

# ICTV Virus Taxonomy Profile: Filoviridae 2024

Nadine Biedenkopf<sup>1</sup>, Alexander Bukreyev<sup>2</sup>, Kartik Chandran<sup>3</sup>, Nicholas Di Paola<sup>4</sup>, Pierre B. H. Formenty<sup>5</sup>, Anthony Griffiths<sup>6</sup>, Adam J. Hume<sup>6</sup>, Elke Mühlberger<sup>6</sup>, Sergey V. Netesov (Нетёсов Сергей Викторович)<sup>7</sup>, Gustavo Palacios<sup>8</sup>, Janusz T. Pawęska<sup>9</sup>, Sophie Smither<sup>10</sup>, Ayato Takada (高田礼人)<sup>11</sup>, Victoria Wahl<sup>12</sup> and Jens H. Kuhn<sup>13,\*</sup>

# Abstract

*Filoviridae* is a family of negative-sense RNA viruses with genomes of about 13.1–20.9 kb that infect fish, mammals and reptiles. The filovirid genome is a linear, non-segmented RNA with five canonical open reading frames (ORFs) that encode a nucleoprotein (NP), a polymerase cofactor (VP35), a glycoprotein (GP<sub>1,2</sub>), a transcriptional activator (VP30) and a large protein (L) containing an RNA-directed RNA polymerase (RdRP) domain. All filovirid genomes encode additional proteins that vary among genera. Several filovirids (e.g., Ebola virus, Marburg virus) are pathogenic for humans and highly virulent. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Filoviridae*, which is available at www.ictv.global/report/filoviridae.

### **Table 1.** Characteristics of members of the family *Filoviridae*

Example	Marburg virus (DQ217792), species Orthomarburgvirus marburgense, genus Orthomarburgvirus
Virion	Enveloped, variously shaped but predominantly filamentous, typically with a single nucleocapsid
Genome	Approximately 13.1–20.9kb of linear, negative-sense, non-segmented RNA
Replication	Ribonucleoprotein complexes serve as templates for transcription and replication. Encapsidated antigenomic RNA is a replication intermediate
Translation	From multiple monocistronic 5'-capped and 3'-polyadenylated mRNAs
Host range	Fish (oblaviruses, striaviruses, thamnoviruses), mammals (cuevaviruses, dianloviruses, orthoebolaviruses, orthomarburgviruses), reptiles (tapjoviruses)
Taxonomy	Realm Riboviria, phylum Negarnaviricota, subphylum Haploviricotina, class Monjiviricetes, order Mononegavirales; >7 genera and >14 species

# VIRION

Filovirids produce virions that are enveloped and diverse in shape and can be branched, toroid, U- or 6-shaped, or long and filamentous in form (Table 1, Fig. 1). Virions contain ribonucleoprotein (RNP) complexes composed of genomic RNA and, typically, structural proteins, including a nucleoprotein (NP), polymerase co-factor (VP35), transcriptional activator (VP30) and large protein (L). Mammalian filovirid particles also contain an RNP-associated protein (VP24) and a matrix protein (VP40) that form a regular layer beneath the viral envelope. Surface spikes formed by glycoprotein ( $GP_{1,2}$ )

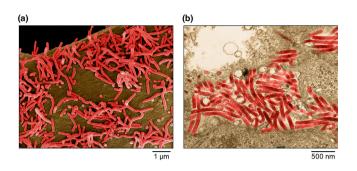
Abbreviations: *GP*, glycoprotein gene; GP<sub>1,2</sub>, glycoprotein; L, large protein; NP, nucleoprotein; ORF, open reading frame; RdRP, RNA-directed RNA polymerase; RNP, ribonucleoprotein; VP, viral protein; VP24, RNP-associated protein; VP30, transcriptional activator; VP35, polymerase co-factor; VP40, matrix protein. 001955



Received 10 January 2024; Accepted 16 January 2024; Published 02 February 2024

Author affiliations: <sup>1</sup>Philipps-University Marburg, Marburg, Germany; <sup>2</sup>The University of Texas Medical Branch at Galveston, Galveston, TX, USA; <sup>3</sup>Albert Einstein College of Medicine, New York, USA; <sup>4</sup>United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, MD, USA; <sup>5</sup>World Health Organization, Geneva, Switzerland; <sup>6</sup>Chobanian and Avedisian School of Medicine, Boston University, Boston, MA, USA; <sup>7</sup>Novosibirsk State University, Novosibirsk, Russia; <sup>8</sup>Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; <sup>9</sup>National Institute for Communicable Diseases of the National Health Laboratory Service, Sandringham-Johannesburg, Gauteng, South Africa; <sup>10</sup>Dstl, Porton Down, Wiltshire, UK; <sup>11</sup>International Institute for Zoonosis Control, Hokkaido University, Sapporo, Japan; <sup>12</sup>National Biodefense Analysis and Countermeasures Center, Fort Detrick, Frederick, MD, USA; <sup>13</sup>Integrated Research Facility at Fort Detrick, National Institutes of Health, Fort Detrick, Frederick, Maryland, USA. **\*Correspondence:** Jens H. Kuhn, kuhnjens@mail.nih.gov

Keywords: Ebola; filovirid; Filoviridae; filovirus; ICTV Report; Marburg virus; orthoebolavirus; orthomarburgvirus; taxonomy.



