MiR-577 suppresses epithelial-mesenchymal transition and metastasis of breast cancer by targeting Rab25

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Introduction
Breast cancer (BC) is one of the most common malignant tumors in women. In 2014, approximately 14 million new cases and 8.2 million cancer deaths were recorded worldwide.1 Before BC fully develops, it undergoes usual epithelial hyperplasia, atypical ductal hyperplasia, ductal carcinoma in situ, and invasive carcinoma.2 Approximately 90% of patients with BC die of metastasis as a result of multiple steps and factors. Epithelial-mesenchymal transition (EMT) definitively causes invasion and distant migration of primary tumors.3

Epithelial-mesenchymal transition is a developmental process wherein epithelial cells lose their original properties and acquire migratory traits of mesenchymal cells.4 Moreover, EMT could promote invasion and metastasis. A crucial step in EMT is the downregulation of E-cadherin. Recent studies identified that microRNAs (miRNAs) are critical factors in EMT-related tumor metastasis.

miRNAs are a series of small non-coding RNAs that could negatively regulate gene expression through complementarity to 3′-untranslated regions (UTRs) of messenger RNAs (mRNAs).5–7 Recent studies have proven that miRNAs participate in biological processes, including cell proliferation, apoptosis, and metastasis.8 Moreover, studies have discovered the multifaceted function of miRNAs in BC metastasis. MiR-200c inhibits metastasis of BC tumors.

Abstract
Background: MicroRNAs can act as both tumor suppressor genes and oncogenes and participate in cell proliferation, metastasis, and apoptosis. Low levels of miR-577 are found in several cancers, for example, thyroid carcinoma, glioblastoma, and hepatocellular carcinoma. The aim of this study was to investigate the effect of miR-577 on breast cancer (BC).
Methods: The relative level of miR-577 in 120 BC tissues and cells was detected by real-time PCR. MDA-MB-231 cells with upregulated miR-577 and MCF-7 cells with downregulated miR-577 were established. Transwell invasion assays were used to examine the invasiveness of cells. Epithelial-mesenchymal transition (EMT) markers were evaluated by immunofluorescence and Western blot. Targeted combinations of miR-577 and Rab25 were analyzed by luciferase assays. Xenograft models were used to examine the effect of miR-577 on BC metastasis.
Results: MiR-577 expression was significantly suppressed in BC tissues. Tumor size, tumor stage, and lymphatic metastasis were attributed to miR-577 expression. Moreover, miR-577 overexpression strongly inhibited the invasiveness and EMT of BC cells in vitro. MiR-577 directly regulated Rab25 in BC. Rab25 upregulation by miR-577 decreased the levels of E-cadherin and increased the levels of Vimentin. Notably, Rab25 knockdown inhibited BC invasion; however, an increase in Rab25 counteracted the invasive effect of miR-577 in BC.
Conclusion: Results indicated that miR-577 suppressed EMT by inhibiting Rab25 expression in BC. MiR-577 and Rab25 are considered potential targets of BC treatment.
through the downregulation of Foxf2.9 MiR-335 suppresses the migration and invasion of BC cells by targeting EphA4.10 MiR-452 inhibits the migration and invasion of BC cells by directly targeting RAB11A.11 MiR-140-5p inhibits angiogenesis and invasion by targeting VEGF-A in BC.12 Hence, miRNAs and target genes could comprise an intricate network and play critical roles in BC metastasis.

Recent reports have demonstrated that miR-577 deregulation is related to carcinogenesis. MiR-577 could inhibit tumorigenesis of hepatocellular carcinoma via β-catenin.13 Moreover, miR-577 inhibits glioblastoma growth through the Wnt signaling pathway.14 However, the functions of miR-577 in BC remain unclear.

In this study, we elucidated the downregulation of miR-577 in BC specimens and cells. However, the upregulation of miR-577 reduced cell invasiveness. MiR-577 downregulation also inhibited E-cadherin expression in BC cells by regulating Rab25. We conducted this study to facilitate the development of effective therapies for BC.

