

## Alteration of B cell Development in the Spleen of C57B1/6 Mice by TCDD Treatment

Kaoru Inouye<sup>1,2</sup>, Tomohiro Ito<sup>1,3</sup>, Hidekazu Fujimaki<sup>1,3</sup>, Chiharu Tohyama<sup>1,3</sup>, and Keiko Nohara<sup>1,3</sup>

<sup>1</sup>Environmental Health Sciences Division, National Institute for Environmental Studies; <sup>2</sup>Domestic Research Fellow, JST; <sup>3</sup>CREST, JST

Inhibition of humoral immune response is a sensitive immunologic perturbations induced by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). It has been reported that TCDD suppresses the antigen (Ag)-specific antibody production and decreases the number of antibody forming cells. In germinal centers (GCs), Ag-activated B cells undergo proliferation and selection to differentiate into plasma cells that produce high-affinity antibodies. The purpose of the present study was to elucidate at which stage TCDD affects B cell development in response to Ag immunization. Therefore the effect of TCDD on GC formation was analyzed in the spleen of C57B1/6 mice. Female 6-week-old mice were orally administered 0 (vehicle) or 20 µg/kg of TCDD and immunized with 100 µg of ovalbumin (OVA) absorbed to alum (day 0). Mice were sacrificed for blood and tissue collection on days 7, 10 and 14, since OVA-specific IgG<sub>i</sub> in plasma was detected from day 10 by ELISA and the increased proportion of GC B cells in spleen was detected from day 7 by flow cytometry. TCDD treatment suppressed anti-OVA IgG1 production on days 10 and 14. Significant reduction in the number of GC B cells, as defined by B220<sup>+</sup> Peanut agglutinin (PNA)<sup>+</sup>, was observed in TCDD-treated mice from day 7 through day 14, indicating that TCDD inhibited GC formation from its early stage. Besides, the suppression of GC formation by TCDD was also histochemically detected by PNA staining. TCDD did not affect immunohistochemical staining pattern of follicular dendritic cells that are involved in GC formation. These results suggest that TCDD suppresses antibody production through preventing B cell proliferation or differentiation in GCs.