A014 LPSC

Effects of Dibutyltin Exposures on Translation Regulatory Factor eIF4B in Human Immune Cells

Abstract:

Dibutyltin (DBT) is an organotin that contaminates the environment due to its uses as a stabilizer in polyvinylchloride (PVC) plastics and as a deworming agent in certain poultry products. DBT has been found in drinking water and other beverages due to leaching from PVC plastics used during the distribution of drinking water and storage of beverages such as beers and wines. DBT has been found in human blood at levels as high as 0.3μM. Inflammatory cytokines are key mediators in the response to injury or infection. However, if their levels are increased in the absence of a necessary immune response, chronic inflammation is possible. Chronic inflammation is associated with various disorders including, rheumatoid arthritis, Crohn's disease, atherosclerosis, and cancer. DBT can increase the production of pro-inflammatory cytokines such as interferon gamma (IFNγ), tumor necrosis factor alpha (TNFα), interleukin 1 beta (IL-1β), and interleukin 6 (IL-6) in human immune cells. DBT appears to utilize the ERK 1/2 and/or p38 MAPK pathways to stimulate pro-inflammatory cytokine production in immune cells. MAPK pathways are capable of regulating translation including processes leading to the phosphorylation (activation) of eukaryotic initiation factor 4B (eIF4B). The current study examines the levels and phosphorylation state of eIF4B after 6-hour and 24-hour exposures to DBT in peripheral blood mononuclear cells (PBMCs). DBT (at all concentrations) caused a robust increase in phosphorylation (activation) of eIF4B (S406) within 6-hour exposure across all donors. At 24 hours of exposure, increases in P-eIF4B (S406) begin to taper off with increases observed sporadically amongst donors. These results suggest that DBT may be in part elevating the production of key pro-inflammatory cytokines in immune cells by its ability to activate translation.

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