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EFFECT OF EGF ON THE PROLIFERATION OF HUMAN EPITHELIAL CANCER CELL LINES: CORRELATION WITH THE OCCUPATION OF EGF RECEPTORS

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A large variety of hormones and growth factors may be involved in the regulation of breast tumor proliferation and contribute to a complex series of hormonal interactions in the target tissue. Epidermal growth factor (EGF) has been demonstrated to modulate the growth of the mammary gland as well as the proliferation of hormone-sensitive human breast cancer cells. We have studied the effect of EGF on the proliferation of breast cancer cell lines, as well as the modulation of estrogen- and epidermal growth factor-receptor levels by EGF treatment. We have observed that all the cell lines analyzed were stimulated by EGF in low containing media. The MCF-7AZ cell line, its H-ras transfected MCF-7AZTD5 variant and the MCF-7 cells, all of them containing relative low epidermal growth factor receptor number (3000 sites/cell) were growth stimulated in a dose-dependent manner by 10^{-9} M to 10^{-8} M EGF. The MDA-MB231, A431 and BT20 cells that express high EGF-R levels were stimulated with relatively low concentrations of EGF (5×10^{-13} to 10^{-11} M). However, A431 and BT20 cells were growth-inhibited in the presence of higher EGF concentrations (10^{-10} M to 10^{-9} M) that led to the occupation of low affinity receptors. We also observed that EGF down-regulated epidermal growth factor receptors while up-regulated estrogen receptors. In addition, Scatchard analysis of radiolabeled EGF binding on cell surface demonstrated that the concentrations of growth factor necessary to occupy a given number of epidermal growth factor receptors is inversely correlated to the total level of these receptors. Our findings suggest that the mitogenic effect of epidermal growth factor on cell proliferation is a function of the quantity of EGF-occupied receptors and that the two states of receptor affinity may reflect two regulatory states in the high receptor-containing cells.

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INSULINE RESPONSE TO GLUCOSE TOLERANCE TEST IN FEMALE SUBJECTS WITH BENIGN MASTOPATHY (BM)

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Growth oncogenic factor receptors (GFR) have been detected in mammary carcinoma and since Insuline (Ins) is included in GFRs, to assess if Ins secretion in BM is related to CA₁₅₋₃ antigen, a glucose tolerance test (GTT) was performed, blood sugar (Bls) and Ins levels were measured, in 87 females with BM (age 17-57). In 76 of them TSH and PRL were measured on TRH test. Since no difference to Ins and Bls response to GTT was noticed in relation to age, degree of hirsutism and body weight, except thyroid dysfunction, the population was divided according to TSH response on TRH in Group A (46) $>10 \mu\text{IU/ml}$ and Group B (30) $<10 \mu\text{IU/ml}$. TSH-Bls differed significantly between the groups for basal and response levels to stimulation, while Ins had no difference. Given that adrenal influence pancreatic function, adrenal steroids were correlated with the above parameters. The significant positive correlations of TSH vs Bls₀, PRL₀, "F", negative of TSH₂₀ vs Ins₀, positive of CA₁₅₋₃ vs Bls₀ are suggesting that, in addition to thyroid-hypothalamic, adrenal and pancreatic hormones may well have a direct or indirect effect and play an important role on CA₁₅₋₃ levels, known as a breast tumor marker. This raises the hypothesis that normalisation of hypothalamic-thyroid and adrenal pancreatic functions may prevent further abnormal evolution of the breast tissues.

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NEW CONCEPTS IN THE TREATMENT AND MANAGEMENT OF ADRENAL ADENOCARCINOMA OF NECROTIC INVASIVE TYPE

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Lung metastases occurred, in a 61 years old woman, nearly 3 years after left adrenalectomy for adenocarcinoma-necrotic invasive type. Therapy with o.p.DDD showed paradoxically increased cortisol ("F") levels and BP Mx 220 mmHg. Since "F" and aldosterone decreased significantly on short Metopiron test, a trial of Metopiron and Ketokonazol (total dose 2.5 gr/di and 2 gr/di respectively) was given. "F" and urinary oxosteroids decreased, followed by clinical improvement. Patient, stopping taking regularly the treatment, new metastases were occurred, among them one in the breast dominated by restarting the above trial. After a medical consultation, it was thought to try again with small o.p.DDD doses. "F" ($>80 \mu\text{g/dl}$) and all steroids increased suddenly, while heavy hirsutism and full moon face reappeared. Cis-platinum therapy, had no success. The initial trial normalized clinical and laboratory findings. But new metastases have developed even in the skin of her scalp. CA₁₅₋₃ antigen was $<8 \text{ U/ml}$ and CEA (-). Several laboratory tests, CT-tomography, biochemical and blood analyses were done. Both, clinical and laboratory improvement, suggest that in addition to surgical removal of the adrenal(s), combined Metopiron and Ketokonazol therapy, may well help and benefit in preventing or treating this particularly rare malignant disease.