【P-36】

Induction of COX-2 by TCDD in Human Liver Cell Lines

Ho Il Kang, Miok Eom, Hyukje Kwon, Mi Sun Park, Tai Kyung Ryeom,
Mi Kyung Kang, Seungn Wan Jee and Ok Hee Kim
Division of Genetic Toxicology, National Institute of Toxicological Research

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) displays high toxicity in animals and has been implicated in human carcinogenesis. Although the mechanism of carcinogenesis by TCDD is unclear, it is considered to be a non-genotoxic and tumor promoter. The promotion step is known to induce by various factors such as oxidative stress and/or inflammation. In order to investigate whether inflammatory response is involved in the process of carcinogenesis by TCDD in two human liver cell lines, hepatoma HepG2 and non-tumorigenic fetal hepatic WRL68 cells, we investigated the expression of metabolizing enzyme CYP1A1, proinflammatory enzymes such as cyclooxygenase-2 (COX-2) and the upstream signaling enzymes and transcription factors regulating COX-2 induction. The CYP1A1 mRNA expression level were increased about 5 fold by 0.1nM TCDD in WRL68 cells and 2 fold by 1nM TCDD in HepG2 cells. And in previous studies, we found that the oxidative DNA damage was increased by TCDD in the same cell lines. These results suggest that CYP1A1 enzyme may be involved in the generation of TCDD-inducible ROS and in toxicity by TCDD. Moreover COX-2 is transcriptionally induced in WRL68 cells treated with 0.1nM TCDD, but not in HepG2 cells. c-jun, p65 and phospho-Erk1/2 also slightly induced by TCDD in WRL68 cells. Taken together, it seems that TCDD may be involved in tumor promotion through COX-2 induction pathway.

Keyword : TCDD, human liver cell line, inflammation