

# THE OVARY AS A TARGET ORGAN FOR EDCS A TOXICITY: ACTION OF EDCS PRESENT IN FOLLICULAR FLUIDS ON HUMAN GRANULOSA TUMORS BIOLOGY

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**E**ndocrine disrupting chemicals (EDCs) are natural or synthetic chemicals that alter the functions of the endocrine system and thereby cause adverse health effects. The ovary is a hormone sensitive organ that produces steroid hormones. For this reason it is a target organ for EDCs toxicity. Several epidemiological studies indicated that, EDCs accumulates in reproductive organs and in the ovarian follicular fluid (FF). In the general human population, EDCs has been detected in FF at nanomolar concentrations (such as: perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), hexachlorobenzene (HCB), dichlorodiphenyldichloroethylene (DDE), polychlorinated biphenyl (PCB153). For this reason, EDCs may act on ovarian tissue not only in an endocrine manner (via the serum), but also in a paracrine manner (via ovarian tissue deposits). Thus, these compounds may directly affect the function of granulosa cells within the ovary and may promote granulosa cell tumor (GCT) progression. GCTs exhibit many morphological, molecular and hormonal features of proliferating normal preovulatory granulosa cells. Importantly, our data suggest that persistent organic pollutants found in human FF act as autocrine mitogenic factors on ovarian cancer cells. However, the biological effects of mixtures cannot be predicted based on the activities of the individual components, so we further evaluated the activity of mixtures of these chemicals, and observed that the mixtures also possessed mitogenic properties. Moreover, a mixture of persistent organic pollutants present in FFs can alter granulosa cell function, activating GPR30 and IGF1R signaling. Therefore, questions about the roles of these chemicals in ovarian cancer are an important issue for public health.

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