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Original article

Screening for candidate genes related to breast cancer with cDNA microarray analysis

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Abstract

Objective: The aim of this study was to reveal the exact changes during the occurrence of breast cancer to explore significant new and promising genes or factors related to this disease.

Methods: We compared the gene expression profiles of breast cancer tissues with its uninvolved normal breast tissues as controls using the cDNA microarray analysis in seven breast cancer patients. Further, one representative gene, named IFI30, was quantitatively analyzed by real-time PCR to confirm the result of the cDNA microarray analysis.

Results: A total of 427 genes were identified with significantly differential expression, 221 genes were up-regulated and 206 genes were down-regulated. And the result of cDNA microarray analysis was validated by detection of IFI30 mRNA level changes by real-time PCR. Genes for cell proliferation, cell cycle, cell division, mitosis, apoptosis, and immune response were enriched in the up-regulated genes, while genes for cell adhesion, proteolysis, and transport were significantly enriched in the down-regulated genes in breast cancer tissues compared with normal breast tissues by a gene ontology analysis.

Conclusion: Our present study revealed a range of differentially expressed genes between breast cancer tissues and normal breast tissues, and provide candidate genes for further study focusing on the pathogenesis and new biomarkers for breast cancer.

Keywords: Breast neoplasms; Candidate genes; Microarray

Introduction

Breast cancer is the most frequent cancer among women worldwide. As the latest WHO statistics show that there were 1.67 million new cases diagnosed in 2012, which was 25% of all cancers.[1] And breast cancer is still the leading cause of cancer-related death in women in less developed countries,

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although preventive approaches and treatments have greatly improved in the past decades.[2] The activation and overexpression of oncogenes, as well as the decreased expression or deletion of cancer suppressor genes, have been proven to play important roles in the development of breast cancer.[3–6] Although, a large number of studies on molecular genetics and molecular biology have revealed that multiple genes and factors take part in the pathogenesis of breast cancer, the exact mechanism is still unclear. Therefore, there is a huge need to identify new and promising genes or factors which can be used as biomarkers to predict the prognosis or sensitivity as well as the effect of treatments for breast cancer.

Currently, transcriptional profiling of gene expression achieved by cDNA microarrays has greatly increased our knowledge of the pathomechanisms involved in various types of cancers. This high-through put technique identifying a large number of promising genes has been successfully used in distinguishing subclasses of caner as well as predicting the clinical outcome and the response to particular treatments.[7,8] Thus, we choose to use the cDNA microarray technology to discover the exact changes during the occurrence of breast cancer to look for new promising genes or factors.

In the present study, we compared the gene expression profiles of breast cancer tissue with its uninvolved normal breast tissue as the control using the cDNA microarray analysis. We found that differences existed between the two groups in gene expression profiles. And a large number of genes were identified that were significantly changed during the occurrence of the disease. Furthermore, we confirmed the cDNA microarray results by detecting one selected gene's change of expression by the use of quantitative real-time PCR. Thus, the cDNA microarray analysis here provide plenty of candidate genes for further study focusing on the pathogenesis and biomarkers of breast cancer.

Material and methods

Ethics statement

This study was approved by the Institutional Review Board of the Second Hospital of Shandong University, and written informed consent was obtained from each patient.

Patients

The enrolled specimens were collected from seven women patients with pathologically confirmed invasive breast cancer in the Second Hospital of Shandong University from May 1, 2009 to Feb 28, 2010. All the patients enrolled followed strict eligibility and exclusion criteria as follows: eligibility criteria were female, histologically confirmed invasive breast ductal carcinoma without prior treatment before surgery, patients underwent modified radical mastectomy, having available breast cancer tissue samples as well as normal breast tissue samples, complete basic clinical and pathological information, and a signed informed consent. The exclusion criteria included prior invasive malignancy within five years, pregnancy, receiving neoadjuvant therapy for breast cancer, bilateral breast cancer, and having a family history of breast cancer. The general characteristics of the seven patients enrolled are shown in Table 1.

Clinical tissue sample collections

All tumor tissues and adjacent normal tissues were collected into liquid nitrogen within 30 min after the resection of the mammary tissue. Pathological review of hematoxylin and eosin-stained sections was used for evaluation of the histological characteristics of all specimens. All the adjacent normal breast tissues were obtained from breast cancer patients who underwent

Table 1
The general characteristics of the seven patients enrolled.

No	Age	Pathological type	Histological grade	Tumor size	ER	PR	Her-2	Ki67(%)
1	55	IDC	II	1.5*0.5	+++	±	−	10
2	41	IDC	II	3.0*2.0	+	+++	−	5
3	59	IDC	II	2.0*2.0	+++	+++	−	10
4	53	IDC	II	1.8*1.0	+++	+++	−	10
5	39	IDC	II	1.0*0.8	+++	++	−	30
6	57	IDC	II	1.8*1.5	+++	+++	−	30
7	35	IDC	II	2.3*1.8	+++	+++	−	50