Mechanism of TCDD-Induced Immunotoxicity: The Role of Cell Activation in the Generation of Toxicity

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(ABSTRACT)

2, 3, 7, 8-Tetrachlorodibenzo-*p*-dioxin is well known for its immunotoxic effects on the thymus, as well as on B and T lymphocyte functions. Previous studies suggested that TCDD exerted immunotoxic effects only on cells differentiating in response to antigenic challenge. To this date, no work has been done to characterize the long-term effects of TCDD on the activated cells. Additionally, no studies have been done to determine whether TCDD has any effect on resting T cells. In the current study, therefore, we investigated the effects of TCDD on activated and resting cells within the same animal. T cells in the popliteal lymph node cells were activated by rear footpad immunizations with anti-CD3 antibodies. Distally-located axillary lymph nodes were chosen as a source of naive and resting T cells. Our results demonstrate that TCDD acted at the time of cell differentiation to suppress the immune responses of activated T cells, but failed to suppress, and at times, enhanced the immune responses of resting T cells. The TCDD-induced immunomodulations were temporary; responsiveness of both activated and resting T cells from TCDD-treated animals returned to normal by two weeks post-treatment, suggesting that TCDD does not affect memory cells. Futhermore, we provide direct evidence that the TCDD-induced immunosuppression in activated cells is due to increased apoptosis of $CD3^+$ T cells. TCDD also induced significant changes in cell surface markers expressed by naive and activated T cells. Together our data suggested that TCDD suppresses the proliferative responsiveness of only the activated, but not naive, T cells and that this is accomplished by induction of increased apoptosis of activated T cells. These studies shed new light on the mechanism through which TCDD induces increased susceptibility to infections and cancer in the vertebrate host.

This research was supported in part by grants from Sigma Xi, the American Cancer Society (IM 747), and the National Institutes of Health (AI/AR01392).