PROGESTOGENS AND MEMBRANE-INITIATED EFFECTS ON THE PROLIFERATION OF HUMAN BREAST CANCER CELLS

X. Ruan1, H. Neubauer2, H. Seeger2, T. Fehm2, M.A. Cahill3, Y. Yang Yang4, M.O. Mueck2

1. Beijing Ob/Gyn Hospital; Capital Medical University, Beijing, China
2. University Women’s Hospital, Tuebingen, Germany
3. Charles Sturt University, Wagga Wagga, NSW, Australia
4. Tongji Hospital of Tongji University, Shanghai, China

Objectives: Evidence is accumulating that progestogens may play a crucial role in the development of breast cancer under contraception and hormone therapy in the postmenopause. Progesterone receptor membrane component 1 (PGRMC1) expressed in breast cancer may be important in tumorigenesis and thus may increase breast cancer risk. The aim of this project was to investigate the influence of progesterone and nine synthetic progestins on MCF-7 breast cancer cells overexpressing PGRMC1.

Methods: MCF-7 cells were stably transfected with PGRMC1 expression plasmid (MCF-7/PGRMC1-3HA). To test the effects of progesterone (P) and the synthetic progestins chlormadinone acetate (CMA), desogestrel (DSG), Dienogest (DNG), drospirenone (DRSP), dydrogesterone (DYD), levonorgestrel (LNG), medroxyprogesterone acetate (MPA), nomegestrol (NOM) and norethisterone (NET) on cell proliferation MCF-7 and MCF-7/PGRMC1-3HA (WT-12) cells were stimulated with different concentrations (10-8 M to 10-6 M).

Results: In MCF-7 cells DNG, DRSP, DSG, DYD, LNG and NET increased the proliferation at 10-7 M, the effect being highest for NET with about 20%. In WT-12 cells the same progestins, but additionally MPA, showed a significant increase, which was much higher (30-245%) than in MCF-7 cells. Here again NET showed the highest proliferative effect. No effect was found for CMA, NOM and P.

Conclusion: Synthetic progestins trigger a proliferative response of PGRMC1 overexpressed MCF-7 cancer cells. The effect of progestogens on breast cancer tumorigenesis may clearly depend on the specific pharmacology of the various synthetic progestins, since mainly testosterone-derived progestogens showed the greatest proliferative effect.

ruanxiangyan@163.com