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GENOME ANNOUNCEMENT

Genome Sequence of the First Human Adenovirus Type 14 Isolated in China

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Emergent pathogens may be examined rapidly at high resolution on a molecular level using genomics, allowing an understanding of their evolution. China is a unique environment for studying pathogens, having a large, dense, and generally closed population. Human adenovirus type 14 (HAdV-14) was originally identified as an acute respiratory disease (ARD) pathogen in The Netherlands (1955), with a second isolation in England (1957). Since then, few reports of this virus appeared until an ARD pathogen with a similar genome caused multiple outbreaks in the United States (2006 to 2009). This report presents the first genome of HAdV-B14 isolated in China (2010). As China experienced two recent outbreaks of an emergent ARD pathogen, HAdV-B55, containing much of the HAdV-B14 genome, the availability of this HAdV-B14 sequence will facilitate studies of the epidemiology of these pathogens, as well as provide a foundation for studying adenovirus evolution and the genesis of emergent pathogens. These observations may be invaluable in predicting possible recombination between wild-type viruses and adenoviral gene delivery vectors, including adenovirus vaccines.

Human adenoviruses (HAdVs) have unique simultaneous roles as models for understanding biological concepts, as human and global public health agents and as biotechnological and biomedical tools. These lines of inquiry benefit from cost-effective genome sequencing, which provides high-resolution data. As these pathogens are associated with sporadic civilian and military outbreaks that result in respiratory, ocular, and gastrointestinal diseases, understanding the molecular evolution of adenovirus genomes is important as a first step in developing prophylactic measures and recognizing ramifications of the development and use of laboratory-engineered gene delivery vectors and adenovirus vaccines.

To date, 65 HAdV types have been recognized and classified within seven species (5, 6, 8, 10–12). Among these, HAdV-B14 has been rarely reported since its identification as an acute respiratory pathogen in The Netherlands in 1955, with a second occurrence in England (1957). Fifty-one years later, a re-emerging variant, HAdV-14p1, was associated with several highly contagious outbreaks of acute respiratory disease (ARD), including fatalities, in the United States (2006 to 2009) (2, 4, 7) and Europe (2009 and 2010) (1). Additionally, as one of the two parental viruses contributing to the genome of an emergent ARD pathogen, HAdV-B55 (14, 16), it is valuable to have the genomes of current circulating strains available for study in order to determine if there is a propensity for HAdV-B14 and HAdV-B11 to recombine, creating a "Trojan horse" in which the presenting antibody epitope is of a renal pathogen and the virus chassis and clinical presentation are of a respiratory pathogen (12). The isolation of HAdV-B14 in China is intriguing, as three recent HAdV-B55 outbreaks were in China in 2006 (14, 16) and 2012 (unpublished) and in Singapore in 2005 (3). In a retrospective survey of HAdV infections in southern China (2010 and 2011), human adenovirus B/CHN/GZ01_2010/2010/14[P14H14F14] was isolated from a throat swab of a 17-month-old child with acute suppurative tonsillitis in Guangzhou (October 2010). This is unusual in that the symptoms were not as previously described for published HAdV-B14 and HAdV-B55 infections (1, 2, 3, 7, 14, 16).

The genome (34,767 bases) was sequenced using the Sanger method following PCR amplification of targeted overlapping regions. This, in turn, was followed by resolution on an ABI 3730 Genetic Analyzer, which resulted in sequence data with an average of 3- to 5-fold redundancy, with both strands represented. The 5′ and 3′ ends were sequenced directly using genomic DNA as templates (described previously [15]). Annotation of the genome and a comparative analysis with other HAdVs provided additional quality control. Gaps and ambiguous sequences were PCR amplified using different primers and resequenced for clarity.

Recombination of HAdV genomes plays a role in pathogen genesis (3, 5, 6, 8, 9, 10, 12, 13). This presentation of the first HAdV-B14 isolate in China facilitates an understanding of the evolution of HAdV-B55 and provides awareness of possible recombination events between wild-type viruses and adenoviral gene delivery vectors, with additional information for the development of adenovirus vaccines.

Nucleotide sequence accession number. Genome data for human adenovirus B/CHN/GZ01_2010/2010/14[P14H14F14] are available in the GenBank database under accession no. JQ824845.

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REFERENCES

1. **Carr MJ, et al.** 2011. Deaths associated with human adenovirus-14p1 infections, Europe, 2009-2010. Emerg. Infect. Dis. 17:1402–1408.

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2. **Centers for Disease Control and Prevention.** 2007. Acute respiratory disease associated with adenovirus serotype 14—four states, 2006-2007. MMWR Morb. Mortal. Wkly. Rep. **56**:1181–1184.
3. **Kajon AE, et al.** 2010. Outbreak of febrile respiratory illness associated with adenovirus 11a infection in a Singapore military training camp. J. Clin. Microbiol. **48**:1438–1441.
4. **Kajon AE, et al.** 2010. Molecular epidemiology and brief history of emerging adenovirus 14-associated respiratory disease in the United States. J. Infect. Dis. **202**:93–103.
5. **Liu EB, et al.** 2011. Genetic analysis of a novel human adenovirus with a serologically unique hexon and a recombinant fiber gene. PLoS One **6**:e24491. doi:10.1371/journal.pone.0024491.
6. **Liu EB, et al.** 2012. Computational and serologic analysis of novel and known viruses in species human adenovirus D in which serology and genomics do not correlate. PLoS One **7**:e33212. doi:10.1371/journal.pone.0033212.
7. **Louie JK, et al.** 2008. Severe pneumonia due to adenovirus serotype 14: a new respiratory threat? Clin. Infect. Dis. **46**:421–425.
8. **Matsushima Y, et al.** 2012. Novel human adenovirus strain, Bangladesh. Emerg. Infect. Dis. **18**:846–848.
9. **Robinson CM, et al.** 2009. Computational analysis of human adenovirus type 22 provides evidence for recombination between human adenoviruses species D in the penton base gene. J. Virol. **83**:8980–8985.
10. **Robinson CM, et al.** 2011. Computational analysis and identification of an emergent human adenovirus pathogen implicated in a respiratory fatality. Virology **409**:141–147.
11. **Singh G, et al.** 2012. Overreliance on the hexon gene leading to misclassification of human adenoviruses. J. Virol. **86**:4693–4695.
12. **Walsh MP, et al.** 2010. Computational analysis identifies human adenovirus type 55 as a re-emergent acute respiratory disease pathogen. J. Clin. Microbiol. **48**:991–993.
13. **Walsh MP, et al.** 2011. Computational analysis of two species C human adenoviruses provides evidence of a novel virus. J. Clin. Microbiol. **49**:3482–3490.
14. **Yang Z, et al.** 2009. Genomic analyses of recombinant adenovirus type 11a in China. J. Clin. Microbiol. **47**:3082–3090.
15. **Zhang Q, et al.** 2006. Comparative genomic analysis of two strains of human adenovirus type 3 isolated from children with acute respiratory infection in southern China. J. Gen. Virol. **87**:1531–1541.
16. **Zhu Z, et al.** 2009. Outbreak of acute respiratory disease in China caused by B2 species of adenovirus type 11. J. Clin. Microbiol. **47**:697–703.