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The miR-877-3p polymorphism rs1264440 is associated with susceptibility to breast cancer

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Abstract

Introduction and Objective. Breast cancer (BC) remains the most common malignant tumour among females. Dysregulated microRNAs (miRNAs) are key regulators in carcinogenesis, and single nucleotide polymorphisms (SNPs) represent their most prevalent genetic alterations. The aim of the study is to investigate the influence of rs1264440 on miR-877-3p expression and its subsequent effects on BC cell proliferation and migration.

Materials and Method. Both 160 female BC patients and 160 healthy control (HC) subjects in Maternity and Child Care Center of Qinhuangdao, China, were selected as case and control groups, respectively. Genotyping for the SNP rs1264440 was performed using a TaqMan probe-based RT-qPCR assay. The Cell Counting Kit-8 (CCK-8) assay was used to determine cell viability. Analysis of cell migration and invasion was conducted by transwell assays.

Results. rs1264440 AA genotype (P = 0.006, OR = 0.308, 95% CI=0.129–0.739), A allele (P = 0.003, OR = 0.586, 95% CI = 0.413–0.832) significantly correlated with BC susceptibility. The rs1264440 AA genotype was associated with decreased miR-877-3p levels. High miR-877-3p level could distinguish BC patients from controls with an area under the curve (AUC) of 0.854 (sensitivity=73.13%, specificity=84.38%). Inhibition of miR-877-3p suppressed the proliferative, migratory, and invasive capacities of BC cells in vitro.

Conclusions. The miR-877-3p rs1264440 is a risk predictor for BC, being implicated in miR-877-3p dysregulation and the promotion of cell viability and motility.

Key words

breast cancer, miR-877-3p, single nucleotide polymorphism, viability, motility

Abbreviations

BC – Breast cancer; **SNPs** – Single-nucleotide polymorphisms; **miRNAs** – microRNAs; **SCCC** – Squamous cell cervical carcinoma; **OS** – Osteosarcoma; **HCC** – Hepatocellular carcinoma; **HC** – Healthy control; **BMI** – Body mass index; **NC** – Negative control; **SD** – Standard deviation; **HWE** – Hardy-Weinberg equilibrium; **ORs** – Odds ratios; **CIs** – Confidence intervals; **ROC curve** – Receiver operating characteristic curve; **ER** – Estrogen receptor; **PR** – Progesterone receptor; **HER2** – Human epidermal growth factor receptor 2

INTRODUCTION

Breast cancer (BC) is the most frequently diagnosed cancer worldwide [1], and its incidence is strongly associated with age, as well as with risk factors such as genetics, diet, and excessive alcohol intake [2]. The development of BC is caused by the dysregulation of pathways that control cell viability and apoptosis [3]. Current standard therapeutic strategies for BC include surgical resection, cytotoxic chemotherapy, endocrine therapy, and molecularly targeted agents [4]. Currently, BC faces many challenges in its diagnosis, treatment, and prognosis [5]. Genes influencing BC prognosis is a top priority, as it may lead to new targeted therapies. MicroRNA related single-nucleotide polymorphisms (SNPs) are considered to be the potential biomarkers for early detection of BC [6].

MicroRNAs (miRNAs) are a class of small non-coding RNAs that mediate the post-transcriptional regulation of gene expression [7, 8]. Aberrantly expressed miRNAs are involved in a wide range of human cancers [9–12], where they consistently function as pivotal tumour suppressors or oncogenes. Numerous miRNAs are dysregulated in BC patients [13]. MiR-877-3p has been identified as differentially expressed in BC patients [14]. In mouse models simulating the menstrual phase, elevated levels of uterine miR-877-3p have been observed [15]. MiR-877-3p is upregulated in squamous cell cervical carcinoma (SCCC) tissues, which promotes cervical cell (CC) motility and infiltration by modulating cytoskeletal protein folding [16]. Accumulating

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evidence indicates that miR-877-3p drives the initiation and progression of diverse diseases by governing cell viability. In osteosarcoma (OS), enforced expression of miR-877-3p exerts tumour suppressive effects by targeting the FGF2 signalling axis, thereby attenuating viability and angiogenesis [17]. MiR-877-3p additionally targets the Bclaf1/P53 signalling pathway, promoting early neurological recovery following cerebral ischemia-reperfusion injury by modulating apoptosis [18]. However, miR-877-3p has not yet been studied in BC pathogenesis. A study on hepatocellular carcinoma (HCC) demonstrated that the rs1264440 polymorphism, located in the promoter region of miR-877, regulates miR-877 expression [19]. Given these reasons, it is speculated that rs1264440 might contribute to the susceptibility of BC. Therefore, this study hypothesizes that the rs1264440 polymorphism associated with miR-877-3p may contribute to BC susceptibility.

The aim of the study is to explore the impact of rs1264440 on miR-877-3p expression and its effects on the viability and motility of BC cells.

