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GENOME ANNOUNCEMENT

Genome Sequence of Human Adenovirus Type 55, a Re-Emergent Acute Respiratory Disease Pathogen in China

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Human adenovirus type 55 (HAdV-B55) is an acute respiratory disease (ARD) pathogen first completely characterized in China (2006). This is a unique Trojan horse microbe with the virus neutralization attribute of a renal pathogen and the cell tropism and clinical attributes of a respiratory pathogen, bypassing herd immunity. It appeared to be an uncommon pathogen, with earlier putative, sporadic occurrences in Spain (1969) and Turkey (2004); these isolates were incompletely characterized using only two epitopes. Reported here is the genome of a second recent isolate (China, 2011), indicating that it may occur more frequently. The availability of this HAdV-B55 genome provides a foundation for studying adenovirus molecular evolution, the dynamics of epidemics, and patterns of pathogen emergence and re-emergence. These data facilitate studies to predict genome recombination between adenoviruses, as well as sequence divergence rates and hotspots, all of which are important for vaccine development and because HAdVs are used for epitope and/or gene delivery vectors.

China has a large, dense, and generally closed population that presents a unique environment for studying pathogens in order to understand patterns of their emergence and re-emergence and the dynamics of epidemics. Examples are the human adenoviruses (HAdVs), which comprise highly contagious pathogens that are responsible for sporadic community- and military-based outbreaks associated with respiratory, ocular, and gastrointestinal diseases. Because adenoviruses are global public health disease agents and also, ironically, biotechnological and biomedical tools that have applications in human health, understanding their molecular evolution is important for identifying causes of outbreaks and for developing vaccines and gene and/or epitope delivery vectors. Currently, cost-effective DNA sequencing facilitates the rapid acquisition of complete viral genome sequences, leading to a correct and complete identification of the pathogen and to insights into its evolution and effects on the population (10).

To date, 65 HAdV types are classified within seven species (5–7, 9, 11, 13) using a new paradigm based on genomics (10). Among these, HAdV-B55 is either (i) a very uncommon re-emergent pathogen, first identified as HAdV-B11a from an outbreak during a military training exercise (Spain, 1969), albeit by partial characterization of its hexon and fiber epitopes (3), and with a second appearance in another military training exercise (Turkey, 2004) (1), or (ii) a newly identified emergent acute respiratory disease (ARD) pathogen, fully characterized by whole-genome sequencing, causing two recent outbreaks, one in China in 2006 (15) and one in Singapore in 2005 (4). In 2011, 5 years after the first HAdV-B55-associated ARD outbreak in China (Qishan County, Shanxi Province), this pathogen apparently re-emerged in Beijing, causing several cases of ARD; one sample was obtained from a 29-year-old patient diagnosed with severe community-acquired pneumonia (2).

Human adenovirus B human/CHN/BJ01/2011/55[P14H11F14] was isolated from this patient's throat swab. Its genome (34,773 bases) was sequenced using the Sanger method, following PCR amplification of targeted overlapping regions. Both the 5′ and 3′ end were sequenced directly, using genomic DNA as the templates, as described earlier (16). The sequence data, collected with an ABI 3730 genetic analyzer, provided an average coverage of 3- to 5-fold redundancy, with both strands represented. Genome annotation and a comparative analysis with other HAdVs provided an additional level of quality control. Gaps and ambiguous sequences were PCR amplified using different primers and resequenced for clarity.

Complete genome analysis of the 2006 isolate demonstrated that this virus is a Trojan horse, containing a genome resulting from a recombination which provides the antibody epitope of a renal pathogen, HAdV-B11, and confers the cell tropism, biological, and pathogenicity properties of HAdV-B14, a respiratory pathogen (13). Genome recombination is an important mechanism driving HAdV evolution (4–9, 13, 14) and conferring changes in pathogenicity (11, 12, 17); HAdV-B55 is a vivid example in which the emergence of a novel recombinant virus allows a subversion of herd immunity (13). The genome data of this second HAdV-B55 isolate, recently obtained in China, along with data of future isolates, will provide a foundation for understanding the evolution of HAdV-B55 and the dynamics of epidemics.

Nucleotide sequence accession number. Human adenovirus B human/CHN/BJ01/2011/55[P14H11F14] data have been deposited in GenBank under sequence accession number JX491639.

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