Toll-like Receptor 3 is Involved in Dibutyltin Stimulation of Interleukin-6 Production in Human Immune Cells.

Toll-like receptors (TLR) regulate the production of proinflammatory cytokines such as interleukin (IL) -1β and IL-6 by immune cells. Proinflammatory cytokines, such as IL-1β, and IL-6, regulate the immune response to injury and infection. However, when their production is elevated in the absence of an appropriate stimuli, chronic inflammation may ensue. Chronic inflammation is associated with a number of pathologies, including cancer. Dibutyltin (DBT) is an organotin compound used in the manufacturing of plastics including polyvinyl chloride (PVC) and as a de-wormer in poultry. It has been found in human blood at concentrations as high as 0.3 μM. Previous work has shown that DBT, at certain exposures, increases the production of both IL-1β and IL-6. Due the role of TLRs in regulating the normal production of these cytokines and the fact that DBT is able to increase their production, we hypothesize that TLRs may be involved in DBT-induced stimulation of IL-1β and/or IL-6 production by immune cells. To address this hypothesis, we examined DBT-induced increases IL-1β and IL-6 production in the presence of a selective TLR3 inhibitor (CU CPT 4a). Human peripheral blood mononuclear cells (PBMC) were treated for 1 h with CU CPT 4a or appropriate control, prior to exposure to 0.5, 0.25, and 0.1 μM DBT for 24 h. Secreted IL-1β or IL-6 was measured by ELISA and intracellular IL-1β or IL-6 was determined by Western blot. Results indicate thatTLR3 is involved in DBT-induced increases in IL-6 production but not that of IL-1β. These results provide important information about the mechanism by which DBT may be elevating levels of these critical pro-inflammatory proteins and potentially causing chronic inflammation and increasing the risk of the diseases associated with chronic inflammation.