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Research Article

Expression of PCGEM1 and lincRNA-p21 lncRNAs in breast cancer tissue

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ABSTRACT

Objectives: Long non-coding RNAs (lncRNAs) play critical roles in tumor development, progression, and prognosis. Prostate cancer gene expression marker 1 (PCGEM1) is an oncogenic lncRNA that inhibits apoptosis, whereas lincRNA-p21 promotes apoptosis. This study aimed to investigate the expression of these lncRNAs in breast tumor tissue and adjacent non-tumor tissue.

Methods: The expression levels of PCGEM1 and lincRNA-p21 were assessed by real-time PCR (RT-PCR) in fifty formalin-fixed, paraffin-embedded invasive ductal carcinoma breast tumor tissues and adjacent non-tumor tissues.

Results: The expression of PCGEM1 was significantly higher in tumor tissues compared to adjacent non-tumor tissues (p=0.01). ROC curve analysis indicated that the sensitivity and specificity of PCGEM1 for discriminating breast cancer were %60.87 and 70.21%, respectively, with an area under the curve (AUC) of 0.63 (p=0.01). No significant correlation was observed between PCGEM1 expression and tumor size, histological grade, or lymph node involvement. The expression of lincRNA-p21 was similar in tumor tissues and adjacent non-tumor tissues.

Conclusion: PCGEM1 may contribute to the pathogenesis of breast cancer and could serve as a diagnostic marker in breast cancer.

Keywords: Breast cancer, Long non-coding RNAs (lncRNAs), Prostate cancer gene expression marker 1 (PCGEM1), lincRNA-p21

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Introduction

Breast cancer accounts for approximately one-third of all cancers in women. It is the second most common cancer after lung cancer and the leading cause of cancer-related death among women (1, 2). Early detection of breast cancer is essential for improving survival rates. Therefore, identifying molecular markers with high sensitivity and specificity for early-stage diagnosis is critical (3, 4).

Long non-coding RNAs (lncRNAs) are transcripts longer than 200 nucleotides that play crucial roles in the cytoplasm and other cellular compartments, including the regulation of translation, metabolism, and signaling pathways. Abnormal expression of lncRNAs can contribute to the development of various diseases, including cancer. Given their significant involvement in numerous cellular processes, lncRNAs hold potential as novel biomarkers for the diagnosis, prognosis, and treatment of cancers (5, 6).

Prostate cancer gene expression marker 1 (PCGEM1) is an oncogenic lncRNA that is overexpressed in prostate cancer and various other cancer cell types (7). Elevated PCGEM1 expression of PCGEM1 inhibits apoptosis and autophagy while promoting cell proliferation, indicating its oncogenic role in tumorigenesis and cancer progression (8, 9). However, to date no studies have investigated the expression of this lncRNA in breast cancer.

LincRNA-p21 is another lncRNA that plays a crucial role in various biological processes, including the cell cycle, proliferation, metabolism, reprogramming, and pluripotency (10, 11). Additionally, p21 regulates the transition from the G1 to S phase of the cell cycle, and lincRNA-p21 is essential for controlling p21 levels and cell cycle progression (12). lincRNA-p21 expression is decreased in liver, prostate, colorectal, and lung cancers, while its overexpression suppresses tumor invasiveness by the Notch pathway and inhibits tumorigenesis by directly binding to STAT3 (13, 14). In the present study, we investigated the expression levels of lincRNA-p21 and PCGEM1 in breast cancer and their correlation with pathological parameters.

Materials and Methods

Fifty paraffin-embedded invasive ductal carcinoma breast tumor tissues and 50 paired adjacent non-tumor tissues, confirmed by a pathologist, were collected from Rasul Akram Hospital. This study was approved by the Institutional Ethics Committee of Iran University of Medical Sciences (IR.IUMS.REC.1399.1210) and was conducted in accordance with the Declaration of Helsinki and the guidelines of the Iranian Ministry of Health and Medical Education. The written informed consent was obtained from all the patients. The clinicopathological parameters, including age, tumor size, histological grade, and involvement/non-involvement of lymph nodes were recorded.

