



ICTV Virus Taxonomy Profile: *Kolmioviridae* 2024

Jens H. Kuhn¹, Artem Babaian², Laura M. Bergner³, Paul Dény⁴, Dieter Glebe⁵, Masayuki Horie (堀江真行)⁶, Eugene V. Koonin⁷, Mart Krupovic⁸, Sofia Paraskevopoulou (Σοφία Παρασκευοπούλου)⁹, Marcos de la Peña¹⁰, Teemu Smura¹¹ and Jussi Hepojoki^{11,*}

Abstract

Kolmioviridae is a family for negative-sense RNA viruses with circular, viroid-like genomes of about 1.5–1.7 kb that are maintained in mammals, amphibians, birds, fish, insects and reptiles. Deltaviruses, for instance, can cause severe hepatitis in humans. Kolmiovirids encode delta antigen (DAg) and replicate using host-cell DNA-directed RNA polymerase II and ribozymes encoded in their genome and antigenome. They require evolutionary unrelated helper viruses to provide envelopes and incorporate helper virus proteins for infectious particle formation. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Kolmioviridae*, which is available at ictv.global/report/kolmioviridae.

Table 1. Characteristics of members of the family *Kolmioviridae*

Example:	hepatitis D virus 1 (AF104263), species <i>Deltavirus italicense</i> , genus <i>Deltavirus</i>
Virion	Spherical virions (36–43 nm in diameter) with an outer envelope containing envelope proteins derived from a helper virus and an inner ribonucleoprotein consisting of genomic RNA and a nucleocapsid protein (delta antigen; DAg) that is encoded by the genomic RNA and may occur in two isoforms
Genome	Rod-like ribozyme-containing negative-sense, covalently closed, circular RNA (cccRNA) of about 1.5–1.7 kb
Replication	RNA-directed RNA synthesis by host-cell DNA-directed RNA polymerase II through a double rolling circle mechanism, and autocatalytic cleavage/ligation via encoded genomic and antigenomic ribozymes and re-cyclization in the host-cell nucleus
Translation	mRNA-based translation of DAg (in some cases including an isoform thereof)
Host range	Mammals, amphibians, birds, fish, insects and reptiles
Taxonomy	Realm <i>Ribozyviria</i> ; the family includes >7 genera and >14 species

VIRION

Kolmiovirions are spherical with a lipid envelope containing envelope proteins obtained from an evolutionarily unrelated helper virus (Table 1, Fig. 1). Virions contain a ribonucleoprotein (RNP) complex consisting of distinct isoforms of delta antigen (DAg) that are encoded in and closely associate with deltavirus genomic and antigenomic RNAs [1, 2].

GENOME

Kolmiovirids have a viroid-like, ribozyme-containing, negative-sense, covalently closed circular RNA (cccRNA) genome of about 1.5–1.7 kb (Fig. 2) that forms a rod-like structure through its high degree of self-complementarity. The genome encodes a single protein, DAg, which in some cases occurs in two isoforms [1–8].

Received 25 January 2024; Accepted 31 January 2024; Published 29 February 2024

Author affiliations: ¹Integrated Research Facility at Fort Detrick, Frederick, Maryland, USA; ²University of Toronto, Toronto, Canada; ³MRC-University of Glasgow Centre for Virus Research, Glasgow, UK; ⁴University Sorbonne Paris Nord, Bobigny, France; ⁵Justus Liebig University, Giessen, Germany; ⁶Osaka Metropolitan University, Izumisano, Osaka, Japan; ⁷National Center for Biotechnology Information, Bethesda, Maryland, USA; ⁸Institut Pasteur, Université Paris Cité, Archaeal Virology Unit, Paris, France; ⁹Genome Competence Center (MF1), Robert Koch Institute Berlin, Berlin, Germany; ¹⁰Universidad Politécnica de Valencia-CSIC, Valencia, Spain; ¹¹University of Helsinki, Helsinki, Finland.

*Correspondence: Jussi Hepojoki, jussi.hepojoki@helsinki.fi

Keywords: deltavirus; hepatitis D virus; ICTV Report; *Kolmioviridae*; taxonomy.

Abbreviations: cccRNA, covalently closed, circular RNA; DAg, delta antigen; HBV, hepatitis B virus; L-DAg, S-DAg, large and small delta antigen; L-HBsAg, M-HBsAg, S-HBsAg, large, middle and small hepatitis B virus surface antigen; RNP, ribonucleoprotein.

001963 © 2024 The Authors



This is an open-access article distributed under the terms of the Creative Commons Attribution License.

