



MASTER THESIS PROJECT

Glucocorticoid receptor activating compounds and their effects on energy metabolism in Atlantic cod (Gadus Morhua)

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ABSTRACT

Oceans are great, rich ecosystems that provide essential global resources. Environmental contaminants of many kinds are known to reach the aquatic environments and have diverse harmful effects. Atlantic cod (Gadus Morhua) is a commercially and ecologically relevant species in the North Atlantic that must cope with the presence of these toxicants. Many of the contaminants in the oceans have lipophilic properties and therefore can accumulate in organs such as the liver. At a molecular level, they can bind to target molecules such as nuclear receptors. The glucocorticoid receptor (GR) is expressed in nearly all vertebrates and is involved in several basic processes including glucose metabolism, among others. In this thesis, using a luciferase reporter assay, ligand binding properties of several contaminants were examined. None of the contaminants were found to bind cod GR. Sequence alignments and phylogeny analysis allowed to unravel that the ligand-binding domain (LBD) of the cod's GR shows differences compared to human GR. Further on, precision-cut liver slices were exposed to two commonly found pharmaceuticals, dexamethasone and prednisolone. Pck1 and pfkfb1 are two key genes of the glucose metabolism pathway and modulation of their expression was investigated by qPCR but no significant difference in gene expression was found. These results suggest that Atlantic cod may be susceptible to GR-activating pharmaceuticals and further investigation into the sensitivity and physiological consequences are needed.