Tissue sections were deparaffinized with two pre-warmed xylene and subsequently rehydrated with 96% ethanol. Total RNA was isolated from tissues using Trizol (Geneall, South Korea) reagent according to the manufacturer's instructions, and RNA quality and concentrations were assessed at wavelengths of 260 and 280 with a NanoDrop spectrophotometer. cDNA synthesis was performed by the instructions of the BeyoRT™ II First Strand cDNA Synthesis Kit (SMOBIO,Taiwan). cDNA was used as a template for the RT-qPCR experiment, which was performed using an Eva Green qPCR Mix No ROX (Solis BioDyne, Estonia) at an ABI 7300 Real Time-PCR System (Applied Biosystems, Life Technologies GmbH, Darmstadt, Germany). The sequences of used primers were listed in Table 1. The obtained data were analyzed using the $2^{-\Delta\Delta Ct}$ method.

Statistical Analysis

The normal distribution of data was determined by the Kolmogorov–Smirnov test. Data were nonparametric (non-normal distribution) and reported as median± range. Differences between the two groups were analyzed by the Mann–Whitney U test (nonparametric). To examine the correlations between variables, Spearman's correlation tests were used for non-parametric variables. Receiver operating characteristic (ROC) curve analysis with the calculation of the area under the curve was done to evaluate discrimination between the studied groups. A p value<0.05 was considered significant.

Results

All patients were female and none had undergone chemotherapy or mastectomy. The average age of the patients was 47 years. Thirty-five percent of the patients were over 50 years old, while 65% were under 50. Lymph node involvement was present in 40% of the patients. Additionally, the tumor size was 3 cm

Table 1. Specific forward and reverse primer sequences.

Primer name	Sequence
lincRNA-p21	F: 5′GGGGATAAGCACCACTAATG3′ R: 5′TGTAGGCAATCACAGAGCAC3′
PCGEM1	F:5′-AGTGAGCAGGCTTGGTGCAT-3′ R: 5′-TTTCCAAAGGGTCCGCTGTC-3′
GAPDH	F:5′ GGGAAGGTGAAGGTCGGAGT-3′ R: 5′ TCCACTTTACCAGAGTTAAAAGCAGG-3′

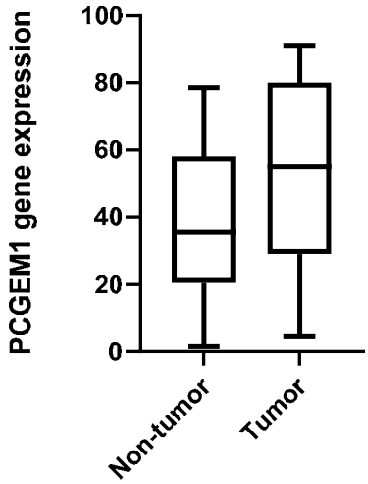

Figure 1. The expression level of PCGEM1 gene in breast tumor tissues compered to adjacent (P value=0.02) non-tumor tissues.

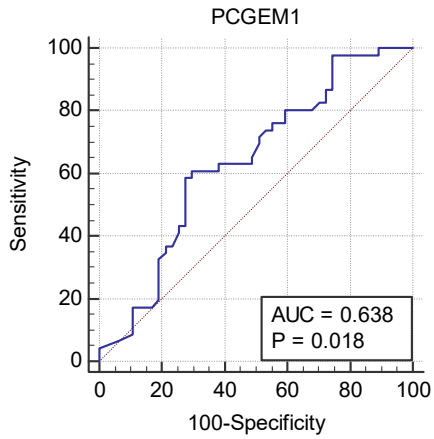

Figure 2. Receiver operating characteristic (ROC) curve analysis for PCGEM1 for breast cancer diagnosis.

or greater in 40% of the cases. As shown in Figure 1, the expression level of the PCGEM1 lncRNA was significantly higher in tumor tissues compared to matched non-tumor tissues (p=0.01). The potential of PCGEM1 serving as a diagnostic biomarker for breast cancer was also evaluated through ROC curve analysis. Figure 2 reveals that the Area Under the Curve (AUC) for PCGEM1was 0.63, with a sensitivity of 60.87% and specificity of 70.21% (p=0.01).

