The Role of Toll-Like Receptors 3, 4, and 8 in Tributyltin Stimulation of Tumor Necrosis Factor α Production by Human Immune Cells

Tributyltin (TBT) significantly contaminates the environment due to its use as a biocide and antifungal agent in various household products, athletic wear, wood preservatives, and marine anti-fouling paints. It is found in several human tissues, including blood at concentrations as high as 200nM. Tumor necrosis factor (TNF) α is a critical regulator of the immune response to injury or infection, and dysregulation of its levels can lead to chronic inflammation, which is associated with several pathologies, including increased invasiveness and metastasis of tumors. Toll-like receptors (TLR) stimulate pathways, including MAP kinase (MAPK) activation, that lead to increased production of TNFα in response to pathogens or injury. Previous studies displayed that TBT (200-2.5 nM) stimulated production of TNFα from peripheral blood mononuclear cells (PBMCs) and that MAPK activation was involved in the mechanism for this TBT-induced increase. The current study examines whether the upstream activators of MAPKs, TLRs 3, 4, and 8, are involved in TBT-induced stimulation of TNFα production. Results indicate that TLR4 is needed for TBT to stimulate TNFα production in human immune cells, thus further elucidating the mechanism by which this compound dysregulates the production of this potent pro-inflammatory cytokine.