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Fish Viruses

J C Leong, University of Hawaii at Manoa, Honolulu, HI, USA

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Glossary

Anadromous Migrating from the sea to freshwater to spawn.

Cardiomyopathy A weakening of the heart muscle or a change in heart muscle structure.

Salmonid Belonging to, or characteristic of the family Salmonidae which includes the salmon trout and whitefish.

Swimbladder An air-filled sac near the spinal cord in many fishes that helps maintain buoyancy.

Introduction

Viruses that infect fish and cause disease are represented in 14 of the families listed for vertebrate viruses by the International Committee on the Taxonomy of Viruses (27 May 2005). The fish viruses containing DNA genomes are listed in the families *Iridoviridae*, *Adenoviridae*, and *Herpesviridae* and those with RNA genomes are listed in the families *Picornaviridae*, *Birnaviridae*, *Reoviridae*, *Rhabdoviridae*, *Orthomyxoviridae*, *Paramyxoviridae*, *Caliciviridae*, *Togaviridae*, *Nodaviridae*, *Retroviridae*, and *Coronaviridae*. As more fish species are brought under culture, there will be additions to this list, and possibly new viruses will be assigned to families not previously characterized in vertebrates.

Viral diseases have had a tremendous economic impact on both wild and farm-reared fish. A herpesvirus outbreak

in 1998 and early 1999 reduced the pilchard (*Sardinops sagax neophilchardus*) fishery in southern Australia by two-thirds. In 2001, infectious salmon anemia virus (ISAV) was discovered in cultured Atlantic salmon in Cobscook Bay, Maine. The discovery of this orthomyxovirus virus forced farmers to destroy about 2.6 million fish in an effort to contain the spread of the disease. The cost to the Maine salmon industry (valued at more than \$100 million) was about \$24 million (USDA Animal and Plant Health Inspections Service (APHIS) estimates). More recently, the rhabdovirus viral hemorrhagic septicemia virus (VHSV), a very serious pathogen of marine and freshwater fish in Europe, was detected in the Great Lakes of North America in 2005. On 24 October 2006, APHIS issued an emergency order that blocked the live export of 37 fish species from any of the eight Great Lakes states. The order caused strong protests from fish farmers who make their living with live bait shipments and fish-stocking programs that sustain the Great Lakes' \$4.5 billion fishing industry. Since vaccines and/or therapeutics for fish viruses are not readily available, containing the spread of these viruses by restricting movement and destruction of the affected population has been the only effective control strategy. Thus, the World Animal Health Organization (OIE) lists nine reportable diseases of fish (Table 1), seven of which are viral diseases.

Known and characterized fish viruses numbered only 16 in 1981, with an additional 11 observed by electron microscopy. Now, there are over 125 described viruses of fish and countless reports of electron microscopic observations of

Table 1 Diseases of fish listed by the OIE, 2006

Epizootic hematopoietic necrosis	Iridovirus
Infectious hematopoietic necrosis	Novirhabdovirus
Spring viremia of carp	Vesiculovirus
Viral hemorrhagic septicemia	Novirhabdovirus
Infectious salmon anemia	Orthomyxovirus
Epizootic ulcerative syndrome	Fungal infection
Gyrodactyloses	Flat worm fluke
Red sea bream iridovirus diseases	Iridovirus
Koi herpesvirus disease	Herpesvirus

viruses in wild-caught and cultured fish. The dramatic increase in reports of new fish viruses correlates with growth of the aquaculture industry that has increased production more than fivefold since 1985 to now represent more than 30% of global fishery production.

RNA Viruses of Fish

Rhabdoviridae

Fish rhabdoviruses are considered among the most serious viral pathogens of aquacultured fish, affecting predominantly salmon and trout. The first fish rhabdovirus was described in 1938 by Schaperclaus in European rainbow trout and, 6 years later, the Sacramento River Chinook virus was reported by Rucker. Since then, these viruses have been isolated, grown in tissue culture cells, and the genomes have been cloned and sequenced. The salmon virus is now called *Infectious hematopoietic necrosis virus* (IHNV) which is the type species for a new genus *Novirhabdovirus* in the *Rhabdoviridae*. Other fish rhabdovirus species assigned to this genus include *Viral hemorrhagic septicemia virus* (VHSV), *Hirame rhabdovirus* (HIRRV), and *Snakehead rhabdovirus* (SHRV). All of these viruses have negative-sense ssRNA genomes with a physical map ordered from the 3'-end as follows: leader-N-P-M-G-NV-L, where N is the nucleoprotein gene, P is the phosphoprotein gene, M is the matrix protein gene, G is the glycoprotein gene, NV is the nonvirion protein gene, and L is the virion RNA polymerase gene. The presence of the NV gene distinguishes the rhabdoviruses in the genus *Novirhabdovirus*, 'novi' standing for nonvirion.

