Expression of microRNAs and interferon-related genes in rainbow trout (Oncorhynchus mykiss Walbaum) infected with Viral hemorrhagic septicemia virus

The fish rhabdovirus Viral hemorrhagic septicemia virus (VHSV) causes severe disease in farmed rainbow trout (Oncorhynchus mykiss). The potential threat from wildlife marine reservoir of VHSV, particularly to sea-farmed fish demands disease protection measures. Identification of biomarkers during infection is important to understand the complex web of interactions involved in the underlying host immune response, which is a requisite to developing effective disease control strategies. MicroRNAs potently mediate post-transcriptional silencing of a broad range of genes by the RNA interference mechanism and have been shown to regulate cellular processes, including immune responses. A microarray experiment in our lab revealed that a number of miRNAs were upregulated in fish liver following VHSV infection. Here, we validated the expression of the miRNAs and analyzed for associated expression of interferon (IFN)-related genes in the liver of VHSV-infected fish. Quantitative RT-PCR verified positive regulation for most of the miRNAs shown to be upregulated by our microarray analysis. Of these, miR-155, miR-462, and miR-731 had the highest expression levels. The increased expression of these miRNAs in infected liver correlated with the upregulation of type I IFN and the type I IFN-inducible Mx and Vig-1 genes, as well as that of IFN-gamma, indicating activation of both general anti-viral IFN response and natural killer cell and/or T cell responses. Further analysis of the expression of the three most highly upregulated miRNAs in fish intramuscularly injected with a type I IFN construct and the general IFN stimulator and TLR-3 agonist, poly I:C showed increased expression of miR-155, miR-462, and miR-731, as well as Mx at the site of injection relative to controls. This suggests that the increased levels of the three miRNAs at the site of administration is associated with type I interferons, which besides their anti-viral effects are known to have major immune regulatory roles in mammals. Besides adding to our understanding of anti-viral immunity, response profiles of miRNAs could serve as molecular signatures of responses to infection. In the future we plan to analyze whether individual variability is associated with differences in disease susceptibility.

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