

Mechanisms for 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)-Induced Suppression of Antigen-Specific Antibody Production - Inhibition of Th2 Cell-Derived Cytokine Production in the Primary Immune Reaction -

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[Introduction].

TCDD has been reported to suppress antigen-specific antibody production, but the precise mechanism remains to be clarified. The type 2 helper T (Th2) cell-derived cytokines, such as IL-4, IL-5 and IL-6, were known to be involved in the antigen-specific antibody production. We have previously demonstrated that TCDD suppresses IL-4 and IL-5 production by splenocytes in the secondary immune response to ovalbumin (OVA). In the present study, we investigated the effects of TCDD on Th2 cell-derived cytokine production in the primary immune reaction, where these cytokines play a pivotal role in the proliferation and differentiation of antigen-specific B cells into antibody-producing plasma cells.

[Methods]

Female C57BL/6 mice (6 week-old) were orally administrated TCDD (20 µg/kg) or vehicle (corn oil containing 4% nonane), and simultaneously immunized with OVA (100 µg/mouse, i.p.) and alum. On Day 4, 7, 10 and 14 after the both treatments, spleen was excised and a single cell suspension (splenocyte) was prepared. T cell and B cell population in splenocytes were analyzed using FACSCalibur (Becton Dickinson). Splenocytes were cultured for 2 days with 100 µg/ml OVA, and then IL-4, IL-5 and IL-6 in the supernatant were measured using an ELISA kit (Biosource).

[Results and Discussion]

On Day 7 and 10, primary immunization of OVA increased T cell and B cell numbers in spleen of vehicle-treated mice, whereas TCDD significantly suppressed the OVA-induced increase in T cell and B cell numbers. IL-4, IL-5 and IL-6 production by control splenocytes re-stimulated *ex vivo* with OVA increased on Day 4 with a gradual decrease whereas TCDD administration significantly suppressed these cytokines on Day 4. The production of IL-5 but not IL-4 and IL-6 was significantly suppressed by TCDD through Day 14. IL-5 was also particularly sensitive to TCDD and significantly suppressed in a dose-dependent manner from a low dose of 1 µg/kg TCDD. Taken together, these results suggest that the suppression of Th2-derived cytokines by TCDD causes the failure of B cell to activate and proliferate. These effects of TCDD may be involved in the impairment of antigen-specific antibody production.