**Virus Taxonomy**

The ICTV Report on Virus Classification and Taxon Nomenclature

*Nodaviridae* Chapter

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**Nodaviridae**


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**Summary**

The family *Nodaviridae* includes two genera, *Alphanodavirus* and *Betanodavirus* (Table 1.*Nodaviridae*). The family name derives from the Japanese village of Nodamura where Nodamura virus was first isolated from *Culex tritaeniorhynchus* mosquitoes. Virions are non-enveloped and spherical in shape with icosahedral symmetry (T=3) and diameters ranging from 25–33 nm. The genome consists of two molecules of positive-sense ssRNA: RNA1 and RNA2. The virion capsid consists of 180 protein subunits arranged on a T=3 surface lattice. Alphanodaviruses infect insects whereas betanodaviruses are pathogens of fish.

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical member:</td>
<td>striped jack nervous necrosis virus (RNA1: AB056571; RNA2: AB056572) species <em>Striped jack nervous necrosis virus</em>, genus <em>Betanodavirus</em></td>
</tr>
<tr>
<td>Virion</td>
<td>Non-enveloped spherical particles, 25–33 nm in diameter, with or without surface projections</td>
</tr>
<tr>
<td>Genome</td>
<td>Bi-partite positive-sense, ssRNA of 3.1 kb (RNA1) and 1.4 kb (RNA2) with 5-terminal caps but without poly(A) tails</td>
</tr>
<tr>
<td>Replication</td>
<td>Cytoplasmic within virus-induced invaginations on the outer mitochondrial membrane</td>
</tr>
<tr>
<td>Translation</td>
<td>From capped genomic and subgenomic RNAs</td>
</tr>
<tr>
<td>Host range</td>
<td>Natural hosts are insects (<em>Alphanodavirus</em>) or fish (<em>Betanodavirus</em>)</td>
</tr>
<tr>
<td>Taxonomy</td>
<td>Two genera, each including four or more species</td>
</tr>
</tbody>
</table>

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**Virion**

Virions are non-enveloped, roughly spherical in shape, 25–33 nm in diameter and have icosahedral symmetry (*Johnson and Reddy 1998*) (Figure 1.*Nodaviridae*). The capsid of virions consists of 180 protein subunits arranged on a T=3 surface lattice. Each subunit is composed of a single capsid protein (CP) or the two products of its cleavage. Electron microscopy of negatively-stained betanodaviruses shows surface projections; these are not observed in alphanodaviruses.
**Physicochemical and physical properties**

Virion Mr is about 8–9 x 10^8; S_{20,W} is about 135–145. Virion buoyant density in CsCl ranges from 1.30 to 1.36 g cm^{-3}. Virions are stable to pH values ranging from 2 to 9 and are resistant to heating at 56 °C for 30 minutes. Infectivity of virions is stable following chloroform extraction.

**Nucleic acid**

The genome consists of two molecules of positive-sense ssRNA: RNA1 and RNA2. Both RNA molecules are required for infectivity and they are encapsidated in the same virus particle. Both molecules are capped at their 5′-ends and lack poly(A) tails at their 3′-ends. The RNA content of the virion is about 16%. The 3′-ends of alphanodavirus RNAs cannot be chemically derivatized even after treatment with denaturing solvents, indicating that the expected 3′-terminal-OH groups are unreactive.

**Proteins**

The capsid of virion consists of 180 protein subunits arranged on a T=3 surface lattice. Each subunit is composed of a single CP or the two products of its cleavage.

**Lipids**

None

**Carbohydrates**

None

**Genome Organization and replication**

Virus replication is cytoplasmic. Infected cells contain ssRNAs corresponding to RNA1 and RNA2, as well as the subgenomic RNA3 (387 nucleotides) which derives from the 3′-terminus of RNA1 (Figure 2. Nodaviridae) and is not packaged into virions. In addition to RNA-dependent RNA polymerase (RdRP) activity, protein A binds to and drives invagination of the outer mitochondrial membrane to provide the compartment where RNA replication occurs. RNA3 encodes either one or two proteins; protein B2 (11 kDa) is encoded by all nodaviruses in a reading frame overlapping that of protein A, and is a suppressor of RNA interference. Some nodaviruses also express protein B1 (11 kDa) which corresponds to the C-terminal region of protein A and is of unknown function. Maturation of non-infectious provirions involves the autocatalytic cleavage of protein α into proteins β (39 kDa) and γ (4 kDa).
Figure 2. Nodaviridae. Flock House virus (Alphanodavirus) genome organization and strategy of replication.