Reverse genetic analysis of the IHNV, SHRV, and VHSV NV genes has, to date, provided mixed results. For IHNV and VHSV, deletion of the NV gene ameliorated virus-induced cytopathic effect (CPE) in tissue culture cells and reduced pathogenicity in fish. However, deletion of the NV gene for SHRV did not affect virus production or virus-induced CPE in tissue culture cells, or reduce pathogenicity in live fish challenges.

IHNV is a virus of salmonid fish and outbreaks of this virus in rainbow trout (*Oncorhynchus mykiss*), sockeye salmon (*O. nerka*), Chinook salmon (*O. tshawytscha*), Atlantic salmon (*Salmo salar*), and masou salmon (*O. masou*) have

been economically devastating to the fish farmers. This virus prefers colder temperatures with optimal growth at 8–15 °C. VHSV is also a serious pathogen of salmonid fish, but its host range is broader and it has been shown to kill Pacific herring (*Clupea pallasii*), Pacific cod (*Gadus macrocephalus*), whitefish (*Coregonus* sp.), European sea bass (*Dicentrarchus labrax*), and turbot (*Scophthalmus maximus*). This broad host range has caused a great deal of concern to authorities in the USA since VHSV was first reported there in 2006 and found to affect freshwater drum (*Aplodinotus grunniens*), round goby (*Neogobius melanostomus*), smallmouth bass (*Micropterus dolomieu*), bluegill (*Lepomis macrochirus mystacalis*), crappie (*Pomoxis nigromaculatus*), gizzard shad (*Dorsoma cepedianum*), and other species occurring in the Great Lakes. HIRRV affects hiram, the Japanese flounder (*Paralichthys olivaceus*), which is a highly prized food fish in Japan. Its host range includes ayu (*Pleuroglossus altivelis*) as well as salmonid fish. SHRV was isolated from snakehead fish (*Channa striatus*) suffering from epizootic ulcerative syndrome (EUS) in Thailand. It is not considered the etiologic agent of EUS which is caused by a fungal pathogen. However, zebrafish (*Brachydanio rerio*), exposed to tissue culture grown SHRV develop, will develop petechial hemorrhages and die.

Spring viremia of carp virus (SVCV), unlike the fish rhabdoviruses described above, does not contain an intervening gene between its glycoprotein and L genes. Analysis of the SVCV genome sequence indicates that it clusters with the members of the genus *Vesiculovirus* that includes vesicular stomatitis virus. SVCV was first identified as the etiologic agent of an acute hemorrhagic disease in common carp (*Cyprinus carpio*) in Europe in 1972. The disease has since been found in Asia, the Middle East, and most recently in South and North America. Outbreaks in the USA have raised concerns that indigenous fish species in the minnow family (*Cyprinidae*), some of which are endangered species, may be susceptible to SVCV. Other virus isolates that are closely related in nucleotide sequence to SVCV are the pike fry rhabdoviruses (PFRV) from a variety of freshwater fish in Europe including pike (*Esox lucius*), common bream (*Abramis brama*), roach (*Rutilus rutilus*), eel virus Europe X (EVEX), eel virus American (EVA); ulcerative disease rhabdovirus (UDRV); the grass carp rhabdovirus isolated from grass carp (*Ctenopharyngodon idella*); trout rhabdovirus 903/87 (TRV 903/87); and sea trout rhabdovirus 28/97 (STRV-28/97).

Phylogenetic analyses comparing aligned data for the N and G genes of members of the family *Rhabdoviridae* have confirmed the classification of the six genera: *Lyssavirus*, *Vesiculovirus*, *Ephemerovirus*, *Cytorhabdovirus*, *Nucleorhabdovirus*, and *Novirhabdovirus*. To date, fish rhabdoviruses are restricted to the genera *Novirhabdovirus* and *Vesiculovirus*. Analyses using the viral P gene sequences indicate that the aquatic vesiculoviruses form a separate cluster from the arthropod-borne vertebrate vesiculoviruses.

Paramyxoviridae

The first description of a paramyxovirus-like virus in fish was reported in 1985. During a routine health assessment of Chinook salmon juveniles in Oregon, tissue culture cells inoculated with a cell-free homogenate of organ tissue exhibited syncytia formation. Electron micrographs of the infected cell line showed enveloped, pleomorphic virus particles with a diameter of approximately of 125–250 nm and a single helical nucleocapsid with a diameter of 18 nm and a length of 100 nm. No disease syndrome was observed in trout and salmon fingerlings in subsequent infectivity trials with the tissue cultured virus. A second fish paramyxovirus that caused epidermal necrosis in juvenile black sea bream (*Acanthopargurus schlegelii*) was identified in Japan by electron microscopy. This virus was never cultured *in vitro*. The most recent description of a fish paramyxovirus was from Atlantic salmon post-smolts suffering from inflammatory gill disease in Norway. The genome of this virus has been cloned and partial sequences from the viral L protein have been used to determine the phylogenetic placement of this virus among the *Paramyxoviridae*. The Atlantic salmon paramyxovirus (ASPV) clustered with the subfamily *Paramyxovirinae*, in the genus *Respirovirus* that includes human parainfluenza virus and Sendai virus.