MATERIALS AND METHOD

Participants. The priori calculation of sample size was performed by GPower 3.1. When effect size = 0.3, α = 0.05, statistic power = 0.95, the total sample size was 220. In order to prevent data loss, a total of 160 female BC patients and 160 healthy control (HC) were recruited from Maternity and Child Care Center of Qinhuangdao between January 2021 – January 2025. The control subjects were matched with the BC patients by age (± 3 years) and body mass index (BMI, ± 2 kg/m^2). The diagnosis of BC was pathologically confirmed by tissue biopsy in all patients. Controls had no history of cancer. All the subjects were from the Chinese Han population.

The study was conducted in accordance with the Declaration of Helsinki and informed consent was signed by every subject before enrollment. Approval was granted by the Ethics Committee of Maternity and Child Care Center of Qinhuangdao, China.

DNA extraction and genotyping. Peripheral venous blood (5 mL) was collected from all subjects into EDTA tubes after 12 h fasting. A GenElute™-E Single Spin Blood DNA Kit (Merck, China, EC196) was used to isolate genomic DNA from blood samples. Genotyping of rs1264440 was performed using a TaqMan SNP genotyping assay (4351379, Thermo Fisher, USA). PCR reaction using 20 μL system contained 40 ng DNA, 10 μL TaqMan Genotyping Master Mix, and 0.5 μL probe. PCR reaction condition was 95 °C for 10 min, followed by 40 cycles of 95 °C for 15 s, 60 °C for 1 min and 72 °C for 4 min. Each sample was performed in triple triplicate. The genotyping was performed by laboratory personnel who were blinded to the status of the samples. All samples were coded with unique identifiers, and the grouping information was not disclosed to the researchers until statistical analysis. Randomly selected 5% samples, using Sanger sequencing, were used to ensure genotyping accuracy

RT-qPCR. Total RNA was obtained using the total RNA Purification Kit (75400, Norgen, Canada) from Plasma according to the provided protocol. RNA concentration and purity were evaluated using NanoDrop 2000. The expression level of miR-877-3p was detected by RT-qPCR. Reverse transcription was performed using the TaqMan MicroRNA Reverse Transcription Kit (4366596, Applied Biosystems, USA). Real-time PCR was carried out using TaqMan Universal Master Mix II (4440038, Applied Biosystems, USA). U6 was used as a reference RNA for normalization. All reactions were performed in triplicate. Relative expression was calculated by the $2^{-\Delta\Delta Ct}$ method.

Cell culture. When the cell monolayer reached approximately 90% confluency, the cells were then harvested and passaged. All cell lines used in this study were purchased from BNCC (Beijing, China). The MDA-MB-231 cells were cultivated in L-15 medium (BNCC339873, BNCC, China) containing 10% foetal bovine serum (FBS, A5256701, Gibco). The MCF7 cells were cultivated in a complete DMEM-H medium (BNCC360905, BNCC, China) containing 10% FBS. The MCF-10A cells were cultivated in a complete medium containing LL-0023 (BNCC376120, BNCC, China) and cholera toxin[20].

Cell transfection. The inhibitor negative control (NC) and miR-877-3p inhibitor were purchased from MedChenExpress (Shanghai, China). Cells (2×10^5 cells/well) were seeded in 6-well plates, then subjected to transfection using either an miR-877-3p inhibitor or an inhibitor NC, with the Lipo8000™ transfection reagent (C0533, Beyotime, China) being used in serum-free medium. After 48 h, cells were harvested for RNA analysis or functional assays.

CCK-8 assay. Following counting, the cell suspension was transferred to 96-well plates at a density of 2,000/well. Incubation was followed by the addition of 20 μL of CCK-8 solution (C0037, Beyotime, China). Absorbance at 450 nm was measured using a microplate reader.

Transwell motility and infiltration assay. MDA-MB-231 and MCF-7 cells (5×10^4 cells) were dispersed in 200 μL serum-free medium. For invasion assays, the upper chambers were pre-covered by Matrigel Matrix (C0372, Beyotime, China). The complete medium has been added in the Lower chambers, containing 600 μL complete medium with 10% FBS. After cultured at 37 °C for 24 h, the cells were collected from the bottom of chambers, fixed with 4% polyoxymethylene for 15 min, and then stained with 0.1% crystal violet for 15 min. Five random fields per well were counted under an inverted microscope (Olympus, Japan) at 200× magnification.

***In silico* survival analysis**. The prognostic value of miR-877-3p was evaluated using UALCAN database (https://ualcan.path.uab.edu/cgi-bin/ualcan-res-mir.pl), which contained survival information from 748 breast cancer patients. Patients were divided into high and low expression groups, based on median miR-877-3p expression, and overall survival was compared using the log-rank test.