The expression level of lincRNA-p21 in breast tumor tissue did not differ significantly from that in adjacent non-tumor tissue (Figure 3). The correlation between PCGEM1 with pathological parameters is presented in Table 2. No significant relationship was observed between PCGEM1 and lincRNA p-21 expression with age, tumor size, tumor grade, or Lymph node involvement (Table 2).

Discussion

Breast cancer is one of the most common cancers and the second leading cause of cancer-related deaths worldwide (15). Extensive research has been conducted to identify the genetic factors responsible for breast cancer, and among the known predisposing genes, long non-coding RNAs (lncRNAs) have emerged as critical contributors (7).

PCGEM1 is an oncogene LncRNA whose expression was first identified in prostate cancer (16). Increased expression of PCGEM1 promotes cell proliferation, migration, and invasion while reducing apoptosis by upregulating RhoA, MMP2, and Bcl-x (17). Overexpression of PCGEM1 stimulates cancer cell growth through increased expression of SNAI1 and Rho, along with induction of p53/p21 p53 and p21 (7). Our study showed that PCGEM1 expression was significantly increased in breast tumor tissues compared to non-tumor tissues, which is consistent with results from other cancers (7, 9, 16, 18-21). Fagan-Solis and colleagues demonstrated that blocking RhoA activity in breast cancer cells by directly inhibiting MMP2

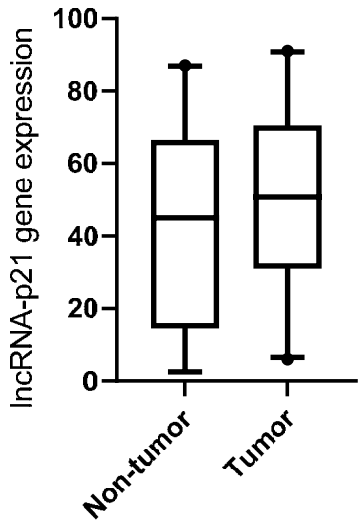

Figure 3. The expression level of lincRNA-p21 gene in breast tumor tissues compered to adjacent (P value>0.05) non tumor tissues.

Table 2. Correlation between PCGEM1 and lincRNA-p21 with pathological parameters.

Variables	PCGEM1		lincRNA-p21	
	r	P	r	P
Age	-0.02	0.8	-0.05	0.07
Tumor size	-0.03	0.7	-0.12	0.4
Tumor grade	0.13	0.3	-0.04	0.7
Lymph node involvement	-0.15	0.29	0.04	0.7

and MMP9 reduced the invasiveness of these cells (22). Therefore, increased PCGEM1 expression may contribute to breast cancer development by inhibiting Ru activity. Li and colleagues also demonstrated that elevated PCGEM1 expression, mediated through miR-129, upregulates STAT3 expression in endometrial cancer(19). Studies have shown that the expression of STAT3, Bcl-xL, and MCL1 is elevated in breast cancer (23), suggesting that increased PCGEM1, via enhanced STAT3 expression, may play a role in breast cancer progression. In this study, no significant association was found between PCGEM1 expression and tumor size, lymph node metastasis, or tumor grade. Additionally, the research demonstrated that the PCGEM1 gene can serve as a diagnostic biomarker for breast cancer, with 60% sensitivity and 70% specificity.

Furthermore, this study examined the expression of lincRNA-p21 in breast cancer tissue and adjacent non-tumoral tissue, but no significant differences were observed. While lincRNA-p21 expression is downregulated in liver, prostate, colon, and lung cancers (10), its expression in breast cancer has not been extensively studied. Therefore, further research with larger sample sizes is needed to better understand the expression of this gene in breast cancer tissue.

To summarize, this study suggests that PCGEM1 may be associated with breast cancer and that its expression levels could serve as a diagnostic tool for patients. However, further research is necessary to elucidate the role of this lncRNA in breast cancer development and to identify the specific genes involved. Additionally, larger-scale studies are required to confirm whether PCGEM1 can serve as a reliable biomarker.

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Conflict of interest

The authors declare that there is no conflict of interest.

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