Orthomyxoviridae

Infectious salmon anemia virus (ISAV) is the only fish orthomyxovirus that has been fully described to date. There are eight RNA segments in the ISAV genome. Segment 1 encodes PB2, a component of the virion RNA polymerase; segment 2 encodes PB1; segment 3, the nucleocapsid protein NP; segment 4, the RNA polymerase PA; segment 5, acetylcholinesterase P3 or fusion protein; segment 6, hemagglutinin; segment 7, protein P4 and P5; and segment 8, proteins P6 and P7. The proteins P4 and P5 may be the ISAV counterparts to the membrane proteins M1 and M2 of influenza A virus; proteins P6 and P7 may be related to the nonstructural proteins NS1 and NEP of influenza A virus. The ISAV hemagglutinin does agglutinate fish red blood cells or mammalian red blood cells.

A comparative sequence analysis of the PB1 gene of ISAV and other members of the *Orthomyxoviridae* led to its assignment as the type species of a new genus *Isavirus*. More recent comparative analyses of the fusion protein gene (segment 5) and the hemagglutinin gene (segment 7) indicate that ISAV isolates can be divided into two subtypes, a North American subtype and a European subtype.

ISAV causes a highly lethal disease with affected farmed Atlantic salmon displaying severe anemia, leucopenia, ascetic fluids, hemorrhagic liver necrosis, and petechiae of the viscera. The virus also causes disease in sea trout (*Salmo trutta*), rainbow trout, and Atlantic herring.

Picornaviridae

The first reported observation of picorna-like viruses in fish was made in 1988 from rainbow smelt (*Osmerus mordax*) in New Brunswick, Canada. Since then, picornaviruses have been isolated from barramundi, turbot, sea bass, grass carp, blue gill, grouper (*Epinephelus tawvina*), Japanese parrotfish (*Oplegnathus fasciatus*), and salmonid fish. In most of these descriptions, the presumptive characterization of the etiologic agent as a picornavirus was based on growth in tissue culture cells and the observation of crystalline arrays in the cytoplasm of small virus particles with a size and morphology consistent with picornaviruses. Analysis of RNA extracted from purified blue gill virus has indicated that it is single-stranded RNA virus. Sequence characterization of the viral genomes has not been carried out and there is some suggestion that at least some of these viruses might actually be betanodaviruses. In many cases, diseased fish infected with these viruses contain picorna-like virus particles in the brain and medulla and the victims display corkscrew-like swimming and eventually die.

Nodaviridae

Members of the *Nodaviridae* that infect fish belong to the genus *Betanodavirus* for which the type species is *Striped jack nervous necrosis virus* (SJNNV). These viruses are nonenveloped with icosahedral symmetry and virion diameters of approximately 30 nm. The viral genome consists of two molecules of positive-sense ssRNA. RNA1, the largest RNA genome segment encodes the viral polymerase. RNA2 encodes the virion capsid protein. A third RNA, transcribed from the 3' terminal region of RNA1, encodes a 75 amino acid protein that bears little similarity with the B2 and B1 proteins encoded by a similar RNA3 in the alphanodaviruses. Despite this, the SJNNV B2 protein RNA has RNA silencing-suppression activity, as does the B2 protein of insect-infecting alphanodaviruses.

The betanodaviruses are the causative agents of viral nervous necrosis or viral encephalopathy and retinopathy in a variety of cultured marine fish. The disease affects young fish and produces a necrosis and vacuolation in the brain, spinal cord, and retina in most cases. It has been reported in striped jack (*Pseudocaranx dentex*), grouper (*Epinephelus* spp.), red drum (*Sciaenops ocellatus*), guppy (*Poecilia reticulata*), barfin flounder (*Verasper moseri*), red sea bream, tiger puffer (*Takifugu rubripes*), Japanese flounder, Atlantic halibut (*Hippoglossus hippoglossus*), amberjack (*Seriola dumerili*), sea bass, and barramundi. The recent detection of betanodaviruses in apparently healthy aquarium fish and invertebrates has raised concerns that the disease could be spread by trade in aquarium fish, particularly from Southeast Asia. Comparative sequence analyses of the coat protein genes for 25 isolates suggest that there are

four genotypic variants: tiger puffer nervous necrosis virus (TPNNV), striped jack nervous necrosis virus (SJNNV), barfin flounder nervous necrosis virus (BFNNV), and red-spotted grouper nervous necrosis virus (RGNNV).

