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Breast cell interactions within a 3D model culture system

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Keywords

Endothelial cells, epithelial cells, fibroblasts, mammary gland, morphogenesis, three-dimensional model

Context

Epithelial-stromal interactions are thought to be important not only in normal cellular proliferation, differentiation and tissue morphogenesis but also in tumour development and progression. To study intercellular communication between specific cell types the authors established a three-dimensional model to analyse the effects of fibroblasts and human umbilical endothelial cells on the growth and morphogenesis of the normal MCF10A breast epithelial cell line and its preneoplastic derivative, the MCF10AT1-EIII8 (EIII8) cell line.

Significant findings

When seeded on a reconstituted basement membrane (Matrigel) normal breast fibroblasts induced MCF10A and EIII8 cells to form discrete islands, with epithelial buds protruding outward from centrally localised fibroblast cells. Fibroblasts derived from benign and malignant breast tissues had the same effect but also led to increased proliferation of both epithelial cell lines as well as increased, organised growth of ductal-alveolar structures. This effect was most pronounced with the EIII8 cells. Inclusion of endothelial cells in the mix had no additional effects when MCF10A cells were present, but further enhanced the growth and morphogenesis seen with EIII8 cells and fibroblasts isolated from benign and malignant breast tissues. Since a pure oestrogen antagonist was able to significantly reduce this epithelial cell proliferation it is possible that the growth effect is at least partly due to oestrogen released from the neoplastic breast fibroblasts. No oestrogenic effect was seen in EIII8 cells co-cultured with fibroblasts obtained from reduction mammoplasty tissue.

Comments

Although this model system exhibits some aspects of the cellular organisation typical of the human breast, the authors themselves point out that this model does not represent normal mammary gland morphology but rather the alterations that take place in early breast cancer. In the normal gland, epithelial cells would not come in contact with fibroblasts as they would be separated from them by the basement membrane. Yet again, no mention is made of the myoepithelial cell and the classic bilayer structure of the ductal-alveolar mammary gland system. MCF10A cells are themselves a heterogeneous cell line, so this may explain the structural organisation seen. It is an interesting model however, and there are clearly differences between the various types of fibroblast as well as reciprocal reactions between epithelial and endothelial cells. This study opens the door for the potential use of therapeutic targeting of 'neoplastic' stromal cells.

Methods

Cell isolation, monolayer and three-dimensional cell culture, cell counts, phase-contrast microscopy, immunocytochemistry of paraffin sections

Additional information

A recent paper looks at the expression of aromatase P450, which catalyses the formation of oestrogens in fibroblasts surrounding breast carcinomas [1].

1. Zhou J, Gurates B, Yang, S, Sebastian, S, Bulun SE: **Malignant breast epithelial cells stimulate aromatase expression via promoter II in human adipose fibroblasts: an epithelial-stromal interaction in breast tumors mediated by CCAAT/enhancer binding protein beta.** *Cancer Res* 2001, **61**:2328-2334 (PubMed abstract).

References

1. Shekhar MPV, Werdell J, Santner SJ, Pauley RJ, Tait L: Breast stroma plays a dominant regulatory role in breast epithelial growth and differentiation: implications for tumor development and progression . Cancer Res. 2001, 61: 1320-1326.