Statistical analysis. Statistical analysis was performed using SPSS 22.0 (IBM, USA). Figures were plotted by GraphPad Prism 9.0.0 software. Normality of continuous variable was assessed using the Shapiro-Wilk test. Continuous variables were presented as mean ± standard deviation (SD) and compared by t-tests or non-parametric tests. Categorical variables were compared using the chi-square test or Fisher's exact test. Hardy-Weinberg equilibrium (HWE) was assessed using a goodness-of-fit chi-square test. Association analysis

between rs1264440 and BC risk was calculated by Chi-square test and presented by odds ratios (ORs) and 95% confidence intervals (CIs). The diagnostic value of miR-877-3p was evaluated by receiver operating characteristic (ROC) curve. $P < 0.05$ was considered statistically significant.

RESULTS

Basic characteristics of BC patients and HC. No significant differences in age or BMI were detected between the BC patients and HC subjects (Tab. 1; $P > 0.05$). Regarding the clinicopathological characteristics, tumours larger than 2 cm were observed in 84 patients (52.5%), while 76 patients (47.5%) had tumours measuring 2 cm or less. Eighty-three patients (51.9%) were classified with TNM stage I, II, and 71 patients (48.1%) were classified as stage III. Only 9.4% of BC patients presented with distant metastasis at the time of diagnosis. Similarly, for key molecular markers including estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), the negative rates were substantially higher than the positive rates among BC patients.

Table 1. Baseline and clinical characteristics of subjects

Characteristics	BC patients (n=160)	Healthy controls (n=160)	*P*
Age	44.89±6.89	45.24±5.81	0.617
BMI	25.78±4.04	25.84±3.88	0.876
Tumour size (cm)			
≤2	76 (47.5)	/	
>2	84 (52.5)	/	
TNM stage			
I+II	83 (51.9)	/	
III	77 (48.1)	/	
Metastasis			
Yes	15 (9.4)	/	
No	145 (90.6)	/	
ER			
Positive	55 (34.4)	/	
Negative	105 (65.6)	/	
PR			
Positive	42 (26.3)	/	
Negative	118 (73.8)	/	
HER2			
Positive	28 (17.5)	/	
Negative	132 (82.5)	/	

BC – breast cancer; BMI – body mass index; ER – estrogen receptor; PR – progesterone receptor; HER2 – human epidermal growth factor receptor 2; / – data not collected

Correlation of miR-877-3p SNP with BC risk. The genotype distribution of the miR-877-3p rs1264440 polymorphism in the control group was in accordance with the HWE test (Tab. 2; $P = 0.383$). Compared with the rs1264440 GG genotype, the GA and AA genotypes were observed at a lower frequency in BC patients than in controls. rs1264440 AA genotype was associated with reduced BC susceptibility ($P = 0.006$, OR = 0.308, 95% CI = 0.129–0.739). Furthermore, the rs1264440 A allele showed a significant correlation with decreased BC risk ($P = 0.003$, OR = 0.586, 95% CI = 0.413–0.832). Under the dominant model, the GA+AA genotype of rs1264440 was found to be inversely associated with BC susceptibility ($P = 0.014$, OR = 0.574, 95% CI: 0.368–0.894). Similarly, under the recessive model, the AA genotype also showed a significant inverse correlation with BC susceptibility ($P = 0.018$, OR = 0.368, 95% CI: 0.157–0.863).

Table 2. Association between miR-877–3p rs1264440 polymorphism and risk of breast cancer

Genotypes	Healthy controls (n=160)	Breast cancer patients (n=160)	*P*	OR (95% CI)
Co-dominant				
GG	74 (46.25)	96 (60.00)	-	-
GA	66 (41.25)	56 (35.00)	0.075	0.654 (0.410–1.044)
AA	20 (12.5)	8 (5.00)	0.006	0.308 (0.129–0.739)
Allele				
G	214 (66.88)	248 (77.50)	-	-
A	106 (33.12)	72 (22.50)	0.003	0.586 (0.413–0.832)
P_{HWE}	0.383			
Dominant				
GG	74 (46.25)	96 (60.00)	-	-
GA+AA	86 (53.75)	64 (40.00)	0.014	0.574 (0.368–0.894)
Recessive				
GG+GA	140 (87.5)	152 (95.00)	-	-
AA	20 (12.5)	8 (5.00)	0.018	0.368 (0.157–0.863)

P_{HWE} of control group was 0.383; OR, odds ratios; 95% CI, 95% confidence interval

Stratified analysis of clinical features of BC patients with different rs1264440 genotypes. The 160 BC patients were stratified into 2 groups based on their rs1264440 genotype: the GG group and the GA+AA group. No significant differences

Table 3. Stratified analysis of clinical features of breast cancer patients with different rs1264440 genotypes

