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ESTROGEN RECEPTOR INDEPENDENT TOXIC MECHANISM OF CHLORPYRIFOS AND CHLORPYRIFOS OXON IN HUMAN BREAST MCF-7 CELLS

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Abstract: Environmental estrogen-like chemicals have been increasingly recognized as potentially hazardous factors for human health. They can act at very low doses, and can affect the synthesis of natural hormones, their release and/or transport. Estrogen receptor alpha (ERα) is the major regulator of breast cancer tumor behavior. In mammary gland, 17β-estradiol (E2) promotes cell proliferation in both normal and transformed epithelial cells by modifying the expression of hormone responsive genes involved in the cell cycle and /or programmed cell death. Chlorpyrifos (CPF) is one of the most widely used organophosphate insecticides in the U.S. CPF is an endocrine disrupter with anti-androgenic and estrogenic properties and reduces serum levels of cortisol and thyroid hormone T4. CPF is metabolizes in human liver to the active metabolite, chlorpyrifos- oxon (CPO) which produces neurotoxicity by inhibiting esterases in the central and peripheral nervous system. The aim of this study was to investigate whether CPF and its metabolite, CPO causes human breast cell death in a concentration-dependent manner, and further investigate whether the toxic effects may be mediated through ER. MCF-7 cells were treated for different exposure times and various concentrations of CPF or CPO in absence and presence of 17β- estradiol (E2). Cell proliferation and viability, and apoptotic cell death were assessed. Our results indicated that exposure to CPF or CPO significantly decreased cell proliferation in a concentration- dependent manner in MCF-7 cells. The ER antagonists, ICI 182,780, and tamoxifen, did not block these effects. By contrast, these antagonists inhibited E2-induced cell proliferation. This study demonstrated that exposure to CPF or CPO can cause toxic effect which may not be directly mediated through an ER receptor. Also, it will provide relevant evidences on the action of CPF and CPO as environmental breast cancer risk factor.

Key Words: Estrogen Receptor Independent Toxic Mechanism, Chlorpyrifos and Chlorpyrifos Oxon Human Breast MCF-7 Cells

Acknowledgements: We acknowledge with thanks UMES Title III office for supporting the Graduate Program in Toxicology.