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Brief Communication

Complete genome sequence of the first human parechovirus type 3 isolated in Taiwan

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Abstract

The first human parechovirus 3 (HPeV3 VGHKS-2007) in Taiwan was identified from a clinical specimen from a male infant. The entire genome of the HPeV3 isolate was sequenced and compared to known HPeV3 sequences. Genome alignment data showed that HPeV3 VGHKS-2007 shares the highest nucleotide identity, 99%, with the Japanese strain of HPeV3 1361K-162589-Yamagata-2008. All HPeV3 isolates possess at least 97% amino acid identity. The analysis of the genome sequence of HPeV3 VGHKS-2007 will facilitate future investigations of the epidemiology and pathogenicity of HPeV3 infection.

Keywords: Clinical isolate; Genome sequence; Human parechovirus

1. Introduction

Human parechovirus (HPeV), a small, round-structured, non-enveloped virus with a single-strand and positive-sense RNA genome, belongs to the *Picornaviridae*.[1] It was first described in 1961 as echoviruses 22 and 23 in the genus *Enterovirus* on identification from an outbreak of diarrhea among children.[2] However, further studies showed that the nucleotide sequence in replication and translation elements of the virus differ from that of other members of the genus *Enterovirus*. So the virus was re-classified into a new genus, *Parechovirus*, and the echoviruses 22 and 23 were re-named HPeV1 and HPeV2, respectively.[3–5] Based on viral protein 1 (VP1) sequence comparison, 16 types of HPeV isolates have been reported.[6]

Most HPeV infections occur in infants <1 year old.[7] HPeV1 may be the most prevalent type in the world, followed by HPeV3.[8–11] Most HPeV infections are asymptomatic but could be associated with gastrointestinal and respiratory tract symptoms, often mild in severity.[12,13] However, HPeV3 notably results in severe diseases of the central nervous system (CNS) and in neonatal sepsis,[14] almost exclusively restricted to infants <3 months old.[15]

In August 2007, HPeV3 VGHKS-2007 was isolated from a throat swab of a 3-month-old male infant in Taiwan, who, at an outpatient visit, presented productive cough with clear nasal discharge and wheezing. After a diagnosis of acute bronchiolitis, the management was supportive treatment. The

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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entire genome of the HPeV3 isolate was sequenced and compared to known HPeV3 sequences.

2. Methods

2.1. Sequence analysis

On the basis of the full-length nucleotide sequences of HPeV3 available in GenBank, 8 pairs of oligonucleotide primers were designed to amplify the different regions of the HPeV3 VGHKS-2007 genome, including the 5′- and 3′-end fragments. All fragments of PCR products were sequenced directly in both directions. The complete genome of this virus is 7349 nucleotides, including the 3′ poly(A) tail. Flanked by a 707-nt 5′ untranslated region (5′ UTR) and a 111-nt 3′ UTR, the predicted polyprotein is encoded by a 6531-nt single open reading frame (ORF). The genome sequence of HPeV3 VGHKS-2007 has been deposited in GenBank (accession no. KM986843).

3. Results

The genome organization of this virus, 5′ UTR–three structural proteins–seven nonstructural proteins–3′ UTR, is identical to that of other HPeVs.[16] However, unlike HPeV1 but similar to other HPeV3 strains, HPeV3 VGHKS-2007 lacks an RGD motif at the C-terminus of the VP1 for binding to integrin on the host cell membrane as part of viral entry process. An alternative receptor may exist, which changes the cellular tropism of HPeV3 and leads to enhanced ability to spread and replicate in the CNS.[16,17]

We aligned the entire genome nucleotide sequence of HPeV3 VGHKS-2007 to the full-length nucleotide sequences of HPeV3 available in GenBank. HPeV3 VGHKS-2007 shares the highest nucleotide sequence similarity, 99%, with 1361K-162589-Yamagata-2008, and more than 87% similarity with other HPeV3 isolates. However, at the polyprotein level, all HPeV3 isolates possess at least 97% amino acid identity.