Nidovirales

The family *Coronaviridae* comprises two genera, *Coronavirus* and *Torovirus*, and is classified with the families *Arteriviridae* and *Roniviridae* in the order *Nidovirales*. Members of the *Coronaviridae* share the common feature of pleomorphic, enveloped virions with diameters of 126–160 nm and prominent surface projections. The nucleocapsid is helical and contains a single molecule of linear, positive-sense ssRNA. Coronavirus-like particles have been isolated from a common carp from Japan showing petechial hemorrhages on the skin and abdomen. A similar virus has also been isolated from moribund colored carp (*Cyprinus carpio*) with ulcerative dermal lesions. The investigators were able to grow the virus in epithelioma papulosum cyprini (EPC) cells and produce the same disease in carp injected with the tissue culture grown virus. Further characterization of these virus isolates was never carried out and there was no confirmation that they are, indeed, coronaviruses.

Recently, a novel virus with morphological features resembling those found in rhabdo-, corona-, and baculoviruses has been detected during the routine diagnostic screening of white bream (*Blicca bjoerkna*) in Germany. Ultrastructural studies indicated that the cell-free virions contain a rod-shaped nucleocapsid similar to that seen in baculoviruses. Virions are bacilliform-shaped structures somewhat reminiscent of plant rhabdoviruses with an envelope containing coronavirus-like spikes. Sequence analysis has indicated that the 26.6 kbp white bream virus (WBV) contains five open reading frames, ORF1a, -1b, -2, -3, and -4, which are produced from a 'nested' set of 3'-coterminal mRNAs. The largest mRNA is of genome length. ORF1a and ORF1b form the viral replicase gene. ORF1a encodes several membrane domains, a putative ADP-ribose 1'-phosphatase, and a chymotrypsin-like serine protease. ORF1b encodes the putative polymerase, helicase, ribose methyltransferase, exoribonuclease, and endoribonuclease activities. These characteristics are consistent with classification of WBV in the order *Nidovirales*. Phylogenetic analyses of the helicase and polymerase core domains indicate that WBV is more closely related to toroviruses than to coronaviruses and it has been suggested that a new nidovirus genus *Bafinivirus* be established (from bacilliform fish nidoviruses).

Togaviridae

The family *Togaviridae* comprises the genera *Alphavirus* and *Rubivirus* among the vertebrate viruses. These viruses have spherical virions, 70 nm in diameter, with a lipid

envelope containing glycoprotein peplomers and a ssRNA genome which is capped at the 5'-end and polyadenylated at the 3'-end. Salmonid alphaviruses (SAVs) cause mortality in salmon and trout in Europe (Norway, France, UK, and Ireland). At least three subtypes of SAV exist: Salmon pancreas disease virus (SPDV/SAV-1) in Atlantic salmon; sleeping disease virus (SDV/SAV-2) in rainbow trout; and Norwegian salmonid alphavirus (NSAV/SAV-3). An early study on the evolutionary relationships of the alphaviruses has indicated that SAVs represent a separate and distant group in the genus *Alphavirus*.

Pancreas disease, due to SPDV (SAV-1) infection, was first described in Scotland in Atlantic salmon. It occurs during the first year at sea following transfer of young fish from freshwater tanks. The fish become anorexic and exhibit sluggish swimming activity with mortality rates reaching 10–50%. Histological examination of the affected fish has shown pancreatic acinar necrosis, and cardiac and skeletal myopathy. In rainbow trout, SDV (SAV-2) infection is characterized by the unusual behavior that fish lie on their side at the bottom of the tank. The lesion responsible for this behavior is red and white muscle degeneration. The histological lesions are similar to those observed in SPDV infection with progressive pancreatic necrosis and atrophy, multifocal cardiomyopathy and muscle degeneration.

Caliciviridae

San Miguel sea lion virus (SMSV) is classified in the species *Vesicular exanthema of swine virus* in the genus *Vesivirus* in the family *Caliciviridae*. Investigators have found that the serotype 7 strain of the virus (SMSV-7), isolated from the opaleye fish (*Girella nigricans*), can produce vesicular exanthema in swine. Thus, it is a virus that can jump from fish to mammals. The same serotype has also been reported in elephant seals and a sea lion trematode. Tissue culture grown serotype 5 SMSV injected into opaleye replicated to high titer 15 °C, producing 10^{7.6} TCID₅₀ per gram of spleen. There is no apparent disease in opaleye caused by this virus.

