2.4 The BVD-Genome

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{multithumb} Pestiviruses have a positive sense single stranded RNA genome [ss (+) RNA]. The BVDV genome has a size of approximately 12'500 nucleotides, the sequence of which is known since 1988 [10]. Some cp strains integrate small variable segments of viral nucleic acid or the host cell genome in certain places of their genome (in NS2 or between NS2 and NS3). Others show duplicates of specific protein coding regions (Npro, NS3), consequently their genome size rises to about 16.5 kb. The genomic RNA has one open reading frame of about 4000 codons [33] which encompasses most of the viral genome. Translation oft the BVDV genome yields one precursor poly protein, which is cleaved co- and postranslationally by viral and host cell encoded proteases (”processing”). Most of the virally encoded cleaving is catalysed by a serine protease domain within NS3 and generates the non-structural proteins NS3 to NS5B, whereas the structural proteins are believed to be cleaved by cellular proteases [33]. Structural proteinsProteinFunctionC Capsid protein (core protein) ErnsEnvelope glycoprotein (rns means Rnase secreted); induces production of antibodies with a weak neutralizing activity [34]

E1Envelope glycoprotein E2Envelope glycoprotein; the least conserved region of the BVD genome codes for E2. It features epitopes that are recognized by the host immune system. Antibodies against these epitopes are essential for the neutralization of viral infectivity. Modification of these epitopes enables the virus to escape neutralization. E2 is relevant for the vaccine development (the more efficiently E2 is presented to the immune system, the better the neutralizing effect).

p7Very small protein with largely unknown function. Essential for the formation of infective virus particles [35].

Non structural proteins

Protein Function NproThe N-terminal protein of BVDV codes for a cysteine protease that cleaves the N-terminus from the core protein (auto-protease) [36][37].

NS23Non-structural protein; serine protease; biggest BVDV-protein with a molecular weight of 125 kD; cp BVDV does not only express NS23 in one piece but also in two separate proteins (NS2, 54 kD and NS3, 80 kD). Therefore, NS3 (with nucleoside triphosphatase/RNA helicase activity [38]) can always be isolated along with NS23 from cp BVDV infections; NS3 serves as a marker protein for cp BVDV [39]. The expression of uncleaved NS23 seems to be essential for the formation of infectious virus particles (both cp and ncp) [40].

NS4A/BNon-structural proteins; NS4A is a cofactor for serine protease NS23[33]; there’s evidence that NS4B plays a role in viral cytopathogenicity [41]; both do not induce an immune response.

NS5ANon-structural protein; part of the replication complex NS5BNon-structural protein with RNA dependent RNA-polymerase activity Non-translated regions Protein Function 5’UTR5’ Untranslated region; the most highly conserved region in the pestivirus genome; start of protein translation

3’UTR3’ Untranslated region ; highly conserved