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Neoplastic Transformation of Immortalized Human Keratinocytes by 2,3,7,8-Tetrachlorodibenzo-P-Dioxin

Mi-Kyung Kang, Ho-Il Kang, Young-Sill Choi, Tai-Kyung Ryeom, Mi-Ok Eom, Mi-Sun Park, Seung-Wan Jee and Ok-Hee Kim

Department of Toxicology, National Institute of Toxicological Research, KFDA, Seoul, Korea

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), a prototype of many halogenated aromatic hydrocarbons, is a ubiquitous, persistent environmental contaminant and the most powerful carcinogen categorized by IARC. It is display high toxicity in animals and is associated with several cancers in human. Although the mechanism of carcinogenesis by TCDD is unclear, it is considered to be a non-genotoxic and tumor promoter. Several studies have shown that the skin is one of target organs for TCDD toxicity, the mechanisms of TCDD-induced carcinogenesis are poorly understood. In this study, we investigated the malignant transformation of human keratinocyte-derived cell line (HaCaT) by the two-stage chemical transformation method using N-methyl-N'-nitro-N- nitorsoguanidine (MNNG) as a initiator and TCDD as a promoter for 2 weeks. We found that subsequent exposure to TCDD for 2 weeks after initial exposure to MNNG markedly induced transformed cells compare to control, MNNG, and TCDD alone. It is suggesting that TCDD can acts as a potent promoter in HaCaT. In addition, these transformed cells showed morphological alternations in soft agar and increased telomerase activity. Therefore, the TCDD treatment of HaCaT cells by initiated with MNNG could promote neoplastic transformation without stimulation by exogenous growth factors. As a result, TCDD has strong potency as a promoter in nontumorigenic immortalized human epidermal keratinocytes.

Keyword : TCDD, MNNG, HaCaT, soft agar, telomerase