Biology

Members of different species in the family Nodaviridae have been obtained from insects and marine fish (Ball and Johnson 1998, Yong et al., 2017). Some members do not show strict specificity for particular hosts. Virions have both horizontal and vertical modes of transmission that can result in disease in their hosts. Alphanodavirus infection results in stunting, paralysis, and death of its insect hosts, while betanodavirus infection of fish causes neural necrosis, encephalopathy or retinopathy and is associated with behavioural abnormalities and high mortality, posing significant problems for marine aquaculture (Iwamoto et al., 2001, Munday et al., 2002).

Antigenicity

Members of the family Nodaviridae are cross-reactive by immunoblot or double-diffusion immunoprecipitation tests, but all the members represent different serotypes (neutralization titer of each antiserum less than 0.5% in heterotypic crosses). In contrast, some members are not cross-reactive by gel immunodiffusion tests.

Derivation of names

Noda from Nodamura virus the type species of the Alphanodavirus genus, first isolated in Nodamura, Japan.

By convention, species of the Alphanodavirus genus are named after the places of isolation of the exemplar viruses (Boolarra virus, Flock House virus, Nodamura virus and Pariacoto virus), or the host from which the exemplar virus was isolated (Black beetle virus, from the black beetle, Heteronychus arator). Species of the Betanodavirus genus contain viruses that are pathogens of fish causing “viral nervous necrosis” and are, therefore named after common name of the host fish from which they were isolated, followed by nervous necrosis virus, as in Barfin flounder nervous necrosis virus, Redspotted grouper nervous necrosis virus, Striped jack nervous necrosis virus, and Tiger puffer nervous necrosis virus (Iwamoto et al., 2001, Munday et al., 2002).

Genus demarcation criteria

The following criteria can be applied to the demarcation of genera within the family Nodaviridae:

- **Biological properties** (host range, vectors, mode of transmission)
- **Virion physical/physicochemical characteristics** (virion sedimentation coefficient and buoyant density)
- **Structural protein characteristics** (electrophoretic mobilities of the CP precursor or its cleavage products)
- **Antigenic properties**
- **Genome molecular characteristics** (in the absence of sequence information, the electrophoretic mobilities of the viral genomic)
- **Phylogeny** (sequence of the two genomic RNAs, and their predicted proteins).

Relationships within the family

Nodaviruses can be classified based on genetic diversity of the RNA2 segment. Isolates with less than 80% identity at the nucleotide level of RNA2 and less than 87% identity at the amino acid level are classified as different species (Schuster et al., 2014). The CP aa sequences of the alphanodaviruses are only about 10% identical to those of the betanodaviruses.
Relationships with other taxa

The omegatetraviruses such as Nudaurelia capensis omega virus (NCoV) and Helicoverpa armigera stunt virus (HaSV) contain bipartite positive-sense ssRNA genomes, but their RNAs are about twice the size of nodavirus RNAs and they have no 3'-terminal blockage. Tetraviruses also have larger capsids with T=4 icosahedral symmetry (Johnson and Reddy 1998).

