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The effects of estradiol and its metabolites on the regulation of CYP1A1 expression.

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2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is the most potent halogenated aromatic hydrocarbon congener that induces expression of several genes including CYP1A1. Exposure to TCDD results in many toxic actions such as carcinogenesis, hepatotoxicity, immune suppression, and reproductive and developmental toxicity. Dramatic differences in dioxin toxicity have been observed between the sexes of some animal species, suggesting hormonal modulation of dioxin action. Many studies have been reported and propose several mechanisms of anti-estrogenic effects of TCDD. In contrast, the effect of estrogen on the regulation of CYP1A1 are not clear at present. There are several reports showing conflicting results. It seems that induction/inhibition of **CYP1A1 may be dependent on cell-type and concentration.**

The purpose of this study was to investigate the regulation of TCDD-induced CYP1A1 gene expression by estradiol and its metabolites. We examined whether estradiol and its metabolites altered TCDD-mediated induction of CYP1A1 enzyme activity. 17β estradiol and 16α estriol at non cytotoxic concentrations caused a significant concentration dependent decline of TCDD-induced EROD activity. To determine whether reduced EROD activity reflected altered CYP1A1 mRNA expression, we measured CYP1A1 mRNA level by RT-PCR. And to examine whether estradiol and its metabolites have effects on TCDD-induced CYP1A1 gene expression at the transcription level, we also performed transient transfection with an AhR responsive reporter plasmid containing the 5′ flanking region of the human CYP1A1 gene to examine whether estradiol and its metabolites have effects on TCDD-induced CYP1A1 gene expression at the transcription level.

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