181-LIPS

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

Due to its industrial use as a flame retardant, Hexabromocyclododecane (HBCD) has become an environmental contaminant found in wildlife samples and human systems. In humans, HBCD has been found in serum, adipose tissue, and breast milk. The innate human immune system can respond to foreign, potentially toxic, substances by producing and secreting cytokines that signal an inflammatory response to neutralize the foreign material. Unintended stimulation of pro-inflammatory cytokine production by a compound such as HBCD can lead to chronic inflammation and the many diseases associated with it, including cancers. The production of pro-inflammatory cytokines, including interleukin (IL)-1β and IL-6, is activated by toll-like receptor (TLR) stimulation of intracellular pathways, of which mitogen activated protein kinases (MAPKs) are one component. HBCD has been shown to increase the production of IL-1β and IL-6 in a MAPK-dependent manner. Additionally, recent results have shown that HBCD stimulation of these cytokines is dependent on TLR4. In response to being activated by ligand binding, TLR expression is altered (as is seen with a number of other receptors). Based on this information, we hypothesize that HBCD may alter the level of expression of TLRs in human immune cells. The current study examines if exposure to HBCD results in alteration of mRNA levels of transmembrane TLRs 1, 2, and 4, as well as intracellular TLRs 3 and 8. Preliminary findings indicate that there are HBCD induced decreases in mRNA expression of certain TLRs. This is consistent with the down regulation of receptor expression that can occur when the receptor has been activated. These results provide further clarification of the mechanism by which HBCD elevates pro-inflammatory cytokines in the absence of appropriate stimuli leading to potential chronic inflammation.