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Amplification at 17q23 in breast cancer

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Keywords

Amplification, breast cancer, overexpression, 17q23

Introduction

Studies using comparative genomic hybridisation (CGH) have demonstrated that chromosome 17q23 is amplified in up to 20% of primary breast tumours. This increase in DNA copy number has been shown to be due to high-level amplification of at least two distinct regions at 17q23. To further characterize this region of amplification in breast tumorigenesis, six genes localised to 17q23 in breast cancer cell lines were analysed for amplification frequency in primary breast tumours.

Aims

To assess amplification frequencies of six genes localised to 17q23 in primary breast carcinoma.

Comments

This report describes the paper cited above and another from the same issue of *Cancer Research*(see Additional information). These two papers take similar approaches in attempting to identify genes associated with the 17q23 amplicon, which is amplified in 20% of breast tumours. The region has been known to contain multiple loci of amplification, and these studies identify five putative genes which may independently or jointly be upregulated to contribute to breast cancer carcinogenesis. The gene-rich nature of this region of the genome, coupled with the demonstrated variability on the 17q23 amplicon mean that much work yet remains to be done to elucidate the precise nature of this common genetic alteration in breast carcinogenesis. The relatively poor correlation seen between amplification and overexpression of some of the genes associated with this amplicon suggests that amplified genes may not necessarily be transcriptionally active, and that activation itself need not occur through amplification, further complicating this important locus in breast cancer.

Methods

Breast cancer cell lines were analysed by Southern and northern hybridisation and FISH to determine amplification and expression of genes which mapped to 17q23. Wu *et al* analysed amplification by Southern hybridisation, and expression by semi-quantitative RT-PCR in 94 primary breast tumours. Barlund *et al*examined amplification in 372 primary breast tumours on a tissue array by FISH, and expression in 12 tumours by LightCycler RT-PCR.

Results

The genes *PAT1*, *PS6K*, and *RAD51C* were identified as being both amplified and overexpressed in the breast cancer cell lines analysed by both groups. In addition, although both groups identified *SIGMA1B*, Barlund *et al* found poor correlation between expression and amplification levels for this gene. However Barlund *et al* did identify *TBX2* as another overexpressed and amplified gene. In primary breast tumours, *PAT1* was amplified in 19% and 8.9% of cases, *PS6K* in 7.5% and 10.2%, and *RAD51C* in 8% and 3.1% in the Wu *et al* and Barlund *et al* studies, respectively. *SIGMA1* was amplified in 12% and *TBX2*in 8.6% of cases in the appropriate study. For each gene, there were instances of amplification without overexpression, and/or vice versa.

Discussion

Both groups have identified genes localised to the chromosome 17q23 amplicon which are amplified and overexpressed in breast cancer cell lines and primary tumours. Taken together, there are at least five genes at 17q23 which appear to be associated with the amplification in breast carcinomas, with potential upregulation of *PAT1*, *PS6K*, *RAD51C*, *SIGMA1B* and *TBX2*. *PS6K* is a serine-threonine kinase involved in G1 to S-phase progression, and provides an excellent candidate for an amplification target gene based on its biological role. However, the equivocal correlation between amplification and overexpression of *PS6K* observed in one of the studies (Wu *et al*) raises doubts as to its oncogenic nature. This correlation is a general feature of all genes investigated across the two studies.

Additional information

Wu G-J, Sinclair CS, Paape J, Ingle JN, Roche PC, James CD and Couch FJ: **17q23 amplifications in breast cancer involve the *PAT1* , *RAD51C* , *PS6K* and *SIGMA1B* genes.** *Cancer Res* 2000, **60**:5371-5375 (PubMed%20abstract).

References

1. Barlund M, Monni O, Kononen J, Cornelison R, Torhorst J, Sauter G, Kallioniemi O-P, Kallioniemi A : Multiple genes at 17q23 undergo amplification and overexpression in breast cancer. Cancer Res. 2000, 60: 5340-5346.