Complete Genome Sequence of the World Health Organization Mumps Reference Strain, MuVi/Sheffield.GBR/1.05

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ABSTRACT   The World Health Organization has designated the MuVi/Sheffield.GBR/1.05 strain as a genotype G mumps reference strain. However, currently only the SH and HN gene sequences are available. We are reporting the complete genome sequence of this strain so that it can now be used as a standard for mumps molecular epidemiology.

Mumps-like infection was first described by Hippocrates in the 16th century (1, 2). In 1934, Johnson and Goodpasture showed that mumps disease was caused by a virus (3). The mumps RNA virus is part of the *Paramyxoviridae* family, in the genus *Rubulavirus*, and humans are the only host identified (4).

A resurgence of mumps has been identified in young adults and in vaccinated populations (5–10). Current genotyping of the small hydrophobic (SH) gene is insufficient, as current outbreaks are due to genotype G strains with minimal genomic diversity in the SH gene (9, 11–13). As a result, whole-genome sequencing is now used to analyze these outbreaks.

The MuVi/Sheffield.GBR/1.05 G reference strain, as designated by the World Health Organization (WHO), was isolated in the United Kingdom in 2005 and is used to compare mumps SH gene sequences (14). Currently, only the SH and hemagglutinin-neuraminidase (HN) gene sequences of the Sheffield strain are publicly available (14, 15). With the increase in whole-genome sequencing to resolve mumps outbreaks, the complete Sheffield sequence would allow this reference strain to remain consistent across different types of sequence analyses.

The MuVi/Sheffield.GBR/1.05 mumps strain was purchased from the National Collection of Pathogenic Viruses (Salisbury, UK) (catalog number 1604296v) and passaged once in Vero cells (ATTC number CCL-81 [16]). Although the effect of cell culture in introducing mumps mutations is unknown, sequential passaging can select for specific strains (17). Our sample underwent one passage in cell culture; therefore, we expect the effect to be minimal.

Nucleic acid was extracted from 200 μl of sample, and first- and second-strand cDNA syntheses were performed as described previously (18). Libraries were prepared using the TruSeq Nano DNA high-throughput library preparation kit (catalog number 20015965; Illumina), with modifications as described previously (18). The library was sequenced on the MiSeq platform (Illumina) using a MiSeq reagent kit v3 (catalog number MS-102-3003).

Using the Galaxy platform (19), FastQ files were aligned using Bowtie 2 (20) with the settings of pair data set collection and a maximum fragment length of 1,000 bases, with a previously described reference sequence (18). BAM Coverage Statistics was used to determine genomic coverage (21). In total 30,768 reads were mapped in the genomic alignment. The alignment was entered into the SNVPhyl pipeline (minimum mean mapping of 28 and single-nucleotide variant [SNV] abundance ratio of 0.75), and a consensus sequence was constructed using the BCFtools consensus (22, 23). All tools were run with default parameters unless otherwise specified.

The MuVi/Sheffield.GBR/1.05 whole genome was successfully sequenced (including the termini), with a genome size of 15,384 nucleotides and a GC content of 42.3%. The minimum

