

ICTV Virus Taxonomy Profile: Bornaviridae

Dennis Rubbenstroth^{1,*}, Thomas Briese², Ralf Dürrwald³, Masayuki Horie (堀江真行)⁴, Timothy H. Hyndman⁵, Jens H. Kuhn⁶, Norbert Nowotny^{7,8}, Susan Payne⁹, Mark D. Stenglein¹⁰, Keizō Tomonaga (朝長啓造)¹¹ and ICTV Report Consortium

Abstract

Members of the family *Bornaviridae* produce enveloped virions containing a linear negative-sense non-segmented RNA genome of about 9kb. Bornaviruses are found in mammals, birds, reptiles and fish. The most-studied viruses with public health and veterinary impact are Borna disease virus 1 and variegated squirrel bornavirus 1, both of which cause fatal encephalitis in humans. Several orthobornaviruses cause neurological and intestinal disorders in birds, mostly parrots. Endogenous bornavirus-like sequences occur in the genomes of various animals. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Bornaviridae*, which is available at ictv.global/report/bornaviridae.

Table 1. Characteristics of members of the family Bornaviridae

Example:	Borna disease virus 1 (U04608), species Mammalian 1 orthobornavirus, genus Orthobornavirus
Virion	Enveloped, spherical virions 90–130 nm in diameter
Genome	Linear negative-sense non-segmented RNA of about 9 kb with three transcription units and at least six ORFs
Replication	Intranuclear. Anti-genomic RNA is generated as a replication intermediate that enables synthesis of progeny genomes. Genomic and anti- genomic RNA molecules are neither capped nor polyadenylated
Translation	From capped polyadenylated mRNA
Host range	Mammals (reservoir: shrews and squirrels; incidental: horses, sheep, humans and other mammals), birds (parrots, finches, aquatic birds), reptiles and fish
Taxonomy	Realm <i>Riboviria</i> , kingdom <i>Orthornavirae</i> , phylum <i>Negarnaviricota</i> , subphylum <i>Haploviricotina</i> , class <i>Monjiviricetes</i> , order <i>Mononegavirales</i> ; several genera and >10 species

VIRION

Where known, bornavirus virions are spherical in shape with a bimodal size distribution of larger (110–130 nm diameter) and smaller particles (70–90 nm diameter) [1, 2]. Virions are enveloped with 7-nm spikes and are believed to bud from host cell membranes (Table 1, Fig. 1). Entry occurs through binding to unknown cell surface receptors via the endosomal route.

GENOME

The bornavirus genome consists of a linear negative-sense nonsegmented RNA with six open reading frames (ORFs) in the order 3'-*N*-*X*/*P*-*M*-*G*-*L*-5' (*Orthobornavirus*) or 3'-*N*-*X*/*P*-*G*-*M*-*L*-5' (*Carbovirus* and *Cultervirus*) [3–6] that encode, at a minimum, a nucleoprotein (N), small accessory protein (X), phosphoprotein (P), matrix protein (M), surface glycoprotein (G) and large protein

*Correspondence: Dennis Rubbenstroth, Dennis.Rubbenstroth@fli.de

Keywords: ICTV Report; Mononegavirales; Bornaviridae; Orthobornavirus; Cultervirus; Carbovirus; Borna disease virus; bornavirus.

Abbreviations: G, surface glycoprotein; L, large protein; M, matrix protein; N, nucleoprotein; P, phosphoprotein; RdRP, RNA-directed RNA polymerase; RNP, ribonucleoprotein; X, small accessory protein. 001613 © 2021



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

Received 14 May 2021; Accepted 14 May 2021; Published 06 July 2021

Author affiliations: ¹Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Greifswald – Isle of Riems, Germany; ²Center for Infection and Immunity and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA; ³Robert Koch Institute, Berlin, Germany; ⁴Hakubi Center for Advanced Research, Kyoto University, Kyoto, Japan; ⁵School of Veterinary Medicine, Murdoch University, Murdoch, Western Australia, Australia; ⁶NIH/NIAID/DCR/Integrated Research Facility at Fort Detrick, Frederick, Maryland, USA; ⁷University of Veterinary Medicine Vienna, Vienna, Austrai; ⁸Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, UAE; ⁹Department of Veterinary Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas, USA; ¹⁰Colorado State University, Fort Collins, Colorado, USA; ¹¹Institute for Frontier Life and Medical Sciences (inFront), Kyoto University, Kyoto, Japan.



