Bornaviridae

Taxonomy

Riboviria › Orthornavirae › Negarnaviricota › Haploviricotina › Monjiviricetes › Mononegavirales › Born aviridae

Derivation of name

Borna refers to the city of Borna in Saxony, Germany, where many horses died in 1885 during an epidemic of a neurological disease, designated as Borna disease (BD), caused by the infectious agent presently known as Borna disease virus (BDV).

Genus Bornavirus

Type species **Borna disease virus**

Virion properties

Morphology

Electron microscopy studies of negatively stained infectious particles of an isolate of Borna disease virus (BDV) have shown that virions have a spherical morphology with a diameter of 90±10 nm containing an internal electron-dense core (50–60 nm).

Physicochemical and physical properties

Virion Molecular weight not known. Virus infectivity is rapidly lost by heat treatment at 56 °C. Virions are relatively stable at 37 °C, and only minimal infectivity loss is observed after 24 hrs incubation at 37 °C in the presence of serum. Virions are inactivated below pH 5.0, as well as by treatment with organic solvents, detergents, and exposure to UV radiation. Infectivity is completely and rapidly destroyed by chlorine-containing disinfectants or formaldehyde treatment.

Nucleic acid

The genome consists of a single molecule of a linear, negative sense ssRNA about 8.9 kb in size and Mr of about 3×10^6). The RNA genome is not polyadenylated. Extracistronic sequences are found at the 3′ (leader) and 5′ (trailer) ends of the BDV genome. The ends of the BDV genome RNA exhibit partial

inverted complementarity. Full-length plus-strand (antigenomic) RNAs are present in infected cells and in viral ribonucleoproteins. Defective RNAs have not been identified in BDV-infected cells and tissues. BDV can be classified into two subtypes based on the complete genome sequences of several BDV strains. With the unique exception of strain No/98, all isolates of BDV to date (independent of year, species and area isolation) have approximately 95% homology at the nt level (subtype 1), while BDV strain No/98 shows only 85–86% nt sequence identity compared to other BDV strains (subtype 2). The nt changes are distributed fairly evenly over the entire genome of BDV. However, all strains predict the same BDV genomic organization and differ by only one nt in absolute genome size.

Antigenic properties

BDV possess a number of distinct antigenic determinants. The so-called soluble antigen (s-antigen) obtained from the supernatant after ultracentrifugation of ultrasonicated BDV-infected brain tissue, contains the viral N, P and M proteins. Serum antibodies from BDV-infected animals frequently recognize all the components of the s-antigen, but rarely recognize the viral G products. BDV field isolates from the same or different animal species, as well as viruses recovered from experimental infections with different histories of passages exhibit strong serological cross-reactivity. There is only one recognized serotype of BDV, but monoclonal antibodies have revealed minor antigenic differences among BDV isolates. Complement independent IgG-specific neutralizing antibodies have been documented in experimentally infected animals. Titers of neutralizing antibodies are usually very low and dependent on the infected host species. BDV G protein has been implicated in virus neutralization.

Borna Disease/Sad horse disease

Horses and sheep have been regarded as the main natural hosts of BDV. In these species BDV can cause a fatal neurologic disease, Borna disease (BD). Evidence indicates that the natural host range of BDV is wider than originally thought. Naturally occurring BDV infections have been documented in cattle, rabbits and cats. In addition, sporadic cases of natural infection with BDV have been reported in several other species, including donkeys, mules and llamas. Moreover, experimental infections have revealed a remarkable wide host range for BDV, from birds to rodents and non-human primates. BDV-induced neurobehavioral abnormalities in animals are reminiscent of some human neuropsychiatric disorders. Serological data and molecular epidemiological studies indicate that BDV can infect humans, and is possibly associated with certain neuropsychiatric disorders.

BDV is thought to be transmitted through salival, nasal, or conjunctival secretions. Infection may therefore result from direct contact with these secretions. Intranasal infection is the most likely route of natural infection, allowing BDV access to the central nervous system (CNS) by intraaxonal migration through the olfactory nerve. Cases of Borna disease (BD) are more frequent in some years than others and tend to occur in spring and early summer, suggesting arthropods as a potential vector. BDV has not been isolated from insects, but ticks have been implicated in the transmission of an infectious encephalomyelitis similar to BD affecting ruminants in the Middle East.

Asymptomatic naturally infected animals of different species have been documented in Europe, North America, Africa and Asia, suggesting that the prevalence and geographic distribution of BDV may have been underestimated. However, a definite natural reservoir of BDV has not been identified. Phenotypic differences have been described among different BDV field isolates, and among viruses with different histories of passages in animals and cultured cells. Despite its wide host range and phenotypic variation, molecular epidemiological data have shown a remarkable sequence conservation of BDV, not only within the same host species but also amongst sequences derived from different animal species.

BDV is highly neurotropic and has a non-cytolytic strategy of multiplication. BDV causes CNS disease in several non-human vertebrate species, which is characterized by neurobehavioral abnormalities that are often, but not always, associated with the presence of inflammatory cell infiltrates in the brain. BDV exhibits a variable period of incubation, from weeks to years, and diverse pathological manifestations that depend on the genetics, age and immune status of the host, as well as route of infection and viral determinants. Classic BD is caused by a T cell-dependent immune mechanism. Inflammatory cells are found forming perivascular cuffs and also within the brain parenchyma. Both $CD4^+$ and $CD8^+$ T-cells are present in the CNS cell infiltrates and contribute to the immune-mediated pathology associated with BD. BDV can also induce distinct deficiencies in emotional and cognitive functions that are associated with specific neurochemical disturbances in the absence of lymphoid infiltration. Heightened viral expression in limbic system structures, together with astrocytosis and neuronal structural alterations within the hippocampal formation are the main histopathological hallmarks of BDV infection.