

Complete Genome Sequences of Two Novel European Clade Bovine Foamy Viruses from Germany and Poland

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Bovine foamy virus (BFV), or bovine spumaretrovirus, is an infectious agent of cattle with no obvious disease association but high prevalence in its host. Here, we report two complete BFV sequences, BFV-Riems, isolated in 1978 in East Germany, and BFV100, isolated in 2005 in Poland. Both new BFV isolates share the overall genetic makeup of other foamy viruses (FV). Although isolated almost 25 years apart and propagated in either bovine (BFV-Riems) or nonbovine (BFV100) cells, both viruses are highly related, forming the European BFV clade. Despite clear differences, BFV-Riems and BFV100 are still very similar to BFV isolates from China and the United States, comprising the non-European BFV clade. The genomic sequences presented here confirm the concept of high sequence conservation across most of the FV genome. Analyses of cell culture-derived genomes reveal that proviral DNA may specifically lack introns in the *env-bel* coding region. The spacing of the splice sites in this region suggests that BFV has developed a novel mode to express a secretory but nonfunctional Env protein.

Brus or spumavirus, belongs to the subfamily of *Spumaretro-virinae* within the *Retroviridae*. Foamy viruses (FV) are complex retroviruses with a unique molecular biology and capacity to cross host species borders (1, 5). There is no obvious disease associated with FV infections, but FVs have high levels of prevalence in their respective animal hosts, while the few human infections are linked to zoonotic transmission of simian FVs to human beings (9, 12).

Here, we report two complete BFV consensus sequences, BFV-Riems from East Germany (GenBank accession number [X307862] and BFV100 from Poland (GenBank accession number JX307861), which were generated by PCR amplification and sequencing of from three to seven individual amplicons per genomic region. BFV genomic DNA templates were obtained from infected primary calf trachea cell cultures (KTR) for BFV-Riems (4) and immortalized canine CF2Th cells for BFV100 (7). The overall genetic organization of both isolates displays all FV characteristics. When comparing the two European isolates, overall and local sequence identity is 98% for coding regions and 97% for the noncoding regions of the long terminal repeats. In contrast, similarity to BFV isolates from the United States (GenBank accession number NC001831.1) (3) and China (GenBank accession number AY134750.1) (13) is 93% across coding and noncoding regions, reflecting high genetic relatedness. Here, we propose a European and a non-European clade of BFV isolates, as clustering of the non-European BFV isolates in phylogenetic analyses suggests common ancestry, perhaps through the sale or husbandry of BFV-positive cattle.

We have recently established serology-based BFV detection systems for animal and human screening, as BFV is known to be present in the human food chain through products such as raw milk (1, 8, 10). Based on data presented here, we are confident that these systems will cover all BFV isolates, at least those from Friesian-Holstein cattle, which are the source of most, if not all, current BFV isolates. Similarly, a recently established BFV integrase PCR (8) probably covers all known BFV isolates. The 3'-terminal region of the integrase could also be suitable for BFV PCR detection, as it is shared by all known BFV isolates but not present in this form in any of the other known FVs or other retroviruses (3; also unpublished data).

All known BFV isolates except BFV-Riems have been propagated *in vitro* in nonbovine cells, which, considering the extreme sequence conservation of all BFV isolates, may be of relevance for evolutionary studies. Analysis of BFV DNA from both isolates reveals that proviral DNA from the 3' end of the coding region may specifically lack introns in the *env-bel* coding region (2, 5, 11). The spacing of the corresponding splice sites in this region and translation of the open reading frames suggest that BFV has developed an alternative mode to express a secretory and nonfunctional Env protein lacking the transmembrane anchor (6).

Nucleotide sequence accession numbers. The BFV100 genomic sequence has been deposited at the GenBank database (accession number JX307861), and the BFV-Riems genomic sequence can be found under accession number JX307862.

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Address correspondence to Martin Löchelt, m.loechelt@dkfz-heidelberg.de. Copyright © 2012, American Society for Microbiology. All Rights Reserved. doi:10.1128/JVI.01875-12 tide sequence and spliced pol mRNA levels of the nonprimate spumavirus bovine foamy virus. J. Virol. **72**:2177–2182.

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