Silencing miRNA-1297 suppresses the invasion and migration of prostate cancer cells via targeting modulation of PTEN and blocking of the AKT/ERK pathway

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Abstract. Phosphatase and tensin homolog (PTEN) loss is a major contributing factor of prostate cancer (PC). miRNA-1297 was reported to serve role in various cancer types; however, the potential roles of miRNA-1297 in PC had not been investigated. In the present study, tumor and adjacent tissues were collected from patients with PC. The gene expression level of miRNA-1297 was measured via polymerase chain reaction. Results indicated that the miRNA-1297 was overexpressed in tumor tissues from PC patients and in PC cell lines. miRNA-1297 also contributed toward the progression of PC. PTEN was confirmed as the direct target of miRNA-1297 and bound with miRNA-1297 via four binding sites. The miRNA-1297 level was negatively associated with the PTEN level. Silencing miRNA-1297 or overexpression of PTEN significantly inhibited the cell migration and invasion. In addition, the AKT/ERK pathway was also inhibited following silencing of miRNA-1297 or overexpression of PTEN. Taken together, the results indicated that silencing miRNA-1297 exerted inhibitory effects on the invasion and migration of PC cells via modulating PTEN and blocking of the AKT/ERK pathway. The results of the present study provided a novel strategy for treatment of prostate cancer cells.

Introduction

Prostate cancer (PC) has become one of the leading causes of mortality in males across the world (1-5). The risk factors of PC are complicated, including genetic factors, age, external exposure and chronic urinary tract infections (6). The incidence of PC has increased markedly over recent years. For example, the incidence of PC increased by nearly one-third between 2015 and 2018 (7). Furthermore, numerous patients with PC exhibit no symptoms and are therefore frequently misdiagnosed (8). It is urgent to elucidate the intrinsic mechanism underlying PC and to find efficient diagnosis methods and treatments for PC.

miRNA is one of the non-protein coding RNAs, which is capable of regulating gene expression at the post-translational level. miRNA functions via binding its target gene, resulting in inhibition of gene expression (9). miRNAs were confirmed as vital functional molecules and are involved in various types of cancer (10-13). The interplay between miRNA and gene expression is complicated. One miRNA often has more than one target gene and one gene is also regulated by different miRNAs (14). As reported previously, miRNAs also serve vital roles in PC (15,16). miR-28-5p was found to exert tumor suppressor effects by mediating SREBF2, which had been confirmed to be involved in PC (15). miR-636 also served a role in bone metastasis of PC via targeting STAB1, MBNL2 and TNS1 (16). Therefore, it may be a promising way to identify the miRNAs that are associated with PC.

Phosphatase and tensin homolog (PTEN) is a common tumor suppressor gene which has been found in many tumor types (17,18). As reported, PTEN was also found to be involved in PC (19). Additionally, loss of PTEN expression indicated an unfavorable prognosis in PC (20,21). The anomaly of DNA methylome and transcriptome was caused by PTEN loss at different stages of PC (22). A previous study indicated that miRNA-1297 promoted cell proliferation via targeting PTEN in testicular germ cell tumors (23). Furthermore, concurrent activation of the ERK/AKT pathway is implicated in PC progression (24). Additionally, PTEN served as a negative regulator of these pathways in PC, and PTEN loss may activate the ERK/AKT pathway and induce PC progression (24). However, the molecular basis of the association between miRNA-1297/PTEN and ERK/AKT is unknown. To further study the intrinsic mechanism of PC, the potential role of miRNA-1297/PTEN axis in PC was investigated in the present study.

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Materials and methods

Cell culture and transfection. RWPE-2 (CRL-11610), DU145 (HTB-81), VCaP (CRL-2876), PC-3 (CRL-1435) and LNCaP (CRL-1740) cells were purchased from American Type Culture Collection (ATCC). DU145, PC-3 and LNCaP cells were cultured in RPMI-1640 medium (ATCC®30-2001™). RWPE-2 cells were cultured in K-SFM (ATCC®17005-042™) and VCaP cells were cultured in Dulbecco's modified Eagle's medium (Gibco; Thermo Fisher Scientific, Inc.). All cells were cultured in medium with fetal bovine serum (FBS; ATCC®30-2020™; 10%) and gentamicin (Gibco; Thermo Fisher Scientific, Inc.; 50 mg/ml) at a density of $2x10^4$/ml in an incubator in an atmosphere with 5% CO_2 at 37˚C. After reaching 70% confluence, the cells were transfected with 10 nM miRNA-1297 inhibitor (Shanghai GenePharma, Inc.; 5'-CACCTGAATTACTTGAA-3'), NC inhibitor (Shanghai GenePharma, Inc.; 5'-ATACTCAAGCTTCTGAC-3') or PTEN-overexpression plasmid (Shanghai GenePharma, Inc.) using Lipofectamine 2000 (Invitrogen; Thermo Fisher Scientific, Inc.), according to the manufacturer's protocols. In brief, the mixture of Lipofectamine 2000 and miRNA-1297 inhibitor or PTEN plasmid was incubated for 10 min at room temperature. Next, the mixture was added into medium and incubated at 37˚C with cells for 48 h. Subsequently, cells were used for the follow-up experiments.

