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Tributyltin-induced Production of Tumor Necrosis Factor α in human Immune Cells Involves Toll-Like Receptor 1/2

Tumor necrosis factor (TNF)α is a pro-inflammatory cytokine and is a critical component of the inflammatory response. If TNFα is elevated in the absence of an appropriate stimulus such as injury or infection, it can lead to a state of chronic inflammation. Chronic inflammation is a factor is a wide number of diseases. These include, inflammatory bowel disease, diabetes, atherosclerosis, and cancer. TNFα is produced by immune and other cells. In immune cells Toll-like receptors (TLR) such as TLR1/2 bind pathogen (or damage) associated molecules and stimulate intracellular components such as MAP kinases (MAPKs). Activation of TLRs then leads to production of TNFα as well as other pro-inflammatory cytokines. Tributyltin (TBT) is an environmental contaminant due to is uses in various household products, athletic wear, and in marine anti-fouling paints as an antimicrobial and antifungal agent (levels in human blood are as high as 200 nM), TBT stimulates production (secreted plus intracellular levels) of TNFα by peripheral blood mononuclear cells (PBMCs) in a MAPK-dependent manner. We hypothesize TLR activation by TBT may also be part of the mechanism by which it stimulates TNFα production in immune cells. To address this hypothesis PBMCs were treated with CU CPT22 (a selective inhibitor of TLR1/2) for 1 h and then exposed to TBT (25, 50, and 100 nM) for 24 h. TNFα secretion was measured by ELISA and intracellular levels by western blot. When TLR1/2 was unavailable TBT- induced production of TNFα production was diminished. These results suggest that TBT interacts with TLR1/2 as part of it mechanism of activating TNFα production by immune cells.