

Viral spillover among diverse animals in the water environment: Risks, mechanisms, and prevention

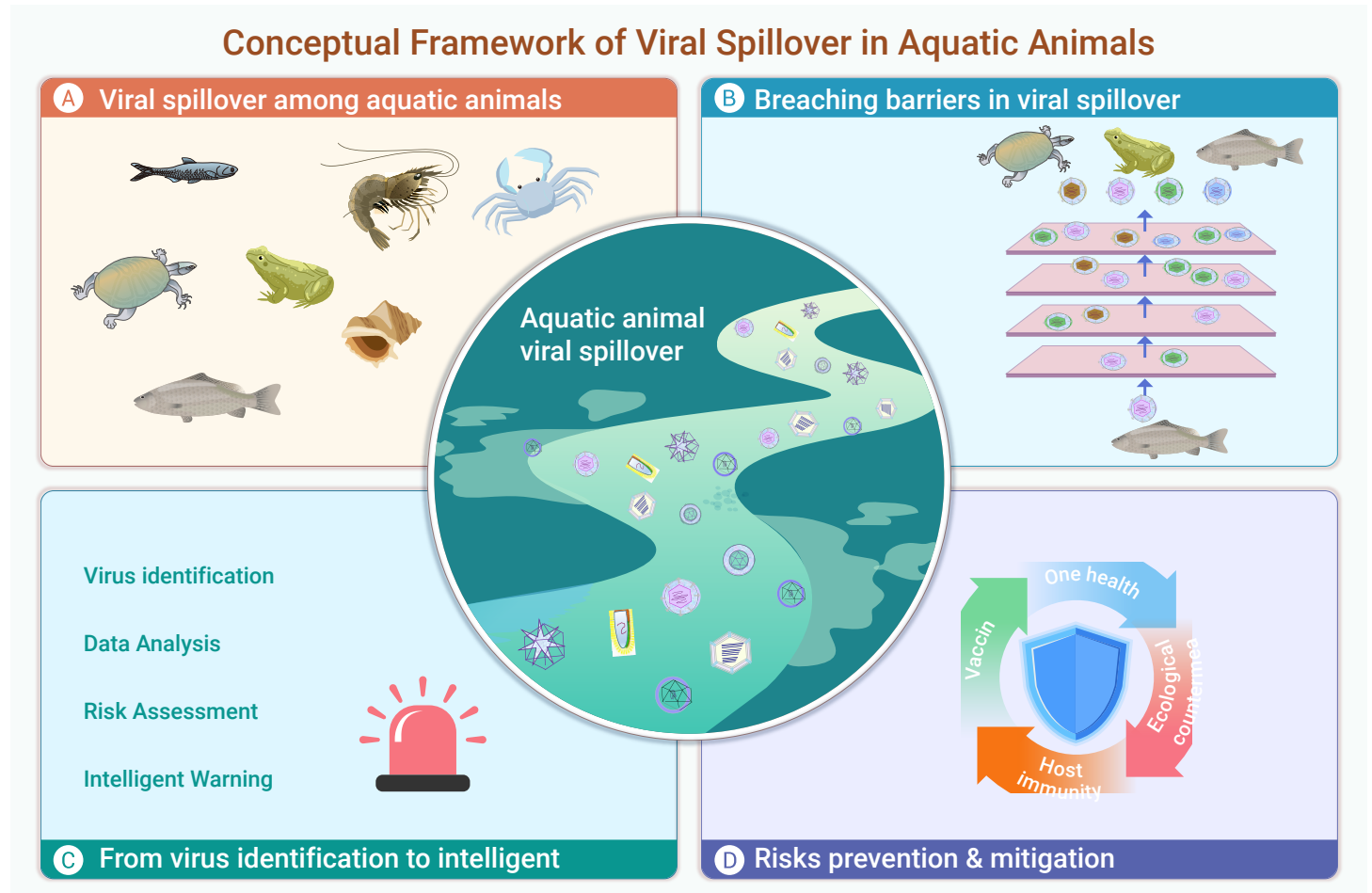
Qi-Ya Zhang,^{1,*} Fei Ke,¹ and Jian-Fang Gui¹

*Correspondence: zhangqy@ihb.ac.cn

Received: August 16, 2026; Accepted: September 8, 2026; Published Online: September 8, 2026; <https://doi.org/10.59717/j.tiw.2026.100014>

© 2026 The Author(s). This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>).

GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Frequent viral spillover (cross-species transmission) severe harm aquaculture and aquatic ecosystems.
- Modelling spillover dynamics builds radial maps illustrating pathogenic aquatic-animal viral spillover.
- Systematic mapping of viral spillover barriers and transmission routes can help uncover their underlying drivers.
- Construct a prevention and control framework integrating multi-source data and multidisciplinary approaches.

Viral spillover among diverse animals in the water environment: Risks, mechanisms, and prevention

Qi-Ya Zhang,^{1,*} Fei Ke,¹ and Jian-Fang Gui¹

¹State Key Laboratory of Breeding Biotechnology and Sustainable Aquaculture, Institute of Hydrobiology, Chinese Academy of Sciences, Wuhan 430072, China

*Correspondence: zhangqy@ihb.ac.cn

Received: August 16, 2026; Accepted: September 8, 2026; Published Online: September 8, 2026; <https://doi.org/10.59717/j.tiw.2026.100014>

© 2026 The Author(s). This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>).

Citation: Zhang Q.-Y., Ke F. and Gui J.-F. (2026). Viral spillover among diverse animals in the water environment: Risks, mechanisms, and prevention. *The Innovation Water* 1:100014.

Viruses are ubiquitous, immensely diverse and vast biomass, forming a pivotal engine of global biogeochemical cycles. However, the frequent outbreak of viral pathogens in aquatic animals poses a serious threat to aquaculture industry, aquatic ecosystems, and environment. It devastates aquaculture industries, drives water quality deterioration through the perturbation of viral ecological functions, and ultimately endangering security of aquatic ecosystems. "Viral spillover in aquatic animals" denotes the cross-species transmission of viruses that can ignite widespread disease outbreaks and cascading ecological impacts in both farmed and wild aquatic animals. While viral spillover involving humans and land animals has received focus, viral spillover in aquaculture remains noticeably missing from global discourse. Thus, the emergence and spillover of novel viruses in aquatic animal loom as a paramount, decades challenge for the global aquaculture sector. To address this challenge, this review focuses on elucidating the diversity, complexity, and ubiquity of spillover of aquatic animal viruses. By simulating spillover dynamics, it constructs radial maps depicting the diffusion of aquatic animal viruses; analyzes representative cases to decipher relevant determinants; deconstructs the viral spillover process to reveal underlying driving mechanisms; and on risk identification and mechanistic analysis, builds an integrated prevention framework that synthesizes multi-source data and multidisciplinary approaches, thereby supporting precise and forward-looking decision-making for health security of aquatic animals and ecosystems.

INTRODUCTION

Viruses can infect all living creatures, and exist in staggering numbers. Virology has made enormous advances in the last 50 years,¹ especially in preceding viral epidemics and pandemics.² The recurrent emergence of pandemic viruses has also aroused a global scale of public vigilance and profound concern.³ From this point on, virology will enter an unprecedented phase of discovery and exploration. Aquatic viruses are widely present in the aquatic environment. Some of them can also cross species barriers,^{4,5} infect and kill diverse aquatic organisms, thereby triggering cascade effect in aquatic ecosystems and biogeochemical cycles.⁶⁻¹¹

Aquaculture, also referred to as "underwater agriculture", is the fastest growing food-producing sector in the world.¹² It had already overtaken beef and overtakes poultry in protein production (<https://sustainablog.org/articles/fish-farming-overtakes-beef/>; <https://www.bluelifehub.com/2025/01/28/aquaculture-accelerates-and-overtakes-poultry-in-protein-production/>).¹³ At present, on the basis of obtaining successful aquaculture paradigms,^{14,15} sublimating the traditional aquaculture wisdom, reutilizing rice-fish integrated farming,¹⁶ and developing new quality of productivity forces have been carried out, and numerous innovative achievements have been produced in fisheries and aquaculture.¹² In addition, clean aquaculture practices and environmental management also offered assistance to aquaculture sustainable development. Especially several fish genetic improvements, such as key gene editing-based approach, have been developed.¹⁷ Through these biotechnology approaches, genome-reconstructed polyploids,^{18,19} and intermuscular bone-free mutants,^{20,21} have been created in fish. And the genome reconstructed *Carassius* polyploid has been demonstrated to possess high resistance to herpesvirus.¹⁹

In different water bodies, however, both farmed and wild aquatic animals have been seriously threatened from various viral and pathogenic infections.^{22,23} Emerging epidemic diseases often originate from the spillover transmission of viral pathogen. In aquatic environments, viruses can even

interact with hosts across vast phylogenetic distances.²⁴ More seriously, the emerging infectious diseases in fish have caused economic losses of up to six billion US dollars per annum,^{25,26} exceeding 40% of global capacity.²⁷

Viral spillover (or cross-species transmission) occurs when a virus jumps into a novel host, establishes infection, and amplifies within the new host population, and thereby triggers a disease outbreak.²⁸ Therefore, viral spillover is no longer a simple one-to-one host jump, but increasingly follows a one-to-many pattern. Even existing evidence suggests that the same virus can replicate in hosts of fungi, plants, and animals, highlighting its potential for cross domain spillover and pathogenicity.^{6,29,30} In some highly pathogenic viruses of aquatic animals, the emergence and spillover also exhibit significant diversity and evolutionary complexity, pose the trend of global spread.³¹ Frequent spillover of RNA viruses further drives cross-species transmission and their host range expansion, increasing the difficulty of disease prevention and control.³² Obviously, aquatic viruses have the ability to spillover (jump from one host species to another) and survive in many unrelated hosts, even lead to catastrophic consequences for the novel host.³³ It is believed that aquaculture will become the primary source of aquatic dietary protein in the next two decades. Therefore, only by prioritizing the research and prevention efforts on the virus spillover among aquatic animals, can we promote sustainable development of aquaculture and ensure the health and welfare of aquaculture organisms and the environmental integrity.³⁴ Of course, only by understanding the characteristics of the spillover virus can the targeted intervention measures be implemented to halt the viral transmission.^{35,36} In short, aquatic viral spillover poses critical questions: why are the viral pathogen so diverse and so prone to outbreaks? How can monitoring and evaluation system be established? The following will delve several deeper comprehensions and discussions into this topic.

VIRUS SPILLOVER FROM AQUATIC ANIMALS

When viruses "spillover", "jump" or "cross-species transmission" occurs from the natural host to new host populations, the risk of epidemic viral disease will soar, and even trigger a public health emergency.³⁷ Although no consensus definition of "viral spillover" exists and the mechanisms governing aquatic animal virus spillover remain largely uncharacterized,³⁸ the risk that spillover events originate from highly pathogenic viral pathogens is escalating rapidly.³⁹⁻⁴³ Additionally, global trade and material flows render future viral spillovers inevitable.^{44,45} Currently, aquatic animal virus spillover has become one of recent research hotspots.^{46,47}

Extensive occurrence of aquatic animal virus spillover

As "a planet of viruses", viral pathogens can coexist with their host animals over extended periods, yet they also have the potential to spill over and spread out on a global scale.⁴⁸ And viruses are significant constraint on aquaculture because they directly lead to reduced fish production. Unlike terrestrial animals, both farmed and wild aquatic animals are more susceptible to common viral pathogens in aquatic environments. Aquatic animal viral spillover can impact the hydrographic environment by polluting water resources, reducing biodiversity, and triggering public health security issues.^{5,49} Historical evidence shows that over the past few decades, spillover-driven epidemics have increased not only in frequency but also grown in scale.⁵⁰ And the number of emerging (or spillover) aquatic viruses is also on the rise.

The viral spillover events have extensively occurred in aquatic animals including *Rhabdoviruses*, *Iridoviruses* (including *Ranaviruses*), and *Herpesviruses* etc., as shown in Figure 1, the radial schematic. The schematic

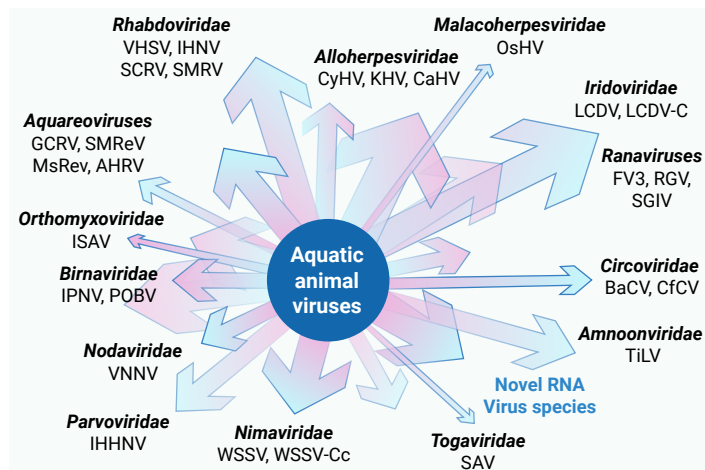


Figure 1. Radial schematic of aquatic animal virus spillover Starting from the upper left and moving clockwise, abbreviations are listed below. **Rhabdoviridae**: VHSV, Viral hemorrhagic septicemia virus. IHNV, Infectious haematopoietic necrosis virus. SCRv, *Siniperca chuatsi* rhabdovirus. SMRV, *Scophthalmus maximus* rhabdovirus. **AlloHerpesviridae**: CyHV, Cyprinid herpesvirus. KHV, Koi Herpesvirus. CaHV, *Carassius auratus* herpesvirus. **Malacoherpesviridae**: OsHV, *Ostreid* herpesvirus. **Iridoviridae**: LCDV, Lymphocystis disease virus. LCDV-C, Lymphocystis disease virus-China. **Ranaviruses**: FV3, Frog virus 3. RGV, *Rana grylio* virus. ADRV, *Andrias davidianus* ranavirus. SCRv, Mandarin fish *Siniperca chuatsi* ranavirus. MSRAV, Largemouth bass *Micropterus salmoides* ranavirus. **Circoviridae**: BaCV, Barbel circovirus. CfcV, European catfish (*Silurus glanis*) circovirus. **Amnoonviridae**: TILV, Tilapia lake virus. **Togaviridae**: SAV, Salmonid alphavirus. **Nimaviridae**: WSSV, White spot syndrome virus. WSSV-Cc, freshwater crayfish *Cambarus clarkii* whispovirus. **Parvoviridae**: IHHNV, Infectious hypodermal and hematopoietic necrosis virus. TIPV, Tilapia Parvovirus. **Nodaviridae**: VNNV, Viral nervous necrosis virus. MrNV, *Macrobrachium rosenbergii* nodavirus. **Birnaviridae**: IPNV, Infectious pancreatic necrosis virus. POBV, *Paralichthys olivaceus* birnavirus. **Orthomyxoviridae**: ISAV, Infectious salmon anemia virus. **Aqueoviruses**: GCHV, Grass carp hemorrhage virus. SMReV, *Scophthalmus maximus* reovirus. MsReV, *Micropterus salmoides* reovirus. AHRV, Atlantic halibut reovirus.

diagram roughly illustrates the groups of representative aquatic animal viruses, the spillover events, and their relative abundances.

Spillover in Rhabdoviruses

Rhabdoviridae is a large family of negative-sense RNA viruses in a broad host range of mammals, birds, reptiles, amphibians, and fishes.⁵¹ And aquatic rhabdoviruses have the potential for alternating spillover and spillback infections between amphibians and fishes.⁴⁶ Over a hundred strains of viral hemorrhagic septicemia virus (VHSV) have been isolated from fishes.^{39,52} This virus is also one of the pathogens that pose a continuous threat to global food security. And the virus can cross species barriers, in which it can infect both freshwater and marine fishes, as well as many kinds of wild marine fishes.^{53,54} Due to wide diversity of host fish species, wide geographical distribution, strong pathogenicity, rapid disease progression, and high mortality rate, the cross species transmission of VHSV has made it one of the most destructive fish viruses in the world.⁵⁵

Researchers have explored the ecology and epidemiology of VHSV using an ecological niche modeling approach. It exhibits high lineage diversity in Eurasia, broad ecological niche and significant ecological plasticity. The virus was detected in over 140 fish species in marine and freshwater ecosystems.^{55,56} This virus can spread to various host species by contaminating water bodies.⁵⁴ From a total of 1,927 samples of 39 wild marine fish species collected from coastal waters and fjord systems, VHSV was detected in 12 samples by real-time reverse transcription polymerase chain reaction (rRT-PCR).⁵⁷ Another rhabdovirus, the infectious hematopoietic necrosis virus (IHHNV), was also tested, by analyzing the glycoprotein (G) gene sequences of 55 viral samples. Its long-distance transmission pathways and mechanisms were revealed.⁵⁸

Spillover in Iridoviridae

The family *Iridoviridae* is composed of seven genera. The viruses in *Iridovirus*, *Chloriridovirus*, *Decapodiridovirus*, and *Daphniairidovirus* infect invertebrate hosts, and the members in *Ranavirus*, *Megalocytivirus*, and

Lymphocystivirus infect cold-blooded vertebrates.^{59,60} *Ranavirus*, *Megalocytivirus*, *Lymphocystivirus*, and *Decapodiridovirus* primarily infect aquatic animals including fishes, amphibians, and reptiles, as well as aquatic crustaceans like shrimp and crabs. Increasing evidence suggests that the emerging viral diseases are one of the primary causes of the worldwide decline in amphibian species.⁶¹ Members of the family *Iridoviridae* are nucleocytoplasmic large DNA viruses (NCLDV) and have been considered as promiscuous pathogens.⁵⁹

Disease caused by lymphocystivirus (lymphocystis disease virus, LCDV) was first discovered in the 19th century. Direct contact and waterborne transmission are the routes accepted for the spreading of LCDV infections.⁶² The morbidity rate caused by this virus can reach up to 70%. And the viral disease has a global distribution that affects more than 125 wild and cultured fish species from marine and freshwater environments.⁶³

Ranaviruses, which originally infected amphibians, have now been detected in a wide range of species across the globe, including anurans (frogs and toads etc.), urodeles (salamanders and giant salamanders etc.), and even fishes. *Ranavirus* isolates have been obtained from various aquatic animals. Not only have ranaviruses with similar genome structures been isolated and identified from amphibians, but also strains with highly homologous genomes have been isolated and identified from different diseased fish species.^{64,65} Some ranavirus strains can cause cross-species infections between anuran and urodele amphibians. The frog-sourced ranavirus (*Rana grylio* virus, RGV) can infect the Chinese giant salamander (*Andrias davidianus*). Conversely, the Chinese giant salamander-sourced ranavirus (*Andrias davidianus* ranavirus, ADRV) can also infect frogs.^{9,66} Based on the genomic sequence information, it is believed that the common ancestor of ranaviruses should be a fish virus, followed by multiple host shifts between amphibians and reptiles. The shift in their host species may also occur from fish to frogs, fish to salamanders, or frogs to turtles, as well as host shifts from amphibians or reptiles back to fishes.⁶⁷

Ranaviruses pose major threats to biodiversity and human livelihoods. Whether in aquatic wildlife or farmed animals, outbreaks of ranavirus disease can lead to massive host mortality and even population collapse.⁶⁸ The discovery that viruses move between species unexpectedly is rewriting ideas about their evolutionary history and may have troubling implications for the threat from emerging diseases. Cross-species transmission events of ranavirus involving aquatic animal viruses have attracted public attention. *Ranaviruses* are widespread across all continents and have been detected in 105 amphibian species in 25 countries.⁶⁹ Recent reports have indicated that with the increasing frequency of ranavirus spillover in the natural world, these viruses have been detected in at least 175 species across six continents.⁷⁰ As evidenced by the presence of frog virus 3 (FV3) in both wild and farmed anuran and caudate amphibians throughout the Americas, Europe, Africa, and Asia. FV3-like strains can cause mortality in genetically diverse and geographically dispersed hosts.⁷¹ Even amphibian chytrid fungi can coinfect their hosts with ranaviruses, and there is a positive correlation between these two pathogens.⁷² There are examples involving ranaviruses jumping from their ancestral fish hosts to other ectothermic animal hosts and subsequently adapting to the new host environments, such as the ATV-like (*Ambystoma tigrinum* virus) group; whereas ranaviruses with amphibian hosts, like FV3s, have jumped from amphibians to fishes.⁷³ Mutated (evolved) ranavirus can spill over from its reservoir host, the frog, into giant salamanders or fishes. Therefore, ranaviruses are considered important emerging pathogens of aquatic animals. With other evidence and possible reasons including (1) Repeated such disease outbreaks in cultured amphibians, fishes and other aquatic animals. (2) Frequent detection of ranavirus infections in invasive species and traded animals in Europe, Asia, and South America. (3) Furthermore, human translocations are believed to have facilitated their range expansion.⁷³

A survey conducted in certain European regions, such as Russia and Portugal indicate that the virus is widely distributed across various host species and altitudinal ranges. The predominant strain is the common midwife toad virus-like (CMTV-like) ranavirus, which is responsible for large-scale mortality in their host events each year.^{74,75} Additionally, recombination has been identified between CMTV-like ranaviruses and FV3-like viruses isolated from the wild,⁷⁶ and the recombined virus has caused massive

mortality among amphibians across continents. FV3 has been identified in turtles in Canada, and the genome sequencing shows that it is a ranavirus similar to the wild-type FV3 DNA sequences.⁷⁷

Ranaviruses exhibit complex interactions with their hosts. The ranavirus replication and transcription machinery was identified as a complicated apparatus containing at least 30 viral and 6 host proteins.⁷⁸ Host proteins play a crucial role in the transcription and replication of viruses, while viruses can also influence the metabolic processes of host cells through various pathways,⁷⁹ and even caused some amphibian species to become extinct.^{80,81} The ranavirus pathogens of cold-blooded vertebrates have the capacity to cross numerous poikilothermic species barriers and the potential to cause devastating disease in their new hosts. They lead to host population decline, alter the composition and structure of host communities, and pose a severe threat to nearly all amphibian populations. Therefore, the amphibian-infected and fish-infected ranaviruses have been listed in the notifiable agents by the World Organization for Animal Health (WOAH).⁶⁸

Ranaviruses infecting reptiles are genetically similar or identical to the viruses that infect amphibians and fishes.⁸² Several cases indicate that the ranaviral infections in native / endemic host species can also cross the barriers of cultured species.⁸³ It is now known that heparan sulfate proteoglycan (HSPG) is a highly sulfated glycosaminoglycan anchored to the cytoplasmic membrane of eukaryotic cells, which can widely mediate virus attachment to cell surfaces.^{84,85} It has been confirmed that the ranaviruses ADRV and RGV, via HSPG, can infect their natural hosts and cells, and also perform cross-species infection.⁸⁶ This is also one of the critical factors why ranaviruses are prone to cross-species transmission or spillover.

