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MOLECULAR CHARACTERIZATION OF CORTISOL RECEPTORS IN FISH.

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In teleost fish, the presence of aldosterone remains doubtful and cortisol is the major corticosteroid controlling a number of physiological processes including both mineralocorticoid and glucocorticoid actions. Regulation of these processes involves cortisol binding to its respective receptor which acts as a ligand inducible transcription factor. A first glucocorticoid receptor (rtGR1) has been cloned in rainbow trout by Ducouret et al. (1995) and this receptor presents all characteristics similar to those of other GRs. Recently, a cDNA encoding a rainbow trout mineralocorticoid-like receptor (rtMR) has been isolated (Colombe et al., 2000). Finally, we have identified in trout a novel cortisol receptor which shows high sequence homology with the other GR and thus is the second GR to be identified in trout (rtGR2). Taking account the homology with the human GR, a three-dimensional (3D) model of the ligand-binding pocket was constructed for each of the trout cortisol receptors. This study allows localisation of the major residues involved in the ligand-induced activation of the receptor and specific of GR or MR. Binding studies or analysis of the transcriptional activity in transfected cell lines confirm that cortisol is the most potent ligand for each of these trout cortisol receptors. However, comparison between rtGR1 and rtGR2 showed differences in transcriptional activity, the later one being more sensitive to cortisol. Analysis of gene expression of these receptors in various tissues indicated a unique transcript size of 7.4 kb for both rtGR1 and rtGR2 and a complex pattern of expression for MR. Interestingly, the three cortisol receptors are differentially expressed in the major osmoregulatory organs, gill, kidney and gut. This suggests a complex regulation of water and ion exchange mechanisms which would involve both the various forms of cortisol receptors and prolactin receptors.