Aquaculture and Fisheries 3 (2018) 1–5

Contents lists available at ScienceDirect

Aquaculture and Fisheries

journal homepage: www.keaipublishing.com/en/journals/aquaculture-and-fisheries/

Review article

Molecular basis of pathogenesis of emerging viruses infecting aquatic animals

Lang Gui [a, *], V. Gregory Chinchar [b], Qiya Zhang [c]

[a] College of Fisheries and Life Science, Shanghai Ocean University, Shanghai 201306, China
[b] Department of Microbiology, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216, USA
[c] State Key Laboratory of Freshwater Ecology and Biotechnology, Institute of Hydrobiology, Chinese Academy of Sciences, Wuhan 430072, China

ARTICLE INFO

Article history:
Received 26 July 2017
Received in revised form
26 December 2017
Accepted 27 December 2017
Available online 1 February 2018

Keywords:
Ranavirus
Herpesvirus
Reovirus
Rhabdovirus
Aquatic animal

ABSTRACT

Aquatic vertebrates are very abundant in the world, and they are of tremendous importance in providing global food security and nutrition. However, emergent and resurgent viruses, such as ranavirus (e.g., Rana grylio virus, RGV and Andriasd avidianus ranavirus, ADRV), herpesvirus (e.g., Carassius carassius herpesvirus, CaHV), reovirus (e.g., grass carp reovirus 109, GCRV-109, Scophthal musmaximus reovirus, SMReV and Micropterus salmoides reovirus, MsReV), and rhabdovirus (e.g., Siniper cachuatsi rhabdovirus, SCRV and Scophthal musmaximus rhabdovirus, SMRV) can cause severe diseases in aquaculture animals and wild lower vertebrates, such as frogs, giant salamanders, fish, and so on. Here, we will briefly describe the symptoms produced by the aforementioned viruses and the molecular basis of the virus–host interactions. This manuscript aims to provide an overview of viral diseases in lower vertebrates with an emphasis on visible symptomatic manifestations and pathogenesis.

1. Introduction

Aquatic animals comprise more than 60% of vertebrate species, including extant fish (32,900 species) and amphibians (7302 species) (The World Conservation Union, 2014). The aquaculture resources from aquatic animals are regarded as important, high-quality protein foods in human diets (Gui & Zhu, 2012). As an alternative to beef, aquatic animals are a benefit not only to human health but also to the environment (Cressey, 2009). However, viruses can cause devastating diseases in aquatic animals (Nakajima, Inouye, & Sorimachi, 1998; Zhang & Gui, 2012). For example, ranaviruses, herpesviruses, reoviruses, and rhabdoviruses have several unexpected consequences. These viral pathogens have different characteristics relative to those infecting terrestrial animals with regard to their morphology, genome, symptom, and pathogen-host interaction in aquatic animals (Zhang & Gui, 2015). The viral diversity in aquatic animals is due to the diversity of viral hosts and the rapid and cross-species transmission of viruses in different populations. We have previously reported several aquatic animal viral genomes as well as the viral genes associated with virus replication and assembly, including RGV (Lei, Ou, Zhu, & Zhang, 2012), CaHV (Wang, Gui, Chen, & Zhang, 2016), SMReV (Ke, He, Pei, & Zhang, 2011) and SCRV (Tao, Zhou, Gui, & Zhang, 2008). To date, sequencing and investigation of viral gene functions have fostered new insights into the molecular pathogenesis of aquatic animal viruses. Our current understanding of viral pathogens, and the roles of several viral genes in virus replication and virus-host interactions were exhibited. The schematic illustration in Fig. 1 briefly describes a framework of symptoms of viral diseases. The molecular basis of virus-host interactions explain viral pathogenesis in aquatic animals.

