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FURTHER BIOCHEMICAL CHARACTERIZATION OF AN ER-PGR+ BREAST CANCER CELL LINE

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We have described (J. Steroid Biochem. 24 : 365, 1986) a variant of the ER-PgR-Evsa-T breast cancer cell line characterized by a progestin binding protein, for which a down-regulation process could be demonstrated in the presence of progestins or antiprogestins. This binding capacity was not modified by sub-culture with phenol red-free medium nor by estradiol; cell growth was totally independent from steroids. In view of the recent finding that steroid hormone receptors are members of a large family of ligand - inducible transcription factors, we examined whether this protein presented biochemical properties ascribed to "true" receptors. Search for PgR by enzyme immuno-assay (Abbott) in cytosols was always positive. Sucrose gradient sedimentations gave the usual 4S and 8S PgR immuno reactive peaks; prior short-term labeling with 3H-ORG 2058 gave an assymetric 8S radioactive peak, while increasing the labeling period or adding KCl favored the 4S form. Addition of various receptor - activating factors to the cytosol increased binding of the labeled receptor to DNA-cellulose. We are now planning to look whether this receptor is modulated by growth factors. Supported by grants from CGER & Fondation Lefèvre.

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COULD THE D5 ANTIGEN REPLACE ESTROGEN AND PROGESTERONE RECEPTORS (ER & PGR) AS A MARKER OF HORMONE DEPENDENCY AND A PROGNOSTIC FACTOR IN EARLY BREAST CANCER (BC) ?

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D5 is a 29 KD protein characterized by a monoclonal antibody raised against purified ER from human myometrium. We confirmed the correlation (r=0.49) between ER (EORTC dextran-coated charcoal method) & D5 (ER-D5 IRMA kit, Amersham) on 177 BC cytosols obtained from early or metastatic BC. This correlation was less evident with PgR. Further analysis of the early BC group at 41 months follow-up (n=78) led to the following interesting observation: 1) pts with D5+ tumors have a statistically significant improvement in relapse-free survival as compared to pts with D5- tumors (log-rank p=0.03), while the difference in survival is approaching statistical significance (log-rank p=0.07); 2) pre and postmenopausal pts do not differ by D5 positivity (around 75%); 3) the ER-PgR+ phenotype seems associated with frequent D5 positivity while PgR is rarely detectable in the presence of a ER-D5- phenotype. With the growing number of potentially important prognostic factors in BC, this single determination could be more cost effective than ER + PgR. Validation through a larger prospective study seems indicated. Supported by grants from CGER & Fondation Lefèvre.

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THERMOSENSIBILITY OF HORMONE RECEPTORS WITH BREAST CANCER

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In 1987 the thermosensibility of progesterone and estradiol receptors localised in the cytosol was investigated among 100 patients who had undergone breast cancer/ breast cancer relapse surgery in the Gyneacological Hospital of the Erlangen University. Hormone receptors were determined by means of a double lignad kit. In order to investigate the thermosensibility the available tumor tissue of the patient was divided in half. One half was preserved in liquid nitrogen immediately after surgery. The other half was stored at room temperature for 1 hour and then deep-frozen at -38,7°C. We found that 1. the receptors of primary breast cancer and breast cancer relapses do not show any differences with regard to thermosensibility. 2. The progesterone receptors localised in the cytosol showed a decrease in receptor density of 30-60% after 1 hour at room temperature and a decrease of 5-30% of the estradiol receptor localised in the cytosol. This leads to the conclusion that progesterone receptors are thermo-sensible to a higher degree. It can be taken form this investigation that deep-freezening hormone receptors immediately after surgery is of utmost importance because otherwise grave mistakes in determining the receptor assay could result which would lead to a false estimation of the patients with regard to prognosis and adequate therapy.

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Example:

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FNC-THERAPY OF METASTATIC BREAST CANCER

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During a prospective study at the Gyneacological Hospital of the Erlangen University 77 patients suffering from metastatic breast cancer were treated following the FNC-scheme of therapy.500 mg/m^2 Fluorouracil, 10 mg/m^2 Novantrone and 500 mg/m^2 Cyclophpsphamid were administered in four -week intervalls.

57 patients had recurrence-free intervalls of less than 2 years and 20 of more than 2 years. 55 patients underwent an adjuvant therapy because of axillary lymph node metastases, 45 of them underwent an adjuvant chemotherapy. 37 patients were preliminarily treated because of the formation of distant metastases. The response rate to FNC (CR+PR+NC) was 72%. Remissions (CR+PR) were observed in 40% of all cases. The therapy was subjectively well-tolerated. The alopecic rate was very low. Bone-marrow depression was determined in individual cases, cardiotoxicity was not observed at all.

Considering the response rate and the subjectively good toleration we find that FNC-therapy is an effective scheme if treatment in cases of metastatic brest cancer.

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