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Toll-like Receptor Activation in Tributyltin-induced Increases in Interleukin 1β Production by Human Immune Cells.

Abstract

Tributyltin (TBT) is an environmental contaminant due to its use as a biocide in a variety of applications including in marine anti-fouling paints. It has been detected in a number of human tissues including blood. Previous studies have shown that exposure to TBT increases the cellular production of the pro-inflammatory cytokine IL-1β by peripheral blood mononuclear cells (PMBCs) and this increase involves MAPK activation. Toll-like receptors (TLR) activate immune cells to produce pro-inflammatory cytokines in response to pathogen associated molecular patterns (PAMPs) and damage associated molecular patterns (DAMPs) by activation of MAPKs as well as other intracellular components. The current study uses selective inhibitors of TLR4 and TLR3 to investigate their roles in TBT-induced production (secreted plus intracellular levels) of IL-1β by PBMCs. Secreted levels of IL-1β were measured using enzyme-linked immunosorbent assay (ELISA) while intracellular levels were determined using Western blot. Inhibition of TLR4 led to diminished ability of TBT to stimulate IL-1β production. In contrast, selective inhibition of TLR3 generally enhanced the TBT-induced production of IL-1β. This indicates that TBT may be either directly or indirectly interacting with certain TLR receptors as part of its mechanism of stimulating pro- inflammatory cytokine production. Contaminant stimulation of IL-1β has the potential to cause chronic inflammation and its attendant pathologies.

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