Collection of clinical samples. The PC tissues and matched para-cancerous normal tissues were collected at the North China University of Science and Technology Affiliated Hospital between January 2016 and December 2017. The distance between the healthy and the cancer tissue was within 5 cm and was confirmed by HE staining. A total of 90 patients who were diagnosed by histopathological examination were enrolled in this study and all patients provided written informed consent. All patients were male and the mean age was 57.2±7.1 (range, 50-79) years. The inclusion criteria were as follows: Primary prostate cancer confirmed by the pathology, without surgery, chemotherapy, radiotherapy or other treatment (25). The exclusion criteria were as follows: Recurrent prostate cancer, treated by surgery, radiotherapy or chemotherapy previously, combined with infectious diseases, malignant tumors, severe liver and kidney disease, pulmonary fibrosis, bone metabolic diseases, secondary renal hypertension, systemic immune diseases and malignant tumor complications (25). The present study was approved by the Ethics Committee of North China University of Science and Technology affiliated Hospital (Approval number 2016-0311).

Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay. MirVana™ miRNA isolation kit (Ambion) was used for the total RNA extraction from tissues and cells. DNA synthesis was performed using TaqMan™ MicroRNA Reverse Transcription kit (kit no. 4366596; Thermo Fisher Scientific, Inc.) or 1st Strand cDNA Synthesis kit (kit no. RR036A; Takara Bio, Inc.). Reverse transcription was performed at 37˚C for 15 min and 85˚C for 5 sec. ABI SYBR® Premix Ex Taq™ II (RR037B; Takara Bio, Inc.) was used for quantification of the gene expression levels of PTEN and miRNA-1297. The 7500 system (Applied Biosystems) was applied for the RT-PCR assay. β-actin served as the internal control. The miRNA-1297 primer (MBS825976) was designed and purchased from MyBioSource company. The primer sequences for PTEN were as follows: Forward, 5'-CGGCAGCATCAAATGTTTCAG-3' and reverse, 5'-AACTGGCAGGTAGAAGGCAACTC-3'. U6 was used as the control and the primer sequences were as follows: Forward, 5'-CTCGCTTCGGCAGCACA-3' and reverse, 5'-AACGCTTCACGAATTTGCGT-3'. The following thermocycling conditions were used: 95˚C for 5 min, followed by 40 cycles of 95˚C for 5 sec and 60˚C for 34 sec. The gene expression level were calculated using the $2^{-\Delta\Delta Ct}$ method (26).

Cell viability assay. RWPE-2 cells were seeded into a 96-well plate following transfection with miRNA-1297 inhibitor for 24 or 48 h. Next, 200 μl medium was added to each well, with 10 μl freshly prepared MTT (5 mg/ml) and 100 μl dissolved formazan liquid (dissolved in PBS). Subsequently, the optical density (OD) at 490 nm of each well was measured. The ratio of viable cells was calculated by dividing OD readings of the transfected groups into the control group.

Transwell assay. The cell migration and invasion were investigated using a Transwell assay. A total of 200 μl PC cells were suspended in serum-free RPMI-1640 medium at a density of $1x10^6$ cells/ml, prior to being added into the upper chambers. Subsequently, 500 μl RPMI-1640 medium containing 10% FBS was added into the lower chambers. Following incubation for 24 h at 37˚C, cells that had migrated to the bottom surface of the insert were fixed with 4% paraformaldehyde for 10 min and stained with 0.1% crystal violet for 30 min both at room temperature. The cells numbers in five randomly selected fields were counted under an inverted microscope (magnification, x40; Olympus Corporation). For the cell invasion assay, the upper chamber was coated with Matrigel (BD Biosciences) and the other procedures were the same with cell migration assay.

