ROLE OF NATURAL AND SYNTHETIC PROGESTINS IN PROGRESSION OF HUMAN BREAST CANCER CELLS IN AN ANIMAL MODEL

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Post-menopausal women with an intact uterus receive combined dose of estrogen and progestin during hormone replacement therapy (HRT) to reduce clinical symptoms such as hot flashes. Progestins, which include natural and synthetic compounds that have progesterone like activities, are added to reduce the known proliferative effects of estrogens on uterine cells that increase the risk of uterine cancer. Unfortunately, recent clinical trials have unexpectedly shown that progestins increase the incidence of breast cancer in women. Our laboratory has recently shown for the first time that the natural hormone progesterone can cause proliferation of breast cancer cells in vivo in an immunodeficient mouse model. Therefore, we hypothesized that synthetic progestins used in clinics have the ability to increase proliferation of breast cancer cells. To prove or disprove our hypothesis we injected 6-week old immunodeficient mice subcutaneously with estrogen pellets, which continuously release estradiol, without which tumor cells cannot be retained. After 48 h BT-474 human breast cancer cells were injected on both flanks of these mice. The mice were then treated with 10 mg/60 day release pellets that contained the most commonly used synthetic progestin medroxyprogesterone acetate (MPA), norgestrel or norethindrone, and tumor volumes were measured over 30-60 days. Our experimental data shows that all the synthetic progestins increased tumor growth in vivo. Thus we conclude that synthetic progestins increase proliferation of human breast cancer cells in vivo resulting in tumor expansion, and we suggest that caution should be exercised when prescribing synthetic progestins for treatment of post-menopausal symptoms in women.