plus two additional proteins -nsp2TF and nsp2N- that are produced after frameshift of the reading frame of viral RNA in the ribosome.

Structural proteins are encoded in ORF 2 to 7 at the 3' end of the virus. At present, 8 structural proteins are known of which 5 are glycoproteins: GP2, E, GP3, GP4, GP5, ORF5a protein, M and N. N protein forms

the viral nucleocapsid. M is the matrix protein and forms a heterodimer with GP5, the major envelope protein. GP2, GP3, GP4 and E proteins form a complex. GP5 is thought to interact with receptors in the cell surface and allows the attachment of the virus to the target cells and the initial internalization. The GP2-GP3-GP4 complex interacts with CD163 and triggers the decapsidation of the virus and the liberation the viral genome.

Non-structural proteins have been identified as the main responsible for the inhibition of the innate immune response of the host, particularly the inhibition of the production of type I interferons. Structural proteins are the ones inducing neutralizing antibody responses. Actually, GP2, GP3, GP4, GP5 and M have been suggested to induce neutralizing antibodies although the precise role and importance of each type of neutralizing antibody is not well known yet.



N

Forms the nucleocapsid. Probably interferes with NF-kβ translocation. Induces cell-mediated immunity (CMI).

GP3

Forms a trimer with GP4 and GP3. Induces neutralizing antibodies.

GP4

Forms a trimer with GP2 and GP3. Induces neutralizing antibodies (decoy epitopes?)

E

Minor envelope protein. Involved in cell specificity.

ORF5a

Minor envelope protein. Essential for virus infectivity.

GP5

Major envelope protein. Induces neutralizing antibodies. Interact with sialoadhesins in cell surface

M

Matrix protein. Forms a heterodimer with GP5. Induces CMI responses.

GP2

Forms a trimer with GP3 and GP4. Induces neutralizing antibodies. Interacts with CD163