

A Spontaneous Deletion of the *US1.67/US2* Genomic Region on the Bovine Herpesvirus 1 Strain Cooper

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Bovine herpesvirus 1 (BoHV-1) is an alphaherpesvirus with a genome of 135 kb. Some BoHV-1 genes are nonessential and may be deleted from the viral genome. Here, a spontaneous gene deletion was identified in the BoHV-1 strain Cooper. Genes of the *US1.67/US2* region were absent, as determined by next-generation sequencing.

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Viruses are continuously undergoing genetic adaptations, where mutations and recombination are major players (1). These can be exemplified by genome rearrangements detected in laboratory-adapted strains of human cytomegalovirus (HCMV) (2). This may be of particular relevance for vaccine strains, which are often subjected to undefined number of passages *in vitro*. In the worst scenario, genetic alterations may lead to changes in genomic composition that may alter the immunizing capacity of a particular vaccine virus.

Here, the detection of a spontaneous deletion of two genes of the genome of a “classical” bovine herpesvirus type 1 (BoHV-1) vaccine strain (NVSL BoHV-1.1 Cooper reference strain) (3) is reported. The virus had been submitted to 12 successive passages in cell culture in our laboratory before sequencing. Virus multiplication was carried out in Madin-Darby bovine kidney cells and concentrated by ultracentrifugation, and DNA was extracted by usual methods (4). Sequencing of the whole viral genome was performed by next-generation sequencing in a MiSeq (Illumina) platform. A total of 645,622 raw reads were generated, with an average length of 139 bp, i.e., a coverage of 674× the whole BoHV-1 genome. Reads were trimmed using the Geneious software. After mapping, the viral genome revealed 99.1% identity to the reference strain Cooper, except for the lack of an 892-bp segment corresponding to the *US1.67/US2* genes.

The virus is believed to have undergone spontaneous deletion during *in vitro* passages. This finding provides additional evidence that, eventually, nonessential BoHV-1 genes may be deleted from viral genomes (5). In this case, no apparent prejudice for viral multiplication was noticed. Because BoHV-1 Cooper is a vaccine strain, the need for constant monitoring of the genomes of vacci-

nal viruses must be stressed, since undesired deletions may alter the immunogenic properties of the end product. This highlights the importance of strict control, including full-genome sequencing, over *in vitro* multiplication of viruses destined to vaccine production.

Nucleotide sequence accession number. The GenBank accession number is [KU198480](https://www.ncbi.nlm.nih.gov/nuclot/KU198480).

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