Characteristics	BC patients (n=160)	GG (n=96)	GA+AA (n=64)	*P*
Age	44.89±6.89	44.69±6.21	46.09±4.95	0.151
BMI	25.78±4.04	25.93±3.94	25.50±3.75	0.504
Tumour size (cm)				0.039
≤2	76 (47.5)	52 (54.2%)	24 (37.5%)	
>2	84 (52.5)	44 (45.8%)	40 (62.5%)	
TNM stage				0.012
I+II	83 (51.9)	42 (43.8%)	41 (64.1%)	
III	77 (48.1)	54 (56.2%)	23 (35.9%)	
Metastasis				0.029
Yes	15 (9.4)	13 (13.5%)	2 (3.1%)	
No	145 (90.6)	83 (86.5%)	62 (96.9%)	
ER				0.013
Positive	55 (34.4)	33 (34.4%)	22 (34.4%)	
Negative	105 (65.6)	63 (65.6%)	42 (65.6%)	
PR				0.033
Positive	42 (26.3)	31 (32.3%)	11 (17.2%)	
Negative	118 (73.8)	65 (67.7%)	53 (82.8%)	
HER2				0.027
Positive	28 (17.5)	22 (22.9%)	6 (9.4%)	
Negative	132 (82.5)	74 (77.1%)	58 (90.6%)	

BC, breast cancer; BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2

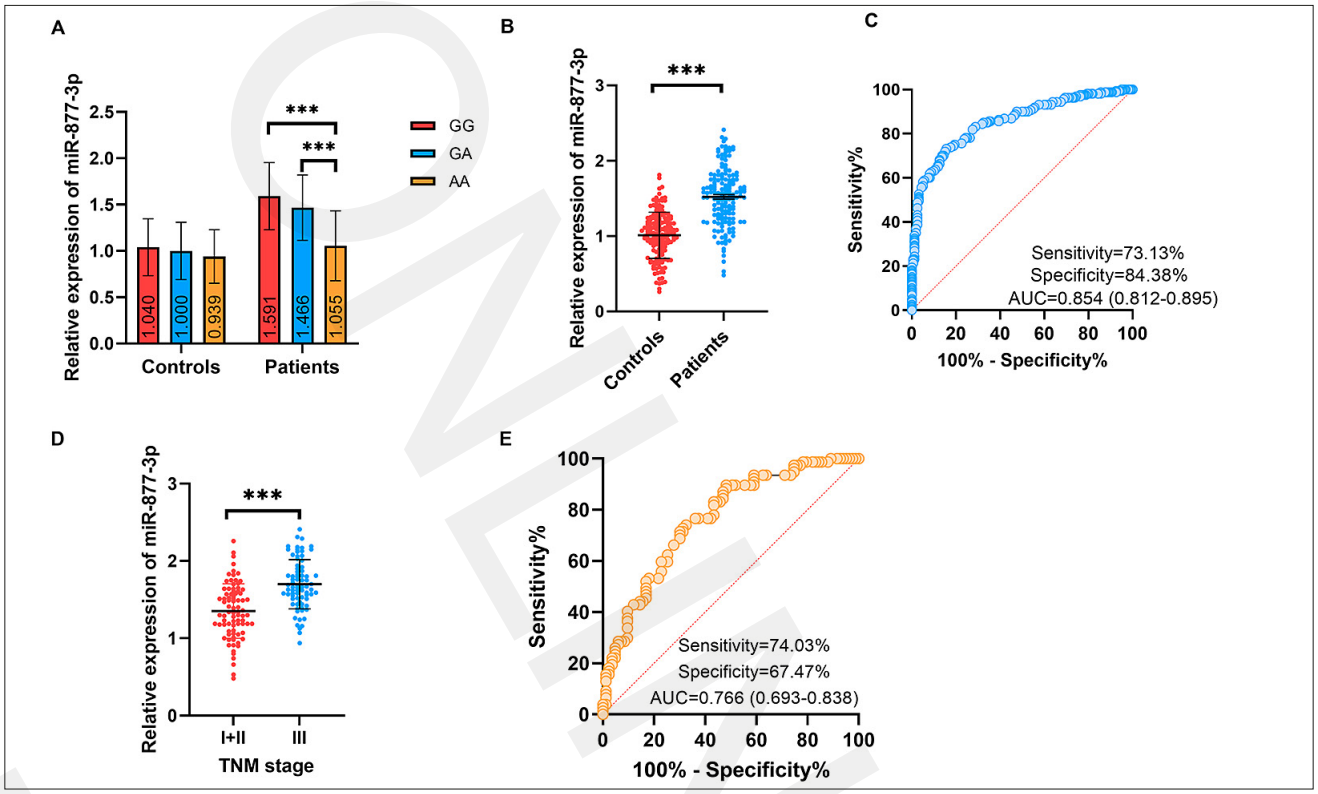


Figure 1. Expression level of miR-877–3p. A. Plasma miR-877–3p expression level varies among different rs1264440 genotypes. miR-877–3p expression in BC patients were 1.591 ± 0.362 for GG, 1.466 ± 0.353 for GA, and 1.055 ± 0.377 for AA. The difference was determined by Mann – Whitney U test. B. Expression level of plasma miR-877–3p shows a significant difference between BC patients and HC subjects. C. ROC curve analysis demonstrates the diagnostic value of miR-877–3p for BC. D. Plasma miR-877–3p expression level differs significantly across TNM stages. E. ROC curve analysis evaluates the utility of plasma miR-877–3p expression in stratifying BC severity (by TNM stage). ***, $P < 0.001$.