2. Ranaviruses

The ranaviruses (family *Iridoviridae*) cause devastating disease and biodiversity decline among farmed and wild aquatic animals around the globe (Chinchar & Waltzek, 2014; Jancovich et al., 2011; Stohr et al., 2015), e.g., fish, frogs, and giant salamanders (Fig. 1). The features of ranaviruses include low host specificity and infectiousness. Typical symptoms cause by ranaviruses include skin erythema, eye exophthalmos, glass sphere turbidity, retinal hemorrhaging, limb necrosis, and systemic hemorrhaging, especially from the mouth (Chen et al., 2013; Schock, Bollinger, & Collins, 2009; ScienceDaily, 2014; Zhang, Li, & Gui, 1999, 2001).

* Corresponding author. College of Fisheries and Life Science, Shanghai Ocean University, 999 Huchenghuan Road, Shanghai 201306, China.
E-mail address: lgui@shou.edu.cn (L. Gui).

https://doi.org/10.1016/j.aaf.2017.12.003
2468-550X/

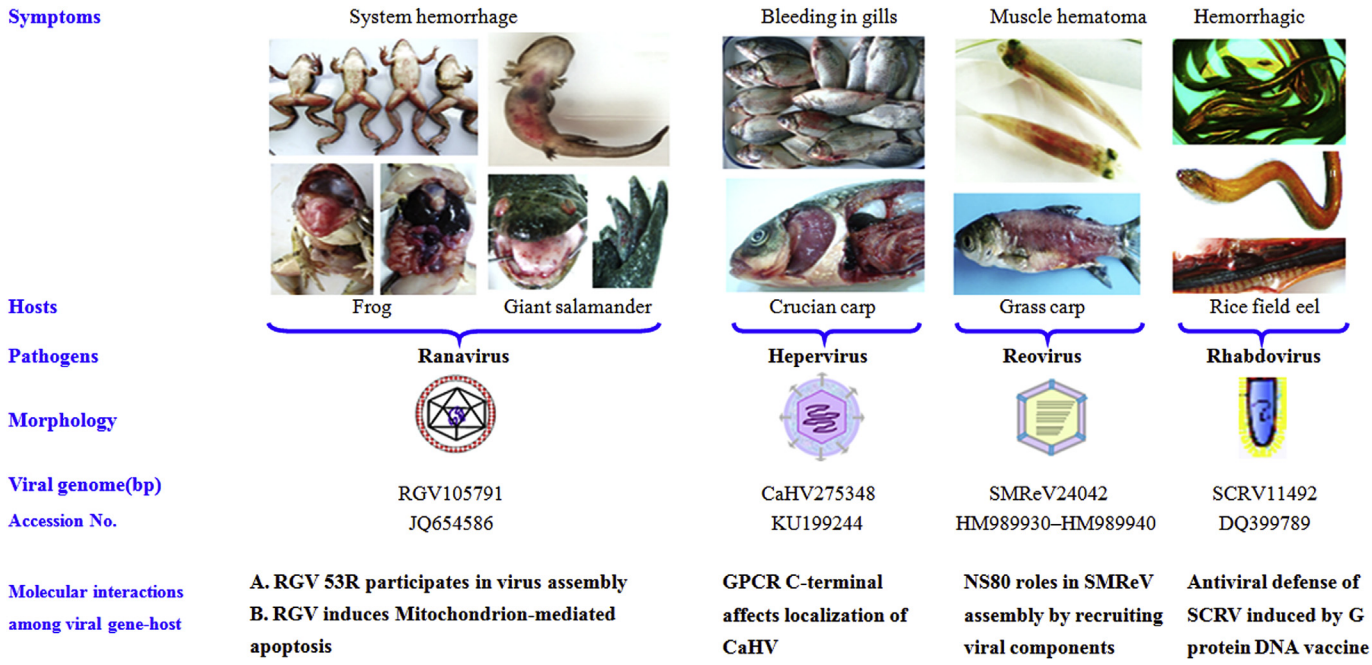

Fig. 1. Symptoms of viral diseases. Four viral pathogens (ranavirus, herpesvirus, reovirus, and rhabdovirus) that can cause disease in five different aquatic animals (frog, giant salamander, crucian carp, grass carp, and rice field eel).

High mortalities occur within days in frogs infected by *Rana grylio* virus (RGV) and Chinese giant salamanders infected by *Andrias davidianus* ranavirus (ADRV).

