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Regulation of CYP 1A1 gene expression by retinoic acid receptor, retinoid X receptor and constitutive androstane receptor in rainbow trout hepatoma cells(RTH 149)

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Exposure of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) causes a variety of biological and toxicology effects, most of which are mediated by aryl hydrocarbon receptor (AhR). The ligand-bound AhR as a heterodimer with AhR nuclear translocator (ARNT) binds to its specific DNA recognition site, the dioxin-responsive element (DRE), and it results in increased transcription of CYP1A1 gene. Retinoic acid (RA) regulates the transcription of various genes for several essential functions through binding to two classes of nuclear receptors, the retinoic acid receptor (RAR) and retinoid X receptor (RXR). Constitutive androstane receptor (CAR) also regulates the transcription of gene. In this study, we have examined how RAR, RXR and CAR regulated CYP1A1 in rainbow trout hepatoma cell (RTH 149) using luciferase reporter gene assay system. We did transient transfection with CYP1A1 luciferase reporter gene and treated with TCDD, all-trans RA, 9-cis RA and phenobarbital. Treatment of all-trans RA, 9-cis RA or phenobarbital decreased the TCDD induced transcription of CYP1A1. When we did transient cotransfection with CYP1A1 luciferase reporter gene and RXR, as increase of RXR concentration, the TCDD induced transcription of CYP1A1 was decreased. Transfection with CAR also decreased the TCDD induced transcription of CYP1A1 in RTH 149 cells.