

ICTV Virus Taxonomy Profile: Nairoviridae

Aura R. Garrison¹, Sergey V. Alkhovsky [Альховский Сергей Владимирович]², Tatjana Avšič-Županc³, Dennis A. Bente⁴, Éric Bergeron⁵, Felicity Burt⁶, Nicholas Di Paola¹, Koray Ergünay⁷, Roger Hewson⁸, Jens H. Kuhn⁹, Ali Mirazimi¹⁰, Anna Papa [Άννα Παπά]¹¹, Amadou Alpha Sall¹², Jessica R. Spengler⁵, Gustavo Palacios^{1,*} and ICTV Report Consortium

Abstract

Members of the family *Nairoviridae* produce enveloped virions with three single-stranded RNA segments comprising 17.1 to 22.8 kb in total. These viruses are maintained in arthropods and transmitted by ticks to mammals or birds. Crimean-Congo hemorrhagic fever virus is tick-borne and is endemic in most of Asia, Africa, Southern and Eastern Europe whereas Nairobi sheep disease virus, which is also tick-borne, causes lethal haemorrhagic gastroenteritis in small ruminants in Africa and India. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Nairoviridae*, which is available at ictv.global/report/nairoviridae.

Table 1. Characteristics of members of the family Nairoviridae

Typical member:	Dugbe virus [S segment: AF434161; M segment: M94133; L segment: U15018], species <i>Dugbe orthonairovirus</i> , genus Orthonairovirus.
Virion	Enveloped, spherical virions 80–120 nm in diameter with heterodimer surface spikes
Genome	Three single-stranded, negative-sense RNA molecules, S, M, and L of about 2 kb, about 5 kb, and about 12 kb, respectively
Replication	Cytoplasmic. The nucleocapsid protein (N) encapsidates the genomic RNA forming ribonucleoprotein (RNP) complexes with the viral RNA-directed RNA polymerase (RdRP)-containing large protein (L). Anti-genomic RNAs are generated and serve as templates for synthesis of nascent RNP complexes containing genomic RNA
Translation	From capped mRNAs that lack poly(A) termini. The 5'-cap structure is derived from cellular mRNAs via cap-snatching
Host range	Birds, humans, rodents, hares, shrews, ruminants, bats, ticks (<i>Orthonairovirus</i>); spider vector (<i>Shaspivirus</i>) or water strider vector (<i>Striwavirus</i>) with unknown host range
Taxonomy	Realm Riboviria, phylum Negarnaviricota, class Ellioviricetes, order Bunyavirales; several genera and >15 species

VIRION

Where known, virions are spherical in shape, 80–120 nm in diameter with a membrane envelope decorated with glycoprotein (GP) spikes composed of G_N and G_C (Table 1,

Fig. 1). Isolated ribonucleoprotein (RNP) complexes are composed of individual segments of genomic RNA encapsidated in nucleocapsid (N) protein. The RNPs are associated with large (L) protein.

Keywords: Bunyavirales; bunyavirus; Nairoviridae; nairovirus; ICTV Report; orthonairovirus; shaspivirus; striwavirus; taxonomy.

Abbreviations: GP, glycoprotein; GPC, glycoprotein precursor; L, large protein; N, nucleocapsid; RdRP, RNA-directed RNA polymerase; RNP, ribonucleoprotein. 001485 © 2020

Received 13 July 2020; Accepted 02 August 2020; Published 25 August 2020

Author affiliations: ¹USAMRIID, Fort Detrick, Frederick, Maryland, USA; ²D. I. Ivanovsky Institute of Virology of N. F. Gamaleya National Center on Epidemiology and Microbiology of Ministry of Health of Russian Federation, Russia; ³University of Ljubljana, Ljubljana Faculty of Medicine, Slovenia; ⁴UTMB, Galveston, Texas, USA; ⁵Viral Special Pathogens Branch, Division of High-Consequence Pathogens and Pathology, CDC, Atlanta, Georgia, USA; ⁶Division of Virology, National Health Laboratory Service and Division of Virology, University of the Free State, Bloemfontein, Republic of South Africa; ⁷Virology Unit. Department of Medical Microbiology, Faulty of Medicine, Hacettepe University, Ankara, Turkey; ⁸Public Health England, Porton Down, UK, Wiltshire, Salisbury; ⁹Integrated Research Facility at Fort Detrick. NIAID, NIH, Fort Detrick, Frederick, Maryland, USA; ¹⁰Folkhalsomyndigheten, Stockholm, Sweden; ¹¹National Reference Centre for Arboviruses and Haemorrhagic Fever viruses, Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; ¹²Institut Pasteur de Dakar, Dakar, Senegal. *Correspondence: Gustavo Palacios, gustavo.f.palacios.civ@mail.mil

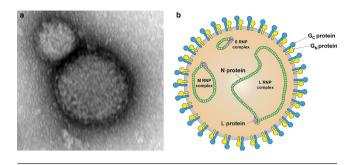


Fig. 1. (a) Transmission electron micrograph of a Crimean-Congo hemorrhagic fever virus particle. (b) Schematic illustration of a nairovirus particle.

