P34

# ARYL HYDROCARBON- AND ESTROGEN-MEDIATED SIGNALS POSSIBLY CROSS TALK TO REGULATE CYP1A1 GENE EXPRESSION

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2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is an environmental toxin that activates the aryl hydrocarbon receptor (AhR) and disrupts multiple endocrine signaling pathways by enhancing ligand metabolism, altering hormone synthesis, down regulating receptor levels, and interfering with gene transcription. And TCDD-mediated gene transactivation via the AhR has been shown to be dependent upon estrogen receptor (ER) expression in human breast cancer cells. In the present study, we have examined the effect of natural estrogen, phytoestrognes and environmental estrogens on the regulation of CYP1A1 gene expression in MCF-7 human breast cancer cell line. that ER and AhR are co-expressed. pCYPIA1-luc reporter gene was transiently transfected into MCF-7 cells. These cells were treated with various chemicals and then luciferase assay was carried out. 17beta-estradiol significantly inhibited TCDD stimulated luciferase activity dose dependently and this inhibition was partially recovered by concomitant treatment of tamoxifen. 17beta-estradiol metabolites, 2-hydroxyestradiol and 16alpha-estriol resulted in less potent inhibitory effect than estradiol and synthetic estrogen, diethylstilbestrol (DES) showed no effect on CYP1A1 gene expression. This study demonstrated that estrogen down-regulated TCDD stimulated CYP1A1 expression via ER mediation. And we have found out that several flavonoids such as genistein, kaempferol, daidzein, naringenin, and alkylphenols such as nonylphenol, 4-octylphenol and resveratrol also inhibited TCDD induced CYP1A1 expression like estrogen. [Supported by grants from the Korean Ministry of Environment]