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Analysis of 2,3,7,8-Tetrachlorodibenzo-P-Dioxin Induced Gene Expression Profile in Hairless Mice Skin Using Pathway Specific cDNA Microarray

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2,3,7,8-Tetrachlorodibenzo-ρ-dioxin (TCDD) displays high toxicity in animals and has been implicated in human carcinogenesis. Although the mechanisms of TCDD-induced carcinogenesis are poorly understood, it considered to be non-genotoxic and tumor promoter. In this study, we investigated the tumor promotion effect of TCDD on the two-stage skin chemical carcinogenesis using hairless mouse (SKH1). We induced papillomas after treatment with N-methyl-N'-nitro-N-nitorsoguanidine (MNNG) as a initiator and TCDD as a promoter for 30 weeks. We found that the incidence or multiplicity of papillomas and hyperplastic nodules was maximally induced at MNNG-TCDD group compare to control, MNNG, and TCDD alone. These results suggesting that TCDD can acts as a potent promoter in the hairless mouse skin. In addition, we have used pathway specific cDNA microarray to detect the transcriptional signature in normal, tumor surrounding and tumor regions of hairless mouse induced by two-stage skin chemical carcinogenesis protocol. We found that 53 genes among 96 genes involved in cell cycle, signal transduction, apoptosis, adhesion molecule, angiogenesis, and invasion were up-regulated in the tumor surrounding region. In the tumor region, only a few genes related with cell cycle and oncogenes were up-regulated but several genes encoding integrin, Akt, Raf were down-regulated. Our data suggest that TCDD promote to development of skin tumor in hairless mouse by changes of multiple integrated network of signaling pathway.

Keyword : TCDD, MNNG, hairless mice, cDNA microarray, gene expression