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Connexin gap junctions in breast cancer

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Keywords

Breast cancer, Cx43, gap junctions, normal breast

Introduction

Gap junctions are intercellular channels that are formed by members of a family of proteins termed the connexins (Cxs). Gap junctions play an important role in cellular functions, including the regulation of cell growth and differentiation.

Aims

To compare the expression of Cx43-mediated gap junctions in normal human breast tissue, breast tumours, breast cancer cell lines, rat mammary gland and experimental rat mammary carcinomas.

Comments

This comprehensive study of Cx43 expression in mammary tissues confirms the loss of Cx43 gap junctions in tumour cells and speculates that this is a critical step in carcinogenesis. Evidence cited from other studies suggests that restoration of this channel function may be a strategy for cancer therapy and may increase the bystander effects of other therapies through renewed intercellular communication. At the very least, the loss of Cx43 gap junctions may be a useful marker for diagnosis of early stages of the disease, although further studies are required to confirm this finding.

Methods

Breast tumour tissue was obtained during surgery for primary cancer from 32 patients who had not received prior treatment, and adjacent normal breast tissue was obtained from 14 of these patients. The breast carcinoma cell lines Hs578T, MDA-231, MDA-468, HBL-100, T47-D and ZR-75 were also used.

Dimethylbenzanthracine (DMBA) - induced rat mammary carcinomas and rat normal mammary tissue from the vehicle-controlled controls were also harvested for analysis. Immunofluorescence confocal microscopy, northern and western blotting were performed to assess Cx43 expression.

Results

Using immunofluorescence, Cx43 gap junctions were undetectable in all grades and types of breast tumour including both *in situ* and invasive disease, but were always present at various levels in the normal breast epithelium examined. This pattern of Cx43 gap junction down regulation in cancerous compared to normal tissues was similar in the rat model used in the study. Furthermore, when Cx43 expression was examined in a series of human breast cancer cell lines, clear down regulation was confirmed which was not due to any gross gene arrangements as assessed by Southern blot analysis.

Discussion

This study demonstrates decreased expression of Cx43 gap junctions as a common phenotype of transformed cells. Other studies have suggested that restoration of Cx43 function can reverse the transformed phenotype. The loss of Cx43 may therefore serve as a diagnostic marker for breast carcinogenesis and specific modulators of gap junction proteins may have therapeutic implications in breast cancer.

References

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