Luciferase reporter assay. The luciferase reporter assay was performed using the Dual-Luciferase Reporter assay system kit (Promega Corporation; E1910), according to the manufacturer's protocols. 293T cells were used as the tool cell to detect the binding of miRNA-1297 and PTEN. As predicted in the targetscan website (http://www.targetscan.org/), there are mainly four binding sites between miRNA-1297 and PTEN. The wild-type (WT) or mutant (MUT) gene located at positions 41-47, 1261-1268, 2619-2626 and 3800-3807 of the PTEN 3'-UTR was cloned into the reporter vector (Beyotime Institute of Biotechnology; D2112). Next, 10 nM the negative control (NC; BBI Life Sciences; 5'-UCACAACCUCCUAGAAAGAGUAGA-3') or miRNA-1297 mimic (BBI Life Sciences; 5'-UUCAAGUAAUUCAGGUG-3') and 100 ng reporter plasmid were co-transfected into the 293T cells. After 48 h, the dual-luciferase reporter assay system (Promega Corporation) was applied for the measurement of the relative luciferase activity. Firefly luciferase activity was normalized to that of *Renilla* luciferase activity.

Western blotting. Total protein was extracted using RIPA lysis buffer (Boster Biological Technology; cat. no. AR0105).

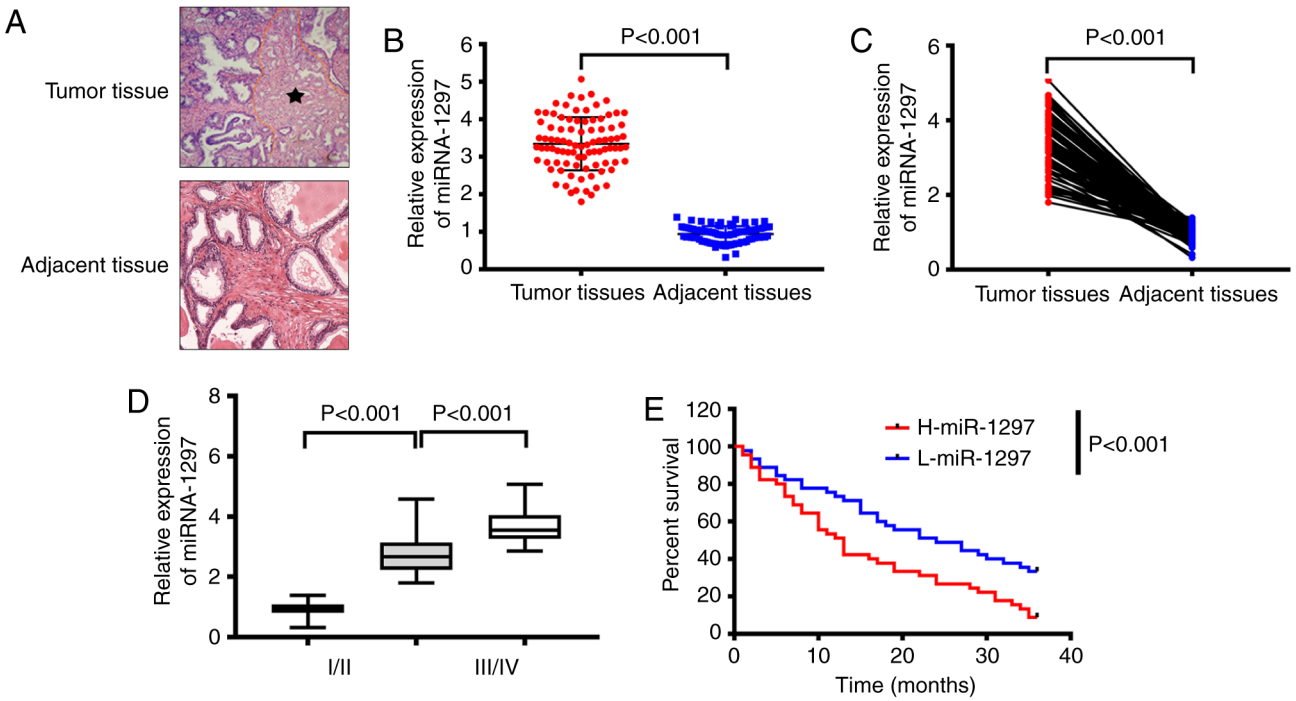

Figure 1. miRNA-1297 is overexpressed in PC tissues and is associated with the progression of PC. (A) PC tissues and matched para-cancerous normal tissues were obtained from 90 patients. The cancer tissue and para-cancerous normal tissue were identified by HE staining. Black star: PC tissue (magnification, x100). (B and C) The miRNA-1297 level in the PC tissue and para-cancerous normal tissue was investigated. (D) The samples were divided into subgroups according to the tumor stage, and the miRNA-1297 level in each subgroup was investigated and compared. Patients were divided into 2 groups according to the median miRNA-1297 expression. The patients with a relative miRNA-1297 expression of >3.285 were included in the high-expression group. The remaining patients were included in the low-expression group. (E) The overall survival rate of patients with high (H-miR-1297) or low miRNA-1297 (L-miR-1297) levels. PC, prostate cancer.

Next, the proteins were quantified using a BCA kit (Beyotime Institute of Biotechnology). A total of 20 μg protein (per lane) was loaded and separated by 10% SDS-PAGE. Next, the PVDF membranes were used for blotting the separated proteins and were then blocked with 5% skimmed milk for 1 h at room temperature. Subsequently, the membranes were incubated with the following primary antibodies: Anti-p-Akt antibody (dilution, 1:1,000; cat. no. ab38449; Abcam), anti-Akt antibody (dilution, 1:1,000; cat. no. ab32505; Abcam), anti-Erk