## Methods

### Patients and tissues

We obtained BC tissues (T) and adjacent non-tumor (ANT) tissues from patients at the Affiliated Hospital of Qingdao University from 2015 to 2016. All specimens were collected and frozen at −80°C. None of the patients had received radiotherapy or chemotherapy before surgery. Informed consent was obtained from each patient. The Research Ethics Committee of Weifang Medical University approved the study.

### Cell culture

MCF-10A, MCF-7, MDA-MB-231 (MDA231), T47D, and MDA-MB-453 were obtained from American Type Culture Collection (Rockville, MD, USA). MCF-10A cells were cultured in Dulbecco’s modified Eagle medium (DMEM)/F12, which contained 10% fetal bovine serum (FBS), 20 ng/mL epidermal growth factor, 0.1 mg/mL cholera toxin, 10 mg/mL insulin, and 500 ng/mL hydrocortisone. MCF-7 cells were cultured in minimum Eagle’s medium containing 10% FBS and 1% sodium pyruvate. T47D, MDA-MB-453, and MDA231 cells were respectively cultured in RPMI1640 and DMEM containing 10% FBS, at 37°C in an atmosphere of 5% CO₂.

### Real-time PCR

Stem-loop quantitative (q)PCR was performed to determine the relative level of miR-577. U6 levels were used for normalization. We used TRIzol to extract RNA from fresh BC tissues and cells. We synthesized complementary DNA with the total RNA using a M-MLV Reverse Transcriptase Kit (Promega, Madison, WI, USA). qPCR was carried out using an Applied Biosystems 7500 Real-time PCR System (Foster City, CA, USA). The following RT sequences were used: (5’-GTCGATATCCAGTGCGTCCAGGTATTC GCACCTGGATACGACCAGGTA-3’), forward primer (5’-ACCGCGCGCGGCTAGATAATATTGG-3’), and reverse primer (5’-ATCCAGTGCAGGCGCAGG-3’).

### Cell transfection

MiR-577 and negative control (NC) mimics, miR-577 inhibitor NC, miR-577 inhibitor, and small interfering RNAs (siRNAs), including Rab25 siRNA, were synthesized by GeneChem (Shanghai, China). We used Lipofectamine 2000 (Thermo Fisher Scientific, Waltham, MA, USA) to transfect the cells following the manufacturer’s protocol. Rab25 complementary DNA was confirmed by DNA sequencing and was cloned into pcDNA3.1.

### Cell proliferation assays

For cell counting kit 8 (CCK-8; Solarbio, Beijing, China) assays, approximately 2 × 10⁴ cells were seeded in 96-well plates. After culture for 24, 48, 72, 96, and 120 hours, cell proliferation capacity was tested by CCK-8 assay. Cell growth curves were plotted using the absorbance value at each time point.

### Cell invasion assay

The invasion assay was assessed using Transwell chambers with Matrigel. After transfection, the cells were added to the upper chamber and incubated at 37°C for 24 hours. A total of 450 μL of complete medium (RPMI 1640, 0.1% bovine serum albumin, and 25 mM 4-[2-hydroxyethyl]-1-piperazinethanesulfonic acid) with 3% FBS was placed in the bottom well. Cells that invaded through the membrane were fixed, stained, photographed, and counted overnight. All assays were repeated in triplicate.

### Immunofluorescence

A total of 1 × 10⁴ cells were planted in 24-well plates on slides overnight and cultured in serum-free medium for 12 hours. Cells were fixed using 4% paraformaldehyde for 25 minutes. Subsequently, the cells were permeabilized with 0.1% Triton X-100 and blocked with 5% bovine serum albumin for 30 minutes at 37°C. The cells were primarily incubated for 12 hours at 4°C. On the next day, cells were washed with phosphate buffered saline and incubated with Alexa Fluor 594 or Alexa Fluor 488-conjugated
secondary antibodies for 1 hour at 37°C. The nucleus was stained with 4',6-diamidino-2-phenylindole for 15 minutes. Finally, the pictures were collected and analyzed using a fluorescence microscope.