SMSV virions are nonenveloped with icosahedral symmetry and are 27–40 nm in diameter. The genome consists of a 7.5–8.0 kbp linear, positive-sense ssRNA that contains a covalently linked protein (VPg) attached to its 5'-end. The 3'-end of the genome is polyadenylated. The nonstructural polypeptides are encoded as a polypeptide in the 5'-end of the genomic RNA, while the single structural protein is encoded in the 3'-end. The identity of nonstructural polypeptides 2C (RNA helicase), 3C (cysteine protease), and 3D (RNA-dependent RNA polymerase) has been suggested by similarity to highly conserved amino acid motifs in the nonstructural proteins of the picornavirus superfamily. Phylogenetic analysis of the capsid protein region of caliciviruses including the

Sapporo-like human caliciviruses indicate that the genus *Vesivirus* includes SMVL-1, SMSV-4, SMSV-13, SMSV-15, SMSV-17, three feline caliciviruses, and the primate calicivirus Pan-1. These viruses are distant from the human caliciviruses and the rabbit caliciviruses.

Retroviridae

The family *Retroviridae* consists of two subfamilies, the *Orthoretrovirinae*, containing six genera, and the *Spumaretrovirinae*, containing only one genus. The piscine retroviruses constitute the genus *Epsilonretrovirus*, a genus established within the *Orthoretrovirinae* to include the piscine retroviruses: walleye dermal sarcoma virus (WDSV), walleye epidermal hyperplasia virus type 1 (WEHV-1), walleye epidermal hyperplasia virus type 2 (WEHV-2), and snakehead retrovirus (SnRV). The genomes of all of these viruses have been sequenced. There are also numerous reports of C-type (retrovirus-like) particles of about 110–150 nm in epidermal papillomas of European smelt (*Osmerus eperlanus*) and in cells cultured from neurofibromas of damselfish (*Pomacentrus partitus*). A retrovirus has also been suggested as the etiological agent of plasmacytoid leukemia in Chinook salmon.

The first report of a retrovirus-like agent in fish was made in 1976 in lymphosarcoma of northern pike and muskellunge (*Esox masquinongy*). The lymphosarcoma lesions contained a reverse transcriptase-like DNA polymerase with a temperature optimum of 20 °C. The first molecular evidence for a piscine retrovirus was reported in 1992 for a type C retrovirus from dermal sarcomas that form on the surface of adult walleye. These tumors are formed on the surface of adult walleye (*Stizostedion vitreum*) in the fall and regress in the spring. The genome of the virus (13.2 kbp) was larger than all other known retroviruses at the time. Sequence analysis indicated that WDSV contained three additional open reading frames: ORF C at the 5' terminal end; and ORF A and ORF B at the 3' terminal end. ORF A encodes a D-cyclin homolog (retroviral cyclin) that locates in the nucleus of tumor cells in interchromatic granule clusters. ORF C encodes a cytoplasmic protein that targets the mitochondria and is associated with apoptosis. It is expressed in regressing tumors when full-length viral RNA is synthesized. The function of the protein encoded in ORF B, which is distantly related to ORF A, remains unknown. The WDSV protease cleavage sites have been identified to contain glutamine in the P2 position. The WDSV reverse transcriptase is rapidly inactivated at temperatures greater than 15 °C; a finding that is consistent with adaptation to growth in a coldwater fish species.

Two additional retroviruses have been cloned from epidermal hyperplasias on walleye. The genome sequences indicate that they are distinctly different from each other (77% identity) and from WDSV (64% identity). Walleye

epidermal hyperplasia viruses 1 and 2 (WEHV-1 and -2) have genome organizations similar to WDSV. Each of the walleye retroviruses produces lesions when a cell-free filtrate from homogenized tumors is injected in naïve walleye juveniles.

Complete nucleotide sequence and transcriptional analyses of snakehead fish retrovirus have also been reported. The proviral genome is arranged in a typical 5'-LTR-gag-pol-env-LTR-3' retrovirus organization. There are three additional ORFs: ORF1 encoding a 52 aa protein (5.7 kDa); ORF2 encoding a 94 aa protein (11 kDa); and ORF3 encoding a 205 aa protein (24 kDa). BLAST searches for possible homologs of these proteins have not produced any meaningful matches and their functions remain unknown. The SnRV genome differs from the retroviruses of walleye in that it has no ORF between the Unique region in the 5' LTR (U5) and the gag region. The pathogenicity of SnRV has also not been determined.

In 2006, a novel piscine retrovirus was identified in association with an outbreak of leiomyosarcoma in the swimbladders of Atlantic salmon. The swimbladder sarcoma virus (SSSV) provirus is 10.9 kbp in length with a simple *gag-pro-pol, env* gene arrangement similar to that of murine leukemia viruses. Phylogenetic analysis of pol sequences suggests that SSV is most closely related to the sequenced zebrafish endogenous retrovirus (ZFERV) and that these viruses represent a new group of piscine retroviruses.

