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GENOME ANNOUNCEMENT

Five Genome Sequences of Subspecies B1 Human Adenoviruses Associated with Acute Respiratory Disease

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Five genomes of human subspecies B1 adenoviruses isolated from cases of acute respiratory disease have been sequenced and archived for reference. These include representatives of two prevalent genomic variants of HAdV-7, i.e., HAdV-7h and HAdV-7d2. The other three are HAdV-3/16, HAdV-16 strain E26, and HAdV-3+7 strain Takeuchi. All are recombinant genomes. Genomics and bioinformatics provide detailed views into the genetic makeup of these pathogens and insight into their molecular evolution. Retrospective characterization of particularly problematic older pathogens such as HAdV-7h (1987) and intriguing isolates such as HAdV-3+7 strain Takeuchi (1958) may provide clues to their phenotypes and serology and may suggest protocols for prevention and treatment.

Human adenoviruses (HAdVs) are causative agents of respiratory, ocular, and gastrointestinal diseases. Susceptible populations include children under the age of 5 years, close-quartered populations such as crowded cities and military training camps, and immunocompromised individuals (2). A genomics-based paradigm for the study of infectious diseases, including past problematic pathogens (8), is possible through high-throughput and low-cost DNA sequencing technologies, along with the growing availability of bioinformatic protocols. Genome sequences allow a more thorough understanding of the molecular mechanisms driving pathogen evolution, including recombination. To understand better the genetic determinants of pathogenicity and the molecular evolution of HAdVs, genomes of five subspecies B1 adenoviruses, isolated from cases of acute respiratory disease (ARD), were sequenced. These include HAdV-7h, HAdV-7d2, HAdV-3+7, HAdV-3/16, and HAdV-16 strain E26. The genome sequences and their annotations facilitate studies on the natural history of emerging and reemerging HAdV pathogens in the context of readily available complete genome sequences.

HAdV-7h strain 87-922 is a recombinant with a type 7-like hexon and a type 3-like fiber, isolated from a fatal case of pediatric pneumonia in Argentina in 1987 (5, 7). HAdV-7d2 strain F52154 was isolated from a patient with ARD at Lackland Air Force Base (AFB) in 2009 (Lisa Lott, Lackland AFB, TX, personal communication). HAdV-3/16 strain Arg827/04, with a type 3-like hexon and a type 16-like fiber, was isolated from a pediatric case of ARD in Argentina (4). HAdV-16 strain E26, isolated from a civilian seeking care for ARD in Egypt, was initially typed by PCR as HAdV-16 (6) and subsequently confirmed by targeted sequencing as having type 16-like hexon and fiber genes (A. E. Kajon, personal observations). HAdV-3+7 strain Takeuchi was isolated from a fatal case of pediatric pneumonia in Japan (1958) and has a unique serological profile (1). These genomes represent additional examples of recombinant genomes, complementing the reported species D recombinants (9–11).

The genome sequences were determined using the 454 GS FLX System, outsourced to Eurofins MWG Operon (Huntsville, AL). These data were assembled using the CLC Genomics software (CLC bio; Cambridge, MA), with an N50 average for the five genomes of 5,260). Gaps, ambiguous sequences, and the inverted terminal repeats were sequenced using an ABI3130xl via PCR amplification. Minimally, the sequence coverages were at 8-fold (Sanger chemistry) and 17- to 20-fold (Next Gen), with the Next Gen data noted by Operon at an accuracy of greater than 99% (Q20 or better).

Recombination plays a major role in generating HAdV genetic diversity (3, 9–13). This has been thoroughly demonstrated by the recent sequencing and bioinformatic analysis of the genomes of newly emergent and prevalent pathogenic strains (3, 9–13). Insights from detailed analysis of a diversity of genomes and their *in silico* proteomes will facilitate the design of experimental strategies to understand the correlation of specific genome attributes with pathogenic phenotypes.

Nucleotide sequence accession numbers. The following genome sequences (accession numbers) have been deposited in GenBank: HAdV-7h (JN860676), HAdV-7d2 (JN860677), HAdV-3/16 (JN860678), HAdV-16 strain E26 (JN860680), and HAdV-3+7 (JN860679). Full bioinformatic analyses of these genomes will be presented in an upcoming report. *Nota bene*, not all of us agree with the nomenclature presented.

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