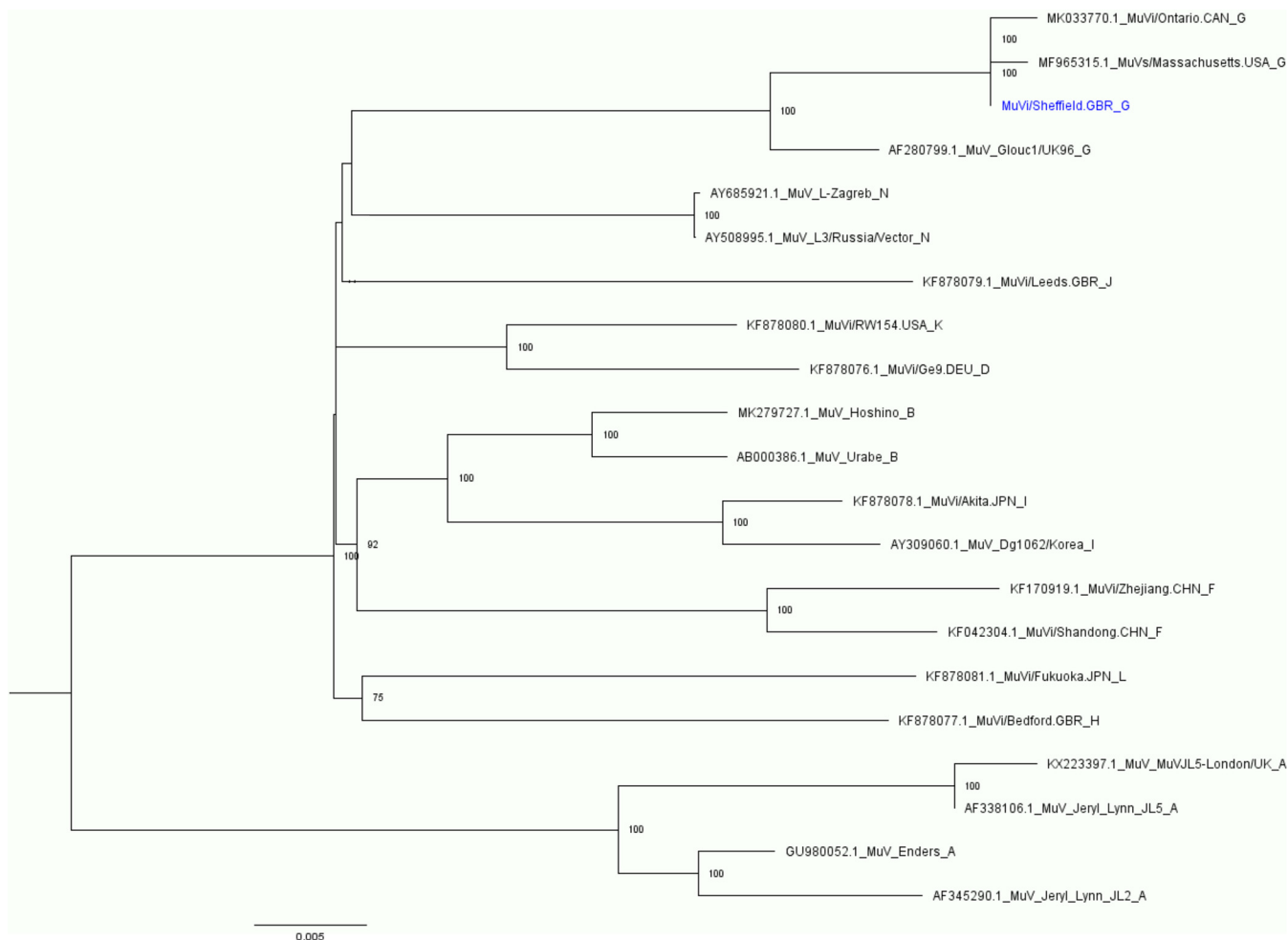Address correspondence to Alberto Severini, alberto.severini@phac-aspc.gc.ca.

FIG 1 Maximum likelihood tree of published mumps complete genome sequences (accession numbers MK279727.1, MK033770.1, MF965315.1, KX223397.1, KF878081.1, KF878080.1, KF878079.1, KF878078.1, KF878077.1, KF878076.1, KF170919.1, KF042304.1, GU980052.1, AY685921.1, AY508995.1, AY309060.1, AF345290.1, AF338106.1, AF280799.1, and AB000386.1) and our sequenced MuVi/Sheffield.GBR/1.05 (shown in blue). A bootstrap analysis of 1,000 was run, with the percentage indicated at each node (values below 70% were removed). The phylogenetic analysis was done using IQ-TREE 2.1.3 (17).

coverage per nucleotide was 4×, the maximum coverage was 8,000×, and the mean coverage per nucleotide was 367.21×.

The Sheffield sequence was analyzed in a maximum likelihood tree with other complete WHO reference strains, vaccine strains, and recent genotype G outbreak strains (Fig. 1). As expected, the MuVi/Sheffield.GBR/1.05 strain clusters with high confidence with outbreak genotype G strains and the alternate WHO genotype G reference strain, MuV Glouc1/UK96 G (Fig. 1).

The MuVi/Sheffield.GBR/1.05 whole-genome sequence adds to the tools available for resolving mumps outbreaks. This will allow for continuity of analysis between SH sequencing and whole-genome sequencing.

Data availability. This genome has been submitted to GenBank under accession number ON148331, and the whole-genome sequencing reads have been submitted to SRA (BioProject accession number PRJNA834753).

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