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Chronic exposure of MCF-7 human breast cancer cells to TCDD results in increased sensitivity to estradiol and decreased sensitivity to an antiestrogen

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Background and significance: 2,3,7,8 Tetrachlorodibenzo-para-dioxin (TCDD) is an ubiquitous persistent organic pollutant. TCDD has been classified as an antiestrogen because it interferes with the estrogenic response in various biological systems. However, acquired resistance to the antiestrogenic effects of TCDD has been observed in in vivo models. Recent epidemiological studies suggest that this compound may be involved in an increased risk of breast cancer. Because of the TCDD's long half-life, it is hypothesized that its effects on breast cancer, if any, might only be evident after a long-term exposure to the compound. Method: MCF-7 human breast cancer cells were cultured for one year in 1 nM of TCDD. These cells (LTTCDD) were tested in the MCF-7 Focus Assay for their response to 17-beta-estradiol (E2) compared with non-exposed MCF-7 cells. The Focus assay relies on the ability of MCF-7 cells to develop dose-dependent three-dimensional multicellular nodules or foci in the presence of E2. TCDD and the antiestrogen ICI 182780 (ICI) inhibit these foci. Results: LTTCDD cells were more responsive to the foci stimulatory effects of E2 and more resistant to the antiestrogenic effects of ICI, as compared to control MCF-7 cells. Moreover, in LTTCDD cells, an additive effect between TCDD and E2 was observed. Conclusion: breast epithelial cells exposed for prolonged periods to TCDD respond with increased sensitivity to the foci stimulatory effects of E2 and are more resistant to antiestrogens and these effects may be altered by the chronic presence of E2.