**Fig. 1.** (a) Scanning and (b) transmission EM images of Marburg virus particles budding from infected Vero E6 cells. Images are colorized for clarity. Courtesy of John G. Bernbaum and Jiro Wada, IRF-Frederick.

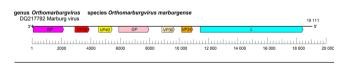
are about 7 nm in diameter and cover the virion surface at roughly 10 nm intervals [1, 2].

# GENOME

Filovirid genomes (Fig. 2) are about 13.1–20.9 kb and lack a 5'-cap or 3'-poly(A) tail. Terminal leader and trailer sequences contain the replication and transcription promoters. Six to ten ORFs are flanked by 3'- and 5'-terminal non-coding regions that contain transcription initiation and termination sites. Five ORFs are shared among all filovirids and encode homologous structural proteins (NP, VP35, GP<sub>1,2</sub>, VP30, L). Cuevaviruses and orthoebolaviruses use co-transcriptional editing to express non-structural proteins [1–3].

# REPLICATION

Filovirions attach to cell surface receptors or attachment factors and enter endosomes in which they engage intracellular receptors. pH-dependent fusion with late endosomes releases virion RNP complexes into the cytoplasm. The virus RNP directs both RNA genome replication and gene transcription. Virus proteins are translated from mRNAs that are synthesized by successive, polar transcription from



**Fig. 2.** Filovirid genome. *GP*, glycoprotein gene; *L*, large protein gene; *NP*, nucleoprotein gene; *VP30*, transcriptional activator gene; *VP24*, RNP-associated protein gene; *VP35*, polymerase co-factor gene; *VP40*, matrix protein gene.

#### References

- Kirchdoerfer RN, Wasserman H, Amarasinghe GK, Saphire EO. Filovirus structural biology: the molecules in the machine. *Curr Top Microbiol Immunol* 2017;411:381–417.
- Kuhn JH, Amarasinghe GK, Perry DL. Filoviridae. In: Howley PM, Knipe DM and Whelan S (eds). *Fields Virology*, 7th edn. Philadelphia, Pennsylvania, USA: Wolters Kluwer/Lippincott Williams & Wilkins; 2020. pp. 449–503.

RNP complexes containing genomic RNA. Replication occurs in the cytoplasm through the synthesis of RNP complexes containing antigenomes that are templates for genomic RNA production. Replication and transcription enzymes include L and VP35. VP30 serves as a transcription enhancer and acts at different gene start sites. Whereas orthoebolaviral and cuevaviral VP30 mediates transcription initiation at the *NP* gene start site, orthomarburgviral VP30 mediates transcription reinitiation at the *GP* gene start site. VP30's function for other filovirids is less defined. In the case of mammalian filovirids, virion assembly, including acquisition of the lipid envelope containing GP<sub>1,2</sub>, occurs by VP40-mediated budding at the plasma membrane [1–4].

# TAXONOMY

Current taxonomy: ictv.global/taxonomy. The family *Filo-viridae* is included in the negarnaviricot order *Mononega-virales*. Filovirids are most closely related to mononegaviral paramyxovirids, pneumovirids and sunvirids [5].

## RESOURCES

Full ICTV Report on the family *Filoviridae*: www.ictv.global/ report/filoviridae.

#### Funding information

This work was supported in part through the Laulima Government Solutions, LLC, prime contract with the US National Institute of Allergy and Infectious Diseases under contract no. HHSN272201800013C. J.H.K. performed this work as an employee of Tunnell Government Services, a subcontractor of Laulima Government Solutions, LLC, under contract no. HHSN272201800013C. This work was funded under Agreement No. HSHQDC-15-C-00064 awarded to Battelle National Biodefense Institute by the Department of Homeland Security Science and Technology Directorate for the management and operation of the National Biodefense Analysis and Countermeasures Center, a Federally Funded Research and Development Center (V.W.). The views and conclusions contained in this document are those of the authors and should not be interpreted as necessarily representing the official policies, either expressed or implied, of the US Government or its departments or of the institutions and companies affiliated with the authors, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government. The full disclaimer is on the Authors page of the full Report.

#### Acknowledgements

We thank Evelien Adriaenssens, Holly Hughes, Elliot J. Lefkowitz, Sead Sabanadzovic, Peter Simmonds, Dann Turner, F. Murilo Zerbini, Luisa Rubino and Arvind Varsani (ICTV Report Editors), and Donald B. Smith (Managing Editor, ICTV Report). We also thank Anya Crane (Integrated Research Facility at Fort Detrick) for critically editing the text.

#### Conflicts of interest

The authors declare that there are no conflicts of interest.

- Pattnaik AK, Whitt MA. Filovirus transcription and replication. In: Pattnaik AK and Whitt MA (eds). *Biology and Pathogenesis of Rhabdoand Filoviruses*. Singapore: World Scientific Publishing; 2015. pp. 515–555.
- Yuan B, Peng Q, Cheng J, Wang M, Zhong J, et al. Structure of the Ebola virus polymerase complex. Nature 2022;610:394–401.
- Wolf YI, Kazlauskas D, Iranzo J, Lucía-Sanz A, Kuhn JH, et al. Origins and evolution of the global RNA virome. mBio 2018;9:e02329–02318.