

Genome Sequence of a Subgenotype 1a Bovine Viral Diarrhea Virus in China

Shandian Gao,^a Junzheng Du,^a Zhancheng Tian,^a Shanshan Xing,^a Jianxun Luo,^a Guangyuan Liu,^a Huiyun Chang,^a Hong Yin^{a,b}

State Key Laboratory of Veterinary Etiological Biology, Lanzhou Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Xujiaping, Lanzhou, Gansu, People's Republic of China^a; Jiangsu Co-Innovation Center for Prevention and Control of Important Animal Infectious Diseases and Zoonoses, Yangzhou, People's Republic of China^b

A bovine viral diarrhea virus (BVDV), GS5, of the BVDV-1a subgenotype was isolated from dairy cattle in Gansu Province, northwest China. Its near-full-length genome was determined to be closely related to an early Belgian BVDV-1a strain, WAX-N, but the relatedness to domestic strains is relatively low, indicating that different genetic evolution occurred between the viral strains in cattle in China.

Received 19 September 2016 Accepted 22 September 2016 Published 10 November 2016

Citation Gao S, Du J, Tian Z, Xing S, Luo J, Liu G, Chang H, Yin H. 2016. Genome sequence of a subgenotype 1a bovine viral diarrhea virus in China. *Genome Announc* 4(6): e01280-16. doi:10.1128/genomeA.01280-16.

Copyright © 2016 Gao et al. This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/).

Address correspondence to Huiyun Chang, changhuiyun@caas.cn, or Hong Yin, yinhong@caas.cn.

Viruses of the genus *Pestivirus* within the family *Flaviviridae* comprise four recognized species, namely, bovine viral diarrhea virus type 1 (BVDV-1), BVDV-2, border disease virus (BDV), and classical swine fever virus (CSFV). Although under natural conditions, BVDV infects mainly cattle, it has been also isolated from animals other than cattle, including sheep, goats, swine, yaks, deer, and members of the Camelidae family (1–3). BVDV-1 is the dominant genotype worldwide, and at least 21 subgenotypes (BVDV-1a to BVDV-1u) have been proposed (4, 5). At least 11 subgenotypes of BVDV (BVDV-1a to -1d, BVDV-1m to -1q, BVDV-1u, BVDV-2a, and BVDV-2b) are circulating among multiple domestic animals in China (5–10). However, the complete genome of domestic isolates was scarcely reported for the classical subgenotypes except for BVDV-1b and BVDV-1d (11–13). In this study, the genome of a Chinese isolate, GS5, which belongs to the BVDV-1a subgenotype, was determined for the first time.

BVDV GS5 in passage cultures was used for viral RNA extraction and reverse transcription-PCR (RT-PCR), using primers that were designed based on the sequences of BVDV strain NADL (GenBank accession number AJ133739). The PCR products were purified and sequenced (Sangon Biotech, Shanghai, China). The near-full-length genome of GS5 is 12,189 nucleotides (nt) in length. Flanked by a 277-nt 5' untranslated region (UTR) and a 215-nt 3' UTR (partially determined), the open reading frame (ORF) is 11,697 nt in length and encodes 3,898 amino acids. Neither a cellular sequence insertion nor duplication of viral protein-coding regions was observed in the viral genome. Blast analysis with the genome sequence revealed that the GS5 strain shared high nucleotide identity (88 to 92%) with the BVDV-1a strains available in GenBank, followed by other subgenotypes of BVDV-1 (80 to 84%). However, it had lower nucleotide identity with strains of BVDV-2 (73%) and atypical bovine pestiviruses (71%). An individual coding region was demonstrated to have the highest nucleotide identity with an early Belgian BVDV-1a strain, WAX-N,

ranging from 88.6% to 96.0%, followed by the North America strain C24V, with 88.6 to 93.9% nucleotide identity. The conserved 5' UTR has 91.1 to 96.0% identity with reference BVDV-1a strains, but the similarity is lower (69.7 to 88.6%) than other subgenotypes of BVDV-1, BVDV-2, and atypical pestiviruses. The coding nucleotides of the immunodominant envelope protein E2 were analyzed, and GS5 is divergent from early North America strains C24V, SD1, and NADL, demonstrating 84.5 to 92.5% nucleotide identity.

Compared with domestic BVDV-1a isolates, GS5 was demonstrated to have nucleotide identity with SH1060 (93.6%) (GenBank accession no. JN248741) and HN01 (90.8%) (GenBank accession no. JX878887) in the 5' UTR, with two camel origin BVDV isolates (88.1% and 87.9%) (GenBank accession no. KC207068 and KC207069) in the N^{pro} coding region, and with GS24 (87.1%) in the E2 coding region (GenBank accession no. KF048838). The genetic relatedness of GS5 to domestic BVDV strains that were identified recently is comparatively lower than that with the Belgian strain WAX-N or early North American strains, suggesting that GS5 may share recent common ancestor with early North American strains, indicating different genetic evolution among different BVDV strains in cattle in China.

