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GENOME ANNOUNCEMENT

Complete Genome Sequence of Two Coxsackievirus A1 Strains That Were Cytotoxic to Human Rhabdomyosarcoma Cells

Qiang Sun,[a] Yong Zhang,[a] Shuangli Zhu,[a] Hui Cui,[b] Huifang Tian,[c] Dongmei Yan,[a] Guohong Huang,[a] Zhen Zhu,[a] Dongyan Wang,[a] Xiaolei Li,[a] Huafang Jiang,[a] Hongqiu An,[a] and Wenbo Xu[a]

WHO WPRO Regional Polio Reference Laboratory, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China[a]; Xinjiang Uygur Autonomous Region Center for Disease Control and Prevention, Urumqi, Xinjiang Uygur Autonomous Region, People's Republic of China[b]; and Shijiazhuang Center for Disease Control and Prevention, Shijiazhuang, Hebei, People's Republic of China[c]

Coxsackievirus A1 (CVA1) belongs to human enterovirus species C within the family *Picornaviridae*, order *Picornavirales*. Two Chinese CVA1 isolates, HT-THLH02F/XJ/CHN/2011 and KS-ZPH01F/XJ/CHN/2011, were isolated from stool specimens of two healthy children in the Xinjiang Uygur autonomous region of China. They were found to elicit cytopathic effects in a human rhabdomyosarcoma cell line, and complete genome sequences of these two CVA1 isolates revealed that natural intertypic recombination events occurred between CVA1 and CVA22.

Human enteroviruses (HEV) are members of the genus *Enterovirus* within the family *Picornaviridae*, order *Picornavirales*, consisting of four species: HEV-A, HEV-B, HEV-C, and HEV-D (3). Coxsackievirus A1 (CVA1) belongs to species HEV-C, which is usually associated with the pathology of acute hemorrhagic conjunctivitis, acute flaccid paralysis, and acute respiratory tract infection (1, 13–15).

The prototypic CVA1 strain (strain Tompkins/USA/1947) was identified in a stool sample from a patient with paralytic illness in New York in 1947 (2). Up to now, only one complete genome sequence of CVA1 (the prototype strain) has been available in the GenBank database. Here, we report two complete genome sequences of CVA1 strains (HT-THLH02F/XJ/CHN/2011 and KS-ZPH01F/XJ/CHN/2011), which were isolated from the stool specimens of two healthy children in the Xinjiang Uygur autonomous region, China, in 2011.

The two CVA1 isolates HT-THLH02F and KS-ZPH01F could infect a human rhabdomyosarcoma (RD) cell line and produce typical cytopathic effect (CPE) 4 to 5 days postinoculation. After purification by plaque assay, the complete genome sequences of the viruses were acquired using the Sanger's dideoxy terminator sequencing method according to the published strategies (1, 8, 18). Sequence raw data were assembled using Sequencher software (version 4.0.5). Sequence alignments and phylogenetic trees were generated using the MGEA program (version 5.0) (12); similarity plot and bootscan analyses were performed using the Simplot program (version 3.5.1) (5).

The genomic organization of these two CVA1 strains is similar to those of other reported HEV genomes. The lengths of the genomes of strains HT-THLH02F and KS-ZPH01F were 7,397 and 7,398 nucleotides (nt), respectively; HT-THLH02F has one base less in the 3′ untranslated region (3′-UTR). Both viral genomes contained a single large open reading frame (ORF) of 6,612 nt, which encoded a 2,202-amino-acid-long polyprotein. The nucleotide similarity and amino acid similarity of these two strains were 99.4% and 99.8%, respectively. Phylogenetic analysis showed that they clustered with the prototype CVA1 strain with respect to the P1 coding region but with CVA22 strains 10427/BAN/1999 (GenBank accession no. DQ995647) and 438913/HK/CHN/2010 (GenBank accession no. JN542510) for the P2 and P3 coding regions. Furthermore, the similarity plot and bootscan analyses indicated that recombination events occurred between CVA1 and CVA22. The two possible crossover sites are located before nt 620 in the 5′-UTR and after nt 4485 in the 2C region. These findings highlight that multirecombinations are common phenomena among HEVs (6, 7, 9–11, 16, 17, 19).

Previous studies have shown that CVA1 can be isolated only from suckling mice and cannot be isolated from cell lines (1, 4). However, in this study, the two CVA1 strains were able to grow and produce typical CPE in RD cells, one of the most common cell lines used for HEV isolation. Our research team is currently using reverse genetic methods to elucidate the inherent mechanism of this phenomenon.

Nucleotide sequence accession numbers. The nucleotide sequences of the complete genomes of the two CVA1 interserotypic recombinant strains HT-THLH02F/XJ/CHN/2011 and KS-ZPH01F/XJ/CHN/2011 have been deposited in GenBank (accession no. JX174176 and JX174177).

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Address correspondence to Wenbo Xu, wenbo_xu1@yahoo.com.cn.

Q.S. and Y.Z. contributed equally to this article.

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