

## **PHYSIOLOGICAL MECHANISMS BEHIND STRESS INDUCED INTESTINAL PRIMARY BARRIER DYSFUNCTION IN RAINBOW TROUT *Oncorhynchus mykiss*.**

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Absorption is an essential function of the gastrointestinal system allowing nutrients, water and electrolytes to cross the epithelium into the blood stream. However, the intestinal epithelium must also function as a selective barrier, facing the complex tasks of blocking pathogens and other harmful substances. Thus, the function and regulation of the intestinal barrier is essential for maintenance of homeostasis and intestinal health and consequently the health and welfare of the animal. We have previously shown that husbandry related acute and chronic stressors in salmonid fish induce intestinal barrier dysfunction, but the physiological mechanisms behind these findings are not understood.

When stressed, both fish and mammals redirect blood flow away from the gastrointestinal tract to the heart and muscles as part of the general stress response. Moreover, in mammals, forced obstruction in intestinal blood flow can result in severe intestinal epithelial damage characterized by intestinal barrier dysfunction which is caused by tissue ischemia and/or reperfusion injuries when the blood flow is restored. The aim of the current study was to investigate if stress induced and experimental reductions in intestinal blood flow in rainbow trout (*Oncorhynchus mykiss*) can explain the intestinal barrier dysfunction previously observed in response to acute stress.

Intestinal blood flow responses were assessed *in vivo* using a surgically implanted blood flow probe before, during and after a 15 min acute stress protocol previously shown to result in intestinal barrier dysfunction in rainbow trout. Barrier function of the proximal and distal intestine was then examined *in vitro* on isolated intestinal tissue from the stressed fish using Ussing chambers, with unstressed fish as control. To specifically study the effect of reduced blood flow to the intestine, the recorded decrease in blood flow during stress was mimicked by mechanically occluding intestinal blood flow for 15 min, followed by assessment of the intestinal barrier function using Ussing chambers directly after occlusion or 24 hours after blood flow to the intestine had been restored. Untreated fish and sham-occluded fish served as controls. Intestinal tissues were also sampled and stored in RNA-later for assessment of transcript abundance of genes associated with intestinal barrier dysfunction using qPCR.

The acute stress protocol resulted in an immediate nearly complete cessation of intestinal blood flow and impaired intestinal barrier function. However, neither the 15 min occlusion, nor the occlusion/reperfusion treatment resulted in any obvious intestinal barrier damages when assessed using Ussing chambers. Our results suggest that the intestinal barrier dysfunction seen after acute stress is not caused by the temporary reduction in blood flow to the intestinal epithelium. Possible alternative mechanisms for the impaired intestinal barrier function will be discussed.

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