Immunotoxic Effects of Dioxins

○Keiko Nohara and Takehiro Suzuki
(Environ. Health Sci. Div., Natl. Inst. Environ. Studies)

Dioxins, including the most potent congener 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), are persistent environmental contaminants. They exert their toxic effects by binding and activating a transcription factor, the arylhydrocarbon receptor (AhR). TCDD has been shown to induce thymus atrophy, suppress antibody production and cytotoxic T lymphocyte (CTL) activity, and generate $CD62L^{lo}CD4^{+}CD25^{+}$ regulatory T cells in an AhR-dependent manner. We previously clarified that TCDD exposure of mice suppresses immunization-induced T cell proliferation and Th2 cytokine production, which was suggested to lead to the suppression of antibody production. To further investigate the role of the AhR in the T cells, we generated transgenic mice expressing a constitutively active mutant of AhR (CA-AhR) only in T cells. Although recent studies have reported that AhR activation in the T cells is necessary for TCDD-induced suppression of T cell function, our studies so far with CA-AhR Tg mice have shown that AhR activation only in T cells are not sufficient for suppression of antibody production and CTL activity. These results suggest that AhR activation in other cell types, such as dendritic cells and other accessory cells, are involved in the immune suppression by TCDD. In contrast to these suppressive effects of TCDD on immune cells, we recently found that pups of dams dosed with 1.0 μg TCDD/kg during pregnancy showed enhanced production of Th2 cytokines and increased levels of antigen-specific serum IgE after immunization. Further studies will be required to clarify whether the increase in the Th2 cytokine production and IgE by maternal TCDD exposure is involved in exacerbation of allergic reaction. Species specific sensitivity of immune system to dioxins also should be clarified to estimate the effects of these compounds on humans.