Related, unclassified viruses

<table>
<thead>
<tr>
<th>Virus name</th>
<th>Accession number</th>
<th>Virus abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrobrachium rosenbergii nodavirus</td>
<td>RNA1: AY231436; RNA2: AY222840</td>
<td>MrNV</td>
</tr>
<tr>
<td>Penaeus vannamei nodavirus</td>
<td>RNA2: EF137180</td>
<td>PvNV</td>
</tr>
<tr>
<td>Wuhan nodavirus</td>
<td>RNA1: AY962576; RNA2: DQ233638</td>
<td>WhNV</td>
</tr>
<tr>
<td>Le Blanc nodavirus</td>
<td>RNA2: JQ943580</td>
<td>LBNV</td>
</tr>
<tr>
<td>Santeuil nodavirus</td>
<td>RNA2: HM030973</td>
<td>SNV</td>
</tr>
<tr>
<td>Orsay virus</td>
<td>RNA2: HM030971</td>
<td>ONV</td>
</tr>
<tr>
<td>Mosinovirus</td>
<td>RNA2: KJ632943</td>
<td>MV</td>
</tr>
<tr>
<td>Lutzomyia nodavirus</td>
<td>RNA2: KR003800</td>
<td>LNV</td>
</tr>
<tr>
<td>bat guano-associated virus</td>
<td>RNA1: HM228873</td>
<td>BGNV</td>
</tr>
<tr>
<td>covert mortality nodavirus</td>
<td>KM112247</td>
<td>CMNV</td>
</tr>
<tr>
<td>Farfantepenaeus duorarum nodavirus</td>
<td>RNA1: KC441519; RNA2: KC441520</td>
<td>FdNV</td>
</tr>
</tbody>
</table>

Virus names and virus abbreviations are not official ICTV designations.

A third group of nodaviruses has been considered by some authors. This group includes the prawn nodaviruses Macrobrachium rosenbergii nodavirus, Penaeus vannamei nodavirus, covert mortality nodavirus and Farfantepenaeus duorarum nodavirus, infecting prawn and shrimp.
Genus: Alphanodavirus

Distinguishing features

Alphanodaviruses have been isolated from insects, although they are capable of infecting cells from a wide range of hosts in the laboratory. They can also infect pigs, mice and hamsters experimentally.

Virion

Virions are non-enveloped, roughly spherical in shape, 32–33 nm in diameter, and have icosahedral symmetry (T=3) ([Johnson and Reddy 1998]. Electron microscopy revealed no distinct surface structure in the virion. Empty shells are rarely seen in virus preparations ([Figure 1. Nodaviridae]

Physicochemical and physical properties

Virion Mr is about 9×10^13; S is 135–145S. Virion buoyant density in CsCl is 1.30–1.34 g cm^-3 and varies with species. The infectivity of aqueous suspensions is stable to extraction with chloroform. The infectivity of Nodamura virus (NoV), black beetle virus (BBV), and Flock House virus (FHV) is stable at room temperature in 1% sodium dodecyl sulfate but Boolarra virus (BoV) is inactivated. Virions are stable at acid pH.

Nucleic acid

The genome consists of two molecules of positive-sense ssRNA: RNA1 (Mr 1.1×10^6, 3.1 kb) and RNA2 (Mr 0.48×10^6, 1.4 kb).

Proteins

The capsid consists of 180 protein subunits (protomers) arranged on a T=3 surface lattice. Each protomer is composed of a single capsid protein (CP, protein α) or the two products of its cleavage (proteins β and γ). Mass spectrometry of the FHV CP indicates that the initiating methionine is removed. Thus, for FHV, the capsid proteins are: protein α: (44 kDa), aa 2–407; protein β: (39 kDa), aa 2–363; protein γ: (4 kDa), aa 364–407. Morphogenesis involves the formation of a non-infectious provirion, which acquires infectivity by autocatalytic cleavage of protein α to form proteins β and γ. Maturation cleavage is often incomplete and virions typically contain residual uncleaved protein α.

Lipids

None.

Carbohydrates

None.