antibody (dilution, 1:1,000; cat. no. 9102; Cell Signaling Technology, Inc.), anti-p-Erk (dilution, 1:1,000; cat. no. 4370; Cell Signaling Technology, Inc.), anti-E-cadherin antibody (dilution, 1:1,000; cat. no. 7559; Cell Signaling Technology, Inc.), anti-N-cadherin antibody (dilution, 1:1,000; cat. no. 3195; Cell Signaling Technology, Inc.), anti-MMP-2 antibody (dilution, 1:1,000; cat. no. 40994; Cell Signaling Technology, Inc.), anti-MMP-9 antibody (dilution, 1:1,000; cat. no. 13667; Cell Signaling Technology, Inc.) and anti-beta actin antibody (dilution, 1:2,000; cat. no. ab8226; Abcam) at 4˚C overnight. Next, the membranes were incubated with HRP-conjugated anti-rabbit IgG secondary antibody for 1 h at room temperature (dilution, 1:5,000; Sigma-Aldrich; cat. no. 12-348). β-actin served as the control. An enhanced chemiluminescence kit (Millipore) was used for visualization of the positive bands. ImageJ software (National Institutes of Health) was applied for quantification of band density.

Statistical analysis. All data in the present study were processed by SPSS software (version 19.0; IBM Corp.). All experiments were repeated at least 3 times. The data are presented as the mean ± standard deviation. The difference between groups was analyzed via student's t test or one-way analysis of variance, followed by Duncan's post hoc test. Paired Student's t-test was used for the comparison of miRNA-1297 expression in tumor tissues and adjacent tissues. Correlation analysis was performed using Pearson's correlation analysis. A survival curve was constructed using the Kaplan-Meier method, followed by the Log rank test. To construct the survival curve, patients were divided into 2 groups according to the median of miRNA-1297 expression (3.285). The patients with a relative miRNA-1297 expression of >3.285 were included in the high expression group and the remaining patients were included in the low expression group. P<0.05 was considered to indicate a statistically significant difference.

Results

miRNA-1297 is highly expressed in PC tissue. The present study first investigated the miRNA-1297 level in tumor tissues and para-carcinoma tissues. The results demonstrated that the miRNA-1297 level was higher in tumor tissues than that in para-carcinoma tissues (Fig. 1A and B). Furthermore, the miRNA-1297 level in tumor tissues from patients with stage I/II PC was higher than that in the non-cancerous tissues but lower than that in the tumor tissues at stage III/IV (Fig. 1C). Subsequently, the effects of miRNA-1297 on overall survival rates were investigated. As shown in Fig. 1D, the overall survival rates in patients with high miRNA-1297

