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Effects of Dibutyltin Exposures on Translation Regulatory Factor S6 in Human Immune Cells.

Abstract

Dibutyltin is an organotin contaminating the environment through its use as a stabilizer in polyvinylchloride, PVC plastics. DBT has been found in drinking water and beverages, such as beer and wine, due to leaching from the PVC plastics used during the distribution of these drinks. Along with PVC plastics, DBT has been used as a deworming agent in poultry, infiltrating additional food products and increasing the exposure of the toxin to humans. Due to its multiple uses, it has entered the food chain and has been detected in human blood at levels as high as 0.3μM. Inflammatory cytokines are important mediators of the response to injury or infection.
However, if their levels are increased in the absence of a needed immune response, chronic inflammation can occur. Chronic inflammation is associated with a number of pathologies including, rheumatoid arthritis, Crohn's disease, atherosclerosis, and cancer. DBT can increase the synthesis 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 use the ERK 1/2 and/or p38 MAPK pathways to stimulate pro-inflammatory cytokine production by immune cells. MAPK pathways have the capacity to regulate translation including processes leading to the phosphorylation (activation) of the S6 ribosomal subunit. The current study examines the levels and phosphorylation state of S6 after 1-hour and 6-hour exposures to DBT in peripheral blood mononuclear cells (PBMCs). The results indicated that, within 1 hour of exposure, DBT (at several concentrations) elevated levels of phospho (P)-S6 and S6. At 6 hours of exposure, DBT caused increased levels of S6, along with significant increases at higher concentrations for P-S6. These results suggest that DBT may be elevating the
synthesis of key pro-inflammatory cytokines in immune cells by its ability to activate translation.

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