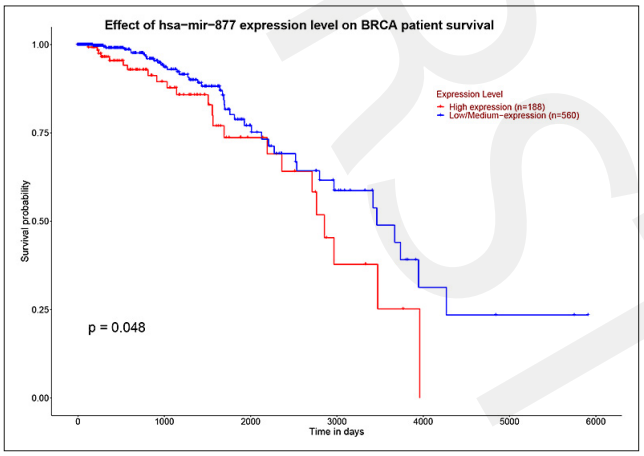
in age or BMI were observed between the 2 groups (Tab. 3; $P > 0.05$). However, significant differences were observed in several clinicopathological characteristics, including TNM stage ($P = 0.012$), metastasis ($P = 0.029$), and tumour size ($P = 0.039$). Furthermore, significant disparities were also detected in key molecular subtype markers, ER ($P = 0.013$), PR ($P = 0.033$), and HER2 ($P = 0.027$).

Effects of rs1264440 for miR-877-3p expression. Genotype analysis revealed significant differences in miR-877-3p levels among BC patients carrying the rs1264440 genotypes. Among them, patients with the GG genotype demonstrated the highest expression levels, and AA genotype carriers had the lowest miR-877-3p levels. Although no statistically significant differences in miR-877-3p expression were observed across rs1264440 genotypes in the HC group, individuals carrying the GG genotype exhibited higher levels than those with other genotypes ($P < 0.001$, Fig. 1A).

Clinical value of plasma miR-877-3p in BC. The RT-qPCR results indicated that the plasma miR-877-3p level was higher in BC patients (1.520 ± 0.378) than in the HC group (1.011 ± 0.306) (Fig. 1B; $P < 0.001$). ROC curve revealed that miR-877-3p levels had potential diagnostic value for distinguishing BC patients from HC subjects, with an area under the curve (AUC) of 0.854 (sensitivity=73.13%, specificity=84.38%) at the cutoff value of 1.285 (Fig. 1C). Subsequent analysis compared the plasma miR-877-3p level across different TNM stages. The results demonstrated a significant upregulation in miR-877-3p expression in TNM stage III patients compared to that in patients in stages I and II (Fig. 1D; $P < 0.001$). ROC curve analysis revealed that miR-877-3p levels could distinguish TNM stage III patients from stages I+II subjects, with an AUC of 0.766 (sensitivity = 74.03%%, specificity = 67.47%) at the cutoff value of 1.515 (Fig. 1E).

***In silico* survival analysis.** The potential prognostic significance of miR-877-3p in BC was analyzed by UALCAN database. As shown in Supplementary Figure 1 ($P = 0.048$), high miR-877-3p expression was significantly associated with shorter overall survival of BC patients.

Effects of miR-877-3p on cell proliferation, migration, and invasion. Compared with MCF-10A cells, both MCF-



Supplementary Figure 1. Overall survival analysis of has-miR-877 on BC patients using UALCAN database.