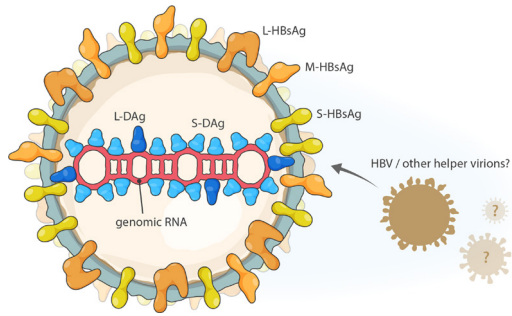


Fig. 1. Schematic of hepatitis D virus 1 particles. L-DAg, S-DAg: large and small delta antigen; L-HBsAg, M-HBsAg, S-HBsAg: large, middle and small HBV surface antigen; HBV: hepatitis B virus.

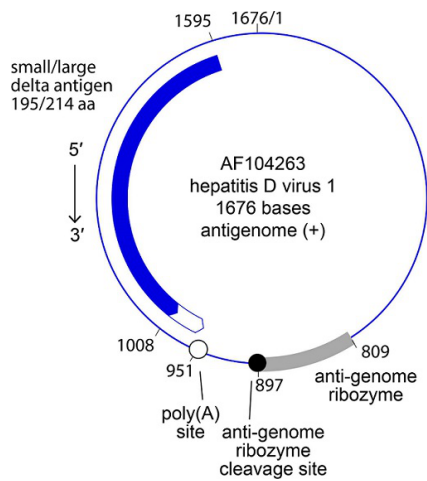


Fig. 2. Antigenome organization of hepatitis D virus 1. Nucleotide numbering according to that for the (complementary) genome.

REPLICATION

Kolmiovirion cell entry is mediated by interaction with cell-surface receptors and envelope proteins that are obtained from helper viruses. Membrane fusion releases the RNP into the cytosol, from where it migrates to the cell nucleus where RNA-directed RNA genome and antigenome synthesis is mediated by host-cell DNA-directed RNA polymerase II through a double rolling circle mechanism; genome- and antigenome-encoded

ribozymes catalyse autocatalytic cleavage of concatenated progeny genomes and ligation/recyclization in the nucleus. DAg isoforms serve as nucleoproteins and regulate replication and packaging [1, 2].

PATHOGENICITY

Deltaviruses cause disease in humans, typically in association with the evolutionarily unrelated hepatitis B virus (HBV, family *Hepadnaviridae*). Coinfection causes hepatitis D, the most severe of WHO-classified viral hepatitis [1, 2].

TAXONOMY

Current taxonomy: ictv.global/taxonomy. Kolmiovirids (realm *Ribozyviria*) are most closely related to viroids and related mobile genetic elements. Kolmiovirids share at least two of the following characteristics: (i) enveloped virions; (ii) circular negative-sense RNA genome containing ribozymes and encoding a DAg homolog; (iii) require an evolutionarily unrelated helper virus for assembly of infectious virions.

RESOURCES

Full ICTV Report on the family *Kolmioviridae*: www.ictv.global/report/kolmioviridae.

Funding information

Production of this Profile, the ICTV Report, and associated resources was supported by the Microbiology Society. This work was supported in part through the Laulima Government Solutions, LLC, prime contract with the U.S. National Institute of Allergy and Infectious Diseases (NIAID) under Contract No. HHSN272201800013C. J.H.K. performed this work as an employee of Tunnell Government Services (TGS), a subcontractor of Laulima Government Solutions, LLC, under Contract No. HHSN272201800013C. The content of this publication should not be interpreted as necessarily representing the official policies, either expressed or implied, of the U.S. Department of Health and Human Services or of the institutions and companies affiliated with the authors.

Acknowledgements

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

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

- Asselah T, Rizzetto M. Hepatitis D virus infection. *N Engl J Med* 2023;389:58–70.
- Dandri M, Volmari A, Lütgehetmann M. The hepatitis delta virus and chronic hepatitis D. *J Hepatol* 2022;77:1448–1450.
- Chang W-S, Pettersson JH-O, Le Lay C, Shi M, Lo N, et al. Novel hepatitis D-like agents in vertebrates and invertebrates. *Virus Evol* 2019;5:vez021.
- Hetzel U, Szivovics L, Smura T, Prähauser B, Vapalahti O, et al. Identification of a novel deltavirus in boa constrictors. *mBio* 2019;10:00014–00019.
- Wille M, Netter HJ, Littlejohn M, Yuen L, Shi M, et al. A divergent hepatitis D-like agent in birds. *Viruses* 2018;10:e0720.
- Paraskevopoulou S, Pirzer F, Goldmann N, Schmid J, Corman VM, et al. Mammalian deltavirus without hepadnavirus coinfection in the neotropical rodent *Proechimys semispinosus*. *Proc Natl Acad Sci U S A* 2020;117:17977–17983.
- Bergner LM, Orton RJ, Broos A, Tello C, Becker DJ, et al. Diversification of mammalian deltaviruses by host shifting. *Proc Natl Acad Sci U S A* 2021;118:e2019907118.
- Lucifora J, Delphin M. Current knowledge on hepatitis delta virus replication. *Antiviral Res* 2020;179:104812.