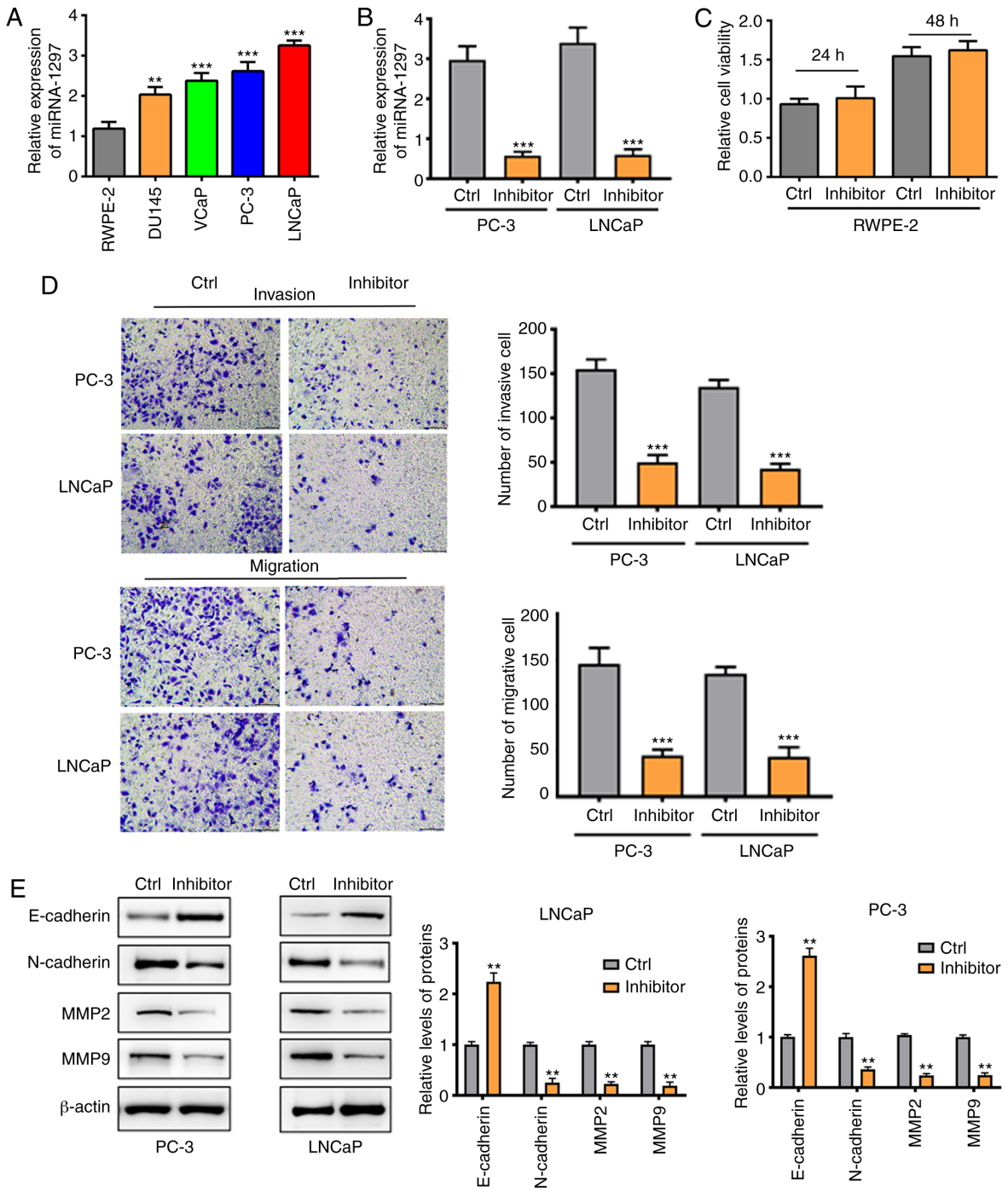

Figure 2. Role of silencing miRNA-1297 on cell migration and invasion. (A) The miRNA-1297 level in the different cell lines was investigated by PCR. **P<0.01 and ***P<0.001 vs. the RWPE-2 group. (B) The miRNA-1297 level in PC-3 and LNCaP cell lines prior to or following miRNA-1297 inhibitor transfection was investigated by PCR. Untransfected PC-3 and LNCaP cells served as the control groups. ***P<0.001 vs. control group. (C) The viability of RWPE-2 cells was assessed prior to or following miRNA-1297 inhibitor transfection. Untransfected RWPE-2 cells served as the control group. (D) The cell invasion and migration level in PC-3 cells and LNCaP cells prior to or following miRNA-1297 inhibitor transfection. ***P<0.001 vs. control group (magnification, x40). (E) The expression of metastasis-associated proteins (E-cadherin, N-cadherin, MMP-2 and MMP-9) in PC-3 and LNcaP cells prior to or following miRNA-1297 inhibitor transfection (**P<0.01 vs. control group). PCR, polymerase chain reaction.

expression were lower than that in patients with low miRNA-1297 expression.