Ranaviruses possess complex replication and transcription machinery, and can also collaborate to complete genome replication, modification, and transcription during cross species spillover. Therefore, it facilitates the ranaviruses crossing the species barrier (species jumping), and infecting different aquatic animals.⁷⁸ Briefly, due to the frequent spillover that crosses the species barrier of poikilotherms to infect and replicate, the ranaviruses have become promiscuous pathogens.^{87,88} Figure 2 shows the schematic diagram of ranavirus spillover among different aquatic animals.

Spillover of Tilapia lake virus

Tilapia Lake virus (TiLV) belongs to the family *Amnoonviridae* within the order *Articulavirales*, genus *Tilapinevirus*. It is a single-stranded RNA virus with 10 genomic segments, but is highly diverged from more familiar *Orthomyxoviruses*, such as influenza.⁸⁹ The family includes a single genus with one species for one virus. TiLV was first reported from Israel.⁹⁰ Its genome size is about 10.3 kb.⁹¹⁻⁹³ Its principal hosts, tilapias of the family *Cichlidae*, are biologically diverse and exhibit complex social behaviors.

Nile tilapia (*Oreochromis niloticus*) is the predominant cultured species. It has been farmed in over 100 countries with an estimated global production of over 6.5 million tons annually.⁹⁴ TiLV is a globally emerging fish virus responsible for episodes of mass mortality in cultured and/or feral tilapia (*Oreochromis* spp. and hybrids).⁹⁵ The virus is becoming an epidemic pathogen that can spread widely through diverse pathways in many countries.⁹⁶ It can cause severe anemia and systemic disease in tilapia,⁹⁷ and also establish a persistent infection in the brain of host fishes. As the persistent infection may pose a risk for viral reinfection and ongoing tissue damage and neuroinflammatory processes, therapeutic intervention and disease management become more challenging.⁹⁸ Vacuolation and necrosis in brain, inclusion body and necrosis in heart, megalocytes and necrosis in intestine have been observed in experimentally infected tilapia.⁹⁹ These viruses are commonly found in both farmed and wild tilapia populations worldwide, causing mass mortality events in cultured and/or wild tilapia (*Oreochromis* spp. and their hybrids). More than 45 countries are believed to be at high risk of TiLV,^{100,101} which have threatened the livelihoods and food security of numerous tilapia farmers.^{102,103}

A laboratory controlled TiLV infection was investigated in 10 warm water fish species. The results revealed that red hybrid tilapia and giant gourami developed clinical signs of infection with a cumulative mortality rate of 60–100%. The presence of TiLV in the brain and liver of infected giant gourami was also confirmed using in situ hybridization. Reports of TiLV infections in different fish species are on the increase. Nowadays, these

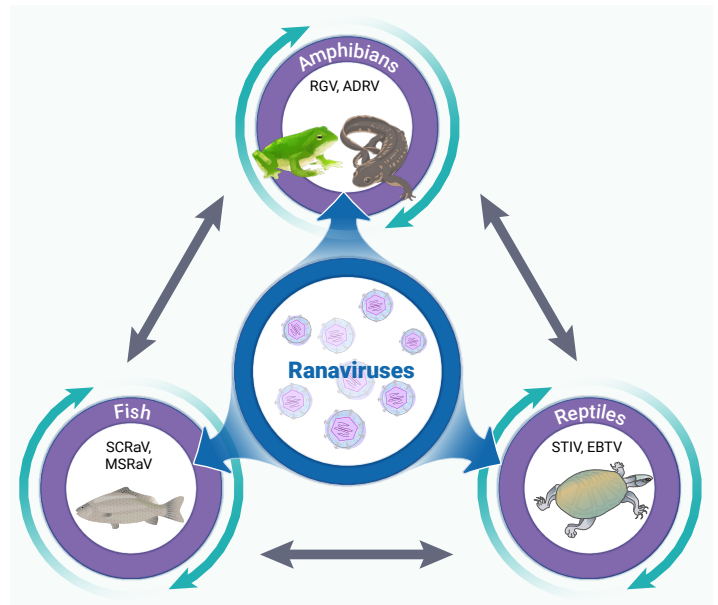


Figure 2. Schematic of ranavirus spillover from different aquatic animals Ranaviruses can jump between frogs, fish, turtles and other aquatic animals, spillover and transmission among different species (arrow-indicated). ADRV, *Andrias davidianus* ranavirus. RGV, *Rana grylio* virus. SCRaV, mandarin fish *Siniperca chuatsi* ranavirus. MSRaV, largemouth bass *Micropterus salmoides* ranavirus. STIV, Soft-shelled turtle iridovirus. EBTv, Eastern box turtles (*Terrapene carolina carolina*) ranavirus. The arrows are mainly based on phylogenetic inferences and partly experimental infection.

viruses are not only commonly found in farmed or wild tilapia populations worldwide, but also infect other fish species.^{104,105} They have also been found in sampled cichlid fish and scaled reptiles (bay tree species) in Africa, Asia, and North America.⁹¹ In addition to tilapia and their hybrids (*Oreochromis* spp., *Tilapia* spp.), this virus can also infect other fish species such as wild cichlids (*Sarotherodon galilaeus*, *Tristramella* spp.) and cause disease.¹⁰⁶ It even infect other species such as river barb (*Barbonymus schwanenfeldii*), infol barbs (*Barbonymus schwanenfeldii*).^{107,108}

The horizontal transmission of TiLV has been demonstrated through the cohabitation of infected fish with susceptible fish, and was also found that the non-fish lake virus may be transmitted vertically.¹⁰⁹ Like the recently reported Covert Mortality Nodavirus (CMNV), which has been listed by WOAH as an important emerging virus in aquaculture. It also spreads through vertically and/or horizontally pathways.¹¹⁰ TiLV can be transmitted between red hybrid tilapia and giant gourami through cohabitation.¹¹¹ TiLV seems a greater tendency to spillover in cultured cells than in fish.¹¹² This may be because cultured cells serving as viral hosts in the dishes lose the physical signals, immune systems, and natural environments that are crucial for their function, resulting in significantly different performance from natural conditions.¹¹³

The emergence of some novel viral pathogens is the result of long-term evolution. Reconstructing the deep phylogenetic history of viruses will help to identify their major evolutionary transitions. The research on the rich biodiversity, continuous evolutionary changes, and extensive geographic distribution of aquatic animal viruses, including rhabdovirus, ranavirus and TiLV, provides evidence for broad spillover potential of aquatic animal viruses. There is evidence to suggest that in the long-term process of evolution, viruses interact and select with their hosts, with genetic variation and changes in transmission modes, viruses break through narrow host ranges and various natural barriers during the infection process, expanding the host range. This resulted new viruses can not only cross species barriers, but also cross kingdoms to infect new hosts.²⁹ It has been revealed that the evolution of the articulaviruses is likely shaped by multiple aquatic-terrestrial transitions and substantial host jumps.¹¹⁴ Biophysical and structural characterisation of RNA-bound oligomers of NP from TiLV have been elucidated. It offers valuable insights into mechanisms of transcription, replication, and genome packaging within the *Articulavirales* order.¹¹⁵

Spillover of herpesviruses

The order *Herpesvirales* is composed of three viral families, namely the families *Herpesviridae* (hosts are reptiles, birds and mammals), *Alloherpesviridae* (hosts are fish and amphibians) and *Malacoherpesviridae* (hosts are molluscs). The family *Alloherpesviridae* contains four genera, *Batrachovirus*, *Cyprinivirus*, *Ictalurivirus*, and *Salmonivirus* (<https://ictv.global/report/chapter/alloherpesviridae/alloherpesviridae>, Posted: November 2024). Herpesviruses are exceptional cases among viral pathogens, exerting pan-species impact via exquisitely orchestrated host–pathogen interactions that span receptor engagement, immune evasion, latency establishment, and reactivation.¹¹⁶

Herpesviruses are common agents in animals of the aquatic environment. The viruses impact a diverse array of aquatic animal species via intricate interactions with host biological systems.^{117,118} They are also important pathogens in fishes which infect a wide range of different species and fish cells.^{119–121} It is now known, at least more than ten herpesviruses cause significant economic losses in aquaculture. They include *Ictalurid herpesvirus* (IcHV) infecting catfish, *Cyprinid herpesvirus* (CyHV) and *Carassius auratus herpesvirus* (CaHV) infecting common carp, crucian carp, and goldfish, *Anguillid herpesvirus* (AngHV) infecting eels, *Acipenserid herpesvirus* (AciHV) infecting sturgeon, and *Salmonid herpesvirus* (SalHV) infecting salmon and trout.^{122,123} In different regions of the world, these viruses can also infect koi, tilapia, grass carp, and other fish species, and lead to host illness and death.¹²⁴ For example, in the late-90s, a devastating outbreak of Koi herpesvirus rapidly spreads to 90% of Israeli carp farms in only a few years, and results in an annual estimated loss of three million USD to the aquaculture industry.¹²⁵ Emerging diseases are usually caused by pathogen spillover and cross-species transmission. Fish herpesviruses can affect other aquatic animal species through complex interactions with host biological systems.¹²⁶

Both symptomatic infections and asymptomatic carriers among fishes can both spillover or transmit herpesviruses to other species, potentially causing disease outbreaks in those populations. Moreover, the genomic sequences of different viral strains can exhibit a high degree of similarity. The CaHV is a representative strain of the cyprinid herpesvirus isolated from diseased crucian carp.¹²⁷ Its genomic sequence has been analyzed and compared with those of koi herpesvirus (KHV), common carp herpesvirus (*Cyprinid herpesvirus*), goldfish herpesvirus (GHV), and *Anguillid herpesvirus* (AngHV). Despite the detection of various mutations, including nucleotide mutations, deletions, insertions, as well as gene duplications, rearrangements, and horizontal transfers in these carp herpesvirus strains, their genomic sequence similarities still reach and even exceed 99%.^{120,128,129} During a long history of coevolution, the genes of herpesviruses can be integrated into the host genome, and herpesviruses have reached a fine-tuned balance with their hosts, allowing them to successfully persist and spread to new hosts.^{123,130,131}

Combining evolutionary approaches with bioinformatics were used to non-viral genome data for viruses by adapting methods from paleovirology. As a result, sequences related to the alloherpesviruses and other large dsDNA viruses were identified in the open access genome data of fifteen species of teleost fishes.¹²⁶ These results from interactions of a great variety of viral and cellular factors together shape the tropism for a particular host, tissue, or cell.¹³⁰ As there are the abilities to establish lifelong relationships with their hosts and trigger recurrent outbreaks, herpesviruses have emerged as formidable players in humans and animals of infectious diseases.¹³² These studies provide valuable insights into the interactions between fish herpesviruses and their hosts, as well as the mechanisms of viral spillover.

Research on fish herpesvirus has made significant progress in various aspects, including its pathogenic characteristics, biological features, and host transmission.^{133–137} In recent years, new advances have also been made in the researches on functional genes of fish herpesviruses and interactions between the virus and the host. Among the proteins encoded by the genome of CaHV, five ring finger proteins have been identified to have diverse structures and functions.¹³⁸ For example, the protein encoded by CaHV-138L can target to mitochondrial protein FoF1 ATPase.¹³⁹ In addition, the resistance to CaHV has been identified deriving from a genomic hotspot region on the chromosome 12B of a novel polyploid.¹⁹ These researches will enhance further understanding of the interactions between viruses and hosts, as well as the mechanisms of fish herpesvirus spillover.

Metagenomic and metatranscriptomic sequencing analyses have revealed extensive risks of cross-species transmission of viruses and other microbial pathogens among non-traditional farmed and wild animals.¹⁴⁰ Herpesviruses are one of the largest and most complex pathogenic viruses and cause a spectrum of diseases, ranging from mild, self-limiting conditions, severe illnesses, to fatal disease. The life cycle of herpesviruses includes two distinct stages: latent infection (reactivation) and lytic replication.¹⁴¹ This increases the probability and complexity of cross-species infections. In short, herpesviruses, through complex interactions with host biological systems, are closely associated with disease progression and impact viral spillover and cross-species transmission.¹⁴²

Spillover of white spot syndrome virus

White spot syndrome virus (WSSV) belongs to the family *Nimaviridae* genus *Whispovirus*. It is an enveloped double-stranded DNA virus and known as one of the largest viruses infecting aquatic animals. It is also the primary pathogen responsible for causing white spot syndrome in crustaceans (such as shrimp, crabs, etc.).

A literature evaluation of WSSV hosts and vectors shows an increase from 33 to 50 families, including 11 families of non-crustacean hosts, which reveals the virus spread across aquatic animals and is causing increasing spillover events.¹⁴³ WSSV can also infect crayfish, other freshwater decapods, and cause their diseases.¹⁴⁴ WSSV has vertical and horizontal routes of transmission, both of which contribute to the rapid disease spread in different shrimp farms and even in nature. Waterborne transmission poses a significant threat, as the infected shrimps continuously release viral particles into the water through gill shedding, secretions, or carcass decomposition, and cause aquatic environmental contamination. Even water with a low level of viral contamination can mediate WSSV spread, and viral shedding can be detected within hours of infection onset.^{145,146} And, the circular stacked capsid structure, the structural transitions during genome release, and the pressure-driven DNA ejection mechanism have been elucidated during WSSV infection.¹⁴⁷ All of the above provide new insights for a better understanding of the WSSV infection process.

PROCESS AND MECHANISM OF VIRUS SPILLOVER

In view of the accelerating trend of viral spillover, it is an urgent need to unravel its complex mechanisms and to develop high-performance, sustainable, and implementable systemic solutions. The core involves structure of viral pathogens, and the dynamic process of viral infection. Detailed research contents should include the variation and evolution of pathogens, their interactions with hosts and environment and the underlying mechanism of virus spillover and driving factors. The top priority at present should construct big and comprehensive datasets, and establish an intelligent monitoring and early warning system. On the whole, existing knowledge of viral spillover is instructive yet far from comprehensive.¹⁴⁸

To achieve cross species spillover, viruses need to break through multiple barriers. In order to complete spillover and transmission, usually, the virus must cross three typical barriers such as accumulation in the natural host, exposure to a new host, and overcoming natural barriers to invade the new host. This multifactorial process hinges on different interlocking dimensions: viral genetic diversity within the reservoir host, biological barriers that constrain cross-species transmission, and ecological or evolutionary drivers that enable the virus to adapt and spread in the novel host species.^{149,150} It is also closely associated with geographical, environmental, and climatic factors, as well as human activities etc.^{49,151,152}

Basic process of viral spillover

Viral spillover hinges on the pathogen's capacity not only to infect its natural host, but also to replicate successfully and sustain transmission within the new host population.¹⁵³ The spillover of viruses from natural hosts to novel hosts (including reservoir host or susceptible hosts), which may subsequently trigger epidemics, is a complex process regulated by multiple factors and accomplished through multiple steps. For example, host range is a viral property that reflects natural hosts that are infected either as part of a principal transmission cycle or as "spillover" infections into alternative hosts.¹⁵⁴ When the genes related to virulence or pathogenicity of a virus undergo

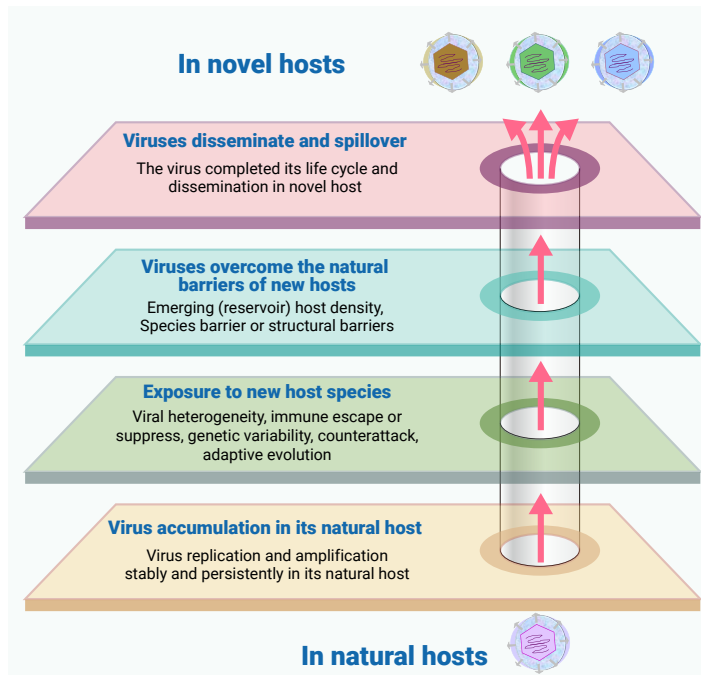


Figure 3. Schematic diagram of viral spillover process The layered barriers (indicated by trapezoidal frames) serve as obstacles to prevent the viral spillover from natural hosts to novel hosts. As each layer of the barrier is breached, the risk of viral spillover progressively increases. The viral spillover process follows a bottom-up pathway (indicated by arrow direction).

genetic drift, there is a possibility of virus spillover and the emergence of epidemics in new hosts.¹⁵⁵ The main steps of virus spillover are illustrated in the trapezoidal diagram of Figure 3. They include (1) Virus accumulation in its natural host. (2) Exposure to new host species. (3) Viruses overcome the natural barriers of new hosts. (4) Viruses disseminate and spillover. The basic process of viral spillover will be described in detail below.