Genome organization and replication

Alphanodaviruses replicate in the cytoplasm of infected cells ([Figure 2. Nodaviridae]). RNA synthesis is resistant to actinomycin D. Infected cells contain three ssRNAs: RNA1 (Mr 1.1×10^6; 3.1 kb); RNA2 (Mr 0.48×10^6; 1.4 kb) and a sgRNA3 (Mr 1.10.13×10^6; 0.39 kb), whose nucleotide sequence corresponds to the 3′-end of RNA1 (387 nt in the case of FHV). Unlike RNAs 1 and 2, RNA3 is not packaged into virions. RNA1 encodes protein A (112 kDa), which is the catalytic subunit of the viral RNA-dependent RNA polymerase (RdRP). RNA2 encodes protein α, the CP precursor (44 kDa). Depending on the virus species, RNA3 encodes one or two small proteins (proteins B1 and B2, 11 kDa). B1 is encoded in the same ORF as protein A. Protein B2 is encoded in an overlapping ORF. The RNA3 of BoV does not encode protein B1 but all known alphanodavirus RNA3 molecules encode protein B2. Protein B2 of FHV functions as a suppressor of RNA interference (RNAi) in Dro sophila melanogaster; cultured Drosophila melanogaster cells (Schneider’s line 2), tobacco plants (Nicotiana benthamiana), and the nematode Caenorhabditis elegans. Similarly, NoV B2 suppresses RNAi in cultured mammalian and mosquito cells. The function of protein B1 is unknown. Cells transfected with isolated RNA1 synthesize RNA1 and overproduce RNA3, but do not make RNA2. RNA2 replication strongly inhibits synthesis of RNA3 and the translation of RNA2 suppresses the translation of RNA1 ([Johnson et al., 2001].

Biology

Host range

Isolates of all species of alphanodaviruses have been obtained from insects, although serological data suggest that NoV also naturally infects pigs and perhaps herons ([Ball and Johnson 1998]. NoV seems to be unique among the nodaviruses in its ability to infect and kill both vertebrates and invertebrates. Other alphanodaviruses do not show strict specificity for particular insect hosts.

In the laboratory, most alphanodaviruses can be propagated in larvae of the common wax moth ([Galleria mellonella] causing paralysis and
death. FHV, BBV, and BoV replicate well in cultured Drosophila melanogaster cells and form plaques on monolayers of these cells. Defective-interfering particles are readily formed unless the viruses are passaged at low multiplicity of infection. FHV, isolated from grass grubs (Costelytra zealandica), also infects several other insect species, including adult common fruit flies (Drosophila melanogaster), tsetse flies (Glossina morsitans morsitans), reduviid bugs (Rhosnius prolixus) and several species of mosquito (Aedes aegypti, Culex pipiens, Armigeres subalbatus and Anopheles gambiae). FHV can be propagated in mammalian cells, plants (Nicotiana benthamiana), yeast (Saccharomyces cerevisiae) and nematodes (Caenorhabditis elegans). Persistent FHV infections, with subsequent resistance to superinfection, occur readily in cultured Drosophila melanogaster cells. NoV, isolated from mosquitoes, also causes paralysis and death in sucking mice and sucking hamsters. NoV infects cultured cells from both mosquitoes and mammals, but not those of Drosophila melanogaster. Interestingly, NoV infection is delayed in mammalian cells compared to mosquito cells. NoV can also be propagated by transfecting mosquito, vertebrate, or yeast (Saccharomyces cerevisiae) cell cultures with virion RNA or cloned cDNA copies of genomic RNAs at temperatures up to 37 °C. PaV infects cultured cells from the beet armyworm (Spodoptera exigua) corn earworm (Helicoverpa zea), and mosquitoes (Aedes a albopictus), but not those of the fruit fly (Drosophila melanogaster) or fall armyworm (Spodoptera frugiperda). Infectious cDNA clones of the genomic RNAs of FHV, NoV and PaV allow the initiation of their respective replicative cycle in many cell types on transfection of plasmid DNA or in vitro transcripts.

Transmission

NoV is transmissible to suckling mice by Aedes aegypti mosquitoes. It causes paralysis and death when injected into sucking mice and sucking hamsters, but no disease in adult animals. In their insect hosts, alphanodaviruses typically cause stunting, paralysis, and death.

Antigenicity

NoV, BBV, FHV and BoV are cross-reactive by double-diffusion immunoprecipitation tests, but all four members represent different serotypes (neutralization titer of each antiserum less than 0.5% in heterotypic crosses). In contrast, Pariacoto virus (PaV) and NoV are not cross-reactive by gel immunodiffusion tests.

Species demarcation criteria

The following criteria can be applied to the demarcation of species within the Alphanodavirus genus:

- **Biological properties** (host range, vectors, mode of transmission). Since the natural host ranges of the nodaviruses have generally not been examined in detail but may in some cases be broad, virus isolation from a new host is not, in itself, evidence of a new nodavirus species.