RGV 53R is a ranaviral envelope protein. RGV 53R is essential for viral assembly (Zhao et al., 2008). RGV 53R initially colocalizes with the endoplasmic reticulum (ER) at an early stage of infection, then the ER components are excluded from the virus factories at the stage of virus assembly (Fig. 2A). RGV infection has been associated with apoptosis (Huang, Huang, Gui, & Zhang, 2007) and dramatic alterations in mitochondrial dynamics, such as mitochondrial fragmentation and crista remodeling. RGV infection induces apoptosis through a mitochondrion-mediated caspase-dependent pathway of cell death (Fig. 2B).

3. Herpesviruses

The fish herpesviruses (family *Alloherpesviridae* in the order *Herpesvirales*) can induce diseases ranging from latent to fatal infection and cause mass mortality. Recently, disease outbreaks with 100% mortality within one week was caused by *Carassius carassius* herpesvirus (CaHV) in crucian carp (Fang et al., 2016). The typical signs of this disease included severe necrosis and heavy bleeding of the gills (Fig. 1).

G protein-coupled receptors (GPCRs) are seven-transmembrane domain receptors and consequently can mediate diverse biological functions via regulation of their subcellular localization. Study of the subcellular localization of CaHV GPCRs may provide valuable information about the precise interactions between herpesvirus and host, and also provide useful targets for antiviral agents in aquaculture. Recently, a series of variants with truncation/deletion/substitution mutations in the GPCR C-terminal of CaHV were constructed (Wang et al., 2016). Different mutations of CaHV GPCR C-terminals have different affects on the subcellular localization of fish herpesvirus-encoded GPCRs. And Lysine-315 (K-315) in C-terminal was a key region. When region K-315 or the intact C-terminal was retained, CaHV GPCR formed aggregates at the nuclear side, and colocalized with the Golgi apparatus (Fig. 3).

4. Reoviruses

Infection by reoviruses (family *Reoviridae*) is associated with high mortality in aquatic animals, such as hemorrhagic disease of grass carp, turbot and largemouth bass caused by grass carp reovirus 109 (GCRV-109), *Scophthal musmaximus* reovirus (SMReV) and *Micropteru ssalmoides* reovirus (MsReV), respectively. The symptoms include obvious hemorrhaging in the muscles of infected fish, eventually leading to death (Fig. 1). Recently, the relationship between the genomic structure of reovirus and host fish in saline environments was revealed (Chen, Gao, & Zhang, 2015).

NS80, the nonstructural protein from reoviruses, is involved in SMReV replication and assembly by recruiting viral components (Ke, He, & Zhang, 2013). After invasion of host cells, NS80 forms a viral factory which then recruits viral proteins. Different regions of NS80 are required for protein interactions. The intercoil region of NS80 is important for self-aggregation, and it is also related to nuclear localization. Other regions of NS80 are required for associations with viral proteins and assembly of new virions that are released, and lead to host cell damage (Fig. 4).

5. Rhabdoviruses

Fish rhabdoviruses (family *Rhabdoviridae*) are classified into three genera, *Novirhabdovirus*, *Perhabdovirus* and *Vesiculovirus*. The genomes of more than 100 fish rhabdovirus strains have been sequenced, and serious rhabdoviral pathogens have been isolated and characterized from diseased aquatic animals in China, such as mandarin fish (*Siniper cachuatsi* rhabdovirus, SCRV), turbot (*Scophthal musmaximus* rhabdovirus, SMRV), flounder (*Paralichthys olivaceus* rhabdovirus, PORV), and farmed rice field eels (*Monopterus albus* rhabdovirus, MoARV) (Ou, Zhu, Chen, & Zhang, 2013; Zhu & Zhang, 2014). Symptoms include anaemia, bulging eyes, ascites, and gangrenous ulcers (Fig. 1) and sick fish gasp at the water surface, and their movements become agitated. Prior to death, abnormal clinical signs include loss of equilibrium, disorganized swimming, accumulation of skin mucus, skin