**Luciferase assays**

Cells (3.5 × 10⁴) were planted in 24-well plates in triplicate overnight. A total of 100 ng mutant (MUT) or wild-type (WT) pGL3-Rab25-3’UTR and 1 ng of pRL-TK Renilla plasmid were transiently transfected according to the manufacturer’s protocol. Renilla and luciferase signals were measured using the Dual-Luciferase Reporter Assay Kit (Promega).

**Western blot**

We used Western blot to analyze protein expression. Cell or tissue protein lysates were electrophoresed on 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis and transferred onto polyvinylidene fluoride membranes. We incubated the membranes with the following primary antibodies, obtained from Cell Signaling Technology (Danvers, MA, USA): Rab25, E-cadherin, Vimentin, and β-actin. We then incubated the membranes with horseradish peroxidase-linked anti-rabbit immunoglobulin G and anti-mouse immunoglobulin G antibodies (Cell Signaling Technology). All assays were repeated in triplicate.

**Statistical analysis**

We analyzed all statistical data using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). A chi-square test was used to analyze the relevance between miR-577 and Rab25 expression and clinicopathological features. A Student’s paired two-tailed t-test or analysis of variance was used to analyze statistical significance. P < 0.05 was considered significant in all cases.

**Results**

*miR-577 expression was decreased in breast cancer (BC) tissues and cells and is related to clinicopathological features*

We hypothesized the potential significance of miR-577 in BC development and progression. We first detected

![Figure 1](image-url) **Figure 1** Expression of miR-577 was decreased in breast cancer (BC) tissues and cells and inhibited migration and invasion of BC cell lines in vitro. (a) Relative expression of miR-577 in BC and adjacent non-tumor (ANT) tissues and (b) various BC cells. (c) Cell proliferation in MDA231 and MCF-7 was evaluated using cell counting kit 8 assay (NC—MDA231/NC, —miR-577—MDA231/miR-577, and —anti-miR—MCF-7/NC, —anti-miR-577—MCF-7/anti-miR-577). (d) Invasion ability of MDA231 was analyzed by Transwell assay (quantification of penetrating cells, left). Transwell invasion assay of MCF-7/anti-miR-577 and MCF-7/NC cells (quantification of penetrating cells, right). (e) Morphological changes of MDA231 and MCF-7 after transfection. (f) Expression changes in E-cadherin and Vimentin after transfection. (g) Immunofluorescence staining. *P < 0.05. OD, optical density.
miR-577 expression in 120 pairs of human BC and ANT tissues. MiR-577 was suppressed almost twofold in BC compared to ANT tissues (Fig 1a). The relationship between miR-577 and the clinicopathological characteristics of the BC patients is summarized in Table 1. Correlations between miR-577 and age and the expression levels of estrogen receptor, progesterone receptor, and Her2 were not statistically significant. However, the results showed that miR-577 was closely related to tumor size, tumor stage, Ki67 expression, and lymph node metastasis.

MiR-577 expression in BC cells was considerably reduced compared to MCF-10A (Fig 1b). MCF-7 cells showed the highest expression of miR-577 compared to MCF-10A (Fig 1b). MCF-7 cells showed the highest expression of miR-577 compared to MCF-10A (Fig 1b).

MiR-577 inhibited the invasion of BC cells

To determine the function of miR-577 in BC progression, MDA231 cells were stably transfected with miR-577 mimics or NC and MCF-7 were transfected with miR-577 inhibitor (anti-miR-577) or NC. The proliferation rates in cells with upregulation and downregulation of miR-577 were unchanged (Fig 1c). We assessed the effect of miR-577 on the invasiveness of MDA231 and MCF-7. MiR-577 upregulation could remarkably decrease the invasiveness of MDA231 compared to NC (Fig 1d left). MiR-577 downregulation in MCF-7 significantly increased its invasiveness (Fig 1d right). These results suggest that miR-577 inhibits the invasion of BC cells.

