SENEGALESE SOLE (*SOLEA SENEGALENSIS*) ISG15: MOLECULAR CHARACTERIZATION AND *IN VIVO* INTERPLAY WITH VIRAL INFECTIONS

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The interferon-stimulated gene 15 (*Isg15*) is strongly induced by type I interferon (IFN I), viral infection, and double-stranded RNA (poly I:C) in several fish species, suggesting that Isg15 protein could play a key role in fish innate immunity against viral diseases. Thus, the aim of the present study was to characterize the molecular structure and transcription pattern of the Senegalese sole (*Solea senegalensis*) *Isg15* gene in response to viral infections.
The molecular characterization shows that the Senegalese sole *Isg15* gene codes for a typical Isg15 protein of 165 aa, containing two ubiquitin-like domains and one conserved LRLRGG conjugating motif at the C-terminal end. The untranslated 5´-end region exhibited the structure of an IFN-stimulated gene promoter, with two interferon stimulated response elements (ISRE). Pairwise alignments based on deduced amino acid sequences showed homologous relationships (72.5-74.2%) between the Isg15 of Senegalese sole and other pleuronectiforms.
The *Isg15* transcription has been studied in head kidneys of Senegalese sole inoculated with poly I:C and with different fish viruses: two Viral Haemorrhagic Septicaemia Virus (VHSV) isolates (highly pathogenic and non-pathogenic to sole), and one reassortant Viral Nervous Necrosis Virus (VNNV) isolate, composed of a RGNNV-type RNA1 and a SJNNV-type RNA2 (pathogenic to sole). These challenges showed that poly I:C induces *Isg15* transcription from 3 to 72 h post-injection (p.i.), whereas the induction in response to viral infections started at 24-48 h p.i. The fast induction of *Isg15* indicates the potential implication of this ISG in the antiviral state stablished by the IFN I system. On the other hand, the interaction between each virus and the IFN I system was evaluated in fish inoculated with poly I:C and subsequently (24 h later) challenged with the different viruses. This challenge showed a viral multiplication decrease in poly I:C treated animals compared with untreated fish. Besides, results showed that only both pathogenic isolates interfered negatively with the *Isg15* stimulation triggered by poly I:C. These results suggest that the Isg15 might play an important role in host defense against RNA virus infection, and the pathogenic isolates used in this study may have mechanisms to evade or limit the Senegalese sole innate host defenses.

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