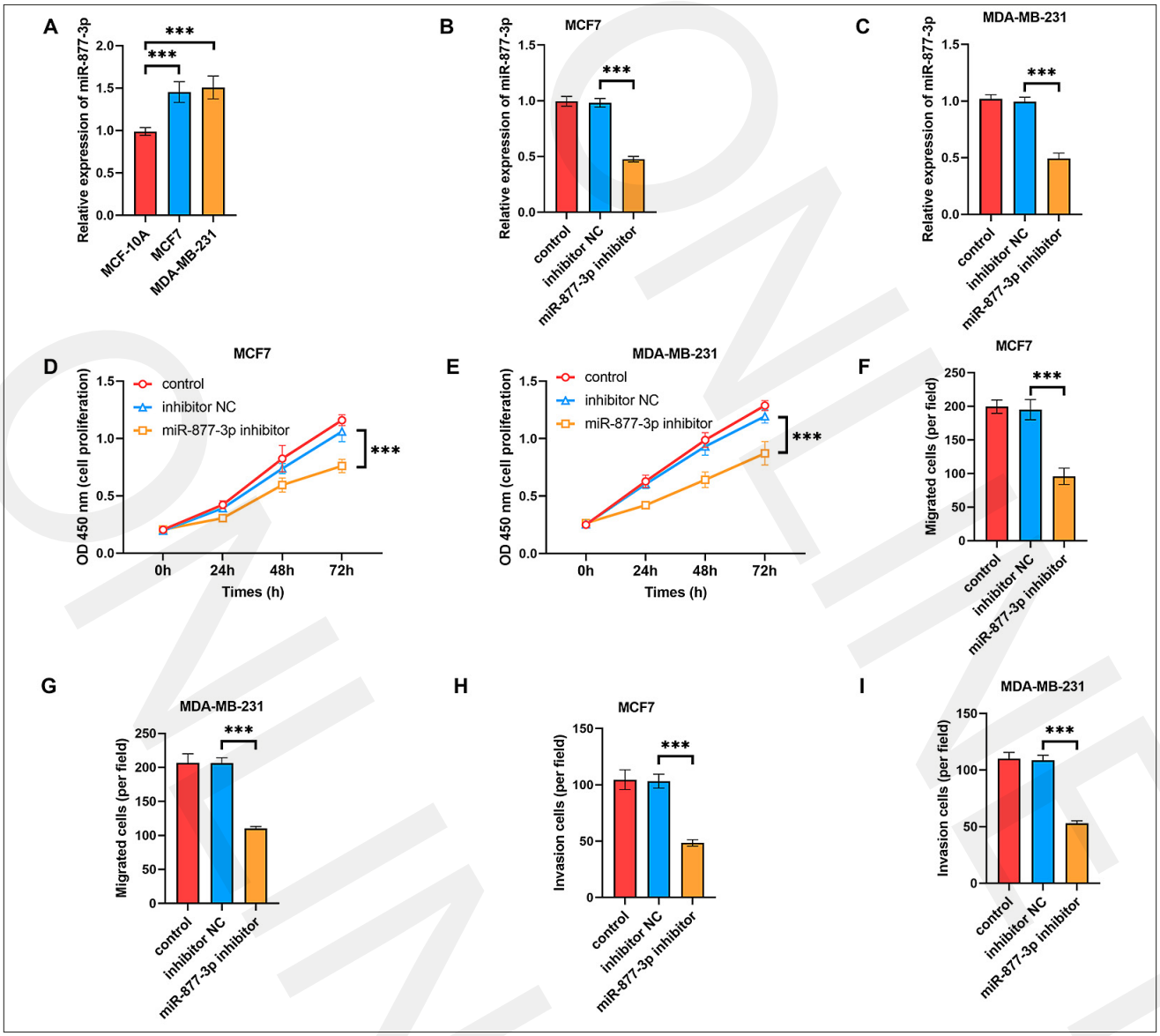


Figure 2. Effect of miR-877–3p expression on BC cell behavior (n = 5). A. Expression level of miR-877–3p in different cell lines. B, C. Validation of miR-877–3p knockdown efficiency following transfection with a miR-877–3p inhibitor. D, E. Effects of miR-877–3p inhibitor on the proliferation of MCF7 and MDA-MB-231 cells. F, G. Impacts of miR-877–3p inhibitor on the migration of MCF7 and MDA-MB-231 cells. H, I. Influences of miR-877–3p inhibitor on the invasion of MCF7 and MDA-MB-231 cells. ***, $P < 0.001$.

7 and MDA-MB-231 lines exhibited elevated miR-877-3p abundance (Fig. 2A; $P < 0.01$), indicating its upregulation in BC cells. MiR-877-3p inhibitor significantly reduced miR-877-3p levels in both MCF-7 and MDA-MB-231 cells (Fig. 2B and 2C; $P < 0.001$), confirming the successful establishment of the miR-877-3p knockdown model. The CCK-8 assay displayed that the proliferative capacity of both MCF-7 and MDA-MB-231 cells in the miR-877-3p inhibitor group was reduced compared to the inhibitor NC (Fig. 2D and 2E; $P < 0.001$). Additionally, the transwell assay showed that the miR-877-3p inhibitor suppressed the motility of BC cells, including cell migration and invasion (Figures 2F-I, $P < 0.001$).

DISCUSSION

Globally, BC accounts for approximately 1/3 of all malignancies in women, and is responsible for about 15% of cancer-related deaths [4]. Multiple studies have indicated that SNPs in miRNAs contribute to the pathogenesis and progression of BC by altering miRNA function. MiR-877-3p has been identified as differentially expressed in BC patients [14]. An independent study further displayed that the rs1264440 polymorphism residing within the miR-877 promoter region functionally modulates miR-877 transcriptional output [19]. These findings suggest that the rs1264440 SNP may contribute to the pathogenesis and progression of BC by altering miR-877-3p expression.

SNPs are the most common variation in the human genome [21]. Multiple studies have indicated that SNPs in miRNAs contribute to the BC pathogenesis and progression by altering miRNA function. This case-control study indicated that rs1264440 AA genotype was associated with a reduced BC risk compared to GG genotype. BC patients carrying rs1264440 AA genotype displayed lower miR-877-3p expression. This is consistent with the study performed by Wang et al., who found that rs1264440 TT genotype carriers had lower miR-877 levels in HCC [19]. These results suggested that rs1264440

was correlated with BC susceptibility by regulating miR-877-3p level. Stratified analysis revealed that BC patients carrying A allele exhibited smaller tumour size, lower TNM stage, absence of metastasis, and negative expression of ER, PR, and HER2. These findings suggest that the rs1264440 A allele carriers contribute to reduced BC progression and phenotype. Nurses and advanced practice providers could use this genetic information, combined with environmental risk factors, to identify high-risk individuals for enhanced surveillance, health education, and earlier referral.