Virus accumulation and genetic drift

Emerging and re-emerging infectious diseases in aquatic animals are frequently caused by viral spillover from natural hosts. The prerequisites for spillover include virus gaining the ability to infect cells of a new host species, adapting to the host, and acquiring the capacity for sustaining transmission within the host population.²⁸ The first stage in viral spillover is extensive accumulation of the virus in its natural or reservoir host, accompanied by genetic drift. These viral pathogens typically undergo amplification and accumulation in their natural hosts (or reservoir hosts), and then they can spread among the new host population. However, the heterogeneity between viruses and hosts, including viral entry into target cells, genome replication and inheritance, viral particle assembly, release, and transmission, can more or less affect the viral life cycle.¹⁵⁶ Viral entry is only the step that a virus must complete to productively infect a cell, produce progeny virions and spread at the intra-host and population levels.¹⁵⁷ Binding susceptible host cells is also one of the key factors responsible for determining host range,¹⁵⁸ and other factors of the host should also be considered,¹⁵⁷ such as receptors are major determinants of host susceptibility to viruses. Animal species sharing host cell receptors that support the binding of multiple viruses can play a key role in virus spillover and the emergence of novel viruses.¹⁵⁹

For spillover to occur, the virus must mutate and develop adequate fitness within the reservoir species before it can be transmitted to a new host. And spillover is part of a continuous evolutionary process. RNA viruses, in particular, are prone to spillover due to their high mutation rates. And recombination, especially of DNA viruses, is a key driving force for the emergence of new variants.²⁸ The genetic drift and evolutionary changes of aquatic viruses play a crucial role in viral spillover, viral diversity, and the biogeochemistry of aquatic ecosystems.¹⁶⁰⁻¹⁶² Genetic drift refers to the random gene changes between generations within a population. Some small changes in viral genes can lead to changes in surface proteins of the virus (e.g. antigenic drift). For a

virus to infect a new host, it needs to undergo genetic changes. These changes can occur within the natural host, the new host, or both. Persistent replication and amplification of the virus in its natural reservoir host may generate high genetic diversity, and thereby maximize the probability of cross-species transmission.

Meanwhile, host population heterogeneity creates multiple distinct pathways that facilitate viral spillover across new recipient species. The same basic evolutionary forces and principles operate at each level, such as mutation and recombination, selection, genetic drift, migration, and adaptive trade-offs.¹⁶³ Some hosts are both the source and the sink for viral spillover.¹⁶⁴ Thus, the virus may form a “reservoir” with high titers following infection in its natural reservoir host.¹⁶⁵

Viral exposure and adaptation to novel hosts

The second stage in a virus's successful spillover lies in acquiring the ability to enter and adapt to a new host. The host range of a virus is governed by multiple molecular interactions. Usually, a virus cannot initiate infection unless it binds to specific receptor molecules on the host cell surface.¹⁶⁶ The capacity for host-switching and cross-species infection stems chiefly from the vast viral genetic diversity and the multifaceted interactions between virus and host.¹⁶⁷ When the virus accumulates heterogeneity, immune escape/suppression ability, genetic diversity, and acquires adaptability in natural host replication and evolution, once it comes into contact with a novel host species, then spillover enters on to the next step. When novel aquatic animal hosts such as fish encounter the virus through direct contact with the natural host or exposure to contaminated water, the risk of spillover rises accordingly.

A host-virus network framework has been proposed to map and forecast viral susceptibility in both animals and humans, which reveals fundamental biological rules that govern cross-species transmission and shapes the global virome.¹⁶⁸ Once healthy aquaculture population coexist in the same aquatic environment with wild aquatic animals infected by viruses, the risk of spillover immediately increases.^{169,170} Under appropriate ecological and evolutionary conditions, viruses may switch to new hosts than coevolve with their native host.¹⁷¹

Virus breaches host defenses, infects a new host and spreads

Viral spillover and onward spread are also restricted by various natural barriers, including receptor compatibility and environmental factors.¹⁷² The third stage in spillover is for the virus to break through natural barriers and enter a new host. The virus must overcome natural barriers such as species incompatibility, immune response in the new host and multiple evolutionary mechanisms for virus-host adaptation, which ultimately determine host susceptibility to a virus.

Viruses do not have a shared universal gene and have multiple origins. The evolution of viruses is closely related to the evolution of their hosts, leading to accelerated evolution of host defense and virus antidefense systems on both sides. Another important complementary feature of this coevolution is exogenous adaptation, where the host acquires viral genes for antiviral defense and other functions. Conversely, viruses hijack host genes for various functions in viral replication, virion morphogenesis, and virus-host interactions, thereby breaking through natural barriers.¹⁷³ For example, the hypermethylated genome of vertebrate iridoviruses is unique among animal viruses. There is no correlation between hypermethylation and viral gene expression, but hypermethylation may help the virus evade the immune system by increasing its genome methylation level.¹⁷⁴ This not only accelerates the emergence of new viruses but also increases the spillover and the pandemic potential.¹⁷⁵ Briefly, for successful cross-species transmission, viruses must progressively overcome molecular, cellular, and ecological barriers. And viral receptor recognition, protease activation, immune evasion, and genomic plasticity are the core drivers of host range expansion.¹⁷⁶

Viruses dominate biosphere and constitute main reservoir of genetic diversity on Earth. In recent years, large-scale mining of metagenomes and meta-transcriptomes has dramatically expanded the world of viruses (virophere), revealing unprecedented diversity. From covert infiltrators to crude disruptors, viruses break through layer-by-layer barriers of infecting new hosts by controlling host gene expression, suppressing immune responses, and redi-

recting cellular resources towards self-replication. Viruses have developed various strategies to ensure their survival and transmission, and they could also trigger new host behavioral alterations.¹⁷⁷

Viral spillover occurs upon crossing tipping point

The fourth stage of viral spillover and spread is to cross the tipping point (overshooting tipping points or breaching the critical threshold), a critical link in the chain. It is also the tipping point for crossing into sustaining community transmission.^{178,179} The progression of viral diseases is a typically dynamic process. Pathological changes accumulate silently in the early stage; once the viral tipping point is breached, the epidemic spreads rapidly, ultimately evolving into a pandemic. The critical transitions are referred to as tipping points. Leveraging dynamic network biomarkers, sample-specific networks, information entropy theories and statistical modeling approach etc. can detect tipping points of spreading viruses in diverse data types.¹⁸⁰⁻¹⁸²

Persistent occurrence of viral epidemics and cross-species transmission of aquatic animal viruses are usually driven by the combined effects of changes in aquatic ecological environments and other multiple factors.¹⁸³ For instance, beyond temperature, rapid climate change further affects the prevalence and severity of aquatic animal epidemics.¹⁸⁴ Viral genetics, host and receptor polymorphisms, as well as ecological, environmental, and population dynamics are all critical parameters to influence viral spillover.¹⁸⁵⁻¹⁸⁷ Aquatic animal viruses can be transmitted horizontally via vectors, contaminated feed, and water sources etc, or transmitted vertically from parent to offspring. Thus, spillover of aquatic animal viruses may increase the risk of disease outbreaks, and sets off a chain reaction of mass die-offs in cultured and wild populations, water pollution, and beyond.

Infectious diseases caused by spillover viruses not only lead to massive mortality in farmed fish and endanger the entire industry,¹⁸⁸ but also pose a significant threat to the economy, human health, and even the global ecosystem.¹⁸⁹⁻¹⁹¹ It is estimated that aquatic diseases, including herpesvirus-associated diseases, cause global economic losses of up to 6 billion US dollars annually.¹⁹² We are on the verge of a potential era of infectious diseases, characterized by rapid spread of emerging and re-emerging of endemic pathogens. This trend is influenced by global connectivity, global travel and trade more affordable and convenient, and shifts in geographic ranges due to climate change.¹⁹¹ Constraint and opportunities coexist in viral spillover. Spillover-derived viruses must either possess or evolve the capacity for cross-species transmission, then establish and sustain transmission chains to successfully emerge.¹⁵⁴ Reassortant viruses have been shown to exhibit distinct tropisms for fish species, differing from those affected by the parental virus strains. This poses an emerging threat not only to aquaculture but also to wild populations.¹⁹³ Viral diseases also exacerbate environmental degradation.⁴⁹ High genetic diversity of wildlife animals can also promote the emergence of novel viral strains, as pathogens evolve and adapt within the varied host populations.^{51,194} The binding of viruses to cellular receptors is a key determinant of replication initiation and tissue tropism. There is evidence that initial step in viral infection is cellular internalization mediated by viral receptor-binding proteins (RBPs), yet the virus still has interspecies barriers in the early stages of infection.¹⁵⁷ Meanwhile, the various factors that lead to virus emergence and spillover often act simultaneously or in parallel. These factors provide more opportunities for viral spillover.

Viral spillover effect frequently occurs and has widespread spatio-temporal influences.¹⁹⁵ Host specificity and environmental factors can shape diversity of the virome.^{43,196} For example, among the 19 recently identified fish viromes, as many as 16 are likely to be new viral species, and extend across multiple families such as *Coronaviridae*, *Hantaviridae*, *Poxviridae*, and *Totiviridae*.^{103,197} This broadens the window of opportunity for viral spillover. Moreover, predators in wild fish populations remove diseased individuals, whereas farmed fish, by contrast, are reared in high-density environments, accelerate viral transmission between individuals, providing ideal conditions for disease outbreaks.

FRONTIER TECHNOLOGIES FOR VIRAL SPILLOVER RISK SURVEILLANCE AND EARLY WARNING

Long-term monitoring and tracing of aquatic animal viruses can help quantify the risk of viral spillover, quickly assess the potential threats, and

provide the targeted control strategies.^{198,199} Detection and analytical methodologies are pivotal for elucidating pathogen properties, monitoring viral spillover, and facilitating early pandemic early warning and containment.^{200,201}

Multiple approaches have been developed to assess the risk of viral spillover. Predictive early warning is foundational to biosecurity management in aquaculture, providing critical information support for viral disease control and prevention. Advances in diagnostic technologies have significantly enhanced the sensitivity and accuracy of aquatic animal disease detection. Furthermore, the application of cutting-edge tools such as drones, sensors, and artificial intelligence has made water quality monitoring, aquatic animal health assessment, and farm behavior observation more cost-effective, efficient, and precise.²⁰² Therefore, it is essential to intensify research in this area and continuously develop and apply novel analytical and evaluation techniques. The following will delve into the strategies for effectively predicting, warning, preventing, and mitigating potential viral disease outbreaks caused by viral spillover

Acquisition and curation of viral datasets

Effective surveillance of viral spillover hinges on constructing a technical framework, for which dataset acquisition and curation, as the cornerstone, should be the first step. Data can be obtained either by direct sampling, preparation, and sequencing, and by collecting raw data from diverse sources, including omics (e.g. viromics) datasets, using open-source tools, and subsequent format conversion and transfer are necessary to resolve multi-source heterogeneity to achieve integrated datasets.²⁰³ Host-virus association databases are increasingly used to explore deep questions in disease ecology, including spillover potential.²⁰⁴ This can provide practical recommendations for database users and managers, and highlights how these tools can serve as starting points in spillover research. The dataset is characterized by its high structure and scalability, which supports online access to a vast collection of analysis templates.²⁰⁵ The rapid growth in number of newly identified viral sequences underscores the need for an accurate and comprehensive classification system for all viral realms at different taxonomic levels.²⁰⁶ Below is a brief overview of several viral datasets.

The Viral Taxonomic Assignment Pipeline (VITAP), is designed to address classification challenges by integrating alignment-based techniques with graphs, offering high precision sequences of both DNA and RNA viruses and providing confidence level for each taxonomic unit. Leveraging virome analyses, it can capture a panoramic view of deep-sea viral diversity.²⁰⁷ Several data warehouses and data platforms of viruses have been built, and a variety of open-source tools purpose-built for virology have also been successively released in recent years.

Global Catalogue of gcMeta (Metagenome) (<https://gcmeta.wdcm.org/>), developed by Chinese scholars, was officially published in 2025. This groundbreaking resource integrates over 2.7 million MAGs (metagenome-assembled genomes), encompassing more than 104k samples across 50 specific biomes. It not only fills the gap in cross-ecosystem microbial comparative analysis but also establishes an efficient transformation pipeline from microbial 'sequence discovery' to 'functional utilization', providing standardized microbial functional data resources directly applicable for artificial intelligence (AI) research to the global scientific community.²⁰⁸

gcVirus (global catalogue of viruses platform, <https://nmcd.cn/gcvirus/>) is aimed at empowering rapid identification, precise tracing, and transmission-trend prediction of emerging viruses, along with online discovery and characterization of novel viruses.

MAG (metagenome-assembled genomes), referred to genomes assembled from metagenomic sequencing data, include metagenome-assembled genomes (MAGs) or draft genomes of individual species. Various computational tools have been developed for constructing and annotating these genomes from metagenomic sequencing data.²⁰⁹

MAGs (Metagenome-assembled genomes) were taxonomically annotated using the Genome Taxonomy Database Toolkit (GTDB-TK, <https://gtdb.ecogenomic.org/>) and validated through maximum likelihood-based phylogenomic tree reconstruction. Through integration of metagenomic and metatranscriptomic data from 191 sediment samples collected across 17 deep-sea cold seep sites globally, 13,336 viral genomes and corresponding

microbial MAGs were obtained. Among the 26,389 defense systems identified, over 60% represent previously unreported candidate defense systems, thereby revealing the coexistence of diverse microbial defense and viral anti-defense systems in extreme environments.²¹⁰

MVIP (Multi-omics Portal of Viral Infection, <https://mvip.whu.edu.cn/>) provides a large number of curated resources on high-throughput sequencing datasets under various virus infections.

OpenVirus is a comprehensive, large-scale data set of viral sequences used to train the LucaVirus model. This repository is dedicated to demonstrate the basic functionality of viruses information. LucaVirus is a 1-billion-parameter virology foundation model that unifies the processing of nucleotide and protein sequences. It is capable of identifying hidden viruses in the genomic "dark matter", annotating the enzymatic activities of uncharacterized proteins, predicting viral evolutionary potential, and identifying antibody candidates for emerging viruses.²¹¹

Vclust (cluster virus genome sequences) is an ultrafast and rigorously clustering engine for viral genomes. Through engineering to absorb the data deluge from viromics and other high-throughput sequencing platforms, it delivers species- to genus-level classification that fully satisfies both International Committee on Taxonomy of Viruses (ICTV) and Minimum Information about an Uncultivated Virus Genome (MIUViG) standards.²¹²

VIBRANT (Virus Identification By iterative AnnoTation) is a tool for automated recovery and annotation of bacterial and archaeal viruses, determination of genome completeness, and characterization of viral community function from metagenomic assemblies. Accurately recovering viruses and investigating their impacts on microbial community metabolism will rapidly advance our understanding of microbiomes, host-microbe interactions, and ecosystem relationships.²¹³

ViOTUcluster (a high-speed, All-in-One Pipeline for Viromic Analysis from Metagenomic Data), is an integrated, lightning-fast, and user-friendly viromics pipeline that delivers one-click processing from raw sequencing reads to viral operational taxonomic unit (VOTU) tables and all downstream essentials, from raw reads to the generation of viral operational taxonomic units (VOTUs) tables, which include abundance, taxonomy, and quality information, as well as assembled viral genomes, AMG prediction, and host prediction. Open-source and available now on GitHub.²¹⁴

VIPR (Virus Pathogen Resource) is a virus pathogen database developed with funding from the U.S. National Institutes of Health (NIH) and a global data platform to better understand viruses. The publicly released data encompass about 20 viral families and nearly 730,000 strains, including both single-stranded RNA and double-stranded DNA genomes.²¹⁵

VIRE (Viral Integrated Resource across Ecosystems), is an integrated comprehensive resource of 1.7 million viral genomes drawn from host-associated, aquatic, terrestrial, and engineered ecosystems. The viral genomes were systematically assembled via a unified and scalable pipeline, and provided detailed information on genome completeness, taxonomic classification, predicted lifestyle, and host assignment based on CRISPR spacer matches.²¹⁶

VirusDIP (Virus Data Integration Platform) serves as a one-stop service platform that integrates viral sequence data from various sources,²¹⁷ including the National GeneBank Database (CNCDB), GISAID, and the National Center for Biotechnology Information (NCBI), helps researchers quickly discover, retrieve, and analyze viruses.

Several new auxiliary tools are also available. For instance, to systematically evaluate agentic viral data retrieval capabilities, VirBench, a manually curated benchmark comprising 120 queries spanning diverse pathogens, taxonomic levels, and combinatorial metadata filters, authentically reflects real-world virology workflows.²¹⁸

In addition, various methods have been used to study marine viruses, such as planktonic DNA viruses in the eastern continental shelf of China (ECSSC), revealing the diversity and spatiotemporal variation patterns of shallow seawater DNA viruses and so on, evaluating their potential impact on biogeochemical cycles, meanwhile yielding a dedicated DNA-virus genome dataset for continental-shelf seas.^{160,219}

Multimodal data integration and application software

Multimodal data integration and cutting-edge artificial intelligence tech-

nologies, have been widely applied in prediction of viral cross-species transmission (viral spillover) and intelligent image annotation.²²⁰⁻²²² Multimodal data integration refers to the integration and analysis of data from multiple sources or types, encompassing a combination of various data forms. Multi-omics, biological imaging and other datasets are ballooning, yet single modalities can no longer capture the multidimensional heterogeneity of viral phenotype, genotype, and environment. Meanwhile, multimodal fusion technologies have emerged as a promising solution for intelligent aquaculture due to their strong environmental adaptability, information complementarity, and high generalization ability.²²³ Embedding multimodal fusion algorithms and scenario-specific system solutions into surveillance networks will open a new frontier for precision early-warning and proactive containment of viral spillovers.

A new batch of multimodal software and frameworks are emerging in the fields of virus-host interaction and aquatic virology research. AquaMonitor dataset is a multimodal and multi perspective image sequence dataset of aquatic invertebrates. Multimodal datasets for aquatic organisms and aquaculture have also been developed and applied. This dataset contains specimen images and their DNA sequences, dry weight, and size data, making it one of the largest multimodal biological datasets to date.²²⁴

CellWhisperer is a chat-style gene-expression search engine. It co-embeds AI-curated RNA-seq atlases and their textual annotations into a unified latent space, giving transcriptomes a "voice". Powered by this space, a large language model can instantly answer cell- or gene-level questions in natural-language conversation, ushering in a new paradigm of interactive single-cell data analysis.²²⁵

DeepHVI, is a multimodal deep-learning framework that fuses protein-sequence embeddings with complementary virus-host features to predict HV-PPIs and pinpoint potential interaction partners for uncharacterized viral proteins.²²⁶ Integrating multimodal and multisource heterogeneous viral data, predictive models quantify spatiotemporal transmission dynamics and reconstruct evolutionary trajectories, enabling forward-looking epidemic early warning (<https://nmdc.cn/gcvirus/>).

Emu3 (evolutionary multimodal understanding third generation) is a family of multimodal models trained solely with next-token prediction. Emu3 equals the performance of well-established task-specific models across both perception and generation, matching flagship systems while removing the need for diffusion or compositional architectures.²²⁷ By only using the goal of "predicting next-token", the model can simultaneously achieve top-tier understanding and generation capabilities.

Multimodal data fusion can be examined from multiple views with high-dimensional, multiscale biomedical data to classify clinical phenotypes and predict outcomes.²²⁸ Integrating multidimensional viral information and building a database for virus mutation spectrum and mutation prediction models are expected to achieve real-time monitoring and intelligent warning of virus mutation.²²⁹

A committee on prevention of viral spillover has been established, and interdisciplinary coordination will be used to strengthen the monitoring and response system for viral spillover risks.²³⁰ Thus, the risk of viral pandemics can be significantly reduced.