miRNA-1297 is overexpressed in PC cells and silencing miRNA-1297 inhibits cell invasion and migration in PC-3 cells and LNCaP cells. To begin with, the miRNA-1297 level was measured in different PC cell lines. The results indicated that the miRNA-1297 level was notably increased in DU145, VCaP, PC-3 and LNCaP cancer cells, compared with normal RWPE-2 cells (Fig. 2A). As cell invasion and migration are important for cancer cells, the role of miRNA-1297 in cell invasion and migration was further investigated. An inhibitor was used to silence miRNA-1297 expression in cancer cells. As shown in Fig. 2B, the miRNA-1297 level was downregulated

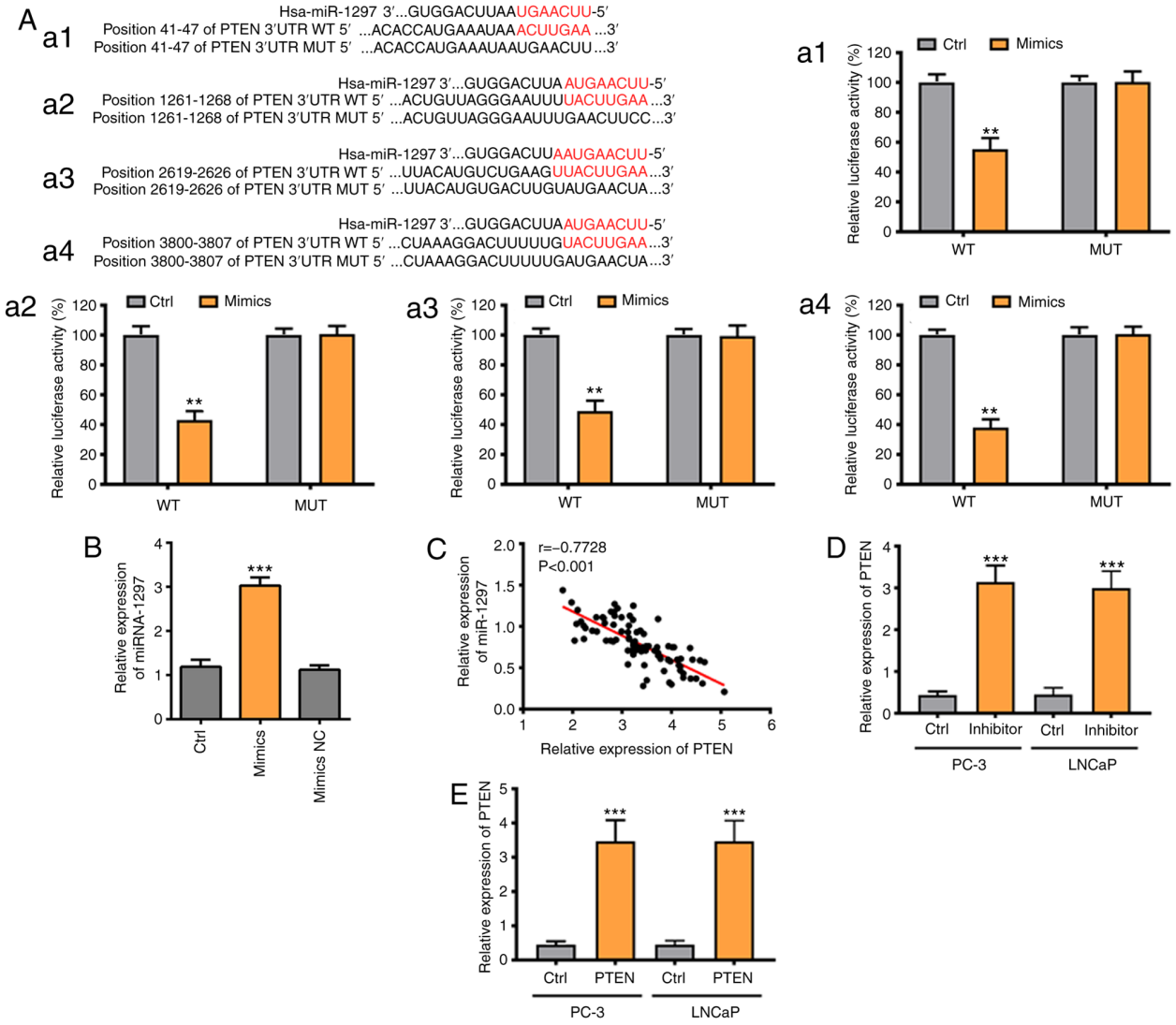

Figure 3. PTEN is validated as the target of miRNA-1297 and is inversely associated with miRNA-1297. (A) The binding sites of miRNA-1297 were predicted by Targetscan; 4 binding sites in PTEN were identified and each predicted binding site (a1, a2, a3 and a4) was verified by a luciferase reporter assay. (B) The miRNA-1297 expression in 293T cells was investigated prior to or following miRNA-1297 mimic transfection. Ctrl: 293T cell without transfection. Mimic NC: 293T cell transfected with negative control mimics. (C) miRNA-1297 expression was negatively associated with the PTEN level. (D and E) The PTEN level was investigated following miRNA-1297 inhibitor or PTEN-overexpression plasmid transfection. miRNA-1297 inhibitor and PTEN-overexpression plasmid transfection upregulated PTEN expression in PC-3 and LNCaP cells. Untransfected PC-3 and LNCaP cells served as the control group. **P<0.01 vs. control group; ***P<0.001 vs. control group. PTEN, phosphatase and tensin homolog.