GENOME

The nairovirus genome (Fig. 2) consists of two to three singlestranded, negative-sense RNA molecules, termed S (small), M (medium; if present), and L (large). These RNAs encode respectively, in the virus-complementary sense, N, the GP precursor (GPC), and L (containing RdRP, helicase, and endonuclease domains).

REPLICATION

Virions attach to unknown cell-surface receptors and enter via the endosomal route [1]. Viral fusion with the host cell results in early or late endosomal release of the virion RNP complex into the cytoplasm. This pH-dependent fusion event likely requires the previous participation of an intracellular receptor [1, 2]. During primary transcription the virion-associated L protein generates antigenomic RNAs, which are capped using host-cell-derived capped primers [3]. Translation is by free (L and S segment mRNAs) or membrane-bound (M segment mRNA) ribosomes. Based on evidence from Crimean-Congo hemorrhagic fever virus, GPC is co-translationally cleaved to yield glycosylated G_N and G_C and non-structural glycoproteins [4]. Antigenome RNA synthesized by the RdRP domain of the L protein serves as a template for genomic RNA replication. Secondary transcription amplifies the synthesis of mRNAs and genome replication. During morphogenesis, G_N and G_C accumulate in the Golgi, are terminally glycosylated, modified host membranes are acquired, and the virions bud into the Golgi cisternae [5, 6].

TAXONOMY

Current taxonomy: ictv.global/report/nairoviridae. Nairoviruses form a family in the polyploviricotine order *Bunyavirales*, and are most closely related to members of the family *Wupedeviridae*. Like most other bunyaviruses, nairoviruses (i) have multisegmented, negative-sense single-stranded RNA genomes; (ii) encode proteins with high sequence identity; (iii) have five conserved motifs (A–E) in their RdRP domain; and (iv) produce enveloped virions.

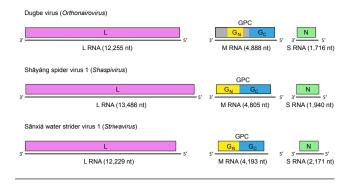


Fig. 2. Schematic representation of nairovirus genome organization.

RESOURCES

Current ICTV Report on the family *Nairoviridae*: ictv.global/ report/nairoviridae

Funding information

Production of this summary, the online chapter, and associated resources was funded by a grant from the Wellcome Trust (WT108418AIA). This work was supported in part through Laulima Government Solutions, LLC's prime contract with the US 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 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 Department of the Army, the US Department of Defense, the US Department of Health and Human Services or of the institutions and companies affiliated with the authors.

Acknowledgements

Members of the ICTV Report Consortium are Stuart G. Siddell, Andrew J. Davison, Elliot J. Lefkowitz, Sead Sabanadzovic, Peter Simmonds, Donald B. Smith, Richard J. Orton and Jens H. Kuhn.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

- Garrison AR, Radoshitzky SR, Kota KP, Pegoraro G, Ruthel G et al. Crimean–Congo hemorrhagic fever virus utilizes a clathrin- and early endosome-dependent entry pathway. Virology 2013;444:45–54.
- Shtanko O, Nikitina RA, Altuntas CZ, Chepurnov AA, Davey RA. Crimean-Congo hemorrhagic fever virus entry into host cells occurs through the multivesicular body and requires ESCRT regulators. *PLoS Pathog* 2014;10:e1004390.
- Holm T, Kopicki J-D, Busch C, Olschewski S, Rosenthal M et al. Biochemical and structural studies reveal differences and commonalities among cap-snatching endonucleases from segmented negative-strand RNA viruses. J Biol Chem 2018;293:19686–19698.
- Bergeron É, Zivcec M, Chakrabarti AK, Nichol ST, Albariño CG et al. Recovery of recombinant Crimean Congo hemorrhagic fever virus reveals a function for non-structural glycoproteins cleavage by furin. PLoS Pathog 2015;11:e1004879.
- Booth TF, Gould EA, Nuttall PA. Structure and morphogenesis of Dugbe virus (*Bunyaviridae*, *Nairovirus*) studied by immunogold electron microscopy of ultrathin cryosections. *Virus Res* 1991;21:199–212.
- Rwambo PM, Shaw MK, Rurangirwa FR, DeMartini JC. Ultrastructural studies on the replication and morphogenesis of Nairobi sheep disease virus, a *Nairovirus. Arch Virol* 1996;141:1479–1492.