Mathematical modeling and machine learning for viral spillover risk prediction

Mathematical modeling and machine learning can decode the genomic sequences to identify potential cross hosts and quantify spillover risks.²³¹ By constructing algorithmic systems for analyzing virus-host interactions and cross-species transmission potential, and deeply integrating them with machine learning, massive data can be rapidly ingested and transmission risks can be predicted in advance. Increasing evidence indicates that high-performance mathematical modeling and machine learning will play an important role in cross-species infection early warning.²³²

Innovations in mathematical modeling have been developed and applied recently. For example, by defining and calculating virus sequencing distances, virus evolution can be combined with epidemiological processes. Researchers have proposed an indicator of "virus sequencing distance", and emphasize that genetic variations in newly emerging viruses can rapidly reshape their transmission ability. Based on millions of publicly available

sequences worldwide, a mathematical modeling method for quantifying the evolution rate of viral strains has been constructed by embedding real-time evolutionary dynamics into epidemiological transmission models.²³³ This method not only facilitates operational ease but also effectively quantifies the evolutionary rate of viral pathogens, significantly enhancing the timeliness and accuracy of virus transmission dynamics predictions.

Based on the construction of the Iridovirus Comprehensive Database and Analysis Platform (IVCDB, <https://www.iridovirus.com/>), the concept of "Pathogenicity Spectrum" for fish viruses was proposed. Research indicates that single-amino-acid polymorphisms in host proteins are key determinants of the cross-species pathogenic spectrum of fish viruses.²³⁴

Utilization of machine learning for metagenomic data analysis has not only become a primary approach for studying diverse virus ecosystems, but also demonstrated enormous potential in novel virus detection.²³⁵ On the basis of high-quality datasets and genomic models, a universal evolutionary prediction framework across virus types and strains has been constructed, which can accurately distinguish viruses from other organisms solely based on genomic features.²²⁰ In using machine learning models to assess the virus spillover risk, researchers have employed two key strategies, expanding the dataset and developing specialized models (e.g. BERT-Infect model, Bidirectional Encoder Representations from Transformers model). Consequently, the essential strategies can be utilized when using machine learning models to evaluate spillover risk.²³⁶

The extensive epidemiological database had been utilized to analyze specific subset of high-consequence spillover events for trends.⁵⁰ Currently, there is significant interest in understanding the evolutionary drivers and mechanisms underlying viral jumps between hosts.¹⁶⁴ A global disease risk distribution map has been constructed, and an infectious disease risk index has been released, by which each country can integrate and evaluate the specific threats with their comprehensive ability to respond to virus spillover.²³⁷

Monitoring diversity distribution of aquatic animal viruses and key viral spillover drivers is critical for epidemic prevention and control. Incorporating the key drivers such as viral diversity distribution maps, host population density, and spatial distribution of multi-species abundance into models, and analyzing transmission dynamics, an effective approach for predicting spillover risk can be provided.²³⁸ By integrating the population dynamic characteristics of reservoir hosts and novel receptor hosts, a modeling framework with stochastic duration has been constructed to characterize the process of cross-species disease transmission.²³⁹

SpillOver (<https://spillover.global/methods>) is an open-source tool for predicting viral risk. It can be used to explore and compare a variety of viral, host, and environmental risk factors to screen the highest viral spillover risk.²⁴⁰ It is also the first open-source risk assessment tool that evaluates wildlife viruses to estimate their zoonotic spillover and pandemic potential. And it effectively creates a watchlist of newly-discovered viruses to help policymakers and health scientists prioritize them for further characterization, surveillance, and risk-reducing interventions. However, machine learning driven virus cross species transmission prediction models still face challenges such as lack of training data, drift in evolutionary paths, phenotype genotype fragmentation, and spatiotemporal dynamic decoupling. Machine learning needs to be made more powerful, such as through the integration of large models and multimodal data, capture complex information and cross many biological environments.^{241,242} Moreover, more and more cutting-edge technologies are emerging and are used for auxiliary detection of pathogens.²⁴³ Actual applications of the above databases, open-source tools, and predictive models in risk surveillance and prevention of aquatic virus spillover still need critical evaluation.

Technological path of monitoring and forecasting of aquatic animal viruses

Viral disease surveillance and early warning serve as the first line of defense in effectively preventing and mitigating risks associated with aquatic animal diseases. Environmental pressures drive continuous evolution of viruses, generate variants with diverse transmissibility and immune evasion capabilities, highlighting the necessity of sustained surveillance and dynamic

adjustment of prevention and control strategies. Understanding the emergence, evolution, spillover, and transmission dynamics of viral pathogens is critical to advancing global health.²⁴⁴ Accurate and efficient viral pathogen detection and control is also a key link in improving the health standards of aquaculture.²⁴⁵ Pathogen spillover risk can be predicted based on host range or genomic composition, while the availability of input data determines whether early warning can be achieved prior to outbreak onset.²⁴⁶

Multiple methods have been adopted for the detection and analysis of viral pathogens in aquatic animals, covering a wide range of fields from traditional techniques to innovative methods. Conventional methods, include cell culture, immunological detection, electron microscopy, and nucleic acid testing.²⁴⁷ Sensitive molecular diagnostic and quantitative analysis technologies have been used to detect and analyze CaHV.²⁴⁸ And innovative methods involve a tremendous diversity of available data analysis (big data analytics, BDA), plaque-mass spectrometry imaging (PMSI), nanoparticle tracking analysis (NTA), and viral biorthogonal non-canonical amino acid tagging (vBONCAT), and other cutting-edge technologies.^{6,249} Some examples are as follows:

High-throughput sequencing and multi-omics analytical methods

Iterative advancement of sequencing technologies has facilitated establishment and maturation of multi-omics integrative analytical methods.²⁵⁰ The advent of high-throughput sequencing technologies has revealed novel and intriguing features of genomes, allowing for comprehensive identification and analysis of whole genomes in a short period of time, with remarkable throughput, accuracy, and scalability.²⁵¹ Multi-omics methods are also providing increasingly rich clues.²⁵² From evolutionary experiments of viruses and other microbial populations to ancient DNA evidence for documenting past pathogen host relationships, multi omics techniques can help trace the evolutionary dynamics of viruses.²⁵³ These data provide a blueprint for various microorganisms, which helps to comprehensively analyze the structure and function of microbial communities in various ecosystems,²⁵⁴ and more and more have been used for diagnosis and monitoring of emerging viral pathogens.²⁵⁵ These comprehensive studies have revealed extensive geographic distribution of global viral communities and vast genetic and functional diversity.²⁰³ Furthermore, using long-read sequencing technology, researchers have analyzed and compared genetic materials of extracellular vesicles (EVs) and virus like-particles (VLPs) in North Pacific and thereby elucidated the potential for horizontal gene transfer (HGT) in aquatic ecosystems, and their evolutionary trajectories.²⁵⁶

Biorecognition and emerging molecular diagnostic technologies

Bionanosensors, recombinase-aided amplification lateral flow dipstick (RAA-LFD), and microfluidic platforms, have been applied to detection of fish viruses and other viral pathogens.^{257,258} Single-cell RNA sequencing (scRNA-seq) can be used to identify undescribed host-virus interactions and investigate their ecological importance and impact.²⁵⁹ Spatial distribution of viral spillover risk can also be predicted by approximating general transmission patterns.²³⁸ Nucleic acid sequence-based amplification (NASBA), as a continuously evolving molecular detection platform, has spawned novel methodologies such as molecular point-of-care testing (POCT). This technology enables rapid acquisition of test results through using portable analytical devices and compatible reagents. Ongoing advances in real-time detection, multiplex amplification, and chip-integrated assays have markedly improved sensitivity and accuracy, reshaping the POCT diagnostic landscape and opening new avenues for faster, more convenient on-site diagnostics.^{260,261}

Big data and AI-driven viral spillover risk prediction

A large-scale spatial epidemiology framework has been applied to investigate how marine environments influence viral disease transmission in Pacific oysters, showing that the disease first broke out in the intertidal farming area and then spread seaward.²⁶² The network science framework and related approaches have identified fundamental biological principles governing cross-species transmission.^{168,263} Some abnormal trends might serve as critical signals for early warning of disease outbreaks. When these signals were combined with information on newly emerging viral hosts, the combined data

sources might provide a foundation for developing tools to predict virus spillover risks. Such tools have already been applied to forecasting high-risk areas for potential spillover events. Data sources-based systems utilizing blockchain and smart contract technologies can effectively share data and facilitate precise disease identification.²⁶⁴ Genomic surveillance of spillover variants, such as wildlife surveillance and risk mapping, would be a powerful complement to predictive approaches. Targeting interventions to regions with the highest genetic risk of spillover can also enhance impact.²⁶⁵

Data sharing network for continuous surveillance of viral spillover

A group of international experts have proposed a universal modular sequencing framework that can flexibly switch among different viral targets to maximize cost-effectiveness.²⁶⁶ World Health Organization (WHO) has announced the International Pathogen Surveillance Network (IPSN), aiming to strengthen global early warning and rapid response capabilities (<https://www.who.int/initiatives/international-pathogen-surveillance-network>, 2023). Recently, a comprehensive viral genome database, named VIRE (a virome resource data platform derived from metagenomics, covering planetary scales with environmental context) has been released. It covers diverse ecosystems, including host-associated, aquatic, terrestrial, and anthropogenic environments, and contains 1.7 million viral genomes from over 100,000 publicly available metagenomes.²¹⁶ Virus spillover can also be predicted based on characteristics of both the host and the virus.²⁶⁷ Tools for virome analysis and virus discovery have also been progressively established. VirID (Virus Identification) has been developed as a comprehensive platform for identifying and characterizing RNA viromes, with a powerful RdRP sequence database that significantly improves the accuracy and depth of virus descriptions.²⁶⁸

But this is still not sufficient. The current tools for evaluating viral spillover in aquatic animals remain notably deficient in timeliness, ease of use, and precision of risk assessment. And the process of virus spillovers and globalization and the global climate change has led viral diseases to be spread faster than before. Therefore, there is an urgent need to establish rapid-response mechanisms to enhance the risk prevention and mitigation for viral spillover.

RISKS PREVENTION AND MITIGATION OF VIRAL SPILLOVER IN AQUATIC ANIMALS

Aquatic ecosystems are the most diverse habitats for animal life on Earth,²⁶⁹ and also harbor an extensive and astonishing array of viral communities. Viruses are also key drivers of global biogeochemical cycles and integral components of ecosystems, and the most distinctive 'survival strategy' lies in continual spillover.²⁷⁰ In the past the spillover effects of aquatic animal viruses are further amplified due to negative impacts of aquatic environmental stress.²⁷¹ As complex replication mechanisms, extensive genomic mutations, and changeable drug resistance of aquatic animal viruses pose severe challenges to existing prevention and control measures, it is very imperative to make innovative response strategies.^{220,272} Thus, prevention and mitigation of spillover risks associated with aquatic animal viruses are of paramount importance. The core objectives should include: (1) to break through the bottlenecks of traditional vaccine development and to open up new avenues for broad-spectrum antiviral strategies; (2) to elucidate the molecular basis of viral drug-resistant mutations and host immune evasion mechanisms; and (3) to integrate emerging biotechnologies to transform antiviral defense systems.²⁷³

To mitigate the potential risks posed by emerging and re-emerging infectious diseases to hosts, WHO has issued a list of high-priority pathogens with pandemic potential.²⁷⁴ Formulated through a comprehensive evaluation framework, the list mainly considers pathogen transmissibility and transmission pathways, feasibility of existing control measures, and lethal risk of associated diseases. Concurrently, some researchers have proposed comprehensive prevention and control strategies that should emphasize three necessary measures including (1) to deepen our understanding of pathogenic mechanisms, (2) to optimize host protective immune responses,

and (3) to utilize artificial intelligence for model construction to inform vaccine and therapeutic development.²⁷⁵

Vaccine development and deployment in aquaculture

Existing commercial aquaculture vaccines primarily encompass: whole-cell inactivated vaccines, live-attenuated vaccines, subunit vaccines, and DNA vaccines. The primary routes of vaccine delivery are injection vaccination, immersion vaccination, and oral vaccination.²⁷⁶ Aquaculture vaccine development has advanced rapidly in recent years. A growing array of next-generation vaccines include subunit, recombinant, mucosal, synthetic peptide, DNA, vectored, monovalent, polyvalent, and reverse vaccinology-designed vaccines.²⁷⁷ This indicates that the translational application of emerging technologies in aquaculture vaccines still holds broad development prospects. However, current vaccines elicit inadequate cross-variant immunity, constraining their protective efficacy against rapidly emerging and continuously evolving pathogens.²⁷⁸

Currently, the antigen optimization approaches are transitioning from traditional empirical screening to rational design, primarily encompassing structure-guided antigen design, immunoinformatics-predicted conserved epitope targeting, consensus sequence optimization, chimeric immunogen engineering, and the integrated application of mRNA technology with virus-like particles (VLPs).²⁷⁹ Leveraging continuous innovations in cutting-edge technologies, the developing strategies include structure- and immunoinformatics-guided antigen design and nanoparticle delivery systems and are opening new avenues for broad-spectrum vaccine development. In addition, the CRISPR/Cas13d-based antiviral system for aquatic animals has been successfully established and can serve as a novel anti-viral strategy.²⁸⁰ For example, *Siniperca chuatsi* rhabdovirus (SCRV) is a lethal virus that infects mandarin fish. By constructing the CRISPR/Cas13d system, viral replication and gene expression of SCRV in fish cells can be effectively targeted and suppressed, and highly efficient target sequences that may serve as potential antiviral-specific sites have been identified.²⁸¹

Enhancement of immune defense capabilities in aquatic animals

Enhancing disease resistance and defense capabilities of aquatic animal hosts should be systematically developed. For example, genetic improvement innovation should be enhanced through disease-resistant molecular breeding to strengthen genetic resistance foundation. And active defense and specific protection should be established via vaccine and immunization program optimization.²⁸²⁻²⁸⁴ Extensive research have shown the integration of natural products (e.g. medicinal plants, probiotics, prebiotics, insect-derived products, aquatic organism derivatives, vitamins, and minerals) into aquaculture practices also presents a promising strategy for sustainable fish health management.²⁸⁵ These natural substances can significantly enhance the innate and adaptive immune responses of freshwater fish, promote growth, and improve resistance to other pathogens. Synergistic effects of these measures are instrumental in improving the health status of farmed aquatic animals, mitigating pathogen infections, and ultimately enhancing aquaculture yield and product quality.²⁸⁶

Ecological prevention and control of viral spillover

Farmed and wild aquatic organism conservation are facing three persistent challenges: elucidating the correlation between viral detection and disease occurrence, quantifying the immune status of animal populations, and establishing a multi-layered integrated prevention and control system.²⁸⁷ The scientific literature on how ecosystems mitigate viral spillover is currently fragmented and inconclusive, hindered by insufficient conceptual frameworks and practical guidance. Though viral disease prevention and control command considerable focus, and scholars are investigating ecological intervention strategies, pathogen spillover risk remains absent from the global priority agenda.

There is growing recognition that ecosystem restoration represents an effective way for reducing the risk of viral spillover. Rebuilding ecological integrity through biodiversity enhancement, ecosystem resilience improvement, and pathogen dynamic regulation can significantly reduce the risks of

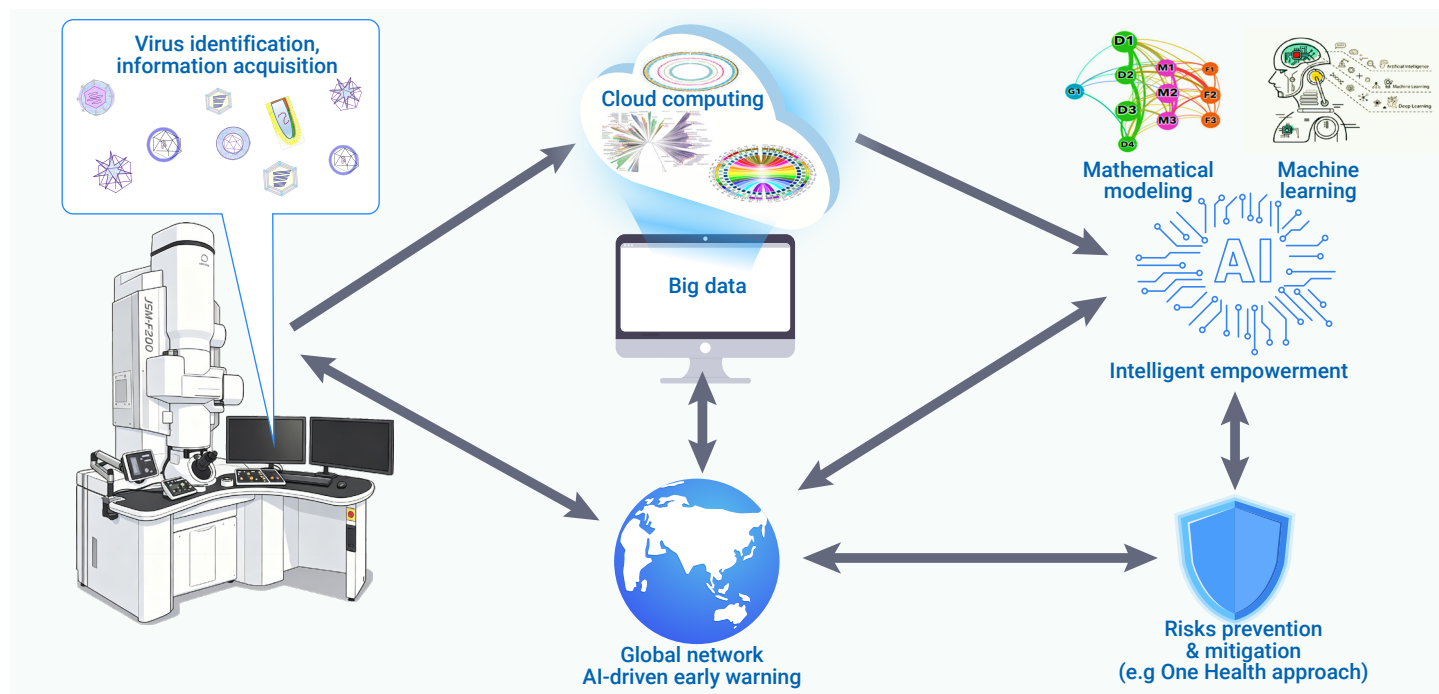


Figure 4. A framework for virus spillover warning, monitoring and preparedness The framework includes: (1) Sample collection and database construction. (2) Big Data and data integration platform. (3) Mathematical modeling and machine learning (e.g. AI empowerment). (4) Globally networked, AI-driven early warning with real-time monitoring and collaborative intelligence. (5) Risk prevention and mitigation for viral spillover, with operationalization of the One Health framework.

viral spillover and transmission.²⁸⁸ Further integration of ecological and biomedical approaches should be carried out to establish a synergistic, comprehensive framework for preventing and controlling viral spillover risks.²⁸⁹ Meanwhile, applying macroecological approaches to predict viral spillover risk and integrating them into the broader One Health framework will provide support for comprehensive prevention and control strategies.²⁹⁰

Leveraging “One Health” to fortify defenses against viral spillover

“One Health” urges human, animal, and environmental health sectors to break down silos between professions, disciplines, and institutions, and to work collaboratively through synthesis approach.²⁹¹ This concept was formally defined in 2021 by the One Health High-Level Expert Panel (OHHLEP), emphasizing the inseparable and close interconnections among human health, animal health (including wildlife), and ecosystem health.²⁹² Based on interdisciplinary systematic thinking, integrating multiple omics, big data science, and remote sensing environmental screening technologies to construct an active monitoring system is expected to fully unleash the greater potential of prediction and early warning.²⁹³ Therefore, in order to support healthy and sustainable development of aquaculture, it is urgent to focus on strategic scientific issues and policy priorities in the field of aquatic animal health. Furthermore, World Organisation for Animal Health (OIE) has also decided to refine and improve biosecurity regulations related to aquaculture, with its content grounded in the established guidelines developed and validated by the International Aquatic Veterinary Biosecurity Consortium (IAVBC).²⁹⁴