MiR-577 reversed epithelial-mesenchymal transition (EMT) of BC cells

To investigate whether miR-577 overexpression prevented BC cell invasion by inhibiting EMT, we observed the morphological changes in BC cells. MDA231/miR-577 could induce significant morphological changes, transforming from a spindle to a cobblestone shape. MCF-7/anti-miR-577 showed a contrary effect (Fig 1e). Western blot analysis was used to detect E-cadherin and Vimentin in all cells. E-cadherin expression was increased in MDA231, while Vimentin expression decreased in MDA231/miR-577 cells compared to MDA231/NC cells (Fig 1f, left). In MCF-7/anti-miR-577 cells, the expression of E-cadherin was downregulated and Vimentin upregulated (Fig 1f, right). The same results were observed after immunofluorescence staining (Fig 1g). As a result, miR-577 repressed the EMT phenotype in BC.

MiR-577 directly regulated Rab25

We excavated target genes using TargetScan bioinformatics prediction software (Whitehead Institute for Biological Research, Cambridge, UK), and the results proved that Rab25 is a target gene of miR-577 (Fig 2a). In addition, we tested the expression levels of Rab25 in MDA231/miR-577 and MDA231/NC cells. Our results showed that the protein level of Rab25 significantly decreased with transient miR-577 expression (Fig 2b), suggesting the important function of Rab25 in miR-577-induced cells. Rab25 expression in MCF-7/anti-miR-577 and MCF-7/NC cells was simultaneously tested, and the protein level of Rab25 significantly increased with transient miR-577 downregulation. Rab25 mRNA levels also significantly increased with transient miR-577 downregulation (Fig 2c). To prove if the predictive binding site of miR-577 on the 3′-UTR of Rab25 was responsible for this regulation, we cloned the WT or MUT Rab25 3′-UTR downstream of a luciferase reporter gene. Moreover, we co-transfected WT or MUT Rab25 vector and miR-577 or anti-NC into 293T cells. The co-transfection of WT Rab25 3′-UTR and miR-577 vector into 293T cells markedly reduced luciferase activity compared to NC and miR-577. The inverse results were observed in 293T cells, which were co-transfected with anti-miR-577 and WT Rab25 3′-UTR (Fig 2d), suggesting that miR-577
directly targets the 3'-UTR of Rab25 mRNA. The results indicate that miR-577 downregulates Rab25 expression by binding its 3'-UTR.

To further confirm that miR-577 directly binds with Rab25, miR-577 and NC were transfected in at least 12 hours. Rab25 was decreased in MDA231/miR-577 compared to MDA231/NC and reached the minimum level at 48 hours (Fig 2e). A similar result was observed in MCF-7 cells (Fig 2e). Moreover, an inverse correlation was observed among the expression levels of miR-577 and Rab25, E-cadherin, and Vimentin in 10 tested clinical specimens (Fig 2f,g). These findings confirm that miR-577 directly regulates Rab25.

**Rab25 participated in EMT-related invasion via miR-577**

To explore whether Rab25 influences EMT-related invasion via miR-577, we transfected RNA interference Rab25 gene in MDA231 cells. Western blot detected Rab25 expression and resembled the EMT markers, and E-cadherin levels were increased with highly efficient knockdown, whereas Vimentin protein levels were decreased to a certain extent (Fig 3a). In particular, Rab25 suppression induced cell morphology, from a spindle to a cobblestone shape (Fig 3b), consistent with the effect of miR-577. The invasiveness of MDA231 cells transfected with siRNA...
fragments was assessed using Transwell assay. The results indicated that Rab25 knockdown significantly impaired cell motility (Fig 3c). We transfected Rab25 and miR-577 in MDA231 cells to determine whether Rab25 would offset the suppressing effect of miR-577. MDA231 cells were cotransfected with NC or miR-577 and pcDNA3.1 or pcDNA3.1-Rab25. Rab25 overexpression can reciprocally neutralize, as shown by the morphological changes (Fig 3d). Vimentin was positively regulated, whereas E-cadherin was negatively regulated, along with the restoration of Rab25, as shown by Western blot analysis (Fig 3e). Transwell assays were performed to investigate the invasion of MDA231 cells. Reduction in the invasiveness initiated by miR-577 in MDA231 cells was counteracted by Rab25 expression (Fig 3f). The results suggest that Rab25 is a functional target gene of miR-577.

