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Comparison of TLR4 and TLR1/2 in Pentachlorophenol Induced Stimulation of IL-1β in Human Immune Cells

The environmental contaminant pentachlorophenol (PCP) is detected in human blood samples at levels as high as 5 μM. Exposure to PCP presents a significant risk to humans. PCP has been associated with respiratory diseases and cancer, showing a strong association with non-Hodgkin's lymphoma, multiple myeloma, and kidney cancer. Interleukin-1 βeta (IL-1β) is a potent pro-inflammatory cytokine produced by immune cells. Production of IL-1β by immune cells is normally stimulated when pathogen- or damage-associated molecular patterns (PAMPS/DAMPS) activate the toll-like receptor (TLR) regulated pathways. Various TLRs are expressed in immune cells and nonimmune cells. TLRs are categorized based on their localization within the cells as either cell surface or intracellular receptors. TLR4 and TLR1/2 are predominately cell surface receptors. It is well known that abnormal production of IL-1β is responsible for chronic inflammation (inflammation in the absence of injury or infection), which is implicated in several diseases such as autoimmune diseases and cancer. Previous work has demonstrated that PCP causes human immune cells to produce elevated levels of IL-1β and that PCP-induced stimulation of IL-1β production was dependent on the activation of MAP kinases, which are components of TLR signaling pathways. It has not yet been established whether PCP associates with TLR4 and TLR1/2. In this study, we examined whether PCP requires TLR4 and TLR1/2 to stimulate the production (secreted + intracellular levels) of IL-1β in human peripheral blood mononuclear cells (PBMC). Cells were treated for 1 h with a selective TLR4 inhibitor (TAK242) and TLR1/2 inhibitor (CUCPT22) or appropriate control, prior to exposure to 5, 2.5, and 1 μM PCP. Secreted IL-1β was measured by ELISA and intracellular IL-1β was determined by Western blot. The results indicate that PCP-induced stimulation of IL-1β productions was diminished in immune cells where TLR4 was inhibited with TAK242. However, the production of IL-1β was not consistently diminished in immune cells where TLR1/2 was inhibited with CUCPT22. The research findings suggest that the PCP-induced production of IL-1β is dependent upon TLR4 receptors and independent of TLR1/2 receptors in human immune cells. These results offer an insight into the mechanism by which PCP may lead to chronic inflammation and its associated pathologies.