

The general population is exposed to a number of hormonally active compounds which are natural or synthetic chemicals that alters the functions of the endocrine system and thereby causes adverse health effects. These compounds known as endocrine disrupting chemicals (EDCs) are present in a number of substrates such as chemical industry pollutants, automobile exhaust, cigarette smoke, grilled meat, milk, water, cosmetic products, fire smoke forest, and volcano dust. Large number of the chemicals has been classified as persistent in the environment and bio-accumulate to high concentrations in wildlife and humans. Recently, epidemiological studies have measured a number EDCs in follicular fluid from women undergoing assisted reproductive technology. Follicular fluid accumulation into the follicle antrum is important for follicular development and oocyte maturation. Evidence suggests that follicular fluid is not only rich in steroids, growth factors, and proteins, but also EDCs. Most frequently among EDCs measured in follicular fluid are identified pesticides (HCB and p-p- DDE), polychlorinated biphenyls (especially PCB153), and perfluoroalkyl acids (PFOA and PFOS). The majority of these chemicals mimics oestrogen action affects oestrogen levels, or bind to oestrogen receptors. For this reason estrogen sensitive tissues in the female reproductive system are the target for their actions. These data suggest that EDCs may act on ovarian tissue not only in an endocrine manner (via serum depots), but also in an paracrine action (via ovarian tissue depots). We believed that EDCs present in follicular fluid are association with various health outcomes, including cancer development and progression. Epidemiological studies have found associations between residing near industries and a risk factor for ovarian cancer mortality. Granulosa cell tumors (GCTs) arise from the granulosa cells and are poorly understood neoplasms with unpredictable biological behavior. The exact etiology of this malignancy remains unknown, with no identification of specific defined risk factors. Thus, it is **hypothesized that mixtures of EDCs presents in follicular fluid activate directly granulosa tumor receptors or acts indirectly by change levels of signaling factors contributes to granulosa cell growth and function and by both mechanisms lead to granulosa tumor progression.** To verify the hypothesis, we intend to identify whether EDCs mixture could stimulate human granulosa tumors spheroids viability, resistant to anoikis, and invasion which are essential for cancer progression. Results of this project may identify biological effects mediated by persistent EDCs in granulosa tumors. Molecular biology and biotechnology based methods allow us to better understand the role of estrogen signaling (ER α , ER β , and GPR30) as well as FSH receptor and IGF1 receptor pathway in the biology of granulosa tumors. In addition, knowledge of the action on endogenous as well as exogenous hormonal active compounds in granulosa tumors will bring us closer to know the etiology of this disease.