**miR-577 overexpression and Rab25 reduction inhibited lung colonization of BC cells in SCID mice**

To further investigate the effect of miR-577 and Rab25 on tumor metastasis in vivo, we adopted SCID mice with BC tumor xenografts. MDA231/NC, MDA231/miR-577, Scr/MDA231, and SiRab25/MDA231 cells were subcutaneously injected into each mouse. After eight weeks, all mice were sacrificed to harvest their xenografts and lungs. The metastatic nodules were smaller in the lungs of SCID mice injected with SiRab25/MDA231 or MDA231/miR-577 compared to Scr/MDA231 and MDA231/NC groups (Fig 4a,b). Rab25 expression in the xenograft was lower in SCID mice injected with MDA231/miR-577 and SiRab25/MDA231 cells compared to MDA231/NC and Scr/MDA231 (Fig 4c). We also detected miR-577 expression in tumors in SCID mice injected with

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**Figure 3** Rab25 participated in epithelial-mesenchymal transition (EMT)-related invasion in breast cancer cells via miR-577. (a) Changes in E-cadherin and Vimentin levels, (b) morphological changes, and (c) relative cell invasion of MDA231 after transfection with small interfering Rab25 (siRab25) and control group transfection with scrambled-siRNA (Scr). (d) Morphological changes of MDA231. (e) Expression of Rab25 and EMT-related markers transfected with different plasmid. (f) MDA231 invasion using Transwell assay. *P < 0.05.
MiR-577 targets Rab25 to suppress EMT

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Figure 4 MiR-577 overexpression and Rab25 reduction inhibited lung colonization of breast cancer (BC) cells in SCID mice. (a) Lung metastasis nodes in SCID mice implanted with MDA231/NC, MDA231/miR-577, scrambled-siRNA (Scr)/MDA231, and small interfering Rab25 (siRab25)/MDA231 cells visualized by hematoxylin and eosin staining. (b) The number of metastatic lung nodes was calculated. (c) Rab25 expression in MDA231 transfected with different plasmid. (d) miR-577 expression was tested in SCID xenograft tumors. NC, negative control.

MDA231/NC, MDA231/miR-577, Scr/MDA231, and SiRab25/MDA231 cells. MiR-577 expression was remarkably increased in SCID mice injected with MDA231/miR-577 and siRab25/MDA231 cells (Fig 4d). All of these results congruently indicate that miR-577 inhibits lung colonization of BC cells in SCID mice.

Discussion

Previous studies have shown that miRNAs can take effect as either oncogenes or tumor suppressor genes, resulting in oncogenesis and progression.\(^{15}\) Moreover, one study suggested that miR-577 is downregulated in colorectal cancer specimens and cells. Restoration of miR-577 significantly suppresses proliferation and induces a G0/G1 cell cycle arrest in colorectal cancer cells.\(^{16}\) The relative expression of miR-577 is lower in hepatocellular carcinoma tissues than in ANT. Low expression of miR-577 is related to large tumor size and advanced tumor node metastasis stage.\(^{13}\) Consistent with previous findings, we discovered that miR-577 expression is markedly decreased in BC tissues compared to expression in paired ANT and miR-577, which serves as a tumor suppressor gene in BC.

Two primary factors in human cancers, especially for malignant tumors, are metastasis and invasion, of which EMT is a fundamental step. MicroRNA interprets an important role in the EMT of BC. MiR-520c-3p can
negatively regulate EMT by targeting IL-8 and suppresses the invasion and migration of BC.

Our results prove that miR-577 reverses EMT in BC cells.

Rab25 is frequently amplified in cancers and is implicated in solid tumors. Rab25 expression enhances the aggressiveness of a subset of BC cells. Mitra et al. showed that Rab25 acts as an oncogene in luminal B BC and is associated with snail-driven EMT. Our results show that Rab25 influences the EMT-related invasion of BC cells. MiRNAs could negatively target gene expression through complementarity to 3'UTRs of mRNAs and miR-577 downregulated Rab25 expression. In short, the overexpression of Rab25 abolished the inhibitory effect of miR-577 on the invasion of BC cancer.

In summary, our findings imply that miR-577 downregulation might result in the increased expression of Rab25, which promotes invasion and metastasis in BC cells in vitro. We might reasonably conclude that miR-577 inhibits Rab25 and both may be suitable as potential therapeutic targets of BC.

