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Estrogen receptor β in breast cancer

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Keywords

ERa, ERβ, normal breast

Introduction

Approximately 30-40% of hormone receptor positive breast cancers do not respond to endocrine therapy. The recent discovery of ERβ suggests that the mechanism of action of estrogens is more complex than at first thought. Estrogens bind ERβ with affinity similar to ERα and the transcriptional activation is identical for both receptor forms. Furthermore ERα and ERβ can form biologically functional receptor heterodimers. However, little is known about ERβ expression and its role in breast cancer.

Aims

To identify ERβ expression by immunohistochemistry (IHC) and by mRNA *in situ* hybridization in a set of unselected breast carcinomas and to correlate the findings with known clinicopathological indicators of malignant potential.

Comments

This very interesting paper tries to clarify the role of estrogen receptorβ (ERβ) in invasive breast cancer by examining its expression. ERβ is often coexpressed with ERa and progesterone receptor (PR) and is also associated with low grade tumors and negative axillary lymph node status. Whether it has any independent therapeutic or survival implications remains to be established. Although its precise role remains to be determined, the paper highlights a number of possible mechanisms of action for ERβ and how it may interact with ERα. So far it has been difficult to obtain a good antibody to ERβ and whether the antibody used in this paper stands the test of time awaits to be seen.

Methods

Fresh frozen tissue was obtained from 79 invasive ductal carcinomas, 6 lobular and 7 intraductal carcinomas. IHC was performed for ERβ with a rabbit polyclonal antibody (PAI-313, Affinity Bioreagents, Golden, CO, USA; dilution 5μg/ml) using a streptavidin-biotin-peroxidase complex technique. Adjacent frozen sections were stained for ER#945; and PR (Abbott Laboratories, Naperville, IL, USA) and for c-erbB2 (Novocastra Laboratories, Newcastle, UK). DNA flow cytometry was also performed on frozen sections. Four different antisense oligonucleotide probes (nucleotides 542-589, 1089-1136, 1326-1373, 1384-1431) were used for the *in situ* hybridization detection of ERβ mRNA.

Results

The ERβ antibody showed strong nuclear immunoreaction and weak cytoplasmic and extracellular background staining. Nuclear staining was confined to normal and malignant epithelial cells. A cutoff of 20% was used to classify tumors as ERβ-positive; 55 out of 92 (59.8%) tumors were subsequently defined as ERβ-positive. The specificity of ERβ IHC was confirmed by mRNA *in situ*hybridization and by using a blocking immunogen peptide.

ERβ expression was seen in 46/79 invasive ductal carcinomas, 4/6 invasive lobular and 5/7 intraductal carcinomas. Of the ERα-positive tumors, 48/63 (76%) were positive for ERβ; however, 7/29 (25%) of ERα-negative tumors also expressed ERβ. Furthermore, 76% of the PR-positive tumors and 42% of the PR-negative tumors were also positive for ERβ. Of the tumors that were negative for both ERα and PR, 22% were positive for ERβ.

Expression of ERβ correlated with axillary lymph node negative status ($P < 0.0001$), low histological grade ($P = 0.0003$), diploid DNA content ($P = 0.03$), a lower S-phase fraction ($P = 0.002$) and with pre- and perimenopausal rather than postmenopausal patients ($P = 0.04$). There was no correlation with tumor size ($P = 0.11$), or *erbB2* overexpression ($P = 0.08$).

Discussion

ERβ is often coexpressed with ERα and PR in breast cancer and in normal ductal epithelium. The majority of breast cancers retained coexpression of ERβ and ERa suggesting that ERβ may be an equal target with ERα for hormone therapy. In addition, the anti-estrogen-ERβ complex inhibits gene transcription when bound to estrogen response elements but works as an agonist when bound to AP1 elements. Therefore, it is possible that anti-estrogens may have agonistic effects in ERβ-positive tumors. Alternatively the coexpression of ERα and ERβ could result in the formation of heterodimers that may have a significant role in breast cancer. The independent predictive value of ERβ, however, remains to be established.

References

1. Jarvinen TAH, Pelto-Huikkl M, Holli K, Isola J: Estrogen receptor β is coexpressed with ERa and PR and associated with nodal status, grade, and proliferation rate in breast cancer. Am J Pathol. 2000, 156: 29-35.