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Chimeric Bovine Viral Diarrhea (BVDV) Npro deletion mutants as modified live vaccine candidates

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BVDV, a worldwide distributed Pestivirus of cattle, causes major economic losses due to clinical disease and reduced fertility. BVDV is divided into two genetically and antigenically different genotypes: BVDV 1 and BVDV 2. Protection against BVDV-2 after vaccination with commercial vaccines which are licensed for the German market is limited. In this study, BVDV 1 and BVDV 2 Npro (N-terminal protease) deletion mutants were generated as live vaccine candidates. Safety and efficacy were evaluated in vaccination-challenge experiments in calves. The recombinants mediated complete protection and sterile immunity from a virulent challenge infection with the respective homologous genotype. However, BVDV 1 del_Npro as well as the combined simultaneous or sequential application of BVDV 1 del_Npro and BVDV 2 del_Npro could not prevent limited challenge virus replication after BVDV 2 test infection. To exclude mutual growth interference, we constructed chimeric BVDV-1/ 2□del Npro recombinants based on the backbone of the cDNA clone pBVDV 1b_del Npro. The envelope glycoproteins E2 or E1/E2 were replaced by E2 or E1/E2 of BVDV type 2. The chimeras markedly reduced the outcome of a heterologous BVDV 2 challenge infection. Sequence analyses of the full-length clones revealed 2 amino acid substitutions within immunogenic domains of the E2 protein (L32P and Q43H) which persistently reoccurred during plasmid propagation. The stabilised chimeric recombinant BVDV-1b□Del_Npro_E1E2 BVDV 2 was generated as a promising modified live BVDV-2 vaccine candidate.

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