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## Evidence Of Two Subpopulations In MCF-7 Human Breast Cancer Cells Chronically Exposed To TCDD That Differentially Express Estrogen Receptor Alpha.

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Estrogens play a key role in the development and evolution of breast cancer tumors. Estrogen receptor alpha (ER\_alpha) mediates many of the biological activities of estrogens. The expression of ER\_alpha has been associated with low invasiveness and good prognosis. Recent epidemiological reports suggest that long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) may be implicated in the increased incidence of breast cancer in exposed women. TCDD interferes with the expression of some ER\_alpha-dependent genes and inhibits estradiol (E2)- dependent growth of breast cancer cells in vitro. However, E2-dependent xenographs of MCF-7 human breast cancer cells resumed growth after two weeks of TCDD exposure. The mechanisms involved in the resumption of cell growth are not completely understood. My previous studies indicated that exposure for more than one year to 1.0 nM TCDD (LTDX cells) resulted in decreased levels of ER\_alpha protein expression as compared with control MCF-7 cells. We investigated whether this reduced expression of ER $\alpha$ ; was either the result of decreased expression of ER\_alpha in all the cells or the inhibition of expression of ER\_alpha in some of the cells. Single cell clones were obtained from LTDX cells and their ER $\alpha$ ; protein expression was analyzed by Western immunoblots. Four out of five LTDX-derived clones expressed ER\_alpha at levels comparable to those in MCF-7 cells. Removal of TCDD treatment for 16 days restored the expression of ER\_alpha in the ER\_alpha-negative cells (X2B cells). These results suggest that cells chronically exposed to TCDD contain at least two cell subpopulations that may respond differently to the ER\_alpha-mediated effects of TCDD.