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

SUM-159PT: an ER-independent breast cancer model

ArticleInfo		
ArticleID	:	3697
ArticleDOI	:	10.1186/bcr-2000-66660
ArticleCitationID	:	66660
ArticleSequenceNumber	:	63
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 2000–3–15 OnlineDate : 2000–3–15
ArticleCopyright	:	Current Science Ltd2000
ArticleGrants	:	
ArticleContext	:	1305822

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Keywords

Estrogen independent, MCF-7, metastases, SUM-159PT

Introduction

While 5 year survival rates for breast cancer are gradually improving, the survival rates for metastatic disease remain in the order of 20%. Phenotypic changes are associated with breast cancer progression from a hormone-sensitive disease to a more aggressive hormone-independent state. New *in vitro* models are required to understand the processes which contribute to metastasis.

Aims

To determine the *in vitro* and *in vivo* characteristics of a novel oestrogen-independent cell line, SUM-159PT, suitable for the study of metastatic breast cancer.

Comments

Most current *in vitro* models for breast cancer use established breast cancer cell lines. However, these may not be truly representative of the many phenotypic changes, such as oestrogen independence, which often occur with breast cancer progression. This is particularly true of the MCF-7 cell line, often regarded as the "gold standard" of breast cancer research, which was actually developed from a pleural effusion rather than a primary carcinoma. In order to understand the processes involved in tumour metastasis, it is essential to have newer, more representative cell line models, which mimic the phenotypic changes observed during evolution of a tumour metastasis. The development and characterisation of the metastatic cell line described in this paper, SUM-159PT, may prove useful to our understanding of the biochemical and molecular changes involved in the later stages of metastasis. However, to understand the process more fully, other cell lines representing the early and intermediate stages of metastasis must also be developed.

Methods

The SUM-159PT breast cancer cell line was isolated from an anaplastic primary tumour. A range of *in vitro* and *in vivo* assays were used to characterise the cell line and these were compared to the oestrogen-dependent MCF-7 cell line. These measurements included growth in nude mice and invasion and growth in Matrigel. Analysis of vimentin and E-cadherin, both implicated in the transition to a metastatic phenotype, and the epithelial marker cytokeratin 18 was performed by western blotting. Oestrogen receptor expression was determined by immunohistochemistry and ligand binding assay. Cellular response to known growth inhibitory substances including dihydroxy vitamin D3, transforming growth factor (TGF)-α1 and 12-O-tetradecanoyl-phorbol-13acetate (TPA) were also performed.

Results

Western blot analysis of SUM-159PT confirmed the epithelial nature of the cells by expression of cytokeratin 18, a marker of epithelial cell differentiation. However, oestrogen receptor was undetectable, both by western blot and ligand binding assay, confirming the cells were oestrogen-independent. Expression of vimentin was increased in SUM-159PT compared with the oestrogen-dependent cell line MCF-7, while the reverse was observed with E-cadherin, confirming the metastatic nature of the cells. The invasive capacity of the cells was further confirmed by an *in vitro* invasion assay, where the cells readily invaded through Matrigel and adopted a stellate morphology, further indications of a metastatic phenotype. SUM-159PT also formed tumours in the mammary fat pad of nude mice, with doubling times comparable to rapidly growing human breast tumours. Despite clear oestrogen independence, SUM-159PT were growth inhibited by dihydroxy vitamin D3, TGF-α 1 and TPA.

Discussion

This paper has described the characterisation of a new cell line, which represents the later stages of breast tumorigenesis. Because of its distinct phenotype, the cell line represents a good model for studying mechanisms associated with metastasis. Additionally, it has potential for studying the efficacy of new therapeutic agents for treatment of advanced breast cancer.

References

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