







Complete Genome Sequences of Mumps and Measles Virus Isolates from Three States in the United States

 Laura C. Magaña,^a  Alex Espinosa,^b  Rachel L. Marine,^c  Terry Fei Fan Ng,^c Christina J. Castro,^a Anna M. Montmayeur,^d Jill K. Hacker,^b Samantha Scott,^e Thomas Whyte,^e Bettina Bankamp,^c M. Steven Oberste,^c Paul A. Rota^c

Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee, USA^a; Viral and Rickettsial Disease Laboratory, California Department of Public Health, Richmond, California, USA^b; Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA^c; CSRA, Atlanta, Georgia, USA^d; Wisconsin State Laboratory of Hygiene, Madison, Wisconsin, USA^e

ABSTRACT We report here the full coding sequence of nine paramyxovirus genomes, including two full-length mumps virus genomes (genotypes G and H) and seven measles virus genomes (genotypes B3 and D4, D8, and D9), from respiratory samples of patients from California, Virginia, and Alabama obtained between 2010 and 2014.

Members of the *Paramyxoviridae* family of single-stranded, negative-sense, non-segmented RNA viruses are causative agents of highly transmissible diseases in humans, including measles (genus *Morbillivirus*) and mumps (genus *Rubulavirus*) (1, 2). Infections are generally mild but can lead to serious complications, including secondary infections causing pneumonias or gastrointestinal infections in measles cases and aseptic meningitis, encephalitis, and orchitis in mumps cases (3, 4). Vaccination eliminated measles from the United States; however, outbreaks have occurred due to importation from countries in which measles is endemic (5). In recent years, there have been numerous mumps outbreaks in the United States (4). Genetic characterization of circulating measles and mumps viruses is vital for surveillance. The mumps virus (MuV) genome is 15,384 nucleotides (nt) in length, with the 12 mumps genotypes delineated based on SH and HN gene sequences (6–8). The measles virus (MeV) genome is 15,894 nt in length and assigned to one of 24 genotypes based on the highly variable 450-nt coding for the carboxyl terminus of the nucleocapsid protein (N-450) (7, 9). Though genotyping protocols are well established, SH and N-450 sequences often do not provide sufficient resolution to accurately map transmission pathways. Application of next-generation sequencing (NGS) methods will expand the amount of sequence information available for MuV and MeV. The genomic sequences reported here were generated at a CDC/Association of Public Health Laboratories (APHL) training workshop to assist the Vaccine Preventable Disease Reference Centers in implementing NGS protocols (5).

Viral isolates of MeV and MuV were passaged in Vero/hSLAM cells, and clinical specimens containing MeV were filtered and nuclease-treated prior to RNA extraction using the QIAmp viral RNA mini kit with an on-column DNase treatment (Qiagen). Random amplicons were prepared from viral RNA using sequence-independent single-primer amplification and size-selected using AMPure XP beads (Beckman Coulter, Inc.) (10). Nextera XT libraries were prepared and sequenced on an Illumina MiSeq 500-cycle paired-end run. Sequence data were processed through an in-house bioinformatics pipeline modified from a previous study (11), and genomes were annotated using Sequin.

Received 26 June 2017 Accepted 28 June 2017 Published 17 August 2017

Citation Magaña LC, Espinosa A, Marine RL, Ng TFF, Castro CJ, Montmayeur AM, Hacker JK, Scott S, Whyte T, Bankamp B, Oberste MS, Rota PA. 2017. Complete genome sequences of mumps and measles virus isolates from three states in the United States. *Genome Announc* 5:e00748-17. <https://doi.org/10.1128/genomeA.00748-17>.

This is a work of the U.S. Government and is not subject to copyright protection in the United States. Foreign copyrights may apply. Address correspondence to Bettina Bankamp, bfb9@cdc.gov.

The MuV genomes were genotypes H (MuVs/Virginia.USA/10.12) and G (MuVs/California.USA/40.11). MuVs/California.USA/40.11 was from a university outbreak in California in 2011 (12), in which the source patient traveled to western Europe during the exposure period. Mumps virus genotype G is the most commonly detected genotype in the United States, Canada, and western Europe (1, 6). The predicted I protein, of unknown function (13), for MuVs/California.USA/40.11 ends prematurely by six amino acids. Truncated I proteins have been observed in at least 11 other MuV sequences deposited in GenBank. For MeV, two sequences were D4 genotype (MV/California.USA/47.13 and MVi/California.USA/16.12), three were genotype B3 (MV/California.USA/05.14, MV/California.USA/08.14/3, and MV/Alabama.USA/13.14), one was genotype D8 (MV/California.USA/49.10), and one sequence was genotype D9 (MVi/California.USA/19.10). To our knowledge, MVi/California.USA/19.10 represents the first complete genomic sequence for genotype D9.

The nine sequences described here will expand the sequence databases for MeV and MuV. These data help to improve the resolution of virologic surveillance for MuV and MeV and develop more robust methods to support molecular epidemiological studies (13–15).

Accession number(s). The sequences of MV/California.USA/47.13, MV/California.USA/05.14, MV/California.USA/08.14/3, MVi/California.USA/16.12, MV/California.USA/49.10, MVi/California.USA/19.10, MuVs/California.USA/40.11, MVs/Alabama.USA/13.14, and MuVs/Virginia.USA/10.12 have been deposited in GenBank under accession no. [KY656518](#) and [KY969476](#) through [KY969483](#).

