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GENOME ANNOUNCEMENT

Complete Genome Sequence of a Coxsackievirus A22 Strain in Hong Kong Reveals a Natural Intratypic Recombination Event

Cyril C. Y. Yip,[1] Susanna K. P. Lau,[1,2,3,4] Patrick C. Y. Woo,[1,2,3,4] Kwok-Hung Chan,[1] and Kwok-Yung Yuen[1,2,3,4]*

Department of Microbiology,[1] State Key Laboratory of Emerging Infectious Diseases,[2] Research Centre of Infection and Immunology,[3] and Carol Yu Centre for Infection,[4] The University of Hong Kong, Hong Kong

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Coxsackievirus A22 (CVA22) belongs to the species human enterovirus C in the *Picornaviridae* family. We report the first complete genome sequence of CVA22 with natural intratypic recombination between CVA22 prototype strain Chulman and CVA22 strain ban99-10427, identified in the stool of a patient in Hong Kong.

Human enterovirus species C (HEV-C) consists of 21 types, poliovirus (PV) 1 to 3, coxsackievirus A1 (CVA1), CVA11, CVA13, CVA17, CVA19 to CVA22, CVA24, EV-C95, EV-C96, EV-C99, EV-C102, EV-C104, EV-C105, EV-C109, EV-C113, and EV-C116, which cause diseases ranging from herpangina, acute hemorrhagic conjunctivitis, and aseptic meningitis to acute flaccid paralysis (1; http://www.picornaviridae.com/enterovirus/hev-c/hev-c.htm). The prototype strain Chulman of CVA22 was identified in a stool sample from a patient without illness (10). Previous studies demonstrated that CVA22, which did not grow in various cell cultures, could be isolated in suckling mice (7, 11). To date, only 3 complete genome sequences of CVA22, including the prototype strain Chulman (New York, 1955), strain USA75-10624 (California, 1975), and strain ban99-10427 (Bangladesh, 1999), are available in GenBank. The role of CVA22 in disease is not fully understood.

We report a CVA22 strain, 438913, found in a patient in Hong Kong in 2010. Her stool sample was positive for enterovirus by PCR using primers targeting the 5′ untranslated region (UTR) as described elsewhere (13). Complete genome sequencing was performed according to our published strategies for positive-sense single-stranded RNA viruses (3, 4, 5, 6, 15, 16, 17, 18, 19). Sequence alignment was performed using ClustalX 2.1 (12). Phylogenetic trees were constructed using PhyML 3.0 (2). Bootscan and similarity plot analyses were performed using SimPlot 3.5.1 (8).

The genome of CVA22 strain 438913 is 7,404 bp in length, after excluding the polyadenylated tract, and the G+C content is 43.75%, which is similar to that of the other sequenced CVA22 strains. Its genome organization is similar to those of other reported enterovirus genomes, with the characteristic gene order 5′-VP4, VP2, VP3, VP1, 2A, 2B, 2C, 3A, 3B, $3C^{pro}$, $3D^{pol}$-3′. Both 5′ (712 bases) and 3′ (71 bases) ends of the genome contain UTRs. Downstream of the 5′ UTR, the genome contains a large open reading frame of 6,621 bases, which encodes potential polyprotein precursors of 2,206 amino acids. Phylogenetic analysis showed that CVA22 strain 438913 was clustered with CVA22 strain Chulman for the P1 region but with CVA22 strain ban99-10427 for the P2 and P3 regions. In the bootscan analysis, the result showed that from the 5′ end of the genome to position 3400, high bootstrap support for clustering between CVA22 strain Chulman and CVA22 strain 438913 was observed. From position 4000 to the 3′ end of the genome, high bootstrap support for clustering between CVA22 strain ban99-10427 and CVA22 strain 438913 was observed. Thus, recombination had possibly occurred between nucleotide positions 3400 and 4000, corresponding to the 2A-2B region. In the similarity plot analysis, CVA22 strain 438913 showed high sequence similarity (>79%) to CVA22 strain Chulman before position 3700 but shared higher similarity (>83%) with CVA22 strain ban99-10427 after position 3700. These findings revealed that a potential recombination site was located at 2A, which was shown to be a recombination hot spot in enteroviruses (9, 14). This is the first time that evidence for natural intratypic recombination is documented for CVA22.

Nucleotide sequence accession number. The nucleotide sequence of the genome of the CVA22 recombinant strain 438913 has been lodged within the GenBank sequence database under accession no. JN542510.

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* Corresponding author. Mailing address: State Key Laboratory of Emerging Infectious Diseases, Department of Microbiology, The University of Hong Kong, University Pathology Building, Queen Mary Hospital, Hong Kong. Phone: (852) 22554892. Fax: (852) 28551241. E-mail: kyyuen@hkucc.hku.hk.

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