Reoviridae

Reoviruses that infect aquatic animals are grouped in the genus *Aquareovirus* in the family *Reoviridae* and are characterized by a nonenveloped double capsid shell, 11 segments of double-stranded RNA and seven structural proteins. John Plumb isolated the first finfish reovirus, golden shiner virus, GSRV, from golden shiner (*Notemigonus crysoleucas*) in 1979. Since then, several reovirus-like agents have been reported in piscine, molluscan, and crustacean hosts. Each has 11 segments of dsRNA and grow at temperatures that reflect their host range. The aquareoviruses have been divided by RNA–RNA hybridization kinetics into six groups (A–F) and several tentative species (Table 2). The type species of the genus *Aquareovirus* is *Aquareovirus A* which includes striped bass (*Morone saxatilis*) reovirus (SBRV). Like other reoviruses, the aquareoviruses are either resistant and resistant to acid to pH3.

Most aquareovirus isolates are nonpathogenic or of low virulence in their host species. Grass carp virus (GCV; species *Aquareovirus C*) is the exception and appears to be the most pathogenic aquareovirus. GCV was isolated from grass carp in the People's Republic of China, causing severe hemorrhagic disease and affecting about 85% of infected fingerling and yearling populations.

Table 2 Species and tentative species of aquareoviruses

<i>Aquareovirus A</i>	
Angelfish reovirus AFRV	
Atlantic salmon reovirus HBR	
Atlantic salmon reovirus ASV	
Atlantic salmon reovirus TSV	
Chinook salmon reovirus DRC	
Chum salmon reovirus CSV	
Threadfin reovirus	
Herring reovirus HRV	
Masou salmon reovirus MSV	
Smelt reovirus	
Striped bass reovirus	
<i>Aquareovirus B</i>	
Chinook salmon reovirus B	
Chinook salmon reovirus LBS	
Chinook salmon reovirus YRC	
Chinook salmon reovirus ICR	
Coho salmon reovirus CSR	
Coho salmon reovirus ELC	
Coho salmon reovirus SCS	
<i>Aquareovirus C</i>	
Golden shiner reovirus ^a	
Grass carp reovirus	
<i>Aquareovirus D</i>	
Channel catfish reovirus	
<i>Aquareovirus E</i>	
Turbot reovirus	
<i>Aquareovirus F</i>	
Chum salmon reovirus PSR	
Coho salmon reovirus SSR	
Tentative species of Aquareoviruses	
Chub reovirus	
Landlocked salmon reovirus	
Tench reovirus	

^aGrass carp reovirus and Golden shiner reovirus are variants of the same virus. Table 2 taken from ICTVdB-The Universal Virus Database, version 4. <http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB>.

Full-length and partial genome sequences for several members of the genus *Aquareovirus* have been reported. The complete sequence is available for several isolates of GCV, golden shiner reovirus (species *Aquareovirus C*), chum salmon (*O. keta*) reovirus (species *Aquareovirus A*), golden ide (*Leuciscus idus melanotus*) reovirus (tentative species), and striped bass reovirus (species *Aquareovirus A*). Segment 6 of the guppy reovirus has been determined and threadfin (*Eleutheronema tetradactylus*) reovirus (untyped) segments 10, 6, and 11 are available. Segment 1 encodes a putative guanylyl/methyl transferase; segment 2 encodes the RNA-dependent RNA polymerase; segment 3 encodes a dsRNA binding protein with NTPase and helicase activity; segment 4, a nonstructural protein; segment 5, a NTPase core protein; segment 6, the outer capsid protein; segment 7, a nonstructural protein; segment 8, a core protein; segment 9, a nonstructural protein; segment 10, the external capsid protein; and segment 11, a nonstructural protein. Phylogenetic comparisons of the available sequences support the

current taxonomic classification of the aquareoviruses and orthoreoviruses in two different genera, a distinction that was made originally on their genome segment number and specific econiches.

Birnaviridae

Members of the *Birnaviridae* have single-shelled non-enveloped capsids and genomes comprising two segments of double-stranded RNA. There are three genera in this family: *Aquabirnavirus*, *Avibirnavirus*, and *Entomobirnavirus*. The names of each genus denote the host specificity. The larger genome segment A encodes a polyprotein containing the virion capsid protein VP2, an autocatalytic protease NS, and an internal capsid protein VP3 in the physical order 5'-VP2-NS-VP3-3' in the positive sense. There is an additional 17 kDa protein encoded in a second reading frame at the 5'-end of RNA segment A and it has been shown to be a novel anti-apoptosis gene of the Bcl-2 family. Segment B encodes the virus RNA-dependent RNA polymerase. There is no evidence of 5'-capping of any of the viral mRNAs.

