PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

*ERBB2*detection and associated chromosomal alterations

ArticleInfo		
ArticleID	:	3689
ArticleDOI	:	10.1186/bcr-2000-66652
ArticleCitationID	:	66652
ArticleSequenceNumber	:	55
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2000–1–27 OnlineDate : 2000–1–27
ArticleCopyright	:	Current Science Ltd2000
ArticleGrants	:	
ArticleContext	:	1305822

Chris Jones

Keywords

CGH, *ERBB2*, FISH

Introduction

Amplification of the *ERBB2* oncogene is found in 20-30% of human breast cancers, and overexpression of the protein may play an important role in the progression of the disease. The amplification of *ERBB2* has been implicated as a prognostic as well as a predictive factor, and has recently been used as a target for therapy. It is not clear to what extent breast tumors with *ERBB2* amplification and/or overexpression contain other genetic aberrations.

Aims

To define *ERBB2*-associated chromosomal alterations and to examine the sensitivity of comparative genomic hybridization (CGH) compared with fluorescence *in situ* hybridization (FISH) and immunohistochemistry (IHC) in detecting *ERBB2* status.

Comments

Overexpression of erbB2 in breast carcinomas has been reported to be associated with resistance to hormone therapy. Some studies have suggested that erbB2 overexpression in estrogen receptor (ER)-positive patients is associated with a relative resistance to tamoxifen, while ER-positive, erbB2-negative patients were more likely to respond. There have also been reports stating that patients with erbB2-overexpressing tumors had a better clinical outcome after doxorubicin-containing therapy than those patients with non-overexpressing tumors. The evidence here that tumors overexpressing the protein show a different pattern of genetic alterations to those which do not, provides clues as to the underlying mechanisms of the differential therapeutic responses.

Methods

Four breast cancer cell lines and thirty three invasive ductal breast carcinomas were examined using CGH, FISH and IHC.

Results

Analysis by CGH demonstrated that 14 of the breast carcinomas showed a copy number gain at chromosome 17q12 by CGH. *ERBB2* amplification was detected by FISH in twelve cases, ten of which also showed this copy number gain by CGH. Twelve cases also stained positively for erbB2 overexpression by IHC. The total number of changes detected by CGH in the *ERBB2*-amplified tumors was higher than in the non-amplified groups using all three of the methods.

Gain of chromosome 20q, and the loss of 18q, were significantly greater for the *ERBB2*-amplified sets than in the non-amplified group. Gains of 16p and 17q22-q24 and losses on 8p also tended to be more common in the *ERBB2*-amplified tumors than in the control group. Concordance between the three methods was: 91% between IHC and FISH; 82% for FISH and CGH; and 84% for IHC and CGH.

Discussion

The results indicate that breast tumors showing erbB2 overexpression or gene amplification are genetically distinct from erbB2-negative tumors. These differences may relate to the mechanisms underlying altered responses to adjuvant therapies, and may define the responsiveness to erbB2-directed immunotherapy. The prognostic significance of 20q amplification has been previously demonstrated, so the finding that this change is more common in *ERBB2*-amplified tumors suggests that the prognostic associations of *ERBB2* should be stratified for chromosome 20q status in multivariate statistical analyses.

References

1. Isola J, Chu L, DeVries S, Matsumura K, Chew K, Ljung BM, Waldman FM: Genetic alterations in *ERBB2*-amplified breast carcinomas. Clin Cancer Res. 2000, 5: 4140-4145.