Prevention of virus spillover risks based on “One Health”

Under a One Health approach, incorporating spillover-associated data, including ecological shifts, wildlife migration, and fisheries trade, into monitoring frameworks facilitates identification of potential outbreak zones and supports early warning of viral spillover, and ultimately improves intervention efficacy.^{295–297} Simultaneously, an interdisciplinary governance system should be built to integrate basic research, quantitative risk assessment, interdisciplinary collaboration, and coordinated governance, and thereby to achieve the co-construction and co-governance of aquatic animal health and sustainable aquaculture development.²⁹⁸

Aquaculture biosecurity and integrated control strategies

Biosecurity Management in Aquaculture is of indisputable importance as the foundation of success in the aquaculture sector. Aquaculture industry could not just flourish but also play a critical role in increasing global food security by effectively addressing global concerns, embracing innovation, and upholding environmental responsibility.²⁹⁹ Aquaculture is currently facing a series of global challenges, particularly disease outbreaks, environmental stress, and the urgent pressures brought about by meeting the growing global demand for aquatic products etc. Biosecurity in aquaculture is a holistic disease prevention, control, and management approach. It includes a wide range of strategies, from strictly enforced quarantine and advanced monitoring systems to selective breeding for disease resistance. The investment in epidemic prevention and control is essentially a strategic investment in long-term global stability.^{300,301} A visualized framework for viral spillover investigation grounded in the One Health paradigm has been constructed, aiming to translate scientific findings into actionable intervention roadmaps. This framework encompasses: identifying pathogen characteristics, transmission contexts, and risk factors, as well as elucidating the host reservoirs and environmental conditions that facilitate spillover events.³⁰² Furthermore, employing phylogenetics and molecular evolution approaches to elucidate viral evolutionary patterns can provide theoretical support for developing targeted strategies to prevent and control viral spillover.³⁰³ Recent advances in disease diagnostics, surveillance systems, and immunological approaches have demonstrated how innovation drives progress in disease prevention and aquatic health management.^{304,305}

To enhance the ability to predict virus spillover, comprehensive methods can further integrate multidimensional data such as virus mutation rate, host susceptibility, and environmental driving factors to construct a systematic prediction model, thereby achieving early identification and early warning of potential spillover events. Currently, significant breakthroughs have been made in emerging technologies and methods such as machine learning prediction models, spatial Durbin models, molecular imaging techniques, and acoustofluidics integrated molecular diagnostic chips (AIMDx) in this field. The AIMDx enables high-throughput, highly sensitive detection of immunoglobulins (IgA, IgG, and IgM) and nucleic acids. This technology facilitates on-chip enrichment and rapid lysis of viral RNA, followed by nucleic acid amplification via Reverse Transcription Loop-Mediated Isothermal

Amplification (RT-LAMP). Concurrently, it supports electrochemical detection of antibodies, including IgA shielded by mucin. Furthermore, AIMDx allows for efficient recovery of both viral particles and antibodies.³⁰⁶ Using a deep learning framework (LucaProt) that integrates protein amino acid sequences and predicted protein functional structural information, 161,979 potential RNA virus species and 180 RNA virus supergroups were predicted.³⁰⁷ Furthermore, by constructing integrated comprehensive databases, and applying machine learning, Spatial Durbin models, and phylogenetic analysis, the integrated approach can help figure out how viruses “spill over”.³⁰⁸ And pairing the right viral animal models with suitable molecular imaging tools can reveal what pathogens look like, how they interact with hosts, and what that means—giving us valuable information.³⁰⁹

To enhance the timeliness and accuracy of prediction and prevention, there is an urgent need to construct a more robust and systematic framework for aquatic-animal virus analysis and surveillance. This framework should integrate innovative tools for virus detection and surveillance, and more comprehensive prevention, early warning, and control measures for emerging infections across species interfaces should be proposed. How to design an excellent virus spillover warning and surveillance framework for primary prevention and the development of risk-targeted early warning and monitoring systems? The core components of the framework should cover: acquiring comprehensive information, integrating multi-source data, intelligent analysis and judgment. Collectively, monitoring, early-warning, and other functional modules should be integrated to establish a risk prevention system as shown in Figure 4.

CONCLUSION

This paper systematically reviews the latest advances in viral spillover in aquatic animals and its risk monitoring and prevention, with a focus on the spillover risk characteristics of different viral taxa, the processes and mechanisms of spillover, and strategies for monitoring and preventing spillover risks. Taking ranavirus as a typical case study, we construct an overview map of viral spillover across different taxonomic groups. Further highlighting the crucial need to integrate emerging scientific methods into the following: (1) vaccine and antiviral drug development, (2) host immunity enhancement, (3) pathogen spread prevention, and (4) the practice of the “One Health” paradigm. In addition, a novel framework for early warning, surveillance, and risk prevention is constructed, providing theoretical support and practical guidance for tracing the source and precise prevention and control of aquatic animal diseases.

REFERENCES

- Holmes E. C., Krammer F. and Goodrum F. D. (2024). Virology-The next fifty years. *Cell* **187**:5128–5145. DOI:10.1016/j.cell.2024.07.025
- Havens J. L., Kosakovsky Pond S. L., Zehr J. D., et al. (2026). Dynamics of natural selection preceding human viral epidemics and pandemics. *Cell* **189**:2762–2775 e2711. DOI:10.1016/j.cell.2026.02.006
- Wei X., Li H., Huang Z. Y. X., et al. (2026). A global-scale assessment of zoonotic virus diversity and spillover potential in urban-adapted mammal species. *Nat. Microbiol.* **11**:1410–1423. DOI:10.1038/s41564-026-02311-9
- Zhang Q. Y. (2020). An overview on several large DNA viruses in freshwater ecosystems. *Acta Hydrobiologica Sinica* **44**:961–975. DOI:10.7541/2020.112
- Zhang Q. Y. and Gui J. F. (2018). Diversity, evolutionary contribution and ecological roles of aquatic viruses. *Sci. China Life Sci.* **61**:1486–1502. DOI:10.1007/s11427-018-9414-7
- Zhang Q.-Y., Ke F., Gui L., et al. (2022). Recent insights into aquatic viruses: Emerging and reemerging pathogens, molecular features, biological effects, and novel investigative approaches. *Water Biology and Security* **1**:100062. DOI:10.1016/j.watbs.2022.100062
- Poulton A. J. (2021). Shunt or shuttle. *Nat. Geosci.* **14**:181–183. DOI:10.1038/s41561-021-00718-z
- Carreira C., Lonborg C., Acharya B., et al. (2024). Integrating viruses into soil food web biogeochemistry. *Nat. Microbiol.* **9**:1918–1928. DOI:10.1038/s41564-024-01767-x
- Zhang Q. Y. and Ke F. (2025). Cross-domain aquatic viruses. *Acta Hydrobiologica Sinica* **49**:012506. DOI:10.7541/2025.2024.0330
- Ke F., Liu A. K. and Zhang Q. Y. (2025). Extra peptidase of a cyanophage confers its stronger lytic effect on bloom-forming *Microcystis aeruginosa*. *Int. J. Biol. Macromol.* **304**:140979. DOI:10.1016/j.ijbiomac.2025.140979
- Zhang X., He T., Zhou J., et al. (2025). Viruses are a key regulator of the microbial carbon cycle in the deep-sea biosphere. *Environ. Sci. Ecotechnol.* **27**:100609. DOI:10.1016/j.ese.2025.100609
- Gui J. F. (2024). Chinese wisdom and modern innovation of aquaculture. *Water Biology and Security* **3**:100271. DOI:10.1016/j.watbs.2024.100271
- FAO (2018). The State of World Fisheries and Aquaculture 2018 - Meeting the sustainable development goals. <https://openknowledge.fao.org/handle/20.500.14283/9540en>
- Gui J. F., Tang Q. S., Li Z. J., et al. (2018). Aquaculture in China: Success stories and modern trends. Wiley-Blackwell. <https://www.wiley.com/en-us/shop/general-aquaculture-fisheries-fish-science/aquaculture-in-china-success-stories-and-modern-trends-p-9781119120766>
- Naylor R. L., Hardy R. W., Buschmann A. H., et al. (2021). A 20-year retrospective review of global aquaculture. *Nature* **591**:551–563. DOI:10.1038/s41586-021-03308-6
- Ren W., Hu L., Guo L., et al. (2018). Preservation of the genetic diversity of a local common carp in the agricultural heritage rice-fish system. *Proc. Natl. Acad. Sci. USA* **115**:E546–E554. DOI:10.1073/pnas.1709582115
- Gui J.-F., Zhou L. and Li X.-Y. (2022). Rethinking fish biology and biotechnologies in the challenge era for burgeoning genome resources and strengthening food security. *Water Biology and Security* **1**:100002. DOI:10.1016/j.watbs.2021.11.001
- Wang T., Gong G., Li Z., et al. (2024). Genomic anatomy of homozygous XX females and YY males reveals early evolutionary trajectory of sex-determining gene and sex chromosomes in silurus fishes. *Mol. Biol. Evol.* **41**:msae169. DOI:10.1093/molbev/msae169
- Lu M., Zhang Q. C., Zhu Z. Y., et al. (2025). Manipulating unisexual-sexual reproduction transition to engineer genome-reconstructed polyoids. *Adv. Sci. (Weinh)* **12**:e06024. DOI:10.1002/adv.202506024
- Gan R. H., Li Z., Wang Z. W., et al. (2023). Creation of intermuscular bone-free mutants in amphitriploid gibel carp by editing two duplicatedrunx2b homeologs. *Aquaculture* **567**:7393. DOI:10.1016/j.aquaculture.2023.739300
- Nie C. H., Hilsdorf A. W. S., Wan S. M., et al. (2020). Understanding the development of intermuscular bones in teleost: Status and future directions for aquaculture. *Rev. Aquacult.* **12**:759–772. DOI:10.1111/raq.12348
- Uma A. (2025). Pathogen and disease transmission in aquatic animals. In management of fish diseases, S.K. Mallik, N. Shahi, and P.K. Pandey (eds). (Springer). DOI: 10.1007/978-981-96-0270-4_2
- Elabd H., Othman R. and Mahboub H. (2024). Diseases in aquaculture. In essentials of aquaculture practices, N.M. Faudzi, M.D. Shah, N. Mazlan, et al. (eds). (Springer). DOI: 10.1007/978-981-97-6699-4_6
- Hwang Y., Roux S., Coclet C., et al. (2023). Viruses interact with hosts that span distantly related microbial domains in dense hydrothermal mats. *Nat. Microbiol.* **8**:946–957. DOI:10.1038/s41564-023-01347-5
- Stentiford G. D., Sritunyalucksana K., Flegel T. W., et al. (2017). New paradigms to help solve the global aquaculture disease crisis. *PLoS Pathog* **13**:e1006160. DOI:10.1371/journal.ppat.1006160
- Akazawa N., Alviai A., Baloi A. P., et al. (2014). Reducing disease risk in aquaculture (English). Agriculture and environmental services discussion paper. <http://documents.worldbank.org/curated/en/110681468054563438>
- Israngkura A. and Sae-Hae S. (2002). A review of economic impacts of aquatic animal disease. In primary aquatic animal health care in rural, small-scale aquaculture development, technical proceedings of the Asia regional scoping workshop, J.R. Arthur, M.J. Phillips, R.P. Subasinghe, et al. (eds). (FAO), pp:55–61. <https://www.fao.org/4/Y3610E/y3610E25.htm#:~:text=This%20study%20develops%20three%20approaches%20in%20studying%20the,via%20the%20farmer%27s%20investment%20decision%20in%20disease%20control>
- Pauciullo S., Zulian V., La Frazia S., et al. (2024). Spillover: Mechanisms, genetic barriers, and the role of reservoirs in emerging pathogens. *Microorganisms* **12**:2191. DOI:10.3390/microorganisms12112191
- Telengech P., Hyodo K., Ichikawa H., et al. (2024). Replication of single viruses across the kingdoms, Fungi, Plantae, and Animalia. *Proc. Natl. Acad. Sci. USA* **121**:e2318150121. DOI:10.1073/pnas.2318150121
- Jancovich J. K., Zhang Q. Y. and Chinchar V. G. (2025). Ranavirus replication: New studies provide answers to old questions. In ranaviruses: Emerging pathogens of ectothermic vertebrates (2nd ed), M.J. Gray, and V.G. Chinchar (eds). (Springer). DOI: 10.1007/978-3-031-64973-8
- Costa V. A. and Holmes E. C. (2024). Diversity, evolution, and emergence of fish viruses. *J. Virol.* **98**:e0011824. DOI:10.1128/jvi.00118-24
- Ahmadivand S., Savage A. and Palic D. (2025). Biosecurity and vaccines for emerging aquatic animal RNA viruses. *Viruses* **17**:768. DOI:10.3390/v17060768
- Ebel G. D. (2017). Promiscuous viruses-how do viruses survive multiple unrelated hosts. *Curr. Opin. Virol.* **23**:125–129. DOI:10.1016/j.coviro.2017.05.002
- Stentiford G. D., Bateman I. J., Hinchliffe S. J., et al. (2020). Sustainable aquaculture through the One Health lens. *Nat. Food* **1**:468–474. DOI:10.1038/s43016-020-0127-5
- Vora N. M., Hannah L., Lieberman S., et al. (2022). Want to prevent pandemics. Stop spillovers. *Nature* **605**:419–422. DOI:10.1038/d41586-022-01312-y
- Vora N. M., Hannah L., Walzer C., et al. (2023). Interventions to reduce risk for pathogen spillover and early disease spread to prevent outbreaks, epidemics, and pandemics. *Emerg. Infect. Dis.* **29**:1–9. DOI:10.3201/eid2903.221079