The type species of the genus *Aquabirnavirus* is *Infectious pancreatic necrosis virus* (IPNV). Infectious pancreatic necrosis is a highly contagious viral disease of salmonid fish. The disease most characteristically occurs in fry of rainbow trout, brook trout (*Salvelinus fontinalis*), brown trout (*S. trutta*), Atlantic salmon, and several species of Pacific salmon. In salmonid fish, the virus causes an acute gastroenteritis and destruction of the pancreas. The signs of the disease are typically darkening, a pronounced distended abdomen, and a spiral swimming motion. The virus has also been associated with disease in Japanese eels (*Anguilla japonica*) in which it causes nephritis, menhaden (*Brevoortia tyrannus*) in which it causes a 'spinning disease', and in yellowtail fingerlings (*Seriola quinqueradiata*). A birnavirus has been associated with hematopoietic necrosis, causing high mortalities in turbot with renal necrosis, and birnaviruses have been isolated from clams exhibiting darkened gills and gill necrosis. A nontypical apoptosis has been observed in cultured cells infected by IPNV.

Transmission of the virus can occur via the feces of piscivorous birds. Fish that survive an IPNV outbreak become IPNV carriers and continue to shed the virus for life. Most IPNV isolates are antigenically related and belong to one large serogroup A. There is only one virus in serogroup B, a clam Tellina virus. More recent studies using comparisons of the deduced VP2 amino acid sequence have identified six genogroups. Genogroup 1 (equivalent to serotype A1) comprises four subgroups: genotypes 1, 2, 3, and 4. With increased culture of marine species of fish, there have been increasing reports of mortalities in yellow tail and amberjack in Japan from marine aquabirnaviruses.

Several vaccines have been developed for IPNV, including bacterially produced capsid protein and a DNA vaccine. The protein vaccine has been moderately effective in reducing the lethal effects of IPNV infection in Atlantic salmon in Norway. However, control methods still rely on quarantine and certification of eggs/fry as disease free.

DNA Viruses of Fish

Iridoviridae

In the family *Iridoviridae*, the genera *Iridovirus*, *Lymphocystivirus*, *Ranavirus*, and *Megalocystivirus* contain all of the known iridoviruses that infect fish. Their common features are icosahedral virions, 120–350 nm in diameter, that may acquire an envelope, and a viral genome consisting of one molecule of linear dsDNA of 100–303 kbp. Lymphocystis disease was one of the first fish diseases to be described due, in large part, to the characteristic giant cells observed in the connective tissue and benign nodules in the skin of plaice (*Pleuronectes platessa*) and flounder (*Platichthys flesus*). The causative agent, lymphocystis disease virus (LCDV), has been detected in more than 140 species of freshwater, estuarine, and marine fishes.

Six iridovirus genomes have been completely sequenced, including those of the *Lymphocystis disease virus 1* (LCDV-1, genus *Lymphocystivirus*), Chilo iridescent virus (CIV, species *Invertebrate iridescent virus 6*, genus *Iridovirus*), Tiger frog virus (TFV, species *Frog 3 virus*, genus *Ranavirus*), *Infectious spleen and kidney necrosis virus* (ISKNV, genus *Megalocystivirus*), *Abystoma tigrinum virus* (ATV, genus *Ranavirus*), and Singapore grouper iridovirus (SGIV, tentative species, genus *Ranavirus*). Comparisons of the different iridovirus genomes have revealed that many genes have been conserved during evolution and, among closely related species, the gene order is well preserved. The number of genes (ORFs) in viruses of this family range from 93 (ATV) to 468 (CIV). There are 195 ORFs in LCDV-1 and 120 ORFs in GIV.

Other iridovirus diseases of fish include epizootic hematopoietic necrosis which is caused by viruses in the species *Epizootic hematopoietic necrosis virus* (EHNV, genus *Ranavirus*) in perch and rainbow trout, European sheatfish virus (ESV, genus *Ranavirus*) in sheatfish (*Silurus glanis*), and European catfish virus (ECV, genus *Ranavirus*) in catfish. ESV and ECV are classified as the same species, *European catfish virus*. *Santee-Cooper ranavirus* (SCRV) is the species name given to three iridoviruses: largemouth bass iridovirus (LMBV), doctor fish virus (DFV-16), and guppy virus (GV-6). The white sturgeon iridovirus group (WSIV) is comprised of a group of unassigned viruses that infect sturgeon in North America and Russian sturgeon (*Acipenser guldenstadti*) in Europe. Red seabream

iridoviruses (RSIV) (genus *Megalocystivirus*) causes mortality in cultured juvenile red sea bream in Japan. It has also been observed in grouper in Thailand. Two goldfish iridovirus-like viruses (goldfish virus 1 and 2, GFV-1 and -2) have been isolated from swimbladder tissue culture of healthy goldfish. Electron microscopic observations of iridoviruses in the cytoplasm of erythrocytes (viral erythrocytic necrosis, VEN) have been observed in many marine and anadromous bony fish.

