IS 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN AN IMMUNOSTIMULATOR ?

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Abstract

Peripheral blood mononuclear cells (PBC) were preincubated with 10 nM 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) for 24 h and were thorougly washed prior to Concanavalin A (Con A)-stimulated coculture period. Pretreatment of PBC resulted in increase of mitogen-induced proliferation. Preliminary data show significant increase of interleucin-1ß (IL-1ß) mRNA synthesis in TCDD-treated monocytes (Mo).

Introduction

TCDD possesses an extremely high degree of polyfunctional biological activity. The suppression effect of TCDD on proliferation and differentation of immunocompetent cells is well known (Silkworth et al., 1989). The opposite effects, like increase in proliferativ activity and differentation has been shown in TCDD-treated epidermal cells, which possess a much lower proliferative activity in pretreated period, if compared with thymocytes or lymphocytes stimulated by mitogen or antigen (Puhvel and Sakamoto, 1987). From our standpoint the estimation of consequences of TCDD action on resting and stimulated human PBC can be an importend step to understanding the mechanism of this xenobiotic effects on the immune system in general.

Methods

Monomolecular leukocytes were isolated from heparinized whole blood by centrifugation over Ficoll-verografin ($d = 1.077$ g/cm^3) and were resuspended in complete RPMI-1640. PBC were pretreated with 10 nM TCDD for 24 h, washed three times, resuspended in culture medium and treated with Con (25 µg/ml) in 96 well microtiter plates (1×10^5 cells per well) for 96 h at 37°C in a moist incubator equilibrated with 5% CO_2 atmosphere. Proliferation was mesured by ^{3}H-thymidine uptake during the last 16 h of the culture. Mo was purifed from PBC by adherence to plastic petri dishes and was treated with 10 nM TCDD for 24 h. IL-1ß and P-450 mRNA synthesis in TCDD treated and non-treated Mo was estimated by dot-hybridation assey.

Results and Discussion

TCDD treatment of non-stimulated PBC did not influence the viability or spontaneous proliferation of these cells. Nevertheless, TCDD treated PBC abundantly proliferated in response to Con A stimulation (Figure).

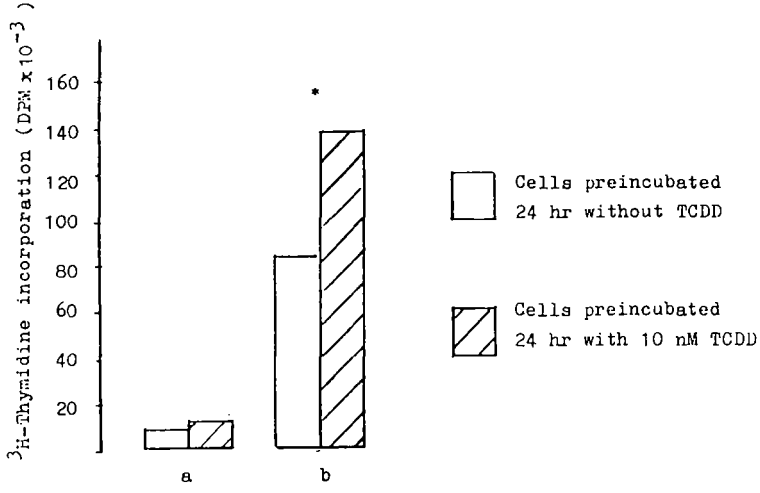

Figure: Preincubation of PBC with TCDD
a) spontaneous proliferation
b) Con A-stimulated proliferation
Asterisk indicate significant difference ($P<0.01$) from control cells, preincubated without TCDD

IL-1ß plays a key role in mitogen-induced proliferation. Dot-hybridization assay showed a significant augmentation of IL-1ß and P-450 mRNA synthesis in TCDD treated Mo (two experiments). One experiment showed a marked IL-1ß and P-450 mRNA synthesis after 4 h TCDD incubation. In both cases IL-1ß mRNA augmentation was observed in 24 h TCDD treated Mo. In conclusion, results here presented show that TCDD may intensify functional activity of resting immunocompetent cells. There can be no doubt that widespread xenobiotic acts as a highly active immunodulator with a complex mechanism of action.

References

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