

# Complete Genome Sequence of a Street Rabies Virus from Mexico

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**A canine rabies virus (RABV) has been used as a street rabies virus in laboratory investigations. Its entire genome was sequenced and found to be closely related to that of canine RABV circulating in Mexico. Sequence comparison indicates that the virus is closely related to those in the “cosmopolitan” group, with high homology (89 to 93%) to clade I of rabies viruses. The virus is now termed dog rabies virus-Mexico (DRV-Mexico).**

Rabies remains a public health threat around the world, as it causes an almost invariably fatal encephalomyelitis (3). Although effective vaccines are available, rabies still causes more than 55,000 human deaths annually throughout the world, with most of them in the developing countries of Asia and Africa (11). Rabies virus (RABV) belongs to the genus *Lyssavirus* in the family *Rhabdoviridae*. Its genome is a single-strand and negative-sense RNA of approximately 12 kb (8, 12). Based on phylogenetic analysis of the nucleoprotein (N) and/or the glycoprotein (G) gene sequences, previous studies have divided all RABVs (genotype 1 of lyssaviruses) into two major clades, one comprising those isolated from terrestrial animals around the world and the other containing viruses isolated from bats and raccoons in the Americas (1, 2, 6, 9). A strain of rabies virus has been used as a street (wild-type) RABV in the laboratory (5) for investigation of rabies pathogenesis. Although it has been described as a dog virus, its exact origin was not known. To identify the origin and species of the virus, total RNA was extracted from a suckling mouse brain infected with the virus using TRIzol LS reagent (Invitrogen, Carlsbad, CA). Ten pairs of oligonucleotide primers to amplify regions of the RABV genomes were designed based on the genomic sequences of the HEP-Flury and CVS-11 strains (4, 10). PCR products were purified using QIAquick gel extraction kit (Qiagen, Germantown, MD) and cloned into the pCR-Blunt II vector (Invitrogen). Cloned DNA was sequenced using a BigDye terminator cycle sequencing ready reaction kit and an ABI Prism 3730 sequencer. The genomic sequence was assembled with the aid of SeqMan software (DNASTAR Inc.). Homology searches and comparisons of all the sequences obtained were performed using the Lasergene package (DNASTAR Inc.). Sequences of encoded proteins were aligned with MEGA version 5 (7). The complete genome of the DRV-Mexico is 11,924 nucleotides in length, similar to other street RABV published to date (12). The lengths of the coding sequences are as follows: 1,353 nucleotides (nt) for the N, 891 nt for the phosphoprotein (P), 609 nt for the matrix protein, 1,575 nt for the G, and 6,384 nt for the RNA-dependent RNA polymerase genes. It was found that P has only 296 amino acids (aa) in DRV-Mexico due to a double stop codon (TGATAA), while the P from other RABV has 297 aa. Sequence comparison indicates that this virus belongs to the “cosmopolitan” group, which includes all the vaccine strains and street viruses isolated from terrestrial animals from all over the world. This strain belongs to this group and is closely related to other Mexican isolates (V590, V682, and V680) (9). It is thus

termed DRV-Mexico, and it shares high homology (89 to 93%) with other cosmopolitan viruses but only low homology (84 to 85%) with viruses isolated recently in Asia (13). The complete genome analysis of DRV-Mexico identified this virus as a dog isolate from Mexico and will facilitate further laboratory investigations of rabies epidemiology and pathogenesis.

**Nucleotide sequence accession number.** The complete genome sequence of DRV-Mexico is available in GenBank under accession number [HQ450386](https://www.ncbi.nlm.nih.gov/nuccore/HQ450386).

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## REFERENCES

1. Bourhy H, et al. 1999. Ecology and evolution of rabies virus in Europe. *J. Gen. Virol.* 80:2545–2557.
2. Davis PL, Bourhy H, Holmes EC. 2006. The evolutionary history and dynamics of bat rabies virus. *Infect. Genet. Evol.* 6:464–473.
3. Dietzschold B, Rupprecht CE, Fu ZF, Koprowski H. 1996. Rhabdoviruses, p 1137–1159. *In* Fields B, Knipe D, Howley PM (ed), *Fields virology*, 3rd ed. Lippincott-Raven Press, Philadelphia, PA.
4. Ito N, et al. 2003. Improved recovery of rabies virus from cloned cDNA using a vaccinia virus-free reverse genetics system. *Microbiol. Immunol.* 47:613–617.
5. Kuang Y, Lackay SN, Zhao L, Fu ZF. 2009. Role of chemokines in the enhancement of BBB permeability and inflammatory infiltration after rabies virus infection. *Virus Res.* 144:18–26.
6. Nadin-Davis SA, Sampath MI, Casey GA, Tinline RR, Wandeler AI. 1999. Phylogeographic patterns exhibited by Ontario rabies virus variants. *Epidemiol. Infect.* 123:325–336.
7. Tamura K, Dudley J, Nei M, Kumar S. 2007. MEGA4: Molecular Evolutionary Genetics Analysis (MEGA) software version 4.0. *Mol. Biol. Evol.* 24:1596–1599.
8. Tordo N, Poch O, Ermine A, Keith G, Rougeon F. 1986. Walking along the rabies genome: is the large G-L intergenic region a remnant gene? *Proc. Natl. Acad. Sci. U. S. A.* 83:3914–3918.
9. Velasco-Villa A, et al. 2006. Molecular diversity of rabies viruses associated with bats in Mexico and other countries of the Americas. *J. Clin. Microbiol.* 44:1697–1710.

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10. Wang L, Cao S, Du J, Dong G, Tang Q. 2010. Sequencing of complete genome of rabies virus CVS-11 strain. *Zhongguo Sheng Wu Zhi Pin Xue Za Zhi* 23:455–459. (In Chinese.)
11. World Health Organization. 2005. WHO Expert Committee on Rabies, 2004. First report, WHO technical report series 931. World Health Organization, Geneva, Switzerland.
12. Wunner WH. 2007. Rabies virus, p 23–68. *In* Jackson AC, Wunner WH (ed), Rabies. Elsevier/Academic Press, London, United Kingdom.
13. Zhang YZ, et al. 2009. Genetic diversity of Chinese rabies viruses: evidence for the presence of two distinct clades in China. *Infect. Genet. Evol.* 9:87–96.