The Effects of Hexabromocyclododecane (HBCD) on Toll-like receptors (TLRs) Expression in Human Immune Cells

Hexabromocyclododecane(HBCD) is recognized as an environmental contaminant used in applications like insulation for buildings, furniture upholstery, and textiles. HBCD has also been found in many environments including wildlife, breast milk along with blood. Toll Like Receptors (TLRs) are critical defensive proteins. They are considered the 1st line of defense for the immune system against pathogens. TLRs are found to initiate signal pathways involving mitogen-activated protein kinases (MAPKs), which activates transcription factors like NF-κB and AP-1, leading to the production of pro-inflammatory cytokines which are ideal for induction of the host immune response against pathogens. There has been previous research that demonstrated HBCD promoting an up regulation of pro-inflammatory cytokines including interleukin 1-beta IL-1β and IL-6. Previous studies have demonstrated that HBCD promotes the upregulation of IL-1β and IL-6 in a MAPK-dependent manner, with this cytokine stimulation relying on TLR4. Based on these findings, we hypothesize that HBCD may influence the protein expression levels of TLRs in human immune cells. This study explores the effects of HBCD on the protein expression of transmembrane TLRs 1, 2, and 4, as well as intracellular TLRs 3 and 8.Preliminary data suggest variations in protein expression levels across different TLRs, with donor-specific differences observed. These findings indicate that HBCD may directly or indirectly interact with specific TLR receptors, contributing to its mechanism of stimulating pro-inflammatory cytokine production. This preliminary evidence provides insight into how HBCD elevates pro-inflammatory cytokines in the absence of appropriate stimuli, potentially leading to chronic inflammation.