Fish and Shellfish Immunology 74 (2018) 627–636

Contents lists available at ScienceDirect

Fish and Shellfish Immunology

journal homepage: www.elsevier.com/locate/fsi

Full length article

Genes related to cell-mediated cytotoxicity and interferon response are induced in the retina of European sea bass upon intravitreal infection with nodavirus

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ARTICLE INFO

Keywords:
Nodavirus
European sea bass
Retina
Innate immune response
Adaptive immune response
Interferon
Cytotoxicity

ABSTRACT

Viral diseases are responsible for high rates of mortality and subsequent economic losses in modern aquaculture. The nervous necrosis virus (NNV) produces viral encephalopathy and retinopathy (VER), which affects the central nervous system, is considered one of the most serious viral diseases in marine aquaculture. Although some studies have localized NNV in the retina cells, none has dealt with immunity in the retina. Thus, for the first time, we intravitreally infected healthy specimens of European sea bass (*Dicentrarchus labrax*) with NNV with the aim of characterizing the immune response in the retina. Ultrastructural analysis detected important retinal injuries and structure degradation, including pycnosis, hydropic degeneration and vacuolization in some cell layers as well as myelin sheaths in the optic nerve fibres. Immunohistochemistry demonstrated that NNV replicated in the eyes. Regarding retinal immunity, NNV infection elicited the transcription of genes encoding proteins involved in the interferon (IFN) and cell-mediated cytotoxicity (CMC) responses as well as B and T cell markers, demonstrating that viral replication influences innate and adaptive responses. Further studies are needed to understand the retina immunity and whether the main retinal function, vision, is affected by nodavirus.

1. Introduction

Nodavirus (NNV) has become one of the most devastating marine fish viruses worldwide, and it represents a serious economic threat to aquaculture [1], affecting both marine and freshwater fish species [1–3]. The virus causes viral encephalopathy and retinopathy (VER), which is characterized by symptoms of neurological damage and high mortality rates of up to 100%, especially in larvae and juvenile European sea bass (*Dicentrarchus labrax*), one of most susceptible species to the virus [4,5], which is extremely important in Mediterranean aquaculture. NNV is a bipartite, naked, icosahedral virus of 25–30 nm, composed of 2 positive single-stranded RNA fragments, RNA1 and RNA2, which are capped but not polyadenylated. The capsid protein (CP) is encoded by the RNA2 and is involved in host specificity whilst RNA1 codes for the non-structural protein RNA-dependent RNA polymerase (RdRp) [6,7]. In addition, a sub-genomic RNA1 transcript, RNA3, encodes the protein B2 which seems to be pivotal for virus accumulation since it antagonizes hosts siRNA and is only expressed in newly infected fish cells [8–10].

NNV infects cells from the brain, spinal cord and retina, causing extensive tissue degradation and altering their functioning [1]. The first evidence of retina damage was described several decades ago, when extensive vacuolation, especially in cells from the bipolar and ganglionic layers, was observed in a variety of fish species [11–14]. This injury to the retina structure is associated with the presence of NNV in the tissue and represents one of the key histopathological features of VER disease. For example, viral particles have been detected in the nuclear and ganglion cell layers and adjacent to the circumferential

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https://doi.org/10.1016/j.fsi.2018.01.034
Received 18 July 2017; Received in revised form 18 January 2018; Accepted 21 January 2018
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