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INDUCTION OF TELOMERASE BY 2,3,7,8- TETRACHLORODIBENZO-*p*-DIOXIN (TCDD) AND ESTROGEN IN BEWO CELLS

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In an attempt to clarify the underlying mechanism of tumor progression by TCDD, westudied its effect on telomerase activity. Since telomerase is associated with tumor progression and also controlled by sex steriods, effects of TCDD on this enzyme might be one of the pathways towards its tumorigenic action. We used Be Wo cells derived from human placental choriocarcinoma as a model system. Stretch PCR analysis showed that TCDD and estrogen induced telomerase activity in Be Wo cells. However, an increase in activity was high with TCDD as compared to an equimolar concentration of estrogen. Co-treatment of TCDD and estrogen resulted in a partial decrease in telomerase activity as compared to TCDD alone. The expression of *hTERT*, a regulatory subunit of telomerase as determined by RT-PCR, was affected by TCDD alone, E_2 alone and TCDD+E2 in a similar manner that to telomerase. Furthermore, the expression of *c-myc*, a positive regulator of *hTERT*, was also increased by TCDD, suggesting the up-regulation of telomerase was *c-myc* dependent. Co-treatment with E2 and TCDD decreased expression of *c-myc* and was comparable to estrogen alone. Since telomerase activity is often associated with proliferating cells, we performed FACS analysis which revealed that both estrogen and TCDD increased cells from G1 to S phase. In contrast, co- treatment of estrogen and TCDD resulted in a decrease in S phase. Our findings do provide evidence that a low concentration of TCDD(1 and 10 nM) activated telomerase as an estrogen agonist while there is the possibility that TCDD(1 and 10 nM) acts as a partial antagonist in the presence of E2 or that the suppression may be due to a yet unknown mechanism.