Abstract: P7

Oestrogen differential interactions with ER + -responsive and ER−-non-responsive human tumour cells

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1. Introduction

Oestrogen receptor (ER) in malignant breast tissue is significantly higher than in normal breast tissue. The high ER content of malignant breast tissue from postmenopausal women is due to the absence of circulating progesterone to downregulate the ER. Oestrogen is associated with a cascade of reactions during the ovulatory cycle leading to cell proliferation and breast cancer initiation (Hakim, World Conference on breast cancer, 29 July 1999). The proliferative effects of oestrogen (E) are mediated through an intracellular receptor, the ER. Oestrogens pass through the cell membrane and bind the ER, transforming the receptor into an active transcription factor, which binds DNA as a dimer at specific oestrogen response elements (EREs) and regulates the expression of a variety of genes.

2. Object

The present studies examined the effect of 17 β-oestradiol (E) alone and combined with progesterone (Pg) on the levels of transforming growth factors (TGF-α TGF-β), insulin growth factor (IGF), C-erbB-2/Neu, Ras p21, p53 and caspase activities).

3. Materials and methods

Micro-explants from primary (10), invasive (15) breast tumours, the oestrogen-responsive ER + (MCF-7, TsTD and ZR75-1) and non-responsive ER− (MDA-MB-231 and MDA-MB-468) established in breast cancer cell lines were cultured *in-vitro* in presence of tunicamycin (Tn), oestrogen (E) and progesterone (Pg) each alone and combined. Amplified C-erbB-2/Neu and mutated p53 and Ras p21 were determined [1,2] using the immunoblotting technique [3,4]. Cell membrane glycopeptide patterns were established as described earlier [5]. The caspases 1, 2, 3, 6, 7 and 8 were examined histochemically with the antibodies clones B24-1, G310-124B, CPP-32 and B25-2, respectively.

4. Results

In the ER− oestrogen-non-responsive breast tumours and established cell lines, there was a positive relationship between C-erbB-2/Neu amplification, *TP53* mutation and Ras p21 triphosphate turnover, with a significant decrease in cellular caspase (apoptosis) which is accompanied by a significant increase in the GP-6, GP-7 cell membrane glycopeptides. These changes correlated significantly with the aggressiveness of the breast cancer cells. Caspase levels correlated with the apoptotic cells.

5. Conclusion

ER modulates the synthesis of the oncogenes.

References

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Abstract: P8

Short term results of a computerised program for breast carcinoma risk analysis

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1. Introduction

New selective modulators of the oestrogen receptor (ER) that are protective against the development of breast cancer will soon be proposed for use as mamma-protective preventive medication in women with a high risk for breast cancer. We present the short-term results of a computerised mass screening programme that enables calculation of the individual risk of breast carcinoma.

2. Objective

To test the predictive value of a newly developed computerised program for the assessment of individual risk for breast cancer. Calculation of risk of 943 women participating in a mammography screening programme was compared with the results of mammography and pathology of biopsies.

3. Methods

An interactive d-Base program requests input from women who present for early breast cancer screening. Basic risk according to age is adjusted for most known risk factors. The program returns: (a) a summary of the protective and risk-enhancing factors of the individual; (b) a crude risk for developing breast cancer expressed in number per 100 000 woman-years (crude breast carcinoma risk score — CBCRS); (c) the relative risk compared with other women of the same age. An individualised advice for further follow-up or use of preventive mamma-protective medication can easily be incorporated.

4. Results

From April 1992 to February 1993 detailed information of 943 women presenting for mammographical screening was obtained. 13 women had suspect lesions on mammography and required further analysis. 6 of these had cancer, while the remaining 7 had a negative biopsy or a negative supplementary diagnostic work-out. The mean CBCRS was 989 versus 153 in the 6 women with suspected mammography and breast cancer (true-positive mammography), 462 versus 128 in the 7 women with suspected mammography and no breast cancer (false-positive mammography) ($P = 0.02$) and 430 versus 312 in the 778 women with normal mammography and no breast cancer ($P = 0.0003$).

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