Tributyltin-induced Production of Interleukin-6 in Human Immune Cells Requires MyD88 activation

Interleukin 6 (IL-6) is a pro-inflammatory cytokine produced by a variety of cell types including immune cells and is a critical component of the inflammatory response. If IL-6 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 in a wide number of diseases. These include, inflammatory bowel disease, diabetes, atherosclerosis, and cancer. IL-6 production as well as that of other inflammatory cytokines is regulated by activation of Toll-like receptors (TLR). 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 260 nM), Previous studies have shown that TBT is able to stimulate production of IL-6 by peripheral blood mononuclear cells (PBMCs) and that this TBT-induced production involved TLR-4, which is linked to the intracellular adapter protein MyD88, but not those TLRs that do not use MyD88 such as TLR3. Based on this information, we hypothesize that blocking MyD88 function will greatly diminish the ability of TBT to stimulate IL-6 production in immune cells. To address this hypothesis PBMCs were treated with TJ-M2010-5 (a selective inhibitor of MyD88) for 1 h and then exposed to TBT (25, 50, and 100 nM) for 24 h. IL-6 secretion was measured by ELISA and intracellular levels by western blot. When MyD88 was unavailable TBT- induced production of IL-6 was blocked. These results suggest that MyD88 is critical in the mechanism of TBT stimulation of IL-6 production by immune cells.