



GÖTEBORGS UNIVERSITET

Intestinal Mucosal Immunology of Salmonids

Response to Stress and Infection and Crosstalk with the Physical Barrier

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Dissertation abstract

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The effect of environmental factors and pathogens on the intestinal epithelium of fish has received increased attention in recent years. Studies focusing on effects of stress, nutrient uptake as well as vegetable ingredients in fish feed have all shown that the intestine is affected by environmental factors. The signs of inflammation during exposure to detrimental environmental conditions have brought to attention the local immune system in the gut. The gut is further one of the main routes for pathogen infection in fish. Therefore this thesis aims at investigating the mucosal immune factors and systems that are affected by environmental stressors and pathogen interactions.

In this thesis the effect of long term environmental stress on the mucosal intestinal epithelium was investigated. Results showed an ongoing inflammation in the intestine that was manifested as a compromised barrier integrity, infiltration of immune cells and an affected immune response. Atlantic salmon was co-habitant infected with infectious pancreatic necrosis virus as well as immune challenged with the viral mimicker, double stranded RNA Poly I:C, where after the mucosal immune response was studied. Both treatments clearly demonstrated an antiviral response including alterations of IFN type I and the Mx protein. When the fish were exposed to a stressor and immune stimulation in combination, the fish immune response was delayed. This stresses the importance of minimize stressful situations for the animals in, for example aquaculture. The demonstrated increase in intestinal epithelial permeability together with inductions of the mucosal immune system raises the question of whether stress or inflammation is the causative agent of the barrier dysfunction.

To address this, the effect of the immune system on the intestinal epithelia was assessed using an in vitro Ussing chamber approach in which the intestinal epithelia was exposed to recombinant cytokines. Exposure to IL-1 β and IL-6 showed negative impact on the intestinal permeability, suggesting that the immune system of the fish is contributing to the inflammation seen during prolonged stress. Further, the tight junction proteins create an extracellular network between the epithelial cells and by that controls the intestinal paracellular permeability was shown to be affected by the two cytokines. The interactions between stress, the immune system and the epithelial barrier function are therefore highly complex and important for our understanding of the physiology of health, welfare and disease.

Keywords: Inflammation, IPNV, Poly I:C, Recombinant cytokines, CD8, MHC-I, Claudins, Permeability, Environmental stress, Cortisol, DNA constructs, IL, IFN
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Abbreviations

MALT	Mucosal-associated lymphoid tissue
GALT	Gut-associated lymphoid tissue
M cell	Microfold cell in the Payers patches
NF- κ B	DNA transcription factor Nuclear Factor κ B
IL	Interleukin
IFN	Interferon
TNF	Tumor necrosis factor
TGF	Transforming growth factor
Mx	Myxovirus resistance (by origin)
CD	Clusters of differentiation antigen on T cells. Different types on different cell types
B cell	Antibody producing lymphocyte
T cell	Lymphocyte derived from the thymus (T)
T _h	T helper cells
T _c	Cytotoxic T cells
CD8 ⁺	CD8 positive – associated with Tc
CD4 ⁺	CD4 positive – associated with Th

List of papers which are referred to in the text by their Roman numbers

I

Disturbance of the intestinal mucosal immune system of farmed Atlantic salmon (*Salmo salar*), in response to long-term hypoxic conditions. *Fish and Shellfish Immunology* (2011). Niklasson L.; Sundh H.; Fridell F.; Taranger G L.; Sundell K. *Fish and Shellfish Immunology* 31:1050-4648

II

High stocking density and poor water quality disturbs the intestinal physical and immunological barriers of the Atlantic salmon. Sundh H.; Niklasson L.; Finne-Fridell F.; Ellis T.; Taranger G L., Pettersen E F.; Wergeland H I.; Sundell K. (Under revision for publication in *Fish and Shellfish Immunology*)

III

Modulation of innate immune responses in Atlantic salmon by chronic hypoxia-induced stress (2013). Bjørn Olav Kvamme; Koestan Gadan; Frode Finne-Fridell; Lars Niklasson; Henrik Sundh; Kristina Sundell; Geir Lasse Taranger; Oystein Evensen. *Fish and Shellfish Immunology* 34:1095-9947

IV

Cortisol effects on the intestinal mucosal immune responses during cohabitant challenge with IPNV in Atlantic salmon (*Salmo Salar*). Niklasson L.; Sundh H.; Olsen R-E.; Jutfelt F.; Skjødt K.; Nilsen T O.; Sundell K. (Submitted for publication in *PLOS ONE*)

V

Recombinant cytokines interleukin 1 beta and interleukin 6 increases intestinal epithelial permeability in Rainbow trout (*Oncorhynchus mykiss*). Niklasson L.; Sundell K.; Martin S.; Secombes C.; Sundh H. (Manuscript)

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