Fig. 1. (a) Electron micrograph of a Borna disease virus 1 particle. Scale bar, 100 nm. Courtesy of Dr M. Eickmann. (b) Illustration of an orthobornavirus particle. Grey - bilaminar lipid envelope.

(L) containing RNA-directed RNA polymerase (RdRP), helicase and endonuclease domains.

REPLICATION

Studies of Borna disease virus 1 indicate that N encapsidates the genomic RNA, forming the viral nucleocapsid, and, together with L and P, forms the ribonucleoprotein (RNP) complex [3]. The genome is transcribed and replicated in the host cell nucleus [7]. Differential use of transcription and termination signals and alternative splicing of polycistronic primary transcripts generate an array of mRNAs (Fig. 2) [8]. Full-length antigenomic positive-sense RNA intermediates are used as templates for generating progeny negative-sense genomic RNA. Nuclear import of viral RNP components after translation of viral mRNA is mediated by their nuclear localization signals; nascent RNPs probably translocate into the cytosol from the nucleus by nuclear export signals [9].

TAXONOMY

Current taxonomy: www.ictv.global/taxonomy. Bornaviruses form a family in the haploviricotine order *Mononegavirales*,



Fig. 2. Orthobornavirus genome organization and transcripts. Dashed lines - introns. ORFs (depicted on the negative-sense strand) encode N, nucleoprotein; X, accessory protein; P, phosphoprotein; M, matrix protein; G, glycoprotein; L, large protein containing an RdRP domain. S, transcription initiation site; T, transcription termination site.

most closely related to members of the families *Mymona-viridae*, *Nyamiviridae* and *Xinmoviridae*. Like most other mononegaviruses, bornaviruses (i) have linear negative-sense non-segmented RNA genomes, (ii) have five conserved motifs (A–E) in the amino-acid sequence of their RdRP domain and (iii) produce enveloped virions.

RESOURCES

Current ICTV Report on the family *Bornaviridae*: www.ictv. global/report/bornaviridae.

Funding information

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 work of D. R. was supported by the Zoonotic Bornavirus Consortium (ZooBoCo) funded by the Federal Ministry of Education and Research of Germany (grant no. 01KI2005B). 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 Health and Human Services or of the institutions and companies affiliated with the authors. Production of this Profile, the ICTV Report, and associated resources was funded by a grant from the Wellcome Trust (WT108418AIA).

Acknowledgements

Members of the ICTV Report Consortium are Stuart G. Siddell, Elliot J. Lefkowitz, Sead Sabanadzovic, Peter Simmonds, F. Murilo Zerbini, Donald B. Smith, Richard J. Orton, and Jens H. Kuhn. We thank Anya Crane and Jiro Wada (Integrated Research Facility at Fort Detrick) for editing the manuscript and figure creation, respectively.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

- Kohno T, Goto T, Takasaki T, Morita C, Nakaya T, et al. Fine structure and morphogenesis of Borna disease virus. J Virol 1999;73:760–766.
- Zimmermann W, Breter H, Rudolph M, Ludwig H. Borna disease virus: immunoelectron microscopic characterization of cellfree virus and further information about the genome. J Virol 1994;68:6755–6758.
- Cubitt B, Oldstone C, de la Torre JC. Sequence and genome organization of Borna disease virus. J Virol 1994;68:1382–1396.
- Schneemann A, Schneider PA, Lamb RA, Lipkin WI. The remarkable coding strategy of borna disease virus: a new member of the nonsegmented negative strand RNA viruses. *Virology* 1995;210:1–8.
- Hyndman TH, Shilton CM, Stenglein MD, Wellehan JFX. Divergent bornaviruses from Australian carpet pythons with neurological disease date the origin of extant *Bornaviridae* prior to the end-Cretaceous extinction. *PLoS Pathog* 2018;14:e1006881.
- Shi M, Lin XD, Chen X, Tian JH, Chen LJ, et al. The evolutionary history of vertebrate RNA viruses. Nature 2018;556:197–202.
- Briese T, de la Torre JC, Lewis A, Ludwig H, Lipkin WI. Borna disease virus, a negative-strand RNA virus, transcribes in the nucleus of infected cells. *Proc Natl Acad Sci U S A* 1992;89:11486–11489.
- Schneider PA, Schneemann A, Lipkin WI. RNA splicing in Borna disease virus, a nonsegmented, negative-strand RNA virus. J Virol 1994;68:5007–5012.
- Honda T, Tomonaga K. Nucleocytoplasmic shuttling of viral proteins in borna disease virus infection. *Viruses* 2013;5:1978–1990.