ACKNOWLEDGMENTS

This work was made possible through support from the Advanced Molecular Detection (AMD) program at the CDC. This research was also supported in part by an appointment to the Research Participation Program at the CDC administered by the Oak Ridge Institute for Science and Education (ORISE) through an interagency agreement between the U.S. Department of Energy and the CDC; by the APHL; and through cooperative agreement number U60HM000803 with the CDC and the Assistant Secretary for Preparedness and Response.

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official views of CDC, the Association of Public Health Laboratories, and/or the Assistant Secretary for Preparedness and Response.

REFERENCES

- Hviid A, Rubin S, Mühlemann K. 2008. Mumps. *Lancet* 371:932–944. [https://doi.org/10.1016/S0140-6736\(08\)60419-5](https://doi.org/10.1016/S0140-6736(08)60419-5).
- Kutty P, Rota J, Bellini W, Redd SB, Barskey A, Wallace G. 2013. Measles, p 7-1–7-21. In Roush SW, Baldy LM (ed), *Manual for the surveillance of vaccine-preventable diseases*, 6th ed. CDC, Atlanta, GA.
- Coughlin MM, Beck AS, Bankamp B, Rota PA. 2017. Perspective on global measles epidemiology and control and the role of novel vaccination strategies. *Viruses* 9:E11. <https://doi.org/10.3390/v9010011>.
- Parker Fiebelkorn A, Barskey A, Hickman C, Bellini W. 2012. Mumps, p 9-1–9-18. In Roush SW, Baldy LM (ed), *Manual for the surveillance of vaccine-preventable diseases*, 6th ed. CDC, Atlanta, GA.
- Association of Public Health Laboratories. 2016. Vaccine preventable diseases. https://www.aphl.org/programs/infectious_disease/Pages/VPD.aspx. Accessed 10 July 2017.
- Jin L, Örvell C, Myers R, Rota PA, Nakayama T, Forcic D, Hiebert J, Brown KE. 2015. Genomic diversity of mumps virus and global distribution of the 12 genotypes. *Rev Med Virol* 25:85–101. <https://doi.org/10.1002/rmv.1819>.
- Rota PA, Brown K, Mankertz A, Santibanez S, Shulga S, Muller CP, Hübschen JM, Siqueira M, Beirnes J, Ahmed H, Triki H, Al-Busaidy S, Dosseh A, Byabamazima C, Smit S, Akoua-Koffi C, Bwogi J, Bukenya H, Wairagkar N, Ramamurthy N, Incomserb P, Pattamadilok S, Jee Y, Lim W, Xu W, Komase K, Takeda M, Tran T, Castillo-Solorzano C, Chenoweth P, Brown D, Mulders MN, Bellini WJ, Featherstone D. 2011. Global distribution of measles genotypes and measles molecular epidemiology. *J Infect Dis* 204(suppl 1):S514–S523. <https://doi.org/10.1093/infdis/jir118>.
- Mühlemann K. 2004. The molecular epidemiology of mumps virus. *Infect Genet Evol* 4:215–219. <https://doi.org/10.1016/j.meegid.2004.02.003>.
- Bankamp B, Liu C, Rivaller P, Bera J, Shrivastava S, Kirkness EF, Bellini WJ, Rota PA. 2014. Wild-type measles viruses with non-standard genome lengths. *PLoS One* 9:e95470. <https://doi.org/10.1371/journal.pone.0095470>.
- Ng TF, Marine R, Wang C, Simmonds P, Kapusinszky B, Bodhidatta L, Oderinde BS, Wommack KE, Delwart E. 2012. High variety of known and new RNA and DNA viruses of diverse origins in untreated sewage. *J Virol* 86:12161–12175. <https://doi.org/10.1128/JVI.00869-12>.
- Montmayeur AM, Ng TF, Schmidt A, Zhao K, Magaña L, Iber J, Castro CJ, Chen Q, Henderson E, Ramos E, Shaw J, Tatusov RL, Dybdahl-Sissoko N, Endegue-Zanga MC, Adeniji JA, Oberste MS, Burns CC. 2017. High-throughput next-generation sequencing of polioviruses. *J Clin Microbiol* 55:606–615. <https://doi.org/10.1128/JCM.02121-16>.
- Zipprich J, Murray EL, Winter K, Kong D, Harriman K, Preas C, Wadford D, Messenger S, Talarico J, Watt JP, Berreman J, Gregory B, Cameron P, Buchman B, Nunez JJ. 2012. Mumps outbreak on a university campus—California, 2011. Office of Surveillance E and Laboratory Services, Centers for Disease Control and Prevention, Atlanta, GA.
- Penedos AR, Myers R, Hadeb F, Aladin F, Brown KE. 2015. Assessment of the utility of whole genome sequencing of measles virus in the charac-

- terisation of outbreaks. PLoS One 10:e0143081. <https://doi.org/10.1371/journal.pone.0143081>.
14. Gardy JL, Naus M, Amlani A, Chung W, Kim H, Tan M, Severini A, Krajden M, Puddicombe D, Sahni V, Hayden AS, Gustafson R, Henry B, Tang P. 2015. Whole-genome sequencing of measles virus genotypes H1 and D8 during outbreaks of infection following the 2010 Olympic winter games reveals viral transmission routes. J Infect Dis 212:1574–1578. <https://doi.org/10.1093/infdis/jiv271>.
 15. Gouma S, Sane J, Gijselaar D, Cremer J, Hahné S, Koopmans M, van Binnendijk R. 2014. Two major mumps genotype G variants dominated recent mumps outbreaks in the Netherlands (2009–2012). J Gen Virol 95:1074–1082. <https://doi.org/10.1099/vir.0.062943-0>.