Furthermore, we randomly selected 15 completed genomes of HPeV1-8 available in GenBank for SimPlot analysis: HPeV1 strains Harris (accession no. L02971), SH1 (accession no.FJ840477), and 7555312 (accession no.FM178558); HPeV2 strain Williamson (accession no.AJ005695); HPeV3 strains 1361K-162589-Yamagata-2008 (accession no.AB668029), Can82853-01 (accession no.AJ889918) and A308/99 (accession no.AB084913); HPeV4 strains K251176-02 (accession no.DQ315670) and Fuk2005-123 (accession no.AB433629); HPeV5 strains T92-15 (accession no.AM235749) and CT86-6760 (accession no.AF055846); HPeV6 strains NII561-2000 (accession no.AB252582) and 2005-823 (accession no.EU077518); HPeV7 strain PAK5045 (accession no.EU556224); and HPeV8 strain BR/217/2006 (accession no. EU716175) (Fig. 1). Throughout the whole ORF, HPeV3 VGHKS-2007 consistently had similarity scores of at least 98% with 1361K-162589-Yamagata-2008, which had resulted in an epidemic of myalgia in 22 adults in Japan.[18] However, if 1361K-162589-Yamagata-2008 was excluded, HPeV3 VGHKS-2007 had higher similarity with HPeV3 strain Can82853-01 in the highly variable capsid-encoding regions VP0, VP3 and VP1 and with HPeV4 strain K251176-02 in the more conserved regions from 2B to 3C. Such findings may have resulted from a recombination event during HPeV evolution.[19]

4. Discussion

HPeV3 VGHKS-2007 is the first HPeV3 isolated in Taiwan. Importantly, our study revealed the existence of

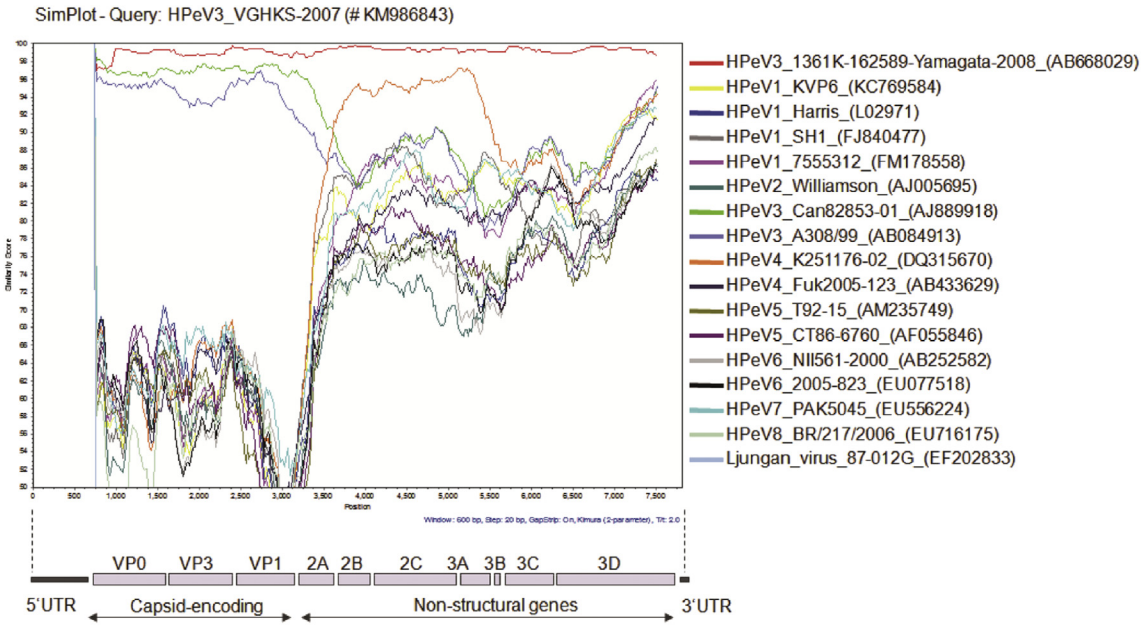

Fig. 1. SimPlot comparison of complete genome sequence of HPeV3 VGHKS-2007 and genomes of other HPeV strains or types. The viral genome structure is shown.

endemic circulation of HPeV in Taiwan.[20] These data suggest HPeV3 could be one of the pathogens causing clinical abnormalities in newborns or young infants, which should be noted in the clinical care system. The availability of the genome sequence of HPeV3 VGHKS-2007 will facilitate future investigations of the epidemiology and pathogenicity of HPeV3 infection disease. For example, the genome information would be required for viral strain identification and evolution analysis of epidemic HPeV3.[21] In addition, with the viral genome sequence, the individual viral protein genes could be further cloned for molecular study to understand the pathogenic mechanism of HPeV3.[22,23]

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