Aberrant expression of miRNAs is closely related to the occurrence and progression of cancers [22, 23]. The current study revealed an up-regulation of miR-877-3p in BC patients relative to HC, consistent with the conclusions of Khadka et al. [14]. They revealed that miR-877-3p is overexpressed in BC. Intriguingly, these findings contrast with those reported in other cancer types, suggesting a cancer-specific role for miR-877-3p. For instance, miR-877-3p is downregulated in bladder cancer [24]. This may be due to tissue-specific regulatory mechanisms and variability in downstream targets. ROC analysis indicated that miR-877-3p not only acts as a potential biomarker for distinguishing BC patients from HC subjects, but also stratifies stage III patients from TNM I+II stages. Although survival data were unavailable in this cohort, analysis using the UALCAN database indicated that high miR-877-3p expression was significantly linked with poor BC overall survival. This observation supports the clinical relevance of miR-877-3p as a potential prognostic biomarker. These findings suggest that miR-877-3p acts as a diagnostic or staging biomarker for BC.

Functional assays perfomed by the authors of the current article revealed that miR-877-3p inhibitor significantly suppressed the proliferation, migration, and invasion of BC cells, which was consistent with the function of miR-877-3p for SCCC [16]. Xiang et al. found that suppressed miR-877-3p could inhibit the gastric cancer cells through SOCS2/Jak2/Stat3 axis [25]. However, this contradicts the findings of Fukuda et al., who observed that miR-877-3p overexpression suppressed viability, motility, and infiltration in oesophageal squamous cell carcinoma (ESCC) cell lines by targeting ZNF177 [26]. Additionally, Xie and colleagues found that Platycodin D could inhibit the proliferation, migration, and invasion of non-small cell lung cancer by upregulating miR-877-3p [27]. These results collectively indicate that miR-877-3p appears to be cancer-type dependent by regulating downstream target gene repertoires and cellular signaling networks. The context-dependent functional duality of miR-877-3p is probably dictated by its distinct downstream targets and the unique cellular microenvironment.

Limitations of the study. Although the present research obtained significant findings, this study has several limitations. Firstly, although the sample size was large enough to provide sufficient statistical power for the primary correlation analyses, it was not sufficient for the disease-stratified analyses. The single-centre nature of the study may have limited the generalizability of the findings. Future investigations should be conducted through large-scale, multi-centre collaborations to validate and extend the results obtained. Secondly, the study was performed exclusively on a single-centre and ethnic cohort. The association between this SNP and BC phenotype is influenced by population-specific genetic diversity and environmental factors. Future research will focus on multi-ethnic cohorts to validate the findings and elucidate heterogeneity. Additionally, while the study provides preliminary functional evidence, the scope of the cellular experiments conducted was limited. Therefore, a more comprehensive functional characterization is imperative in future research to confirm the findings, and to provide deeper mechanistic insights. Finally, while the study identifies a significant genetic association, it does not address the fundamental gap in understanding the mechanistic role of the miR-877-3p locus, particularly the rs1264440 variant, in BC pathogenesis. Future research must therefore focus on deciphering its functional impact on downstream signaling pathways and cellular phenotypes. Future studies should also translate these molecular insights into nursing practice via risk assessment tools, education, and care pathways, fostering translation to enhance patient outcomes and nursing quality.

CONCLUSIONS

In conclusion, the study showed that miR-877-3p was increased in BC patients. The rs1264440 GG genotype may promote BC risk by upregulating miR-877-3p which, in turn, enhances the viability, migration, and invasion of BC cells. Furthermore, this genotype was correlated with unfavourable clinicopathological features in TNM stage III patients, including larger tumour size, metastatic status, and positive expression of ER, PR, and HER2. These findings indicate that miR-877-3p rs1264440 may serve as a potential therapeutic target and prognostic biomarker for BC.

