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Oestrogen receptor mutations and their influence on breast cancer growth

Amoils, Karin Dagmar

2012-03-12
http://hdl.handle.net/10539/11415

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ABSTRACT

Oestrogen receptor (ER) mutations have been identified fo
previous studies. The effects of the deletion variants due
clinical parameters, prognosis and treatment were exam
carcinoma patients and 13 control samples from elective reduct
procedures, respectively. RNA extracted from fine needle
breast tissue was reverse transcribed and using nested
analysis the presence of the deletion variants ERβ2 and
tested using Fisher's exact test to determine their significance with respect to clinical parameters s
nodal involvement, stage, presence or absence of metasta
and hormone responsiveness was examined. Kaplan-Meier survival analysis w
also determined.

The T47D breast cancer cell line was cloned with two clone
further analysis, namely TCA3 (hormone sensitive) and TCC
These clones were treated for ten passages with 17β-oestroge
oestradiol and oestriol; oestrogen precursors, androstenedi
anti-oestrogen, 4-hydroxytamoxifen; and the aromatase in
aminoglutethimide, respectively. RNA was extracted from
after the tenth passage and ERα and ERβ2 exon profiles were exam
RT-PCR and sequence analysis. After the tenth passage hor
were performed every 24 hours (up to 96 hours) with
determined using the MTT assay.

The results indicate that ER² variants do not have any affect
to menstrual status and nodal involvement (N). Expression
required by the mouse monoclonal® antibody 1D5 (DAKO
immunocytochemical assay used for the recognition of
assess ER status and therefore show significance. ER±"
previous investigations, the variant ER±"3 were not foun
tumourigenesis. ER±"5 was observed to be more prevale
patients and was usually expressed with the complete ER±5 i
heterodimerization. ER±"5 showed no significance with res
disease or response to hormone treatment.

An increase in the ratio of type ER±"4 to ER±4 indicated an increa
metastatic potential of diseased tissue. ER±4 and ER±"4
present in MCF7D clones and after 10 passages the TCA3 c
10^{-8}M aminoglutethimide indicated a complete loss of ER±
hormone responsiveness. Results suggest that ER±"4 may pla
progression of disease but not in the acquisition of tamoxif

ER±"6 was observed in 15% of patient tumour samples. An increase in the expression of ER±"6 in MCF7D cultures in the control samples
significantly increased their mean ($p = 0.018$). ER±"6 was also
observed as significant with respect to oestrogen ($p = 0.023$) indicating the
possible relevance of ER±"6 in progression of the disease.

ER±”7 was the most frequently observed variant and did no
significance with regard to any of the clinical parameters e
of ER±”7 did not show significance with regard to hormone
vitro the presence of this variant, as a heterodimer with the w
ER±7, conferred greater sensitivity to tamoxifen in the ta
TCC1.

Multiple exon deletions of ER± were also observed. The
multiple deletion variants were ER±”4, namely ER±”6
and ER±”4/6. The multiple variants may be involved in
tumour progression.

ER² variants were not examined in as much detail as ER
insufficient material available for analysis. The binding doma
domain and the ligand binding domain, of ER² were analy
patients and in 47 cell lines. They were not found to be sig
respect to the clinical parameters investigated and the ER
and TCC1 lines remained unchanged after 10 passages unde
conditions.