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Disclosure

No authors report any conflict of interest.

References

1 McGuire S. World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015. Adv Nutr 2016; 7: 418–9.
2 Pinder SE, Ellis IO. The diagnosis and management of pre-invasive breast disease: Ductal carcinoma in situ (DCIS) and atypical ductal hyperplasia (ADH)—current definitions and classification. Breast Cancer Res 2003; 5: 254–7.
3 Guarino M. Epithelial-mesenchymal transition and tumour invasion. Int J Biochem Cell Biol 2007; 39: 2153–60.
4 Kalluri R, Weinberg RA. The basics of epithelial-mesenchymal transition. J Clin Invest 2009; 119: 1420–8 (Published erratum appears in J Clin Invest 2010;120:1786).
5 Ventura A, Jacks T. MicroRNAs and cancer: Short RNAs go a long way. Cell 2009; 136: 586–91.
6 Calin GA, Croce CM. MicroRNA-cancer connection: The beginning of a new tale. Cancer Res 2006; 66: 7390–4.
7 Sun L, Zhang B, Liu Y, Shi L, Li H, Lu S. MiR125a-5p acting as a novel Gab2 suppressor inhibits invasion of glioma. Mol Carcinog 2016; 55: 40–51.
8 Iorio MV, Croce CM. microRNA involvement in human cancer. Carcinogenesis 2012; 33: 1126–33.
9 Zhang T, Wan JG, Liu JB, Deng M. MiR-200c inhibits metastasis of breast tumor via the downregulation of Foxf2. Genet Mol Res 2017. https://doi.org/10.4238/gmr16038971
10 Dong Y, Liu Y, Jiang A, Li R, Yin M, Wang Y. MicroRNA-335 suppresses the proliferation, migration, and invasion of breast cancer cells by targeting EphA4. Mol Cell Biochem 2018; 439: 95–104.
11 Li W, Li G, Fan Z, Liu T. Tumor-suppressive microRNA-452 inhibits migration and invasion of breast cancer cells by directly targeting RAB11A. Oncol Lett 2017; 14: 2559–65.
12 Lu Y, Qin T, Li J et al. MicroRNA-140-5p inhibits invasion and angiogenesis through targeting VEGF-A in breast cancer. Cancer Gene Ther 2017; 24: 386–92.
13 Wang LY, Li B, Jiang HH, Zhuang LW, Liu Y. Inhibition effect of miR-577 on hepatocellular carcinoma cell growth via targeting beta-catenin. Asian Pac J Trop Med 2015; 8: 923–9.
14 Zhang W, Shen C, Li C et al. miR-577 inhibits glioblastoma tumor growth via the Wnt signaling pathway. Mol Carcinog 2016; 55: 575–85.
15 Chen CZ. MicroRNAs as oncogenes and tumor suppressors. N Engl J Med 2005; 353: 1768–71.
16 Jiang H, Ju H, Zhang L, Lu H, Jie K. microRNA-577 suppresses tumor growth and enhances chemosensitivity in colorectal cancer. J Biochem Mol Toxicol 2017; 31 (6): e21888.
17 Tang CP, Zhou HJ, Qin J, Luo Y, Zhang T. MicroRNA-520c-3p negatively regulates EMT by targeting IL-8 to suppress the invasion and migration of breast cancer. Oncol Rep 2017; 38: 3144–52.
18 Xue Y, Xu W, Zhao W, Wang W, Zhang D, Wu P. miR-381 inhibited breast cancer cells proliferation, epithelial-tomesenchymal transition and metastasis by targeting CXCR4. Biomed Pharmacother 2017; 86: 426–33.
19 Cheng KW, Agarwal R, Mitra S et al. Rab25 increases cellular ATP and glycogen stores protecting cancer cells from bioenergetic stress. EMBO Mol Med 2012; 4: 125–41.
20 Mitra S, Federico L, Zhao W et al. Rab25 acts as an oncogene in luminal B breast cancer and is causally associated with Snail driven EMT. Oncotarget 2016; 7: 40252–65.