ICTV Virus Taxonomy Profile: *Hepeviridae*

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**Abstract**

The family *Hepeviridae* includes enterically transmitted small non-enveloped positive-sense RNA viruses. It includes the genera *Piscihepevirus*, whose members infect fish, and *Orthohepevirus*, whose members infect mammals and birds. Members of the genus *Orthohepevirus* include hepatitis E virus, which is responsible for self-limiting acute hepatitis in humans and several mammalian species; the infection may become chronic in immunocompromised individuals. Extrahepatic manifestations of Guillain–Barré syndrome, neuralgic amyotrophy, glomerulonephritis and pancreatitis have been described in humans. Avian hepatitis E virus causes hepatitis–splenomegaly syndrome in chickens. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the taxonomy of the *Hepeviridae*, which is available at www.ictv.global/report/hepeviridae.

**Table 1. Characteristics of the family *Hepeviridae***

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<th>Typical member: human hepatitis E virus Burma (M73218), species <em>Orthohepevirus A</em>, genus <em>Orthohepevirus</em></th>
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**VIRION**

The virions of human hepatitis E virus are icosahedral, non-enveloped, spherical particles with a diameter of approximately 27–34 nm (Table 1, Fig. 1). The capsid is formed by capsomeres consisting of homodimers of a single capsid protein, forming the virus shell. Each capsid protein contains three linear domains forming distinct structural elements: S (the continuous capsid), P1 (three-fold protrusions) and P2 (two-fold spikes). Neutralizing epitopes have been found in the P2 domain. Each domain contains a putative polysaccharide-binding site that may interact with cellular receptors. Native T=3 capsids contain flat dimers, with less curvature than those of T=1 virus-like particles [1].

![Fig. 1. Negative contrast electron micrograph of human hepatitis E virus virions from a case stool collected in Nepal. (A) virion and (B) empty capsid. The bar represents 100 nm (photograph from M. Purdy).](image-url)

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Genome

Viral genomes are positive-sense monopartite RNA of about 6.4 to 7.2 kb, with three ORFs flanked by short 5′- and 3′-terminal non-coding regions; ORF2 overlaps ORF3 but neither overlaps ORF1. The 5′-end is m7G-capped and the 3′-end is polyadenylated (Fig. 2). Non-structural proteins encoded by HUD, MT, methytransferase; P, a putative papain-like cysteine protease; RNA polymerase [7, 8]. ORF2 encodes a capsid protein and is followed by a unique domain, also called the Z domain [7]; PP, a hypervariable polyproline region that is dispensable for virus infectivity; Macro, macro domain; Hel, helicase; and RdRP, RNA-dependent RNA polymerase [7, 8]. ORF2 encodes a capsid protein and is followed by a short 3′ NCR. ORF3 overlaps ORF2 but follows ORF1 in a different reading frame and encodes a small phosphoprotein with a multi-functional C-terminal region. The scale is in bases.

Replication

The replication of human hepatitis E virus is not well understood. The viral RNA-dependent RNA polymerase associates with the host endoplasmic reticulum through residues encoding a predicted transmembrane domain in order to begin replicating the viral genome. It appears that replication involves temporal separation and alternating cycles of positive- and negative-sense RNAs to produce capsid, ORF3 protein, ORF1 polypeptide and new genomes, resulting in the generation of progeny virions [2, 4].

Taxonomy

Orthohepevirus. Members of this genus infect a wide range of mammals, including humans, domestic and wild swine, deer, sheep, rabbits, camels, mongooses, (Orthohepevirus A members), rats, ferrets, shrews, bandicoots, mink (Orthohepevirus C members), bats (Orthohepevirus D members), and birds (Orthohepevirus B members) [5]. Unclassified viruses have been detected in moose and foxes, and in droppings from little egrets and kestrels. Human hepatitis E virus can cause self-limiting acute hepatitis in humans and is transmitted by contaminated water or the consumption of undercooked or raw meat and dairy and other products from infected animals. Human hepatitis E virus is the leading cause of acute hepatitis in developing countries [6].

Piscihepevirus. This genus includes a single species whose typical isolate, cutthroat trout virus, infects trout, although its pathogenicity and full host range are unknown [5].

Resources