37. Bell D., von Agris J., Tacheva B., et al. (2025). Natural spillover risk and disease outbreaks: Is over-simplification putting public health at risk. *J. Epidemiol. Glob. Health* **15**:65. DOI:10.1007/s44197-025-00412-y
38. Gavotte L., Gauchere C. and Frutos R. (2023). Environmental spillover of emerging viruses: Is it true. *Environ. Res.* **233**:116416. DOI:10.1016/j.envres.2023.116416
39. Zhang Q. Y. and Gui J. F. (2015). Virus genomes and virus-host interactions in aquaculture animals. *Sci. China Life Sci.* **58**:156–169. DOI:10.1007/s11427-015-4802-y
40. Letko M., Seifert S. N., Olival K. J., et al. (2020). Bat-borne virus diversity, spillover and emergence. *Nat. Rev. Microbiol.* **18**:461–471. DOI:10.1038/s41579-020-0394-z
41. Rohde R. E. and McNamara R. P. (2021). Virus spillover and emerging pathogens pick up speed. Contagion live. <https://www.contagionlive.com/view/virus-spillover-and-emerging-pathogens-pick-up-speed>
42. Grange Z. L., Goldstein T., Johnson C. K., et al. (2021). Ranking the risk of animal-to-human spillover for newly discovered viruses. *Proc. Natl. Acad. Sci. USA* **118**:e2002324118. DOI:10.1073/pnas.2002324118
43. Zhao J., Wan W., Yu K., et al. (2024). Farmed fur animals harbour viruses with zoonotic spillover potential. *Nature* **634**:228–233. DOI:10.1038/s41586-024-07901-3
44. Zhou Z., Tran P. Q., Martin C., et al. (2025). Unravelling viral ecology and evolution over 20 years in a freshwater lake. *Nat. Microbiol.* **10**:231–245. DOI:10.1038/s41564-024-01876-7
45. Brown C. (2013). Spillover: Animal infection and the next human pandemic. *Emerg. Infect. Dis.* **19**:349. DOI:10.3201/eid1902.121694
46. Emmenegger E. J., Bueren E. K., Conway C. M., et al. (2024). Host jump of an exotic fish rhabdovirus into a new class of animals poses a disease threat to amphibians. *Viruses* **16**:1193. DOI:10.3390/v16081193
47. Song H. C., Elsheikha H., Yang T., et al. (2025). Global spillover of land-derived microbes to Ocean hosts: Sources, transmission pathways, and one health threats. *Environ. Sci. Ecotechnol.* **27**:100603. DOI:10.1016/j.ese.2025.100603
48. Zimmer C. (2021). A Planet of Viruses (3rd ed) (University of Chicago Press). <https://press.uchicago.edu/ucp/books/book/chicago/P/bo89967708.html>
49. Goncalves do Amaral C., Pinto Andre E., Maffud Cilli E., et al. (2024). Viral diseases and the environment relationship. *Environ. Pollut.* **362**:124845. DOI:10.1016/j.envpol.2024.124845
50. Meadows A. J., Stephenson N., Madhav N. K., et al. (2023). Historical trends demonstrate a pattern of increasingly frequent and severe spillover events of high-consequence zoonotic viruses. *BMJ Glob. Health* **8**:e012026. DOI:10.1136/bmjgh-2023-012026
51. Hierweger M. M., Koch M. C., Rupp M., et al. (2021). Novel filoviruses, hantavirus, and rhabdovirus in freshwater fish, Switzerland, 2017. *Emerg. Infect. Dis.* **27**:3082–3091. DOI:10.3201/eid2712.210491
52. Walker P. J., Bigarre L., Kurath G., et al. (2022). Revised taxonomy of rhabdoviruses infecting fish and marine mammals. *Animals (Basel)* **12**:1363. DOI:10.3390/ani12111363
53. Schonherz A. A., Lorenzen N. and Einer-Jensen K. (2013). Inter-species transmission of viral hemorrhagic septicemia virus (VHSV) from turbot (*Scophthalmus maximus*) to rainbow trout (*Onchorhynchus mykiss*). *J. Gen. Virol.* **94**:869–875. DOI:10.1099/vir.0.048223-0
54. Mohammadisefat P., Zorriehzahra M. J., Adel M., et al. (2023). Viral hemorrhagic septicemia virus (VHSV), past, present and future: A review. *International Aquatic Research* **15**:191–203. DOI:10.22034/IAR.2023.1983457.1424
55. Escobar L. E., Escobar-Dodero J. and Phelps N. B. D. (2018). Infectious disease in fish: Global risk of viral hemorrhagic septicemia virus. *Rev. Fish Biol. Fisheries* **28**:637–655. DOI:10.1007/s11160-018-9524-3
56. Ito T., Kurita J., Mori K. I., et al. (2018). Virulence marker candidates in N-protein of viral haemorrhagic septicaemia virus (VHSV): Virulence variability within VHSV Ib clones. *Dis. Aquat. Organ.* **128**:51–62. DOI:10.1038/dao03215
57. Sandlund N., Gjerset B., Bergh O., et al. (2014). Screening for viral hemorrhagic septicemia virus in marine fish along the Norwegian coastal line. *PLoS One* **9**:e108529. DOI:10.1371/journal.pone.0108529
58. Breyta R. B., Batts W. N. and Kurath G. (2022). Genetics reveal long-distance virus transmission links in pacific salmon. *Animals (Basel)* **12**:2120. DOI:10.3390/ani12162120
59. Chinchar V. G., Hick P., Ince I. A., et al. (2017). ICTV virus taxonomy profile: Iridoviridae. *J. Gen. Virol.* **98**:890–891. DOI:10.1099/jgv.0.000818
60. Chinchar V. G., Waltzek T. B. and Subramaniam K. (2017). Ranaviruses and other members of the family Iridoviridae: Their place in the virosphere. *Virology* **511**:259–271. DOI:10.1016/j.virol.2017.06.007
61. Luedtke J. A., Chanson J., Neam K., et al. (2023). Ongoing declines for the world's amphibians in the face of emerging threats. *Nature* **622**:308–314. DOI:10.1038/s41586-023-06578-4
62. Leiva-Rebollo R., Labella A. M., Valverde E. J., et al. (2020). Persistence of lymphocystis disease virus (LCDV) in seawater. *Food Environ. Virol.* **12**:174–179. DOI:10.1007/s12560-020-09420-6
63. Borrego J. J., Valverde E. J., Labella A. M., et al. (2017). Lymphocystis disease virus: Its importance in aquaculture. *Rev. Aquacult.* **9**:179–193. DOI:10.1111/raq.12131
64. Chen Z. Y., Gui J. F., Gao X. C., et al. (2013). Genome architecture changes and major gene variations of *Andrias davidianus* ranavirus (ADRV). *Vet. Res.* **44**:101. DOI:10.1186/1297-9716-44-101
65. Yu X.-D., Ke F., Zhang Q.-Y., et al. (2023). Genome characteristics of two ranavirus isolates from mandarin fish and largemouth bass. *Pathogens* **12**:730. DOI:10.3390/pathogens12050730
66. Ke F., Gui J. F., Chen Z. Y., et al. (2018). Divergent transcriptomic responses underlying the ranaviruses-amphibian interaction processes on interspecies infection of Chinese giant salamander. *BMC Genomics* **19**:211. DOI:10.1186/s12864-018-4596-y
67. Jancovich J. K., Bremont M., Touchman J. W., et al. (2010). Evidence for multiple recent host species shifts among the Ranaviruses (family Iridoviridae). *J. Virol.* **84**:2636–2647. DOI:10.1128/JVI.01991-09
68. Bates K. A., Rosa G. M. and Garner T. W. J. (2025). Ranavirus. *Trends Microbiol.* **33**:701–702. DOI:10.1016/j.tim.2025.02.008
69. Duffus A. L. J., Waltzek T. B., Stöhr A. C., et al. (2015). Distribution and host range of ranaviruses. In: *Ranaviruses: Lethal pathogens of ectothermic vertebrates*, M.J. Gray, and V.G. Chinchar (eds). (Springer), pp:9–57. DOI: 10.1007/978-3-319-13755-1_2
70. Pan W., Liang M., You Y., et al. (2024). Viral genomic methylation and the interspecies evolutionary relationships of ranavirus. *PLoS Pathog* **20**:e1012736. DOI:10.1371/journal.ppat.1012736
71. Lesbarreres D., Balseiro A., Brunner J., et al. (2012). Ranavirus: Past, present and future. *Biol. Lett.* **8**:481–483. DOI:10.1098/rsbl.2011.0951
72. Whitfield S. M., Geerdes E., Chacon I., et al. (2013). Infection and co-infection by the amphibian chytrid fungus and ranavirus in wild Costa Rican frogs. *Dis. Aquat. Organ.* **104**:173–178. DOI:10.3354/dao02598
73. Price S. J., Ariel E., MacLaine A., et al. (2017). From fish to frogs and beyond: Impact and host range of emergent ranaviruses. *Virology* **511**:272–279. DOI:10.1016/j.virol.2017.08.001
74. Rosa G. M., Sabino-Pinto J., Laurentino T. G., et al. (2017). Impact of asynchronous emergence of two lethal pathogens on amphibian assemblages. *Sci. Rep.* **7**:43260. DOI:10.1038/srep43260
75. Lisachova L. S., Lisachov A. P., Ermakov O. A., et al. (2025). Continent-wide distribution of CMTV-like ranavirus, from the Urals to the Atlantic Ocean. *EcoHealth* **22**:173–184. DOI:10.1007/s10393-025-01703-3
76. Vilaca S. T., Bienentreu J. F., Brunetti C. R., et al. (2019). Frog virus 3 genomes reveal prevalent recombination between ranavirus lineages and their origins in Canada. *J. Virol.* **93**:e00765–00719. DOI:10.1128/jvi.00765-19
77. Carstairs S. J., Kyle C. J. and Vilaca S. T. (2020). High prevalence of subclinical frog virus 3 infection in freshwater turtles of Ontario, Canada. *Virology* **543**:76–83. DOI:10.1016/j.virol.2020.01.016
78. Ke F., Yu X.-D., Wang Z.-H., et al. (2022). Replication and transcription machinery for ranaviruses: Components, correlation, and functional architecture. *Cell & Bioscience* **12**:6. DOI:10.1186/s13578-021-00742-x
79. Liu L., Zhang Y., Yuan M. D., et al. (2024). Integrated multi-omics analysis reveals liver metabolic reprogramming by fish iridovirus and antiviral function of alpha-linolenic acid. *Zool. Res.* **45**:520–534. DOI:10.24272/j.issn.2095-8137.2024.028
80. Earl J. E., Chaney J. C., Sutton W. B., et al. (2016). Ranavirus could facilitate local extinction of rare amphibian species. *Oecologia* **182**:611–623. DOI:10.1007/s00442-016-3682-6
81. Rosa G. M., Botto G. A., Mitra A. T., et al. (2022). Invasive fish disrupt host-pathogen dynamics leading to amphibian declines. *Biol. Conserv.* **276**:109785. DOI:10.1016/j.biocon.2022.109785
82. Wirth W., Schwarzkopf L., Skerratt L. F., et al. (2018). Ranaviruses and reptiles. *PeerJ* **6**:e6083. DOI:10.7717/peerj.6083
83. Herath J., Ellepola G. and Meegaskumbura M. (2021). Patterns of infection, origins, and transmission of ranaviruses among the ectothermic vertebrates of Asia. *Ecol. Evol.* **11**:15498–15519. DOI:10.1002/ece3.8243
84. Simon David D. A. and Parish C. R. (2013). Heparan sulfate: A ubiquitous glycosaminoglycan with multiple roles in immunity. *Front Immunol.* **4**:470. DOI:10.3389/fimmu.2013.00470
85. Cagno V., Tseligka E. D., Jones S. T., et al. (2019). Heparan sulfate proteoglycans and viral attachment: True receptors or adaptation bias. *Viruses* **11**:596. DOI:10.3390/v11070596
86. Ke F., Wang Z. H., Ming C. Y., et al. (2019). Ranaviruses bind cells from different species through interaction with heparan sulfate. *Viruses* **11**:593. DOI:10.3390/v11070593
87. Chinchar V. G. and Waltzek T. B. (2014). Ranaviruses: Not just for frogs. *PLoS Path.* **10**:e1003850. DOI:10.1371/journal.ppat.1003850.g001
88. Herath J., Sun D., Ellepola G., et al. (2023). Emerging threat of ranavirus: Prevalence, genetic diversity, and climatic drivers of Ranavirus (Iridoviridae) in ectothermic vertebrates of Asia. *Front Vet. Sci.* **10**:1291872. DOI:10.3389/fvets.2023.1291872
89. Wang X. and Osterrieder N. (2025). A plasmid-based reverse genetics system for tilapia lake virus (TiLV). *Aquaculture* **595**:741575. DOI:10.1016/j.aquaculture.2024.741575
90. Eyngor M., Zamostiano R., Kembou Tsoufack J. E., et al. (2014). Identification of a novel RNA virus lethal to tilapia. *J. Clin. Microbiol.* **52**:4137–4146. DOI:10.1128/JCM.00827-14
91. Koonin E. V., Krupovic M., Surachetpong W., et al. (2023). ICTV virus taxonomy profile: Amnoonviridae 2023. *J. Gen. Virol.* **104**:001903. DOI:10.1099/jgv.0.001903

92. Tang K. F. J., Bondad-Reantaso M. G., Surachetpong W., et al. (2021). Tilapia lake virus disease strategy manual. FAO Fisheries and Aquaculture Circular No. 1220. (FAO). DOI:10.4060/cb7293en
93. Surachetpong W., Roy S. R. K. and Nicholson P. (2020). Tilapia lake virus: The story so far. *J. Fish Dis.* **43**:1115–1132. DOI:10.1111/jfd.13237
94. Fracalossi D. M. and Turchini G. M. (2022). Tilapia. *Rev. Aquacult.* [https://onlinelibrary.wiley.com/doi/toc/10.1111/\(ISSN\)1753-5131.Tilapia](https://onlinelibrary.wiley.com/doi/toc/10.1111/(ISSN)1753-5131.Tilapia)
95. Waltzek T., Frasca Jr S., Ferguson H., et al. (2019). Tilapia lake virus (TiLV): A globally emerging threat to tilapia aquaculture. *Edis* **2019**:FA213. DOI:10.32473/edis-fa213-2019
96. Saranya S. R., Priya V., Manishkumar A. T., et al. (2023). Isolation and identification of pathogens from fish: Tilapia lake virus (TiLV). In *aquaculture microbiology. Springer protocols handbooks.*, J. Thomas, and N. Amarasena(eds). (Springer), pp:49–58. DOI:10.1007/978-1-0716-3032-7_8
97. Turner J. K., Sakulpolwat S., Kuchanon S., et al. (2023). Tilapia lake virus (TiLV) causes severe anaemia and systemic disease in tilapia. *J. Fish Dis.* **46**:643–651. DOI:10.1111/jfd.13775
98. Kembou-Ringert J. E., Hotio F. N., Steinhagen D., et al. (2024). Knowns and unknowns of TiLV-associated neuronal disease. *Virulence* **15**:2329568. DOI:10.1080/21505594.2024.2329568
99. He T., Zhang Y.-Z., Gao L.-H., et al. (2023). Identification and pathogenetic study of tilapia lake virus (TiLV) isolated from naturally diseased tilapia. *Aquaculture* **565**:739166. DOI:10.1016/j.aquaculture.2022.739166
100. Dong H. T., Ataguba G. A., Khunrae P., et al. (2017). Evidence of TiLV infection in tilapia hatcheries from 2012 to 2017 reveals probable global spread of the disease. *Aquaculture* **479**:579–583. DOI:10.1016/j.aquaculture.2017.06.035
101. Aich N., Paul A., Choudhury T. G., et al. (2022). Tilapia Lake Virus (TiLV) disease: Current status of understanding. *Aquaculture and Fisheries* **7**:7–17. DOI:10.1016/j.aaf.2021.04.007
102. FAO (2017). Outbreaks of Tilapia lake virus (TiLV) threaten the livelihoods and food security of millions of people dependent on tilapia farming. Global information and early warning system on food and agriculture (GIEWS). https://www.fao.org/fileadmin/user_upload/newsroom/docs/GIEWS%20Special%20Alert%20338%20Global%2017326EN.pdf
103. Kibenge F. S. (2019). Emerging viruses in aquaculture. *Curr. Opin. Virol.* **34**:97–103. DOI:10.1016/j.coviro.2018.12.008
104. Machimbirike V. I., Jansen M. D., Senapin S., et al. (2019). Viral infections in tilapines: More than just tilapia lake virus. *Aquaculture* **503**:508–518. DOI:10.1016/j.aquaculture.2019.01.036
105. Jansen M. D., Dong H. T. and Mohan C. V. (2018). Tilapia lake virus: A threat to the global tilapia industry. *Rev. Aquacult.* **11**:725–739. DOI:10.1111/raq.12254
106. Yamkasem J., Piewbang C., Techangamsuwan S., et al. (2021). Susceptibility of ornamental African cichlids *Aulonocara* spp. to experimental infection with Tilapia lake virus. *Aquaculture* **542**:736920. DOI:10.1016/j.aquaculture.2021.736920
107. Abdullah A., Ramly R., Mohammad Ridzwan M. S., et al. (2018). First detection of tilapia lake virus (TiLV) in wild river carp (*Barbonymus schwanenfeldii*) at Timah Tasoh Lake, Malaysia. *J. Fish Dis.* **41**:1459–1462. DOI:10.1111/jfd.12843
108. Abdullah A., Pazzi A. M., Ridzwan M. S. M., et al. (2022). Persistent detection of Tilapia lake virus in wild tilapia and tin foil barbs. *Vet. World* **15**:1097–1106. DOI:10.14202/vetworld.2022.1097-1106
109. Yamkasem J., Tattiyapong P., Kamlangdee A., et al. (2019). Evidence of potential vertical transmission of tilapia lake virus. *J. Fish Dis.* **42**:1293–1300. DOI:10.1111/jfd.13050
110. Xu T., Xia J., Wang C., et al. (2025). Horizontal and vertical transmission of covert mortality nodavirus in the marine fish. *Aquaculture* **607**:742620. DOI:10.1016/j.aquaculture.2025.742620
111. Jaemwimol P., Rawiwan P., Tattiyapong P., et al. (2018). Susceptibility of important warm water fish species to tilapia lake virus (TiLV) infection. *Aquaculture* **497**:462–468. DOI:10.1016/j.aquaculture.2018.08.028
112. Li B., Zheng S., Wang Y., et al. (2022). Susceptibilities of ten fish cell lines to infection with Tilapia lake virus. *Microb. Pathog.* **166**:105510. DOI:10.1016/j.micpath.2022.105510
113. Subramanian S., Busch C. J., Molawi K., et al. (2022). Long-term culture-expanded alveolar macrophages restore their full epigenetic identity after transfer in vivo. *Nat. Immunol.* **23**:458–468. DOI:10.1038/s41590-022-01146-w
114. Petrone M. E., Parry R., Mifsud J. C. O., et al. (2023). Evidence for an ancient aquatic origin of the RNA viral order Articulavirales. *Proc. Natl. Acad. Sci. USA* **120**:e2310529120. DOI:10.1073/pnas.2310529120
115. Arragain B., Pelosse M., Huard K., et al. (2025). Structure of the tilapia lake virus nucleoprotein bound to RNA. *Nucleic. Acids. Res.* **53**. DOI:10.1093/nar/gkaf112
116. Yao Q., Mercier A., Nayak A., et al. (2025). Structural and mechanistic insights into herpesvirus helicase-primase and its therapeutic inhibitors. *Nat. Microbiol.* **10**:3191–3201. DOI:10.1038/s41564-025-02168-4
117. Quijano Carde E. M. and Soto E. (2024). A review of latency in the *Alloherpesviridae* family. *J. Fish Dis.* **47**:e14016. DOI:10.1111/jfd.14016
118. Dorfman B., Lamichhane S., Marcos-Hadad E., et al. (2026). Differences in CyHV-3 infection and infectivity among common carp and Asian carp species. *Aquaculture* **625**:744303. DOI:10.1016/j.aquaculture.2026.744303
119. Jiang Q.-Q., Li Z., Zhang Q.-Y., et al. (2024). A novel cell line established from skin tissue of gibel carp (*Carassius gibelio*) is susceptible to *Carassius auratus* herpesvirus infection. *Water Biology and Security* **3**:100253. DOI:10.1016/j.watbs.2024.100253
120. Bergmann S. M., Wang Y., Li Y., et al. (2024). Occurrence of herpesvirus in fish. *J. Vet. Res.* **68**:73–78. DOI:10.2478/jvetres-2024-0008
121. Bergmann S. M., Todte M., Jager L., et al. (2025). Molecular detection and characterisation of herpesviruses in asymptomatic Russian sturgeon (*Acipenser gueldenstaedtii*) from European aquaculture. *J. Vet. Res.* **69**:169–175. DOI:10.2478/jvetres-2025-0028
122. Hanson L. A., Doszpoly A., van Beurden S., et al. (2024). Chapter 8-Alloherpesviruses of Fish. In *aquaculture virology*. 2nd ed. F.S.B. Kibenge, and M.G. Godoy (eds). (Academic Press), pp:165–189. DOI:10.1016/B978-0-323-91169-6.00013-3
123. He B., Sridhar A., Thiry M., et al. (2025). Genomic and phenotypic characterization of a novel virulent strain of *Cyprinus cyprinidalo2* originating from an outbreak in the Netherlands. *Viruses* **17**:658. DOI:10.3390/v17050658
124. Thangaraj R. S., Nithianantham S. R., Dharmaratnam A., et al. (2021). Cyprinid herpesvirus - 2 (CyHV - 2): A comprehensive review. *Rev. Aquacult.* **13**:796–821. DOI:10.1111/raq.12499
125. Perelberg A., Smirnov M., Hutoran M., et al. (2003). Epidemiological description of a new viral disease afflicting cultured *Cyprinus carpio* in Israel. *Israeli Journal of Aquaculture - Bamidgheh* **55**:5–12. DOI:10.46989/001c.20337
126. Aswad A. and Katzourakis A. (2017). A novel viral lineage distantly related to herpesviruses discovered within fish genome sequence data. *Virus Evol.* **3**:vex016. DOI:10.1093/ve/vex016
127. Ke F. and Zhang Q. Y. (2023). Advances on genomes studies of large DNA viruses in aquaculture: A minireview. *Genomics* **115**:110720. DOI:10.1016/j.ygeno.2023.110720
128. Zeng X. T., Chen Z. Y., Deng Y. S., et al. (2016). Complete genome sequence and architecture of crucian carp *Carassius auratus* herpesvirus (CaHV). *Arch. Virol.* **161**:3577–3581. DOI:10.1007/s00705-016-3037-y
129. Yang J., Wen J., Xiao S., et al. (2022). Complete genome and molecular characterization of a new cyprinid herpesvirus 2 (CyHV-2) SH-01 strain isolated from cultured crucian carp. *Viruses* **14**:2068. DOI:10.3390/v14092068
130. Adler B., Sattler C. and Adler H. (2017). Herpesviruses and their host cells: A successful liaison. *Trends Microbiol.* **25**:229–241. DOI:10.1016/j.tim.2016.11.009
131. Radosavljevic V., Glisic D., Maksimovic-Zoric J., et al. (2025). Emergence and persistence of *Cyprinus cyprinidalo2* 2 (CyHV-2) in Prussian carp in Serbian lakes. *Aquaculture* **597**:741956. DOI:10.1016/j.aquaculture.2024.741956
132. Sudomova M. and Hassan S. T. S. (2023). Herpesvirus diseases in humans and animals: Recent developments, challenges, and charting future paths. *Pathogens* **12**:1422. DOI:10.3390/pathogens12121422
133. Zhao Z., Yu F., Hao K., et al. (2022). A brief review on virology researches of fish herpesviruses. *Journal of Fisheries of China* **46**:322–336. DOI:10.11964/jfc.20210712945
134. Boutier M., Morvan L., Delrez N., et al. (2021). Fish and amphibian Alloherpesviruses (*Herpesviridae*). In *encyclopedia of virology*, pp:306–315. DOI:10.1016/b978-0-12-809633-8.20931-x
135. van Beurden S. and Engelsma M. (2012). Herpesviruses of fish, amphibians and invertebrates. In *herpesviruses*, G.D. Magel, and S. Tyring (eds). (Intech), pp:217–242. DOI:10.5772/29575.
136. Burioli E. A. V., Prearo M. and Houssin M. (2017). Complete genome sequence of Ostreid herpesvirus type 1 microVar isolated during mortality events in the Pacific oyster *Crassostrea gigas* in France and Ireland. *Virology* **509**:239–251. DOI:10.1016/j.virol.2017.06.027
137. Delisle L., Petton B., Burguin J. F., et al. (2018). Temperature modulate disease susceptibility of the Pacific oyster *Crassostrea gigas* and virulence of the Ostreid herpesvirus type 1. *Fish Shellfish Immunol.* **80**:71–79. DOI:10.1016/j.fsi.2018.05.056
138. Wang Z. H., Ke F., Zhang Q. Y., et al. (2021). Structural and functional diversity among five RING finger proteins from *Carassius auratus* herpesvirus (CaHV). *Viruses* **13**:254. DOI:10.3390/v13020254
139. Zhao Y. H., Zeng X. T. and Zhang Q. Y. (2020). Fish herpesvirus protein (CaHV-138L) can target to mitochondrial protein FoF1 ATPase. *Virus Res.* **275**:197754. DOI:10.1016/j.virusres.2019.197754
140. Shi Y., Li Y., Li H., et al. (2025). Extensive cross-species transmission of pathogens and antibiotic resistance genes in mammals neglected by public health surveillance. *Cell* **188**:6591–6605 e6514. DOI:10.1016/j.cell.2025.08.016
141. Knipe D. M. and Cliffe A. (2008). Chromatin control of herpes simplex virus lytic and latent infection. *Nat. Rev. Microbiol.* **6**:211–221. DOI:10.1038/nrmicro1794
142. Dotto-Maurel A., Arzul I., Morga B., et al. (2025). Herpesviruses: Overview of systematics, genomic complexity and life cycle. *Virol. J.* **22**:155. DOI:10.1186/s12985-025-02779-7
143. Desrina, Prayitno S. B., Verdegem M. C. J., et al. (2022). White spot syndrome virus host range and impact on transmission. *Rev. Aquacult.* **14**:1843–1860. DOI:10.1111/raq.12676
144. Ke F., Gui L., Li T., et al. (2021). A footprint in the genome of freshwater crayfish whispovirus (WSSV-Cc). *Journal of Fisheries of China* **45**:1491–1499. DOI:10.11964/jfc.20210512878

