P-17

Aryl Hydrocarbon Receptor (AhR) -dependent Inhibition of AP-1 DNA binding by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in LPS-activated B cells

Jaehong Suh[1], Young Jin Jeon[2], Hwan Mook Kim[2], Norbert E. Kaminski[3], and Kyu-Hwan Yang[1]

[1]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, [2]Korea Research Institute of Bioscience and Biotechnology, Taejon, Korea, and [3]Department of Pharmacology and Toxicology, Michigan State University, U.S.A.

B cell has been identified as the sensitive cellular target responsible for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) -induced immune suppression. In isolated cell systems, the differentiation of B cells into antibody secreting plasma cells is believed to be inhibited by TCDD. We also have previously demonstrated IgM secretion was suppressed by TCDD in LPS-activated murine B cell line, CH12.LX. But the mechanism responsible for this inhibition by TCDD is still unclear. In the present studies, we examined the DNA binding activities of transcription factors to look at the change in cellular signaling pathway by TCDD in activated B cells. Among several transcription factors investigated in LPS-activated CH12.LX cells, TCDD (1 nM) inhibited AP-1 binding significantly at 48 and 72 hours after cell activation, but produced little effects in early time (2 hours). However, no inhibition was found by TCDD treatment in BCL-1 cells, AhR-deficient murine B cell line. Additionally, α -naphthoflavone and PCB52 (2,2',5,5'-tetrachlorobiphenyl), which has antagonistic effects on AhR-mediated biochemical responses, reversed low dose (0.1 and 0.3 nM) of TCDD-mediated inhibition of AP-1 binding. Furthermore, inhibition of AP-1 activity by TCDD was also found in the LPS-activated primary culture of splenocytes from B6C3F1 mice. Western blotting for the component of AP-1 complex, c-Jun, revealed low level expression of this protein in the nucleus of TCDD-treated cell compared to vehicle control. Collectively, these results suggest that TCDD-induced suppression of B cell differentiation is at least partially caused by inhibition of AP-1. (This work was supported by the grant from the Ministry of Environment, Korea)