

**1301 IDENTIFICATION AND CHARACTERIZATION OF TIG1, A NOVEL TCDD-INDUCIBLE GENE.**

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TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) is a prototype of a class of halogenated aromatic hydrocarbons, which are mostly byproducts of industrial processes and combustion of fuels. Many of the chemicals are persistent environmental contaminants. TCDD elicits a wide range of toxic responses in animals and impose a threat to human health. The aryl hydrocarbon receptor is a ligand-activated receptor/transcription factor, which, together with other factors, mediates the biological effects of TCDD and related chemicals. The mechanism of action of AhR involves transcriptional regulation of gene expression of target genes. However, current knowledge on the target genes and their roles in TCDD toxicity is limited and does not adequately explain the wide spectrum of TCDD toxicity. To gain new insights into the mechanism of TCDD action, we have utilized the mRNA differential display technique to identify new genes that are regulated by TCDD. We report here the identification of a new TCDD-inducible gene (TIG1) in mouse cell lines. Analyses of the partial sequence of TIG1 suggest that it represents a novel gene product. The induction of TIG1 by TCDD is both time- and dose-dependent. Cycloheximide, an inhibitor of protein synthesis, superinduces TIG1 in the presence of TCDD. Cell genetic analyses of the induction reveal that it requires AhR and Arnt. Furthermore, these analyses demonstrate that the transcription activation functions of both AhR and Arnt are required for the induction of the gene. Finally, treatment of C57BL/6 mice with low doses of TCDD induces TIG1 mRNA expression in liver. Thus, TIG1 is a novel target gene of

TCDD in both cultured cell and intact animal; the induction of the gene by TCDD is mediated through the AhR/Arnt signaling process. These findings provide new insights into the mechanism of gene regulation by AhR. Current research is aimed at analyses of the sequence and cellular function(s) of TIG1.