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17q aberrations in breast cancer

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Amplification, breast cancer, CGH, chromosome 17q, imbalance

Introduction

A number of known cancer genes map to the long arm of chromosome 17, among which *ERBB2*, *BRCA1* and *NME1* have been shown to be the most frequently involved in breast cancer. Recent reports have suggested the existence of at least four regions of allelic imbalance (AI) along 17q, one at 17q21, two in the 17q22-q24 region and one at 17q25. However, the nature of the anomalies involving these regions remains uncertain.

Aims

To determine the nature of the genetic events affecting the respective regions of AI detected on 17q in breast cancer.

Comments

The long arm of chromosome 17 has been implicated in a range of genetic abnormalities associated with a number of cancers, including breast tumours. The data presented here do much to narrow down a number of regions along 17q showing both loss and gain of genetic material in breast cancer. Such an approach will aid in the identification of the genes involved which may be associated with the progression of the disease. This paper also makes the important point that allelic imbalance studies, while generally taken as corresponding to losses of genetic material, may in fact correlate to DNA amplifications. Concurrent molecular cytogenetic analysis by CGH and FISH can be used to further characterise these regions.

Methods

Allelotyping analysis using 19 CA repeat markers mapping in the 17q21-q25 region was carried out on 178 pairs of breast tumour and cognate normal DNA. Comparative genomic hybridisation (CGH) was carried out on a subset of 43 tumours presenting variable patterns of imbalance. Fluorescent *in situ* hybridisation (FISH) was carried out using bacterial artificial chromosome (BAC) clones on 6 breast cancer cell lines and 14 breast cancer specimens.

Results

Frequency of allelic imbalances ranged from 34.3% to 54.2% of the informative cases according to the marker and, overall, 66% of the tumours presented AI at one of the markers tested. Analysis of the patterns of imbalances revealed at least five common regions of overlap, termed SRO 1-5. CGH analysis of 43 of the breast tumours showed that AI could correlate with loss of chromosome 17, gain of 17q, gain of 17q22-q24, loss of 17q11-q21 and/or loss of 17q25-qter. Gains were most commonly observed at 17q23-q24, which corresponded with SRO 2 and SRO 3. FISH experiments with BAC clones showed amplification in 4 of 6 cell lines and in 10 of 14 tumours at these regions. Clinico-pathological correlations indicated that imbalance at 17q preferentially occurred in high grade, progesterone receptor (PR)-positive and *ERBB2*-amplified tumours.

Discussion

Allelotyping data defined five discrete regions of imbalance along 17q. Three of these regions of overlap are believed to correspond to chromosomal losses, as further evidenced by CGH analysis. SRO 1, which maps to 17q21, is known to comprise *BRCA1* and other tumour suppressing genes, while SRO 4 and SRO 5 map at 17q25 and could correspond to growth inhibiting activities observed in chromosome transfer experiments. CGH and FISH data on the other two regions strongly suggest that these SROs represent DNA amplifications. Overall, correlations with clinico-pathological data suggest that genetic alterations on 17q occur preferentially in aggressive breast cancer.

References

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