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

Mammaglobin as a marker in breast cancer

ArticleInfo		
ArticleID	:	3726
ArticleDOI	:	10.1186/bcr-2000-66689
ArticleCitationID	:	66689
ArticleSequenceNumber	:	92
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 2000–8–9 OnlineDate : 2000–8–9
ArticleCopyright	:	Current Science Ltd2000
ArticleGrants	:	
ArticleContext	:	1305822

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Keywords

Mammaglobin, metastasis, RT-PCR

Introduction

Despite apparent curative resection, subsequent development of metastatic spread presents a major clinical problem in about 30% of all breast cancer patients. In recent years the RT-PCRtechnique has been used as a means of detecting circulating carcinoma cells in blood or bone marrow. Epithelial markers which have been used to date include cytokeratins, muc-1, epidermal growth factor receptor (EGF-R) or erbB2; however, these markers are not always specific for tumour cells. Recently, expression of the human mammaglobin (hMAM) gene has been suggested as a more specific marker for detecting circulating breast tumour cells in blood.The hMAM gene belongs to the uteroglobin gene family and is found on chromosome 11q12.3-13.1, a region frequently amplified in breast cancer.

Aims

To compare gene expression of hMAM with that of the more conventional markers, cytokeratin-19 (CK19) and EGF-R and to examine the relationship between expression of these markers and clinical outcome.

Comments

The development of suitable methods to detect blood-borne metastasis has been the goal of many laboratories recently. Although initial studies were promising, it was subsequently shown that many of the markers used were not entirely tumour-specific. Here, expression of mammaglobin, a mammary-gland-specific gene, was compared with other more conventionally used molecular markers. The high specificity of mammaglobin for breast cancer cells suggests that a specific marker of blood borne metastasis of breast cancer cells has finally been identified. This has potential use as a marker to detect early metastatic spread.

Methods

Blood samples were collected from patients with ductal carcinoma *in situ*(n = 12), invasive breast cancer (n = 133), haematological malignancies (n = 20) and healthy volunteers (n = 31). Primary human tumour material from 40 breast cancer patients was also analysed. Total RNA was extracted and reverse transcribed into cDNA. This was amplified by nested RT-PCR using primers designed to detect hMAM, EGF-R and CK-19 genes and analysed by gel electrophoresis. RNA from the cell line MDA-MB-361 served as a positive control.

Results

hMAM, EGF-R and CK-19 were detected in breast cancer tissue and the cell line MDA-MB-361. None of the blood samples from healthy volunteers or from patients with haematological malignancies was positive for hMAM. CK-19 was detected in blood from 39% of normal volunteers, while EGF-R and erbB2 were found in blood samples from patients with haematological malignancies (25% and 10%, respectively). In blood samples from patients with invasive breast cancer, mRNAs for hMAM, EGF-R and CK-19 were found in 8%, 10% and 48% respectively. Expression of EGF-R or CK19 in blood samples from breast cancer patients was not correlated with clinicopathological features; however, there was a correlation between expression of hMAM and node status, metastasis and levels of serum CA15-3.

Discussion

In comparison with other molecular markers, the presence of hMAM transcripts in blood of breast cancer patients represents a superior marker to detect breast cancer spread. hMAM correlates with established clinical prognostic indicators; however, prospective studies are required to establish its possible prognostic impact.

References

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