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GENOME ANNOUNCEMENT

Complete Genome Sequence of Hepatitis E Virus from Rabbits in the United States

Caitlin M. Cossaboom, Laura Córdoba, Dianjun Cao, Yan-Yan Ni, and Xiang-Jin Meng

Department of Biomedical Sciences and Pathobiology, College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg, Virginia, USA

Hepatitis E virus (HEV) is a single-strand positive-sense RNA virus in the family *Hepeviridae*. The disease caused by HEV, hepatitis E, is an important public health problem in developing countries of Asia and Africa and is also endemic in many industrialized countries, including the United States. HEV has been identified from several other animal species in addition to humans, including the pig, chicken, mongoose, deer, rabbit, ferret, bat, and fish. Here we report the complete genome sequence of the first strain of HEV from rabbits in the United States. Sequence and phylogenetic analyses revealed that the U.S. rabbit HEV is a distant member of the zoonotic genotype 3 HEV, thus raising a concern for potential zoonotic human infection. A unique 90-nucleotide insertion within the X domain of the ORF1 was identified in the rabbit HEV, and this insertion may play a role in the species tropism of HEV.

Hepatitis E virus (HEV) is an important human pathogen in the family *Hepeviridae* (5). Hepatitis E is generally an acute, self-limiting disease with a mortality of up to 25% in infected pregnant women (14). Chronic HEV infection with considerable morbidity and mortality has recently been documented in immunocompromised individuals such as organ transplant recipients (9). As a zoonotic pathogen, HEV has been genetically identified from humans and a number of other animal species, including chickens, pigs, deer, rabbits, cutthroat trout, mongooses, rats, bats, and ferrets (1, 4, 6, 8, 13, 15, 17, 18). The first animal strain of HEV, swine HEV, is zoonotic and infects humans (12, 13). Among the four recognized major genotypes of HEV, genotypes 1 and 2 are restricted to humans, whereas genotypes 3 and 4 are zoonotic and infect several other animal species (10).

We report here the complete genomic sequence of the first strain of HEV from rabbits in the United States. Rabbit fecal samples collected from a rabbit farm in Virginia tested positive for HEV RNA by a nested reverse transcription-PCR using degenerate primers (2). Overlapping fragments covering the complete genome of U.S. rabbit HEV were subsequently amplified using the primer walking strategy. The extreme 5′ and 3′ ends of the viral genome were amplified using the rapid amplification of cDNA ends (RACE) technique. The complete genomic sequence was assembled and analyzed using the MegAlign computer software.

Excluding the poly(A) sequence, the complete genome of the U.S. rabbit HEV is 7,282 bp in length, and the G/C content is 55.6%. The genome organization of the U.S. rabbit HEV is similar to those of other mammalian HEVs, with a 5′ untranslated region (UTR) (nucleotides [nt] 1 to 26), followed by ORF1 (nt 27 to 5195), ORF2 (nt 5230 to 7212), ORF3 (nt 5192 to 5560), and the 3′ UTR (nt 7213 to 7306). The U.S. rabbit HEV shares approximately 74%, 73%, 79%, and 75% nucleotide sequence identities across the entire genome with the genotypes 1, 2, 3, and 4 mammalian HEVs, respectively. Phylogenetic analysis revealed that rabbit HEV is a distant member of genotype 3 HEV, which is zoonotic and capable of infecting across species barriers (10, 11, 16). Rabbit HEV can cross species barriers and infect pigs (3) and thus may infect humans.

A unique 90-nt insertion within the X domain of the ORF1 was identified in the rabbit HEV, rat HEV, and one genotype 3 human HEV, compared to the known genotype 1 to 4 mammalian HEVs (7). Since a 171-nucleotide insertion of a human S17 ribosomal protein gene in the hypervariable region adjacent to the X domain of a genotype 3 HEV genome has been linked to an expanded host range of cross-species infection (16), this unique 90-nt insertion in rabbit HEV may play a role in species tropism.

Nucleotide sequence accession number. The complete genome sequence of the first U.S. rabbit HEV strain was deposited in the GenBank database under the accession number JX565469.

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Address correspondence to Xiang-Jin Meng, xjmeng@vt.edu.

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