REFERENCES

1. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. Br J Radiol. 2022;95(1130):20211033.
2. Xu Y, Gong M, Wang Y, et al. Global trends and forecasts of breast cancer incidence and deaths. Sci Data. 2023;10(1):334.
3. Katsura C, Ogunmwonyi I, Kankam HK, Saha S. Breast cancer: presentation, investigation and management. Br J Hosp Med (Lond). 2022;83(2):1–7.
4. Xiong X, Zheng LW, Ding Y, et al. Breast cancer: pathogenesis and treatments. Signal Transduct Target Ther. 2025;10(1):49.
5. Jiang B, Bao L, He S, et al. Deep learning applications in breast cancer histopathological imaging: diagnosis, treatment, and prognosis. Breast Cancer Res. 2024;26(1):137.
6. Bahreini F, Rayzan E, Rezaei N. microRNA-related single-nucleotide polymorphisms and breast cancer. J Cell Physiol. 2021;236(3):1593–605.
7. Du R, Flynn MJ, Mahe K, et al. miRNA modules for precise, tunable control of gene expression. Mol Cell. 2026;86(1):194–212 e7.
8. Jelski W, Okrasinska S, Mroczko B. microRNAs as Biomarkers of Breast Cancer. Int J Mol Sci. 2025;26(9).
9. Lameirinhas A, Torres-Ruiz S, Garrido-Cano I, et al. Involvement of microRNAs-449/FASN axis in response to trastuzumab therapy in HER2-positive breast cancer. Mol Med. 2025;31(1):116.
10. Sirek T, Sirek A, Zmarzly N, et al. Impact of MiRNAs on Wnt-related gene activity in breast cancer. Sci Rep. 2025;15(1):16211.
11. Ghanbari M, Karari K, Altalebi SAR, et al. The role of microRNAs in breast cancer: Diagnostic and therapeutic implications. Int J Biol Macromol. 2025;321(Pt 4):146386.
12. Gao H, Zhang C. miR-3133 is an unfavorable prognosis factor and tumor suppressor in colon cancer. Funct Integr Genomics. 2023;23(2):132.
13. Lin Y, Wang YY, Xu ZB, et al. miRNAs Associated with Axillary Lymph Node Metastasis in Breast Cancer: A Systematic Review and Meta-Analysis. Ann Surg Oncol. 2025.
14. Khadka VS, Nasu M, Deng Y, et al. Circulating microRNA Biomarker for Detecting Breast Cancer in High-Risk Benign Breast Tumors. Int J Mol Sci. 2023;24(8).

15. Watters M, Walker CA, Murray AA, et al. Uterine miR-877-3p and let-7a-5p are increased during simulated menstruation in a mouse model. Reprod Fertil. 2022;3(1):L3–l5.
16. Mendaza S, Fernández-Irigoyen J, Santamaría E, et al. Understanding the Molecular Mechanism of miR-877-3p Could Provide Potential Biomarkers and Therapeutic Targets in Squamous Cell Carcinoma of the Cervix. Cancers (Basel). 2021;13(7).
17. Chen M, Li Z, Cao L, et al. miR-877-3p inhibits tumor growth and angiogenesis of osteosarcoma through fibroblast growth factor 2 signaling. Bioengineered. 2022;13(4):8174-86.
18. Miao Y, Liang X, Chen J, et al. Transfer of miR-877-3p via extracellular vesicles derived from dental pulp stem cells attenuates neuronal apoptosis and facilitates early neurological functional recovery after cerebral ischemia-reperfusion injury through the Bclaf1/P53 signaling pathway. Pharmacol Res. 2024;206:107266.
19. Wang H, Wang B, Wang T, Fan R. A genetic variant in the promoter region of miR-877 is associated with an increased risk of hepatocellular carcinoma. Clin Res Hepatol Gastroenterol. 2020;44(5):692-8.
20. Yang C, Liu Y, Gai L, et al. Artesunate regulates malignant progression of breast cancer cells via lncRNA TUG1/miR-145-5p/HOXA5 axis. PLoS One. 2025;20(8):e0329490.
21. Arancibia T, Morales-Pison S, Maldonado E, Jara L. Association between single-nucleotide polymorphisms in miRNA and breast cancer risk: an updated review. Biol Res. 2021;54(1):26.
22. Morales-Gonzalez S, Calaf GM, Acuna M, et al. The miR-146a Single Nucleotide Polymorphism rs2910164 Promotes Proliferation, Chemoresistance, Migration, Invasion, and Apoptosis Suppression in Breast Cancer Cells. Cells. 2025;14(8).
23. Polcaro G, Liguori L, Manzo V, et al. rs10204525 binding to miR-4717-3p modulates PD-1 expression and predicts the development of immune-related adverse events in patients with advanced cancer treated with anti-PD-1/PD-L1 therapy. J Immunother Cancer. 2025;13(12).
24. Li S, Zhu Y, Liang Z, et al. Up-regulation of p16 by miR-877-3p inhibits proliferation of bladder cancer. Oncotarget. 2016;7(32):51773-83.
25. Xiang X, Ma HZ, Chen YQ, et al. GM-CSF-miRNA-Jak2/Stat3 Signaling Mediates Chemotherapy-Induced Cancer Cell Stemness in Gastric Cancer. Front Pharmacol. 2022;13:855351.
26. Fukuda T, Baba H, Okumura T, et al. miR-877-3p as a Potential Tumour Suppressor of Oesophageal Squamous Cell Carcinoma. Anticancer Res. 2023;43(1):35–43.
27. Xie Z, Zhou Z, Wang S, et al. Platycodin D inhibits non-small cell lung cancer bone metastasis by inducing ferroptosis through miR-877-3P/PNMA5 regulatory axis. Phytomedicine. 2025;149:157534.