in the inhibitor groups, suggesting that miRNA-1297 was silenced successfully. The safety of the miRNA-1297 inhibitor was assessed using RWPE-2 cells. As shown in Fig. 2C, transfection with the miRNA-1297 inhibitor did not influence the proliferation of RWPE-2 cells. Next, the cell migration and invasion were investigated. Results demonstrated that the number of migrated and invasive cells in the inhibitor group was significantly less than that in the control group (Fig. 2D). Furthermore, the protein expression of MMP-2, MMP-9, E-cadherin and N-cadherin was investigated. The Western blotting results indicated that silencing miRNA-1297 may inhibit PC metastasis by decreasing MMP-2, MMP-9 and N-cadherin expression (Fig. 2E).

miRNA-1297 is capable of targeting PTEN. As shown in Targetscan, PTEN was the predicted target of miRNA-1297 with four binding sites (Fig. 3A). The binding sites were all verified via a Luciferase Reporter Assay. The relative luciferase activity in the wild-type of PTEN and in the mimics group was the lowest among all the study groups and the luciferase activity remained unchanged in the remaining groups (Fig. 3A). These results confirmed that miRNA-1297 was able to bind to PTEN via four binding sites. PCR results also indicated that the PTEN level was negatively associated with the miRNA-1297 level in patients with PC (Fig. 3B). Furthermore, the PTEN level in the inhibitor group and the PTEN-overexpression group was markedly increased, compared with the control group (Fig. 3C and D). In conclusion, PTEN was the directive target of miRNA-1297.

Silencing miRNA-1297 inhibits cell invasion and migration of PC via upregulating PTEN and inhibiting the AKT/ERK pathway. As shown in Fig. 4A and B, cell migration and invasion were suppressed in the PTEN-overexpression group,

