ICTV Virus Taxonomy Profile: *Flaviviridae*

Peter Simmonds,1,* Paul Becher,2 Jens Bukh,3 Ernest A. Gould,4 Gregor Meyers,5 Tom Monath,6 Scott Muerhoff,7 Alexander Pletnev,8 Rebecca Rico-Hesse,9 Donald B. Smith,10 Jack T. Stapleton11,12 and ICTV Report Consortium

**Abstract**

The *Flaviviridae* is a family of small enveloped viruses with RNA genomes of 9000–13 000 bases. Most infect mammals and birds. Many flaviviruses are host-specific and pathogenic, such as hepatitis C virus in the genus *Hepacivirus*. The majority of known members in the genus *Flavivirus* are arthropod borne, and many are important human and veterinary pathogens (e.g. yellow fever virus, dengue virus). This is a summary of the current International Committee on Taxonomy of Viruses (ICTV) report on the taxonomy of the *Flaviviridae*, which is available at www.ictv.global/report/flaviviridae.

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

<table>
<thead>
<tr>
<th>Typical member: yellow fever virus-D17 (X03700), species Yellow fever virus, genus Flavivirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virion</td>
</tr>
<tr>
<td>Genome</td>
</tr>
<tr>
<td>Replication</td>
</tr>
<tr>
<td>Translation</td>
</tr>
<tr>
<td>Host range</td>
</tr>
<tr>
<td>Taxonomy</td>
</tr>
</tbody>
</table>

**VIRION**

Virions are typically spherical in shape with a lipid envelope (Table 1, Fig. 1). Virions have a single, small, basic capsid (C) protein and two (genera *Flavivirus*, *Hepacivirus* and *Pegivirus*) or three (genus *Pestivirus*) envelope proteins.

**GENOME**

Virus genomes are positive-stranded, non-segmented RNA of approximately 9.2–11, 12.3–13, 8.9–10.5 and 8.9–11.3 kb for members of the genera *Flavivirus*, *Pestivirus*, *Hepacivirus* and *Pegivirus*, respectively (Fig. 2). They contain a single, long ORF flanked by 5′- and 3′-terminal non-coding regions, which form specific secondary structures required for genome replication and translation. Translational initiation of genomic RNA is cap dependent in the case of members of the genus *Flavivirus*.

---

Received 1 December 2016; Accepted 1 December 2016

**Author affiliations:** 1Nuffield Department of Medicine, University of Oxford, Oxford OX1 3SY, UK; 2Institute of Virology, University of Veterinary Medicine, Hannover D-30559, Germany; 3Copenhagen Hepatitis C Program (CO-HEP), Copenhagen University Hospital, Hvidovre, Denmark; 4Unité des Virus Emergents, Faculté de Médecine Timone, 13385 Marseille Cedex 05, France; 5Institut für Immunologie, Friedrich-Loeffler-Institut, Sueder 10, Greifswald-Riems D-17493, Germany; 6BioProtection Systems/NewLink Genetics Corporation, 94 Jackson Road, Suite 108, Devens, MA 01434, USA; 7Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6015, USA; 8Laboratory of Infectious Diseases, NIAID/NIH, Bethesda, MD 20892, USA; 9Baylor College of Medicine, Houston, TX 77030-3411, USA; 10Centre for Immunity, Infection and Evolution, University of Edinburgh, Edinburgh EH9 3FL, UK; 11Department of Internal Medicine, University of Iowa, Iowa City, IA 52242, USA; 12Department of Microbiology, University of Iowa, Iowa City, IA 52242, USA.

**Correspondence:** Peter Simmonds, peter.simmonds@ndm.ox.ac.uk

**Keywords:** *Flaviviridae*; taxonomy; ICTV Report.
**REPLICATION**

Viral proteins are synthesized as part of a polyprotein that is co- and post-translationally cleaved by viral and cellular proteases. The structural proteins are contained in the N-proximal portion of this polyprotein and the non-structural proteins in the remainder. Replication of members of the family Flaviviridae occurs through the synthesis of an antigenome as the template for genome RNA production. Genome RNA also acts as a translational template for the synthesis of viral proteins. Replication complexes are sequestered with a complex topology in membranous structures within the endoplasmic reticulum. Replication enzymes include a serine protease, an RNA helicase and an RNA-dependent RNA polymerase. These proteins are homologous among all members of genus Flavivirus, contain conserved motifs and are encoded at similar locations in the genome. Virion assembly, including acquisition of a glycoprotein-containing lipid envelope, occurs by budding through intracellular membranes. Particles are transported in cytoplasmic vesicles through the secretory pathway and released by exocytosis.

**TAXONOMY**

**Flavivirus**

This genus consists primarily of >50 species of arthropod-borne viruses, with distinct groups infecting mosquitoes or ticks [1]. Mammals and birds are the usual primary hosts, in which infections range from asymptomatic to severe or fatal haemorrhagic fever or neurological disease. Important human pathogens include yellow fever virus, dengue virus, Japanese encephalitis virus, West Nile virus and tick-borne encephalitis virus. Other members cause economically important diseases in domestic or wild animals. Additional viruses infecting only arthropods or only mammals (e.g. Tamana bat virus) have been described recently.

**Pestivirus**

These viruses infect pigs and ruminants, including cattle, sheep, goats and wild ruminants [2], and are transmitted through contact with infected secretions (respiratory droplets, urine or faeces). Infections may be subclinical or cause enteric, haemorrhagic or wasting diseases, including those by the economically important bovine viral diarrhoea virus and classical swine fever virus.

**Hepacivirus**

This genus includes hepatitis C virus, a major human pathogen causing progressive liver disease [3], and several other viruses of unknown pathogenicity that infect horses, rodents, bats, cows and primates [4]. Infections are typically persistent and target the liver.

**Pegivirus**

Members are widely distributed in a range of mammalian species, in which they cause persistent infections [5]. To date, they have not been clearly associated with disease.

**RESOURCES**


**Funding information**

Production of this summary, the online chapter and associated resources was funded by a grant from the Wellcome Trust (WT108418AIA).

**Acknowledgements**

Members of the ICTV Report Consortium are Elliot J. Lefkowitz, Andrew J. Davison, Stuart G. Siddell, Peter Simmonds, Michael J. Adams, Donald B. Smith, Richard J. Orton and Nick J. Knowles.

**Conflicts of interest**

The authors declare that there are no conflicts of interest.

**References**