Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on Human Tonsillar Lymphocytes

Jeong, Hye Gwang.

Department of Environmental Science, Chosun University

Murine lymphocyte function is quite sensitive to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). However, in contrast to the murine model, the corresponding functional studies have not been undertaken with the human lymphocytes. It was of interest to determine if human tonsillar lymphocytes could also be modulated by direct exposure to this chlorinated hydrocarbon. Therefore, the effects of TCDD on cytochrome P450-dependent drug metabolizing enzyme activity and immune function (proliferation and antibody secretion) in murine splenocytes and human tonsillar lymphocytes (HTL) were examined.

The induction of cytochrome P450 1A1 (P450 1A1) and P450 1A1-specific 7-ethoxyresorufin O-deethylase (EROD) activity by TCDD was investigated in HTL. EROD activity was induced by TCDD in mitogens (Phytohemagglutinine and pokeweed mitogen)-stimulated blast cells, but not in resting cells. TCDD markedly induced a EROD activity in a dose- and time-dependent manner. The expression of P450 1A1 and its mRNA were increased by TCDD in cultured blast cells, as detected by immunoblot and northern analysis, respectively. The induction in P450 1A1 gene transcription by TCDD could be accounted for by increased DNA binding of the dioxin receptor to the xenobiotic responsive element (XRE) sequences, as measured by gel shift analysis. These findings support the conclusion that TCDD bind to Ah receptor in cytosol, resulting in an increase of the expression of P450 1A1 gene synthesis of P450 1A1 protein and EROD activity in mitogens-stimulated HTL. However, EROD was not induced in murine splenocytes under any conditions.

In immune function, no suppression in proliferation and antibody secretion were observed by TCDD in mitogen-stimulated either cells. However, TCDD suppressed the background proliferation without PWM in both murine splenocytes and human tonsillar lymphocytes. Because background proliferation in HTL and murine splenocytes was suppressed by TCDD, we purified human and murine B-cells population. TCDD produced comparable effects on background proliferation and IgM secretion in purified murine and human B-cells in a dose-dependent manner from 0.3-30 nM. These results indicate that TCDD has a direct effect on human tonsillar lymphocyte activity and suggest that B-cells are a sensitive cellular target.

These findings indicate that enzyme induction and suppression of immune function may have different mechanism in murine and human system.