- **Antigenic properties**. Antisera raised against different isolates or strains of a single nodavirus species should exhibit high levels of cross-reactivity in Western blot and/or neutralization analyses. Lower levels of cross-reactivity in these assays using antisera against all previously recognized nodavirus species can provide evidence of a novel nodavirus.

- **Virion electrophoretic mobility**. Intact virus particles migrate with characteristic electrophoretic mobilities in non-denaturing agarose gel.

- **Sedimentation coefficient, buoyant density**. Virion sedimentation coefficient and buoyant density should be compared with those of other nodavirus species.

- **Structural protein characteristics**. The electrophoretic mobilities in SDS-PAGE of the CP precursor or its cleavage products should be compared with those of other nodavirus species.

- **RNA electrophoretic mobilities**. In the absence of sequence information, the electrophoretic mobilities of the viral genomic RNAs should be compared with those of other nodavirus species.

- **Phylogeny**. Within the alphanodaviruses, CP amino acid sequences are 44–87% identical to one another. Different species encode capsid proteins that differ at >20% of nucleotide or >13% of amino acid positions. Because the nodavirus genome is segmented, reassortment can occur and the two genome segments may have distinct evolutionary lineages.

In practice, while the five criteria above may be suggestive of a new species, definitive demarcation is based on the nucleotide sequence of the viral CP gene. The two closest recognized species are BBV and FHV, whose RNA2 sequences show 75–78% identity at the nucleotide level and 81–87% identity at the amino acid sequence level (Figure 1. Alphanodavirus). Their RNA1 sequences, however, are 99% identical.

![Figure 1. Alphanodavirus](image)

**Figure 1. Alphanodavirus**. Phylogenetic analysis of alphanodavirus capsid protein sequences. Complete RNA2 sequences were aligned using MUSCLE (Edgar 2004) within the SSE v1.3 (Simmonds 2012) and a neighbor joining tree produced using evolutionary distances using the JTT matrix within MEGA7 (Kumar et al., 2016). Branches supported by >70% of bootstrap replicates are indicated. Tips are labelled with nucleotide sequence Genbank accession number, virus name and virus species. This phylogenetic tree and corresponding sequence alignment are available to download from the Resources page.
### Member species

**Exemplar isolate of the species**

<table>
<thead>
<tr>
<th>Virus name</th>
<th>Isolate</th>
<th>Accession number</th>
<th>RefSeq number</th>
<th>Available sequence</th>
<th>Virus Abbrev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black beetle virus</td>
<td>black beetle virus</td>
<td>RNA1: X02396; RNA2: X00956</td>
<td>RNA1: NC_001411; RNA2: NC_002039</td>
<td>Complete genome</td>
<td>BBV</td>
</tr>
<tr>
<td>Boolarra virus</td>
<td>Boolarra virus</td>
<td>RNA1: AF329080; RNA2: X15960</td>
<td>RNA1: NC_004142; RNA2: NC_004145</td>
<td>Complete genome</td>
<td>BoV</td>
</tr>
<tr>
<td>Flock House virus</td>
<td>Flock House virus</td>
<td>RNA1: X77156; RNA2: X15959</td>
<td>RNA1: NC_004146; RNA2: NC_004144</td>
<td>Complete genome</td>
<td>FHV</td>
</tr>
<tr>
<td>Flock House virus</td>
<td>Flock House virus</td>
<td>IP-RIA-022011</td>
<td>RNA1: JF461541; RNA2: JF461542</td>
<td>Complete genome</td>
<td>FHV</td>
</tr>
<tr>
<td>Flock House virus</td>
<td>Flock House virus</td>
<td>TNCL</td>
<td>RNA1: EF690537; RNA2: EF690538</td>
<td>Complete genome</td>
<td>FHV</td>
</tr>
<tr>
<td>Flock House virus</td>
<td>Drosophila melanogaster American nodavirus</td>
<td>RNA1: GU976286; RNA2: GU976286</td>
<td>RNA1: NC_003690; RNA2: NC_003691</td>
<td>Complete genome</td>
<td>FHV</td>
</tr>
<tr>
<td>Nodamura virus</td>
<td>Nodamura virus</td>
<td>RNA1: AF174533; RNA2: AF174534</td>
<td>RNA1: NC_002690; RNA2: NC_002691</td>
<td>Complete genome</td>
<td>NoV</td>
</tr>
<tr>
<td>Nodamura virus</td>
<td>Nodamura virus</td>
<td>RNA2: X15961</td>
<td>Partial genome</td>
<td>NoV</td>
<td></td>
</tr>
<tr>
<td>Pariacoto virus</td>
<td>Pariacoto virus</td>
<td>RNA1: AF171942; RNA2: AF171943</td>
<td>RNA1: NC_003691; RNA2: NC_003692</td>
<td>Complete genome</td>
<td>PaV</td>
</tr>
</tbody>
</table>

