ABSTRACT BOOK

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GILTHEAD SEABREAM (*SPARUS AURATA*) MX PROTEINS SHOW POSITIVE AND NEGATIVE SYNERGY IN THEIR ANTIVIRAL ACTIVITY

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Due to their direct antiviral activity, Mx proteins play a main role in the response mediated by the type I interferon against viral infections. The study of the farmed fish gilthead seabream Mx genes is especially interesting, since this species displays an unusually high natural resistance to viral diseases, becoming a potential asymptomatic carrier and/or reservoir for several viruses pathogenic to other fish species. Gilthead seabream has three Mx proteins (Mx1, Mx2 and Mx3) that, separately, display antiviral activity against a wide range of viruses, showing interesting differences in their antiviral specificities.

In this work, the possible synergy between the three Mx isoforms has been studied using *in vitro* systems, consisting of permanently transfected CHSE-214 cells expressing two or the three gilthead seabream Mx proteins. The antiviral activity of these Mx combinations has been tested against the infection by the Infectious Pancreatic Necrosis Virus (IPNV), the Viral Haemorrhagic Septicaemia Virus (VHSV) and the European Sheatfish Virus (ESV) in cells inoculated at 0.1 and 0.01 multiplicity of infection (MOI). The antiviral effect was evaluated by viral titration ($TCID_{50}$ method).

Interestingly, a positive synergistic effect in the antiviral activity against ESV was observed when Mx2 and Mx3 were combined, and this effect was intensified when the three isoforms were present in these cells. In contrast, the presence of more than one Mx isoform interfered with the antiviral activity against IPNV and VHSV showed by the Mx proteins expressed separately. Furthermore, Mx2 combined with Mx3, and the combination of the three Mx proteins exerted a negative synergistic effect against IPNV infection. Specifically, the viral titres were significantly higher in Mx expressing cells than in control cells. In the same way, in Mx1 and Mx2 expressing cells infected with VHSV the viral replication was also increased.

These results suggest the interaction between Mx isoforms, in which the expression level of each isoform might be an important factor, and support the

idea of finely tuned mechanisms controlling the antiviral activity of Mx proteins.

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