The Role of MyD88 in Pentachlorophenol Stimulation of Interleukin-1β Production by Human Immune Cells

Interleukin-1β (IL-1β) is a proinflammatory cytokine produced in response to injury or infection. High levels of IL-1β, in the absence of infection or injury, can lead to chronic inflammation which is linked to increased pathologies including cancer. Pentachlorophenol (PCP) is an environmental contaminant detected in human blood at levels as high as 5μM and is associated with development of several cancers. Previous studies indicate that PCP stimulates the production of IL-1β by immune cells and that this production involves toll-like receptors (TLR), which are linked to the intracellular adapter protein MyD88. Based on this information, we hypothesize that blocking MyD88 function will greatly diminish the ability of PCP to stimulate IL-1β production by immune cells. Cells were treated with a selective inhibitor of MyD88, TJ-M2010-5, and tested for PCP stimulation of IL-1β production using ELISA to determine secreted levels of IL-1β and western blot to determine intracellular levels. Results show that MyD88 is needed for PCP-induced increases in IL-1β. PCP stimulation of IL-1β production was greatly decreased or completely absent in cells where MyD88 function has been blocked These data clarify the mechanism by which PCP could lead to chronic inflammation. As mentioned above, chronic elevation of pro-inflammatory cytokines such as IL-1β can lead to cancer development, such as seen with PCP exposures.