Virus names, the choice of exemplar isolates, and virus abbreviations, are not official ICTV designations.

### Related, unclassified viruses

<table>
<thead>
<tr>
<th>Virus name</th>
<th>Accession number</th>
<th>Virus abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drosophila line 1 virus</td>
<td>not available</td>
<td>DL</td>
</tr>
<tr>
<td>gypsy moth virus</td>
<td>not available</td>
<td>GMV</td>
</tr>
<tr>
<td>Helicoverpa zea alphanodavirus</td>
<td>RNA2: GU976286</td>
<td></td>
</tr>
<tr>
<td>Lymantria ninayi virus Greenwood</td>
<td>not available</td>
<td>LNV</td>
</tr>
<tr>
<td>Manawatu virus</td>
<td>not available</td>
<td>MwV</td>
</tr>
<tr>
<td>New Zealand virus</td>
<td>not available</td>
<td>NZV</td>
</tr>
<tr>
<td>Newington virus</td>
<td>RNA2: U754530</td>
<td>NV</td>
</tr>
</tbody>
</table>

Virus names and virus abbreviations are not official ICTV designations.
Genus: *Betanodavirus*

**Distinguishing features**

Betanodaviruses are pathogens of fish causing a disease called “viral nervous necrosis” and are named after the host fish from which they were isolated, followed by nervous necrosis virus (Munday et al., 2002). They infect more than 50 species of marine and freshwater fish. Five genetic lineages of betanodavirus have been identified.

**Virion**

**Morphology**

Virions are non-enveloped, spherical in shape, 25–33 nm in diameter, and have icosahedral symmetry (T=3). Distinct surface protrusions are observed by electron microscopy of negatively stained preparations (Figure 1. *Betanodavirus*). Image reconstruction of virus-like particles of Malabaricus grouper nervous necrosis virus (MGNNV) indicates that the capsid protein (CP) of betanodaviruses has a two domain structure compared to the single domain structure of the CP of alphanodaviruses. The average diameter of the particle is 31 nm. In contrast with most alphanodaviruses, empty particles have been seen by electron microscopy of some preparations of betanodaviruses.

**Physicochemical and physical properties**

Virion buoyant density in CsCl of striped jack nervous necrosis virus (SJNNV) has not been reported but that of Dicentrarchus labrax encephalitis virus (DlEV), a related but not yet classified betanodavirus, is about 1.31–1.36 g cm$^{-3}$. Virions of DlEV are stable between pH 2 and 9 and resistant to heating at 56 °C for 30 min. Infectivity is resistant to extraction of virions with chloroform.

**Nucleic acid**

The genome consists of two molecules of positive-sense ssRNA: RNA1 (Mr 1.01×10$^6$, 3.1 kb) and RNA2 (Mr 0.49×10$^6$, 1.4 kb). Both RNA molecules are encapsidated in the same virus particle, and both are required for infectivity. Both molecules are capped at their 5’-ends and lack poly(A) tails at their 3’-ends.

**Proteins**

Betanodavirus capsids contain 180 copies of a single structural protein of 42 kDa. In contrast to alphanodaviruses, maturation cleavage of this protein is not observed.

**Lipids**

None.

**Carbohydrates**

None.