145. Iftehimul M., Hasan N. A., Bass D., et al. (2025). Combating white spot syndrome virus (WSSV) in global shrimp farming: Unraveling its biology, pathology, and control strategies. *Viruses* **17**:1463. DOI:10.3390/v17111463
146. Kim M. J., Kim J. O., Jang G. I., et al. (2023). Evaluation of the horizontal transmission of white spot syndrome virus for whiteleg shrimp (*Litopenaeus vannamei*) based on the disease severity grade and viral shedding rate. *Animals (Basel)* **13**:1676. DOI:10.3390/ani13101676
147. Sun M., Liu M., Shan H., et al. (2023). Ring-stacked capsids of white spot syndrome virus and structural transitions with genome ejection. *Sci. Adv.* **9**:eadd2796. DOI:10.1126/sciadv.add2796
148. Shaw C. L. and Kennedy D. A. (2025). Early epidemiological characteristics explain the chance of population-level virus persistence following spillover events. *PLoS Biol.* **23**:e3003315. DOI:10.1371/journal.pbio.3003315
149. Sokolow S. H., Nova N., Pepin K. M., et al. (2019). Ecological interventions to prevent and manage zoonotic pathogen spillover. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **374**:20180342. DOI:10.1098/rstb.2018.0342
150. Ellwanger J. H. and Chies J. A. B. (2021). Zoonotic spillover: Understanding basic aspects for better prevention. *Genet. Mol. Biol.* **44**:e20200355. DOI:10.1590/1678-4685-GMB-2020-0355
151. Borremans B., Faust C., Manlove K. R., et al. (2019). Cross-species pathogen spillover across ecosystem boundaries: Mechanisms and theory. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **374**:20180344. DOI:10.1098/rstb.2018.0344
152. Chen Q. (2025). Linking habitat loss to pathogen spillover. *Nat. Rev. Biodivers.* **1**:752. DOI:10.1038/s44358-025-00111-3
153. Wasik B. R., de Wit E., Munster V., et al. (2019). Onward transmission of viruses: How do viruses emerge to cause epidemics after spillover. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **374**:20190017. DOI:10.1098/rstb.2019.0017
154. Parrish C. R., Holmes E. C., Morens D. M., et al. (2008). Cross-species virus transmission and the emergence of new epidemic diseases. *Microbiol. Mol. Biol. Rev.* **72**:457–470. DOI:10.1128/MMBR.00004-08
155. Chen W., Lu S., Xiong H., et al. (2025). Gene flow and its sporadic spillover: H10 and N5 avian influenza viruses from wild birds and the H10N5 human cases in China. *Viol. Sin.* **40**:15–23. DOI:10.1016/j.virs.2024.12.002
156. Jones J. E., Le Sage V. and Lakdawala S. S. (2021). Viral and host heterogeneity and their effects on the viral life cycle. *Nat. Rev. Microbiol.* **19**:272–282. DOI:10.1038/s41579-020-00449-9
157. Dufloo J., Andreu-Moreno I., Moreno-Garcia J., et al. (2025). Receptor-binding proteins from animal viruses are broadly compatible with human cell entry factors. *Nat. Microbiol.* **10**:405–419. DOI:10.1038/s41564-024-01879-4
158. Maginnis M. S. (2018). Virus-receptor interactions: The key to cellular invasion. *J. Mol. Biol.* **430**:2590–2611. DOI:10.1016/j.jmb.2018.06.024
159. Kuchipudi S. V., Nelli R. K., Gontu A., et al. (2021). Sialic acid receptors: The key to solving the enigma of zoonotic virus spillover. *Viruses* **13**:262. DOI:10.3390/v13020262
160. Guo X., Liang Y., Gao C., et al. (2026). Diversity and ecological potentials of marine viruses inhabiting continental shelf seas. *Adv. Sci. (Weinh)* **13**:e11707. DOI:10.1002/advs.202511707
161. Ke F., Gui L., Li T., et al. (2021). The features of an emerging whispovirus isolate from freshwater crayfish. *Aquacult. Rep.* **20**:100728. DOI:10.1016/j.aqrep.2021.100728
162. Zhang Q. Y. (2020). Genes associated with cyanophage infection: A review. *Microbiology China* **47**:3277–3286. DOI:10.13344/j.microbiol.china.200527
163. Elena S. F. and García-Arenal F. (2023). Plant virus adaptation to new hosts: A multi-scale approach. In viral fitness and evolution. Current topics in microbiology and immunology, E. Domingo, P. Schuster, S.F. Elena, et al.(eds). (Springer). DOI:10.1007/978-3-031-15640-3_5
164. Tan C. C. S., van Dorp L. and Balloux F. (2024). The evolutionary drivers and correlates of viral host jumps. *Nat. Ecol. Evol.* **8**:960–971. DOI:10.1038/s41559-024-02353-4
165. Hoffmann C., Krasemann S., Wurr S., et al. (2024). Lassa virus persistence with high viral titers following experimental infection in its natural reservoir host, *Mastomys natalensis*. *Nat. Commun.* **15**:9319. DOI:10.1038/s41467-024-53616-4
166. Rothenburg S. and Brennan G. (2020). Species-specific host-virus interactions: Implications for viral host range and virulence. *Trends Microbiol.* **28**:46–56. DOI:10.1016/j.tim.2019.08.007
167. da Silva P. G., Mesquita J. R., de Sao Jose Nascimento M., et al. (2021). Viral, host and environmental factors that favor anthroponotic spillover of coronaviruses: An opinionated review, focusing on SARS-CoV, MERS-CoV and SARS-CoV-2. *Sci. Total Environ.* **750**:141483. DOI:10.1016/j.scitotenv.2020.141483
168. Albery G. F., Becker D. J., Brierley L., et al. (2021). The science of the host-virus network. *Nat. Microbiol.* **6**:1483–1492. DOI:10.1038/s41564-021-00999-5
169. Mehle N., Gutierrez-Aguirre I., Kutnjak D., et al. (2018). Water-mediated transmission of plant, animal, and human Viruses. *Adv. Virus Res.* **101**:85–128. DOI:10.1016/bbs.aivir.2018.02.004
170. Yuan L., Yu P., Huang X., et al. (2024). Seasonal succession, host associations, and biochemical roles of aquatic viruses in a eutrophic lake plagued by cyanobacterial blooms. *Environ. Int.* **193**:109125. DOI:10.1016/j.envint.2024.109125
171. Viruses switch hosts to evolve. (2017). *Nature* **543**:466. DOI:10.1038/543466b
172. Le Sage V., Lowen A. C. and Lakdawala S. S. (2023). Block the spread: Barriers to transmission of influenza viruses. *Annu. Rev. Virol.* **10**:347–370. DOI:10.1146/annurev-virology-111821-115447
173. Krupovic M. and Koonin E. V. (2026). Organization and evolution of the virosphere and the replicator space. *C. R. Biol.* **349**:35–75. DOI:10.5802/crbio.193
174. Liang M., Pan W., You Y., et al. (2024). Hypermethylated genome of a fish vertebrate iridovirus ISKNV plays important roles in viral infection. *Commun. Biol.* **7**:237. DOI:10.1038/s42003-024-05919-x
175. Thorne L. G. (2025). Linking innate immune evasion to pandemic potential. *Nat. Rev. Microbiol.* **23**:70. DOI:10.1038/s41579-024-01137-8
176. Wickenhagen A., van Tol S. and Munster V. (2024). Molecular determinants of cross-species transmission in emerging viral infections. *Microbiol. Mol. Biol. Rev.* **88**:e0000123. DOI:10.1128/mmbr.00001-23
177. Yu X., Zhu Y., Yin G., et al. (2024). Exploiting hosts and vectors: Viral strategies for facilitating transmission. *EMBO Rep.* **25**:3187–3201. DOI:10.1038/s44319-024-00214-6
178. Wang X. and Zhang W. (2026). Henipaviruses at the threshold: Preparedness in the era of recurrent spillover. *Emerg. Microbes. Infect.* **15**:2667556. DOI:10.1080/22221751.2026.2667556
179. Kurahashi S., Mukai T., Sekine Y., et al. (2023). A tipping point of spreading viruses: Estimating the risk of household contact transmission of COVID-19. *Frontiers in Physics* **10**:1044049. DOI:10.3389/fphy.2022.1044049
180. Liu X., Chang X., Leng S., et al. (2019). Detection for disease tipping points by landscape dynamic network biomarkers. *Natl. Sci. Rev.* **6**:775–785. DOI:10.1093/nsr/nwy162
181. Lyu C., Chen L. and Liu X. (2024). Detecting tipping points of complex diseases by network information entropy. *Brief Bioinform.* **25**:bbae311. DOI:10.1093/bib/bbae311
182. Schmidt J. P., Park A. W., Kramer A. M., et al. (2017). Spatiotemporal fluctuations and triggers of Ebola virus spillover. *Emerg. Infect. Dis.* **23**:415–422. DOI:10.3201/eid2303.160101
183. Carlson C. J., Albery G. F., Merow C., et al. (2022). Climate change increases cross-species viral transmission risk. *Nature* **607**:555–562. DOI:10.1038/s41586-022-04788-w
184. Rowley A. F., Baker-Austin C., Boerlage A. S., et al. (2024). Diseases of marine fish and shellfish in an age of rapid climate change. *Iscience* **27**:110838. DOI:10.1016/j.isci.2024.110838
185. Tian J., Sun J., Li D., et al. (2022). Emerging viruses: Cross-species transmission of coronaviruses, filoviruses, henipaviruses, and rotaviruses from bats. *Cell Rep.* **39**:110969. DOI:10.1016/j.celrep.2022.110969
186. Nichol S. T., Arikawa J. and Kawaoka Y. (2000). Emerging viral diseases. *Proc. Natl. Acad. Sci. USA* **97**:12411–12412. DOI:10.1073/pnas.210382297
187. Choi Y. K. (2021). Emerging and re-emerging fatal viral diseases. *Exp. Mol. Med.* **53**:711–712. DOI:10.1038/s12276-021-00608-9
188. FAO. (2020). The State of World Fisheries and Aquaculture 2020. Sustainability in action. <https://doi.org/10.4060/ca9229en>
189. Randolph D. G., Refsich J., MacMillan S., et al. (2020). Preventing the next pandemic - Zoonotic diseases and how to break the chain of transmission. The United Nations Environment Programme (UNEP). <https://www.unep.org/resources/report/preventing-future-zoonotic-disease-outbreaks-protecting-environment-animals-and>
190. Jones K. E., Patel N. G., Levy M. A., et al. (2008). Global trends in emerging infectious diseases. *Nature* **451**:990–993. DOI:10.1038/nature06536
191. Baker R. E., Mahmud A. S., Miller I. F., et al. (2022). Infectious disease in an era of global change. *Nat. Rev. Microbiol.* **20**:193–205. DOI:10.1038/s41579-021-00639-z
192. Maezono M., Nielsen R., Buchmann K., et al. (2025). The current state of knowledge of the economic impact of diseases in global aquaculture. *Rev. Aquacult.* **17**:e70039. DOI:10.1111/raq.70039
193. Valero Y. and Cuesta A. (2023). Reassortant viruses threatening fish aquaculture. *Rev. Aquacult.* **15**:1720–1731. DOI:10.1111/raq.12813
194. Waltzek T. B., Stacy B. A., Ossiboff R. J., et al. (2022). A novel group of negative-sense RNA viruses associated with epizootics in managed and free-ranging freshwater turtles in Florida, USA. *PLoS Pathog* **18**:e1010258. DOI:10.1371/journal.ppat.1010258
195. Shepherd F. K., Roach S. N., Sanders A. E., et al. (2024). Experimental viral spillover across 25 million year gap in Rodentia reveals limited viral transmission and purifying selection of a picornavirus. *mBio* **15**:e0165024. DOI:10.1128/mbio.01650-24
196. Yang J. H., Luo C. F., Xiang R., et al. (2025). Host taxonomy and environment shapes insectivore viromes and viral spillover risks in Southwestern China. *Microbiome* **13**:122. DOI:10.1186/s40168-025-02115-9
197. Grimwood R. M., Fortune-Kelly G., Holmes E. C., et al. (2023). Host specificity shapes fish viromes across lakes on an isolated remote island. *Virology* **587**:109884. DOI:10.1016/j.virol.2023.109884
198. Sanchez C. A., Li H., Phelps K. L., et al. (2022). A strategy to assess spillover risk of bat SARS-related coronaviruses in Southeast Asia. *Nat. Commun.* **13**:4380. DOI:10.1038/s41467-022-31860-w
199. Farkas K., Mannion F., Hillary L. S., et al. (2020). Emerging technologies for the rapid detection of enteric viruses in the aquatic environment. *Current Opinion in*

- Environmental Science & Health* **16**:1–6. DOI:10.1016/j.coesh.2020.01.007
200. MacIntyre C. R. (2025). Thinking globally for pandemic early warning systems. *Nat. Med.* **31**:731–732. DOI:10.1038/s41591-024-03460-2
201. Sripada S. A., Hosseini M., Ramesh S., et al. (2024). Advances and opportunities in process analytical technologies for viral vector manufacturing. *Biotechnol. Adv.* **74**:108391. DOI:10.1016/j.biotechadv.2024.108391
202. Bohara K., Joshi P., Acharya K. P., et al. (2023). Emerging technologies revolutionising disease diagnosis and monitoring in aquatic animal health. *Rev. Aquacult.* **16**:836–854. DOI:10.1111/raq.12870
203. Roux S. and Colet C. (2026). Viromics approaches for the study of viral diversity and ecology in microbiomes. *Nat. Rev. Genet.* **27**:32–46. DOI:10.1038/s41576-025-00871-w
204. Lindsley I. C., Juman M. M., Seifert S. N., et al. (2026). Host-virus association databases as tools for understanding viral spillover at varying scales. *PLoS Negl. Trop. Dis.* **20**e0013343. DOI:10.1371/journal.pntd.0013343
205. Zhao Y., Zou X., Wang X., et al. (2025). An open graph dataset organized by scales. *Sci. Data* **12**:898. DOI:10.1038/s41597-025-05077-7
206. Galeeva J., Kuzmichenko P., Manolov A., et al. (2025). Bioinformatics tools and approaches for virus discovery in genomic data: A systematic review. *Viruses* **17**:1538. DOI:10.3390/v17121538
207. Zheng K., Sun J., Liang Y., et al. (2025). VITAP: A high precision tool for DNA and RNA viral classification based on meta-omic data. *Nat. Commun.* **16**:2226. DOI:10.1038/s41467-025-57500-7
208. Sun Y., Chen Q., Fan G., et al. (2026). gcMeta 2025: A global repository of metagenome-assembled genomes enabling cross-ecosystem microbial discovery and function research. *Nucleic Acids Res.* **54**:D724–D733. DOI:10.1093/nar/gkaf1115
209. Yang C., Chowdhury D., Zhang Z., et al. (2021). A review of computational tools for generating metagenome-assembled genomes from metagenomic sequencing data. *Comput. Struct. Biotechnol. J.* **19**:6301–6314. DOI:10.1016/j.csbj.2021.11.028
210. Han Y., Liao J., Li C., et al. (2026). Co-occurrence of diverse defense systems shapes complex microbe-virus relationships in deep-sea cold seeps. *Nat. Commun.* **17**:1427. DOI:10.1038/s41467-025-68174-6
211. Pan Y. F., He Y., Liu Y. Q., et al. (2026). Predicting the evolutionary and functional landscapes of viruses with a unified nucleotide-protein language model: LucaVirus. *Natl. Sci. Rev.* **13**:nwag376. DOI:10.1093/nsr/nwag376
212. Zielezinski A., Gudys A., Barylski J., et al. (2025). Ultrafast and accurate sequence alignment and clustering of viral genomes. *Nat. Methods* **22**:1191–1194. DOI:10.1038/s41592-025-02701-7
213. Kieft K., Zhou Z. and Anantharaman K. (2020). VIBRANT: Automated recovery, annotation and curation of microbial viruses, and evaluation of viral community function from genomic sequences. *Microbiome* **8**:90. DOI:10.1186/s40168-020-00867-0
214. Liu S., Ye Y., Guo B., et al. (2025). ViOTUcluster: A high-speed, All-in-one pipeline for viromic analysis of metagenomic data. *IMetaOmics* **2**e70023. DOI:10.1002/imo2.70023
215. Pickett B. E., Sadat E. L., Zhang Y., et al. (2012). ViPR: An open bioinformatics database and analysis resource for virology research. *Nucleic Acids Res.* **40**:D593–598. DOI:10.1093/nar/gkr859
216. Nishijima S., Fullam A., Schmidt T. S. B., et al. (2026). VIRE: A metagenome-derived, planetary-scale virome resource with environmental context. *Nucleic Acids Res.* **54**:D902–D911. DOI:10.1093/nar/gkaf1225
217. Wang L., Chen F., Guo X., et al. (2020). VirusDIP: Virus data integration platform. *bioRxiv* 2020.2006.139451. DOI:10.1101/2020.06.08.139451
218. Nasri F., Gurev S., Varilly P., et al. (2026). Deterministic access to global viral sequence data enables robust agentic scientific. *arXiv* 2606.06749v06741
219. Wang C., Zheng R. and Sun C. (2025). Deep-sea viral diversity and their role in host metabolism of complex organic matter. *Nat. Commun.* **16**:10134. DOI:10.1038/s41467-025-65207-y
220. Nie Z., Liu X., Chen J., et al. (2025). A unified evolution-driven deep learning framework for virus variation driver prediction. *Nat. Mach. Intell.* **7**:131–144. DOI:10.1038/s42256-024-00966-9
221. Ma K., Liu K., Xin Y., et al. (2026). Multilabel prediction of virus target proteins via multimodal graph representation learning. *PLoS Comput. Biol.* **22**e1014320. DOI:10.1371/journal.pcbi.1014320
222. Lukas P., Gibeaud A., Schumer C., et al. (2026). Multimodal data integration to determine viral and innate immune kinetics in human airway epithelium. *PLoS Comput Biol* **22**e1014248. DOI:10.1371/journal.pcbi.1014248
223. Li W., Du X., Xu X., et al. (2024). A review of aquaculture: From single modality analysis to multimodality fusion. *Comput. Electron. Agric.* **226**:109367. DOI:10.1016/j.compag.2024.109367
224. Impiö M., Rehsen P. M., Laamanen T., et al. (2025). AquaMonitor: A multimodal multi-view image sequence dataset for real-life aquatic invertebrate biodiversity monitoring. *arXiv* 2505.22065v22061
225. Schaefer M., Peneder P., Malz D., et al. (2025). Multimodal learning enables chat-based exploration of single-cell data. *Nat. Biotechnol.* DOI:10.1038/s41587-025-02857-9
226. Wang X., Luo J., Cai X., et al. (2025). DeepHVI: A multimodal deep learning framework for predicting human-virus protein-protein interactions using protein language models. *Biosaf. Health* **7**:257–266. DOI:10.1016/j.bshealth.2025.07.005
227. Wang X., Cui Y., Wang J., et al. (2026). Multimodal learning with next-token prediction for large multimodal models. *Nature* **650**:327–333. DOI:10.1038/s41586-025-10041-x
228. Er A. G., Ding D. Y., Er B., et al. (2024). Multimodal data fusion using sparse canonical correlation analysis and cooperative learning: A COVID-19 cohort study. *NPJ Digit. Med.* **7**:117. DOI:10.1038/s41746-024-01128-2
229. Ren H., Ling Y., Cao R., et al. (2023). Early warning of emerging infectious diseases based on multimodal data. *Biosaf. Health* **5**:193–203. DOI:10.1016/j.bshealth.2023.05.006
230. Vora N. M., Hassan L., Plowright R. K., et al. (2024). The Lancet-PPATS commission on prevention of viral spillover: Reducing the risk of pandemics through primary prevention. *Lancet* **403**:597–599. DOI:10.1016/S0140-6736(23)01064-4
231. Mollentze N., Babayan S. A. and Streicker D. G. (2021). Identifying and prioritizing potential human-infecting viruses from their genome sequences. *PLoS Biol.* **19**:e3001390. DOI:10.1371/journal.pbio.3001390
232. Son H. S. and Cho M. (2025). Prediction of host tropism and cross-species infection of viruses. In *viroinformatics and computational virology in public health* (Springer). DOI: 10.1007/978-981-96-5757-5_7
233. Gui T. and Longini I. (2025). Incorporating genomic sequences into stochastic transmission modeling to improve the analysis of SARS-CoV-2 transmission dynamics. DOI: 10.64898/2025.12.11.25342070 %J medRxiv
234. Qin X., Liang M., Pan W., et al. (2026). STING single amino acid polymorphisms modulate iridovirus immune evasion and pathogenicity spectrum. *Proc. Natl. Acad. Sci. USA* **123**:e2523268123. DOI:10.1073/pnas.2523268123
235. Peng C., Shang J., Guan J., et al. (2024). ViralLM: Empowering virus discovery through the genome foundation model. *Bioinformatics* **40**:btat704. DOI:10.1093/bioinformatics/btat704
236. Kawasaki J., Suzuki T. and Hamada M. (2025). Hidden challenges in evaluating spillover risk of zoonotic viruses using machine learning models. *Commun. Med.* (Londr) **5**:187. DOI:10.1038/s43856-025-00903-w
237. Fanelli A., Cescatti A., Ciscar J. C., et al. (2025). Assessing the risk of diseases with epidemic and pandemic potential in a changing world. *Sci. Adv.* **11**:eadw6363. DOI:10.1126/sciadv.adw6363
238. Golchin M., Di Marco M., Horwood P. F., et al. (2024). Prediction of viral spillover risk based on the mass action principle. *One Health* **18**:100737. DOI:10.1016/j.onehlt.2024.100737
239. Saldana F., Stollenwerk N., Van Dierdonck J. B., et al. (2024). Modeling spillover dynamics: Understanding emerging pathogens of public health concern. *Sci. Rep.* **14**:9823. DOI:10.1038/s41598-024-60661-y
240. Budeski K. and Lipsitch M. (2025). Focusing a viral risk ranking tool on prediction. *Proc Natl Acad Sci USA* **122**:e2419337122. DOI:10.1073/pnas.2419337122
241. Surur F. M., Mammo A. A., Gebresilassie B. G., et al. (2025). Unlocking the power of machine learning in big data: A scoping survey. *Data Science and Management* **8**:519–535. DOI:10.1016/j.dsm.2025.02.004
242. Research Briefing. Machine learning framework reveals a concordant cell-state landscape across single-cell datasets. (2026). *Nat. Biotechnol.* DOI:10.1038/s41587-025-02978-1
243. Liu J., Gao W., Guo C., et al. (2026). Artificial intelligence-assisted pathogen detection: Algorithms, biosensing platforms, and applications. *Biosensors (Basel)* **16**:267. DOI:10.3390/bios16050267
244. Editorial. (2026). Evolving viral threats. *Nat. Rev. Microbiol.* **24**:1–2. DOI:10.1038/s41579-025-01263-x
245. Kang H. Y., Lee Y., Park J., et al. (2025). Environmental RNA - based surveillance of viral hemorrhagic septicemia virus (VHSV) in olive flounder (*Paralichthys olivaceus*) aquaculture: Detection dynamics and risk assessment. *Environmental DNA* **7**:e70083. DOI:10.1002/edn3.70083
246. Mollentze N. and Streicker D. G. (2023). Predicting zoonotic potential of viruses: Where are we. *Curr Opin. Virol.* **61**:101346. DOI:10.1016/j.coviro.2023.101346
247. Zhang Q. Y. and Gui J. F. (2008). Aquatic Virology (Higher Education Press). https://www.hceis.com/home/book_view.aspx?id=6296
248. Zhao Y., Xu D., Ke F., et al. (2024). A droplet digital PCR method (ddPCR) for sensitive detection and quantification of Carassius auratus herpesvirus (CaHV). *Water Biology and Security* **3**:100252. DOI:10.1016/j.watbs.2024.100252
249. Loynd C., Singha Roy S. J., Canarelli S. E., et al. (2026). Cell-selective multiplexed bioorthogonal noncanonical amino acid tagging for nascent proteomics. *Nat. Chem. Biol.* **22**:318–327. DOI:10.1038/s41589-025-02039-3
250. Wu X., Xu W., Deng L., et al. (2024). Spatial multi-omics at subcellular resolution via high-throughput in situ pairwise sequencing. *Nat. Biomed. Eng.* **8**:872–889. DOI:10.1038/s41551-024-01205-7
251. Dongare D. B., Nishad S. S., Mastoli S. Y., et al. (2025). High-throughput sequencing: A breakthrough in molecular diagnosis for precision medicine. *Funct. Integr. Genomics*. **25**:22. DOI:10.1007/s10142-025-01529-w
252. Luo Y., Zhao C. and Chen F. (2024). Multiomics research: Principles and challenges in integrated analysis. *Biodes. Res.* **6**:0059. DOI:10.34133/bdr.0059
253. Editorial. (2026). Microbial ecology and evolution in the genomics era. *Nat. Rev. Genet.* **27**:1–2. DOI:10.1038/s41576-025-00917-z