Herpesviridae

Herpesviruses have been isolated from channel catfish (*Ictalurus punctatus*), common and koi carp (*C. carpio*), common goldfish (*Carassius auratus*), eel (*Anguilla* spp.), rainbow trout, masou salmon, lake trout (*S. namaycush*), sturgeon, walleye, and Japanese flounder. Channel catfish virus is the only fish herpesvirus assigned to the genus, *Ictalurivirus*, and this genus is not assigned to any of the three subfamilies (*Alphaherpesvirinae*, *Betaherpesvirinae*, and *Gammaherpesvirinae*) of the family *Herpesviridae*. The other fish herpesviruses, cyprinid herpesviruses 1 and 2 (CyHV-1 and CyHV-2), koi herpesvirus (CyHV-3), salmonid herpesvirus 1 and 2 (SalHV-1 and -2), eel herpesvirus (*Anguilla* herpesvirus, AngHV-1), and the acipenserid or white sturgeon herpesviruses remain as unassigned members of the family *Herpesviridae*. Electron micrographic evidence of herpesviruses has been found in sharks, eels, pike, flounder, perch, angelfish, grouper, and other fish.

The genomes of fish herpesviruses range in size from 134 to 295 kbp and the physical organization of the genome varies sufficiently to suggest that they have evolved separately from the herpesviruses of birds and mammals. The genome of *Ictalurid herpesvirus 1* (IcHV-1) or Channel catfish virus has a unique long (UL) region flanked by a substantial direct repeat that is similar to the betaherpesviruses of the genus *Roseolovirus*. The SalHV-1 genome is more similar in organization to the alphaherpesviruses of the genus *Varicellovirus* with a unique short (US) region flanked by a unique long (UL) region which is not flanked by a repeat. Phylogenetic comparisons of the individual genes including the DNA polymerase gene, the major capsid protein gene, the intercapsomeric triplex protein gene, and the DNA helicase gene indicate that the three cyprinid viruses are closely related and are distinct from IcHV-1.

These viruses are serious pathogens in their respective hosts. IcHV-1 outbreaks among juvenile catfish result in mortality and fish that survive the infection become carriers. The cyprinid herpes viruses produce a systemic disease with lesions in hematopoietic tissue in goldfish and papillomas on the caudal regions in koi carp. SalHV-2 was isolated from the ovarian fluid of masou salmon and it induces syncytia formation and lysis of

infected cells. Epithelial papillomas are induced in young masou salmon injected with tissue culture-grown virus. The acipenserid herpesviruses cause serious losses in hatchery-reared young of white sturgeon (*Acipenser transmontanus*).

Adenoviridae

Adenovirus particles have been observed in lesions in a number of fish species and have been isolated from white sturgeon, dabs (*Limanda limanda*), cod, and Japanese red sea bream. The white sturgeon adenovirus has been isolated in tissue culture and its hexon protein and protease gene sequences are available. Based on an alignment of partial DNA polymerase gene sequences of the sturgeon adenovirus and 24 other adenovirus types, it is clear that the fish adenovirus is distantly related to the other adenoviruses, and might constitute a fifth genus of the *Adenoviridae*.

Adenovirus infection in cod produces an epidermal hyperplasia. In California, white sturgeon adenovirus affects young fish in hatcheries. Infection is characterized by epithelial hyperplasia and enlarged cell nuclei. A lympholeukemia has been observed in red sea bream and papillomas have been observed in dabs infected with adenoviruses.

See also: Fish and Amphibian Herpesviruses; Fish Rhabdoviruses; Fish Retroviruses; Aquareoviruses; Infectious Pancreatic Necrosis Virus; Infectious Salmon Anemia Virus.

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Flaviviruses of Veterinary Importance

R Swanepoel, National Institute for Communicable Diseases, Sandringham, South Africa

F J Burt, University of the Free State, Bloemfontein, South Africa

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Glossary

Argasid Soft-skinned tick, member of the family *Argasidae*.

Arthropod Any member of the phylum Arthropoda, including insects and arachnids (spiders, scorpions, ticks, and mites).

Culicoid midge Blood-sucking midge of the genus *Culicoides*.

Instar Stage in the life cycle of arthropods, for example, egg, larva, nymph, and adult in mosquitoes; egg, larva, nymph, and adult in ticks.

Ixodid Tick with a hardened shell or scutum.

Microhabitat The environmental niche in which an organism is found.

Phlebotomine fly Blood-sucking sandfly of the genus *Phlebotomus*.

Phylogenetics The study of the genetic relatedness of organisms.

Transovarial transmission of virus Passage of virus infection through the eggs of arthropods to the succeeding generation, thus ensuring perpetuation of the virus.

Vectors Blood-sucking arthropods (mosquitoes, midges, sandflies, and ticks) which transmit viruses from one vertebrate to another.

Virion A complete virus particle with its protein coat and core of DNA or RNA nucleic acid.