**Genome organization and replication**

Betanodaviruses replicate in the cytoplasm. Infected cells contain three ssRNAs: RNA1 (Mr 1.01×10$^6$, 3.1 kb); RNA2 (Mr 0.49×10$^6$, 1.4 kb);
and a subgenomic (sg) RNA3 (Mr about 0.13×10^6; 0.4 kb) derived from RNA1. RNA3 is not packaged into virions. RNA1 encodes protein 1a (110 kDa), the RNA-dependent RNA polymerase (RdRP). RNA2 encodes protein 2a (42 kDa), the CP. The RNA3 of SJNNV encodes protein B2 and has a potent RNA silencing-suppression activity, as also observed for alphanodaviruses (Iwamoto et al., 2001).

**Antigenicity**

Betanodaviruses are cross-reactive by immunoblot analysis using polyclonal antisera but differential reactivity is observed with monoclonal antibodies. Virus neutralization with polyclonal antisera divides four betanodaviruses into three serotypes; serotype A for SJNNV, serotype B for tiger puffer nervous necrosis virus (TPNNV), and serotype C for red-spotted grouper nervous necrosis virus (RGNNV) and barfin flounder nervous necrosis virus (BFNNV).

**Biology**

**Host range**

Isolates of all species of betanodaviruses have been isolated from larvae, juvenile or adult marine fish, in which they cause “viral nervous necrosis” or “viral encephalopathy and retinopathy” associated with behavioral abnormalities and high mortalities. SJNNV and TPNNV have a limited host range: striped jack for SJNNV and tiger puffer for TPNNV. In contrast, RGNNV and BFNNV have a wide range of host fish; RGNNV is isolated from warm-water fishes and BFNNV is isolated from cold-water fishes. These diseases cause significant problems for the marine aquaculture industry.

Betanodaviruses replicate in cultured cells from striped snakehead fish (SNN-1 and E-11) and other cells derived from fish such as groupers (GF-1), sea bass (SBL), turbot (TV-1), and gilthead sea bream (SAF-1). A low level of virus replication is observed in mammalian (COS-1 and HeLa) cells.

**Transmission**

Betanodavirus antigens and/or CP genes are detected in eggs, larvae and ovaries of some inapparently infected hatchery-reared fish species, and the CP gene is frequently detected in a variety of wild fishes without any disease signs, indicating both horizontal and vertical modes of transmission of the virus.

**Species demarcation criteria**

The following criteria can be applied to the demarcation of species within the Betanodavirus genus:

- **Biological properties** (host range, vectors, mode of transmission). They primarily infect fish especially larval and young fish.
- **Antigenic properties**. Strains of betanodavirus fell into 3 major serotypes (A, B, C) and this sero-grouping is in part consistent with their genotypes, i.e. serotype A for striped jack nervous necrosis virus (SJNNV) genotype, serotype B for tiger puffer nervous necrosis virus (TPNNV) genotype, and serotype C for both red-spotted grouper nervous necrosis virus (RGNNV) and barfin flounder nervous necrosis virus (BFNNV) genotypes. The serological relatedness between RGNNV and BFNNV genotypes may result from their relatively higher similarity in RNA2 sequences.
- **Virion electrophoretic mobility**. Intact virus particles migrate with characteristic electrophoretic mobilities in non-denaturing agarose gel.
- **Sedimentation coefficient, buoyant density**. Virion sedimentation coefficient and buoyant density should be compared with those of other nodavirus species.
- **Structural protein characteristics**. The electrophoretic mobilities in SDS-PAGE of the CP precursor or its cleavage products should be compared with those of other nodavirus species.
- **RNA electrophoretic mobilities**. In the absence of sequence information, the electrophoretic mobilities of the viral genomic RNAs should be compared with those of other nodaviruses.
- **Genome sequence**. The nucleotide sequence of the two genomic RNAs should be compared with those of other nodaviruses (Thiéry et al., 2004) (Figure 2. Betanodavirus). Different species encode capsid proteins that differ at >15% of nucleotides and >12% of amino acid positions. Because the nodavirus genome is segmented, reassortment can occur and the two genome segments may have distinct evolutionary lineages.
Figure 2. Betanodavirus Phylogenetic analysis of betanodavirus capsid protein sequences. Complete RNA2 sequences were aligned using MUSCLE (Edgar 2004) within the SSE v1.3 (Simmonds 2012). After excluding sequences that were <2% divergent in amino acid sequence, a neighbor joining tree produced using evolutionary distances using the JTT matrix within MEGA7 (Kumar et al., 2016). Branches supported by >70% of bootstrap replicates are indicated. Tips are labelled with nucleotide sequence accession number, virus name and virus species. This phylogenetic tree and corresponding sequence alignment are available to download from the Resources page.

