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Participation of Toll-like Receptors in Tributyltin-induced Increases in Interleukin 6 Production by human immune cells.

Abstract:
Toll-like receptors (TLR) regulate the production of pro-inflammatory cytokines by immune cells in response to pathogen associated molecular patterns (PAMPs) and damage associated molecular patterns (DAMPs). The intracellular signaling pathways activated by TLRs include MAPKs as well as other intracellular components. The environmental contaminant tributyltin (TBT) has been detected in a number of human tissues including blood. In previous studies, TBT (at levels found in human blood) was shown to increase production of the pro-inflammatory cytokine interleukin 6 (IL-6) by peripheral blood mononuclear cells (PMBCs) and this increase involved MAPK activation. Excessive levels of IL-6 have been associated with a number of pathologies that are associated with chronic inflammation, including cardiovascular disease and cancer. In the current study TLR4 and TLR3 are selectively inhibited to probe their involvement in TBT-induced production (secreted plus intracellular levels) of IL-6 by PBMCs. Measurement of secreted IL-6 used enzyme-linked immunosorbent assay (ELISA) while intracellular levels were determined with Western blot. When TLR4 was inhibited prior to exposure to 100, 50 , and 25 nM TBT, the ability of TBT to stimulate IL-6 production was significantly diminished. Selective inhibition of TLR3 generally diminished the TBT-induced production of IL-6, but the effects were less consistent than those seen with TLR4 inhibition. Results suggest that TLR4, and to some extent TLR3, may be participating in the TBT induced stimulation of IL-6 production in human immune cells. Stimulation of IL-6 production by TBT has the potential to cause chronic inflammation. As mentioned above, chronic inflammation is associated with a wide range of severe pathologies.

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