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IN VITRO ACTIONS OF STEROIDS ON ENDOMETRIAL CANCER CELLS. E.Gurpide, C.F.Holinka, H.Hata, A.Gravanis, F.Schatz and L.Markiewicz. Mount Sinai School of Medicine (C.U.N.Y.), New York

In vitro studies with endometrial tissue fragments have shown differences in enzymatic activities and responsiveness to hormones of normal and neoplastic endometrium. They have also suggested tests that may identify patients with endometrial tumors who are likely to respond to hormonal therapy. Estrogens significantly stimulate $PGF_{2\alpha}$ output by secretory but not by proliferative endometrium under organ culture conditions. The $PGE_2/PGF_{2\alpha}$ ratio in basal output is higher in endometrial cancer than in normal endometrium. Progestins inhibit the basal and estrogen-stimulated $PGF_{2\alpha}$ output, increase estradiol 17β dehydrogenase activity, promote glycogen accumulation and diminish lipocortin output when added to cultures of endometrial fragments. Epithelial cells in primary cultures also produce $PGF_{2\alpha}$ and respond to estrogens, even when derived from proliferative endometria. The basal output of $PGF_{2\alpha}$ by stromal cells is much lower than that of epithelial cells in culture and is not significantly increased by estrogens. A human endometrial adenocarcinoma cell line (Ishikawa), established in Kuramoto's laboratories, was found to be responsive to estrogens. Progesterone receptor levels as well as DNA polymerase and alkaline phosphatase activities were elevated by estradiol (10^{-8}M). Addition of estradiol to quiescent cultures of Ishikawa cells resulted in about 3-fold increases in cell numbers. The estrogen-responsive Ishikawa cell line offers the opportunity to examine hormonal regulation of autocrine factors promoting or inhibiting growth and, by comparison with estrogen-unresponsive cell lines (e.g. HEC-1, HEC-50), to identify differences in the quality and function of specific estrogen binders. Such studies could be extended to the examination of deficiencies progesterone receptors present in Ishikawa cells, especially after estrogen treatment, since these cells do not respond to progestins.

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TISSUE STEROIDS IN ENDOMETRIAL AND BREAST CANCER

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Steroid hormones are present in human tissues in significant amounts, and apart from acting as a hormonal reservoir, these steroids may affect the activity of enzymes concerned with steroid metabolism, e.g. dehydrogenase and aromatase. We have shown that in endometrial tissue and in breast tumour cells androgens are inhibitors of dehydrogenase, an enzyme which is also sensitive to progesterone. Aromatase can be markedly affected by cortisol and by progesterone in vitro. We have therefore investigated tissue steroid concentrations and enzyme activity to seek a possible relationship, and to compare normal and malignant tissue. No relationship between cortisol and aromatase was found, but a negative relationship with progesterone was apparent. Androgen levels were higher, but not significantly so between breast tumour and normal tissue. Dehydrogenase activity was higher in the tumour compared with normal tissue but oestradiol levels were higher than oestrone in tumour and were similar in normals. Thus, androgens and progesterone may play a role in modulating oestrogen metabolism in breast tumours, but whether this mechanism can totally account for the different relationship between oestrone and oestradiol in breast tumours compared with normal tissue requires further investigation.