Member species

<table>
<thead>
<tr>
<th>Species</th>
<th>Virus name</th>
<th>Isolate</th>
<th>Accession number</th>
<th>RefSeq number</th>
<th>Available sequence</th>
<th>Virus Abbrev.</th>
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<tbody>
<tr>
<td>Barfin flounder nervous necrosis virus</td>
<td>barfin flounder nervous necrosis virus</td>
<td>BF93Hok</td>
<td>RNA1: EU826137; RNA2: EU826138</td>
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<td>BFNNV</td>
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<td>Atlantic cod nervous necrosis virus</td>
<td>GmMR11/06</td>
<td>RNA1: EF433472; RNA2: EF433468</td>
<td>RNA1: NC_008040; RNA2: NC_008041</td>
<td>Complete genome</td>
<td>ACNNV</td>
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<td>Atlantic halibut nodavirus</td>
<td>AH95NorA</td>
<td>RNA1: AJ401165</td>
<td>-</td>
<td>Partial genome</td>
<td>AHNV</td>
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<td>RNA2: A2J45641</td>
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<td>AHNV</td>
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<td>red-spotted grouper nervous necrosis virus</td>
<td>SGWak97</td>
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<td>China</td>
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<td>DGNV</td>
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<td>greasy grouper nervous necrosis virus</td>
<td>Singapore</td>
<td>RNA1: AF319555; RNA2: AF319542</td>
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<td>Complete genome</td>
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<td>Redspotted grouper nervous necrosis virus</td>
<td>Japanese flounder nervous necrosis virus</td>
<td>WD</td>
<td>RNA1: FJ478760</td>
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<td>JFNNV</td>
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<td>Japanese flounder nervous necrosis virus</td>
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<td>JFNNV</td>
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<td>Malabaricus grouper nervous necrosis virus</td>
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<tr>
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<td>Solea senegalensis nervous necrosis virus</td>
<td>SpSsIAusc16003</td>
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<td>RNA1: NC_003448; RNA2: NC_003449</td>
<td>Complete genome</td>
<td>SSNNV</td>
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<tr>
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<td>S. senegalensis nervous necrosis virus</td>
<td>03-160</td>
<td>RNA2: AJ698113</td>
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<td>tiger puffer nervous necrosis virus</td>
<td>TPkag93</td>
<td>RNA1: EU236148; RNA2: EU236149</td>
<td>RNA1: NC_013460; RNA2: NC_013461</td>
<td>Complete genome</td>
<td>TPNNV</td>
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</tbody>
</table>

Virus names, the choice of exemplar isolates, and virus abbreviations, are not official ICTV designations.

Related, unclassified viruses

<table>
<thead>
<tr>
<th>Virus name</th>
<th>Accession number</th>
<th>Virus abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dicentrarchus labrax encephalitis virus</td>
<td>RNA2: U39876</td>
<td>DIEV</td>
</tr>
<tr>
<td>KSNNV-KorMu1</td>
<td>RNA2: K778109</td>
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<tr>
<td>Melanogrammus aeglefinus nervous necrosis virus</td>
<td>RNA2: AY547549</td>
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</tr>
<tr>
<td>turbot nodavirus</td>
<td>RNA2: AJ608266</td>
<td>TNV</td>
</tr>
</tbody>
</table>

Virus names and virus abbreviations are not official ICTV designations.
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The chapter in the Ninth ICTV Report, which served as the template for this chapter, was contributed by Thiéry, R., Johnson, K.L., Nakai, T., Schneemann, A., Bonami, J.R. and Lightner, D.V.
Resources: Nodaviridae

Sequence alignments and tree files:

Figure 1. *Alphanodavirus*

Alignment file (FASTA format)

Tree file (newick format)

Figure 2. *Betanodavirus*

Alignment file (FASTA format)

Tree file (newick format)
References: Nodaviridae


Citation: Nodaviridae

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