Endocrine Disruption

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The Effects of Tris(2-Chloroethyl) phosphate (TCEP) on the Expression of Estrogen Receptor Alpha and Tumor Suppressor Gene BRCA-1 in Breast Cancer Cell Lines

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TCEP is an organophosphorus flame-retardant (OPFR) that is used widely in polyurethane foams, furniture, and household products. From these products, TCEP has significant emission into its surrounding environment. Inhalation and dermal absorption are the most common routes of human exposure to OPFRs, which have been measured in human hair, breast milk, and urine. Previous studies of OPFRs have shown their endocrine disrupting actions that have influence on diseases such as cancer. Breast cancer is the second most common cancer among women in the United States, and because of this prevalence, it is imperative to investigate possible causes and treatments for this disease. Due to the endocrine disrupting nature of OPFRs, we are investigating the effects of TCEP on hormone dependent breast cancer cell lines MCF-7 and T-47D. Our study examines the effects of TCEP, alone and in combination with hormones and anti-hormones, on ERα and BRCA1 expression in MCF-7 and T-47D breast cancer cells by utilizing western blot analyses, cellular viability assays, confocal microscopy, apoptosis assays and RT-qPCR analyses. In order to deplete any endogenous steroids or effectors, breast cancer cells were cultured in a medium containing 5% charcoal-stripped fetal bovine serum for six days. Western blot analysis revealed alterations in the expression of ER-alpha after 24 hours of treatment with varying concentrations of TCEP (1µM-2mM). A concentration-dependent decrease of ERα protein levels was noted in the T-47D cell line when compared to the control. BRCA1 protein levels also displayed an altered expression compared to the control through the various concentrations of TCEP. Through our concentration studies, optimum concentrations of TCEP were found to be 100 µM for T-47D and 2mM for MCF-7. For our hormone studies, cell lines were treated with their respective optimum concentration of TCEP as well with combinations of hormones and anti-hormones. After 24-hour treatment of E2, TCEP, and a combination of E2 with TCEP, a decrease in ERα expression was observed when compared to the control in both MCF-7 and T-47D cell lines. A combination of TCEP with ICI treatment revealed a significant down regulation of ERα expression level compared to the control. The same treatment conditions exhibited an increase with BRCA1 expression compared to the control and these effects were sensitive to the presence of antiestrogens in both cell lines. For cell viability studies, cells were treated for 6 days with TCEP concentrations ranging from 10nm-2µM which displayed an increase (40-50%) in cell proliferation compared to the control in both cell lines. Cytolocalization of ERα remained unaltered with the above treatment conditions. Our studies provide interesting findings about the molecular mechanisms of TCEP as a potential endocrine disrupting compound on the steroid receptors and tumor suppressor genes in breast cancer cells.

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