Accession number(s). The genome sequence of BVDV GS5 has been deposited in GenBank under the accession number [KJ541471](https://www.ncbi.nlm.nih.gov/nuccore/KJ541471).

ACKNOWLEDGMENTS

This study was supported by the NSFC (grant 31502104), Gansu Province Youth Science and Technology Fund (grant 1506RJYA151), ASTIP, CAAS, and NBCITS, MOA (CARS-38).

FUNDING INFORMATION

This work, including the efforts of Shandian Gao, was funded by NSFC (31502104). This work, including the efforts of Shandian Gao, was funded by Gansu Province Youth Science and Technology Fund

(1506RJYA151). This work, including the efforts of Hong Yin, was funded by ASTIP, CAAS. This work, including the efforts of Hong Yin, was funded by NBCITS, MOA (CARS-38).

REFERENCES

1. Ames TR. 2005. Hosts, p 171–175. *In* Ridpath JF, Goyal SM (ed), Bovine viral diarrhoea virus: diagnosis, management, and control. Blackwell Publishing, Oxford, United Kingdom.
2. Mishra N, Vilcek S, Rajukumar K, Dubey R, Tiwari A, Galav V, Pradhan HK. 2008. Identification of bovine viral diarrhoea virus type 1 in yaks (*Bos poeophagus grunniens*) in the Himalayan region. *Res Vet Sci* **84**: 507–510. <http://dx.doi.org/10.1016/j.rvsc.2007.05.019>.
3. Gao S, Luo J, Du J, Lang Y, Cong G, Shao J, Lin T, Zhao F, Belák S, Liu L, Chang H, Yin H. 2013. Serological and molecular evidence for natural infection of Bactrian camels with multiple subgenotypes of bovine viral diarrhoea virus in western China. *Vet Microbiol* **163**:172–176. <http://dx.doi.org/10.1016/j.vetmic.2012.12.015>.
4. Giammarioli M, Ceglie L, Rossi E, Bazzucchi M, Casciari C, Petrini S, De Mia GM. 2015. Increased genetic diversity of BVDV-1: recent findings and implications thereof. *Virus Genes* **50**:147–151. <http://dx.doi.org/10.1007/s11262-014-1132-2>.
5. Deng M, Ji S, Fei W, Raza S, He C, Chen Y, Chen H, Guo A. 2015. Prevalence study and genetic typing of bovine viral diarrhoea virus (BVDV) in four bovine species in China. *PLoS One* **10**:e0121718. <http://dx.doi.org/10.1371/journal.pone.0121718>.
6. Xue F, Zhu YM, Li J, Zhu LC, Ren XG, Feng JK, Shi HF, Gao YR. 2010. Genotyping of bovine viral diarrhoea viruses from cattle in China between 2005 and 2008. *Vet Microbiol* **143**:379–383. <http://dx.doi.org/10.1016/j.vetmic.2009.11.010>.
7. Zhong F, Li N, Huang X, Guo Y, Chen H, Wang X, Shi C, Zhang X. 2011. Genetic typing and epidemiologic observation of bovine viral diarrhoea virus in Western China. *Virus Genes* **42**:204–207. <http://dx.doi.org/10.1007/s11262-010-0558-4>.
8. Deng Y, Sun CQ, Cao SJ, Lin T, Yuan SS, Zhang HB, Zhai SL, Huang L, Shan TL, Zheng H, Wen XT, Tong GZ. 2012. High prevalence of bovine viral diarrhoea virus 1 in Chinese swine herds. *Vet Microbiol* **159**: 490–493. <http://dx.doi.org/10.1016/j.vetmic.2012.04.023>.
9. Zhu LQ, Lin YQ, Ding XY, Ren M, Tao J, Wang JY, Zhang GP, Zhu GQ. 2009. Genomic sequencing and characterization of a Chinese isolate of bovine viral diarrhoea virus 2. *Acta Virol* **53**:197–202. http://dx.doi.org/10.4149/av_2009_03_197.
10. Wang W, Shi X, Chen C, Wu H. 2014. Genetic characterization of a noncytopathic bovine viral diarrhoea virus 2b isolated from cattle in China. *Virus Genes* **49**:339–341. <http://dx.doi.org/10.1007/s11262-014-1067-7>.
11. Zhang S, Tan B, Ding Y, Wang F, Guo L, Wen Y, Cheng S, Wu H. 2014. Complete genome sequence and pathogenesis of bovine viral diarrhoea virus JL-1 isolate from cattle in China. *Virol J* **11**:67.
12. Xie Z, Fan Q, Xie Z, Liu J, Pang Y, Deng X, Xie L, Luo S, Khan MI. 2014. Complete genome sequence of a bovine viral diarrhoea virus strain isolated in southern China. *Genome Announc* **2**(3):e00512-14. <http://dx.doi.org/10.1128/genomeA.00512-14>.
13. Cai M, Song Q, Wang J, Zhu Y. 2016. Genomic characterization of three bovine viral diarrhoea virus isolates from cattle. *Arch Virol* **161**(12): 3589–3592. <http://dx.doi.org/10.1007/s00705-016-2910-z>.