254. Szabo G., Eloe-Fadrosh E. A., Pett-Ridge J., et al. (2026). A genomic view of Earth's biomes. *Nat. Rev. Genet.* **27**:13–31. DOI:10.1038/s41576-025-00888-1
255. Torres Montaguth O. E., Buddle S., Morfopoulou S., et al. (2026). Clinical metagenomics for diagnosis and surveillance of viral pathogens. *Nat. Rev. Microbiol.* **24**:61–75. DOI:10.1038/s41579-025-01223-5
256. Weinheimer A. R., Brown J. M., Thompson B., et al. (2025). Single-particle genomics uncovers abundant non-canonical marine viruses from nanolitre volumes. *Nat. Microbiol.* **10**:3245–3257. DOI:10.1038/s41564-025-02167-5
257. Luo S., Yin L., Liu X., et al. (2025). Advances in virus biorecognition and detection techniques for the surveillance and prevention of infectious diseases. *Biosensors (Basel)* **15**:198. DOI:10.3390/bios15030198
258. Gui L., Zhao Y., Xu D., et al. (2022). Quick detection of *Carassius auratus* herpesvirus (CaHV) by recombinase-aid amplification lateral flow dipstick (RAA-LFD) method. *Front. Cell Infect. Microbiol.* **12**:981911. DOI:10.3389/fcimb.2022.981911
259. Fromm A., Hevroni G., Vincent F., et al. (2024). Single-cell RNA-seq of the rare virosphere reveals the native hosts of giant viruses in the marine environment. *Nat. Microbiol.* **9**:1619–1629. DOI:10.1038/s41564-024-01669-y
260. Gavina K., Franco L. C., Khan H., et al. (2023). Molecular point-of-care devices for the diagnosis of infectious diseases in resource-limited settings - A review of the current landscape, technical challenges, and clinical impact. *J. Clin. Virol.* **169**:105613. DOI:10.1016/j.jcv.2023.105613
261. Zhang Q., Zhang X., Yang J., et al. (2026). Point-of-care molecular diagnostics and drug-resistance mechanisms in neglected infectious diseases: Current advances and future therapeutic opportunities. *Front. Cell Infect. Microbiol.* **16**:1769679. DOI:10.3389/fcimb.2026.1769679
262. Pernet F., Fuhrmann M., Petton B., et al. (2018). Determination of risk factors for herpesvirus outbreak in oysters using a broad-scale spatial epidemiology framework. *Sci. rRep.* **8**:10869. DOI:10.1038/s41598-018-29238-4
263. Lloyd-Smith J. O. (2017). Predictions of virus spillover across species. *Nature* **546**:603–604. DOI:10.1038/nature23088
264. Li Z., Meng F., Wu B., et al. (2024). Reviewing the progress of infectious disease early warning systems and planning for the future. *BMC Public Health* **24**:3080. DOI:10.1186/s12889-024-20537-2
265. Whitlock A. O. B., Bird B. H., Ghersi B., et al. (2023). Identifying the genetic basis of viral spillover using Lassa virus as a test case. *R. Soc. Open Sci.* **10**:221503. DOI:10.1098/rsos.221503
266. Hill V., Githinji G., Vogels C. B. F., et al. (2023). Toward a global virus genomic surveillance network. *Cell Host Microbe* **31**:861–873. DOI:10.1016/j.chom.2023.03.003
267. Olival K. J., Hosseini P. R., Zambrana-Torrel C., et al. (2017). Host and viral traits predict zoonotic spillover from mammals. *Nature* **546**:646–650. DOI:10.1038/nature22975
268. Yang Z., Shan Y., Liu X., et al. (2024). VirID: Beyond virus discovery—an integrated platform for comprehensive RNA virus characterization. *Mol. Biol. Evol.* **41**:msae202. DOI:10.1093/molbev/msae202
269. Wang H., Zhang J., Brookes J. D., et al. (2026). The Innovation Water: An international journal of water-associated science and technology. *Innov. Water* **1**:100001. DOI:10.59717/j.tiw.2026.100001
270. Holmes E. C. (2022). The ecology of viral emergence. *Annu. Rev. Virol.* **9**:173–192. DOI:10.1146/annurev-virology-100120-015057
271. Betancourt J. L., Rodriguez-Ramos T. and Dixon B. (2024). Pattern recognition receptors in Crustacea: Immunological roles under environmental stress. *Front. Immunol.* **15**:1474512. DOI:10.3389/fimmu.2024.1474512
272. Editorial (2025). Rethinking approaches to overcome infectious disease. *Nat. Microbiol.* **10**:1791–1792. DOI:10.1038/s41564-025-02093-6
273. Nakamura T., Isoda N., Sakoda Y., et al. (2022). Strategies for fighting pandemic virus infections: Integration of virology and drug delivery. *J. Control. Release* **343**:361–378. DOI:10.1016/j.jconrel.2022.01.046
274. Ukoaka B. M., Okesanya O. J., Daniel F. M., et al. (2024). Updated WHO list of emerging pathogens for a potential future pandemic: Implications for public health and global preparedness. *Infez Med* **32**:463–477. DOI:10.53854/liim-3204-5
275. Wang S., Li W., Wang Z., et al. (2024). Emerging and reemerging infectious diseases: Global trends and new strategies for their prevention and control. *Signal. Transduct. Target Ther.* **9**:223. DOI:10.1038/s41392-024-01917-x
276. Tammam I., Bitchava K. and Gelasakis A. I. (2024). Transforming aquaculture through vaccination: A review on recent developments and milestones. *Vaccines (Basel)* **12**:732. DOI:10.3390/vaccines12070732
277. Behera J. K., Behera B. and Bhattacharya M. (2026). The present landscape of both traditional and innovative biotechnology driven vaccines for fish diseases in global aquaculture. *Aquaculture and Fisheries* **11**:423–443. DOI:10.1016/j.aaf.2025.10.001
278. Gupta A., Rudra A., Reed K., et al. (2024). Advanced technologies for the development of infectious disease vaccines. *Nat. Rev. Drug Discov.* **23**:914–938. DOI:10.1038/s41573-024-01041-z
279. Cao M., Li Y., Song X., et al. (2025). Broad-spectrum vaccines against various and evolving viruses: From antigen design to nanoparticle delivery. *J. Virol.* **99**:e00997–009925. DOI:10.1128/jvi.00997-25
280. Wang Q., Liu Y., Han C., et al. (2021). Efficient RNA virus targeting via CRISPR/CasRx in fish. *J. Virol.* **95**:10.1128/jvi.00461-00421. DOI:10.1128/jvi.00461-21
281. Yu X.-D., Zhang Q.-Y. and Ke F. (2025). CRISPR/Cas13d mediated inhibition of *Siniperca chuatsi* rhabdovirus infection in fish cells. *Aquaculture* **602**:742355. DOI:10.1016/j.aquaculture.2025.742355
282. Tayyab M., Zhao Y. and Zhang Y. (2025). Microbiome engineering to enhance disease resistance in aquaculture: current strategies and future directions. *Front. Microbiol.* **16**:1625265. DOI:10.3389/fmicb.2025.1625265
283. El-Son M. A. M., Elbahnaswy S., Khormi M. A., et al. (2025). Harnessing the fish gut microbiome and immune system to enhance disease resistance in aquaculture. *Fish Shellfish Immunol.* **163**:110394. DOI:10.1016/j.fsi.2025.110394
284. Chen N., Jin J., Zhang B., et al. (2024). Viral strategies to antagonize the host antiviral innate immunity: An indispensable research direction for emerging virus-host interactions. *Emerg. Microbes. Infect.* **13**:2341144. DOI:10.1080/22221751.2024.2341144
285. Awad E. (2025). The role of natural products on the immune status of freshwater fish. *Aquacult. Int.* **33**:396. DOI:10.1007/s10499-025-02035-3
286. Mohamad A., Yasin I. S. M., Azzam-Sayuti M., et al. (2025). Prevention and control of aquatic animal diseases. In management of fish diseases, S.K. Mallik, N. Shahi, and P.K. Pandey (eds). (Springer). DOI: 10.1007/978-981-96-0270-4_18
287. Polinski M. P. (2026). Aquatic animal viruses and antiviral immunity: A closing editorial. *Viruses* **18**:127. DOI:10.3390/v18010127
288. Ecke F., Semenza J. C., Buzan E., et al. (2025). Adaptive ecosystem restoration to mitigate zoonotic risks. *Nat. Ecol. Evol.* **9**:1979–1988. DOI:10.1038/s41559-025-02869-3
289. Plowright R. K., Ahmed A. N., Coulson T., et al. (2024). Ecological countermeasures to prevent pathogen spillover and subsequent pandemics. *Nat. Commun.* **15**:2577. DOI:10.1038/s41467-024-46151-9
290. Di Marco M., Marcolin L., Tonelli A., et al. (2026). Macroecological approaches for the prediction of zoonotic disease risk. *Nat. Sustain.* **9**:35–45. DOI:10.1038/s41893-025-01749-9
291. Lee K. and Brumme Z. L. (2013). Operationalizing the One Health approach: The global governance challenges. *Health Policy Plan* **28**:778–785. DOI:10.1093/heapol/czs127
292. One Health High-Level Expert P., Adisasmito W. B., Almuhairei S., et al. (2022). One Health: A new definition for a sustainable and healthy future. *PLoS Pathog.* **18**:e1010537. DOI:10.1371/journal.ppat.1010537
293. Wang C.-X., Xiu L.-S., Hu Q.-Q., et al. (2023). Advancing early warning and surveillance for zoonotic diseases under climate change: Interdisciplinary systematic perspectives. *Adv. Clim. Change Res.* **14**:814–826. DOI:10.1016/j.accre.2023.11.014
294. Scarfe A. D. and Palić D. (2020). 3-Aquaculture biosecurity: Practical approach to prevent, control, and eradicate diseases. In aquaculture health management, F.S.B. Kibenge, and M.D. Powell (eds). (Academic Press), pp: 75–116. DOI: 10.1016/B978-0-12-813359-0.00003-8
295. Sikkema R. S. and Koopmans M. (2026). Viral emergence and pandemic preparedness in a One Health framework. *Nat. Rev. Microbiol.* **24**:29–44. DOI:10.1038/s41579-025-01243-1
296. Gippet J. M. W., Carlson C. J., Klastenberger T., et al. (2026). Wildlife trade drives animal-to-human pathogen transmission over 40 years. *Science* **392**:178–182. DOI:10.1126/science.adw5518
297. Chen J., Pei S., Huang J., et al. (2026). Fishery trade and the spread of pathogens carried by aquatic life. *Water Biology and Security* **5**:100499. DOI:10.1016/j.watbs.2025.100499
298. Li T., Zhou X. N. and Tanner M. (2025). One Health: Enabler of effective prevention, control and elimination of emerging and re-emerging infectious diseases. *Infect. Dis. Poverty.* **14**:77. DOI:10.1186/s40249-025-01337-1
299. Othman R., Elabd H., Pratiwy F. M., et al. (2024). Biosecurity in Aquaculture: Nurturing health and ensuring sustainability. In essentials of aquaculture practices, N.M. Faudzi, M.D. Shah, N. Mazlan, et al. (eds). (Springer Nature Singapore), pp:139–182. DOI: 10.1007/978-981-97-6699-4_8
300. Vora N. M., Sizer N. and Bernstein A. (2021). Preventing spillover as a key strategy against pandemics. *Nature* **597**:332. DOI:10.1038/d41586-021-02427-4
301. Dobson A. P., Pimm S. L., Hannah L., et al. (2020). Ecology and economics for pandemic prevention. *Science* **369**:379–381. DOI:10.1126/science.abc3189
302. Gurley E. S. and Plowright R. K. (2025). A roadmap of primary pandemic prevention through Spillover investigation. *Emerg. Infect. Dis.* **31**:1501–1506. DOI:10.3201/eid3108.250442
303. Gunthard H. F., Kusejko K. and Kouyos R. D. (2026). Phylogenetics and molecular evolution to understand and curb the HIV pandemic. *Nat. Rev. Microbiol.* **24**:76–92. DOI:10.1038/s41579-025-01202-w
304. Khurana M. P., Tsui J. L., Gutierrez B., et al. (2026). Global approaches to infectious disease surveillance and modeling. *Nat. Med.* **32**:1646–1660. DOI:10.1038/s41591-026-04351-4
305. Öz M., Üstüner E., Çifci S., et al. (2025). Artificial intelligence for fish disease diagnosis and management: Innovations, challenges, and One Health implications. *Aquacult. Int.* **33**:652. DOI:10.1007/s10499-025-02352-7
306. Qian J., Xia J., Chiang S., et al. (2025). Rapid and comprehensive detection of viral antibodies and nucleic acids via an acoustofluidic integrated molecular diagnostics chip: AIMDX. *Sci. Adv.* **11**:eadt5464. DOI:10.1126/sciadv.adt5464

307. Hou X., He Y., Fang P., et al. (2024). Using artificial intelligence to document the hidden RNA virosphere. *Cell* **187**:6929–6942 e6916. DOI:10.1016/j.cell.2024.09.027

308. Wang Y. H., Chen J. J., Ma J., et al. (2025). Early-warning signals and the role of H9N2 in the spillover of avian influenza viruses. *Med* **6**:100639. DOI:10.1016/j.medj.2025.100639

309. Lau C. Y., Martinez-Orengo N., Lyndaker A., et al. (2023). Advances and challenges in molecular imaging of viral infections. *J. Infect. Dis.* **228**:S270–S280. DOI:10.1093/infdis/jiad247

FUNDING AND ACKNOWLEDGMENTS

This work was supported by grants from the National Key R&D Plan of the Ministry of Science and Technology, China (2023YFD2400201), the Project from Chinese Academy of Sciences (KJZD-SW-L11), and the National Natural Science Foundation of China (32573566). The funders had no role in study design, data collection and analysis, deci-

sion to publish, or preparation of the manuscript.

AUTHOR CONTRIBUTIONS

Z.Q.Y: Conceptualization, supervision, funding acquisition, literature collection and analysis, writing – original draft, writing – review and editing. K.F.: Funding acquisition, Writing – review and editing. G.J.F.: Writing – review and editing. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

DATA AND CODE AVAILABILITY

No new data were created or analyzed in this study.