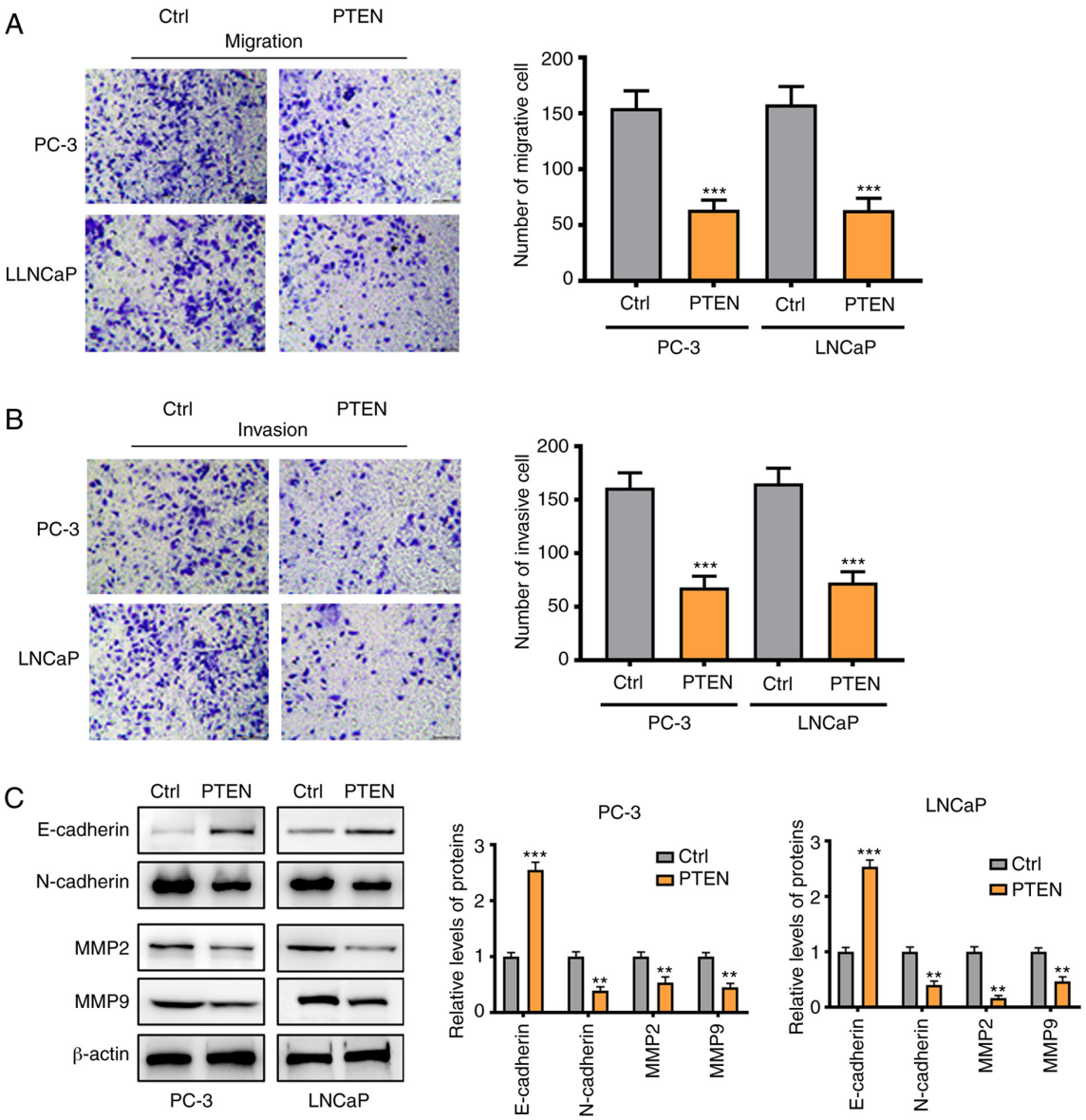

Figure 4. Role of PTEN-overexpression in cell migration and invasion. (A and B) The invasion and migration of PC-3 and LNcaP cells prior to or following PTEN transfection. Overexpression of PTEN exhibited a significant inhibitory effect on cell invasion and migration. (magnification, x40). **P<0.01, ***P<0.001 vs. control group. (C) The expression of metastasis-associated proteins (E-cadherin, N-cadherin, MMP-2 and MMP-9) in PC-3 and LNcaP cells prior to or following PTEN-overexpression. Untransfected PC-3 and LNCaP cells served as the control group. **P<0.01, ***P<0.001 vs. control group. PTEN, phosphatase and tensin homolog.

which was in accordance with the results in the miRNA-1297 inhibitor group (Fig. 2C and D). The Western blotting also yielded similar results. Following overexpression of PTEN, the MMP-2, MMP-9 and N-cadherin protein expression was significantly decreased (Fig. 4C). These results further indicated that PTEN was the downstream target of miRNA-1297. To investigate the signaling pathways influenced by miRNA-1297 and PTEN, the levels of AKT, ERK and their corresponding phosphorylated forms were also investigated in the present study. The expression of p-AKT and p-ERK were significantly inhibited by silencing miRNA-1297 while the total AKT and ERK levels remained unchanged (Fig. 5A). Similar results were found following overexpression of PTEN, and p-AKT and p-ERK expression was decreased in the PTEN-overexpression group (Fig. 5B). All these findings suggested that silencing miRNA-1297 inhibited cell invasion and migration via upregulation of PTEN and suppression of the AKT/ERK pathway.

Discussion

PC is one of the major causes of fatality in males and severely threatens the health of males (27). PTEN loss has been confirmed as a crucial contributor for PC (26-28). PTEN is associated with a poor prognosis and recurrence of PC (28-30). Luminal cells of the prostate, which have been confirmed to be the prime origin of PC, generated tumors with stronger aggressivity under the condition of PTEN loss (31,32). Furthermore, PTEN was also reported to induce abnormal methylome and transcriptome of DNA (22).

miRNA is confirmed as a crucial regulator in various cancer types via binding to its target genes. Regulation of

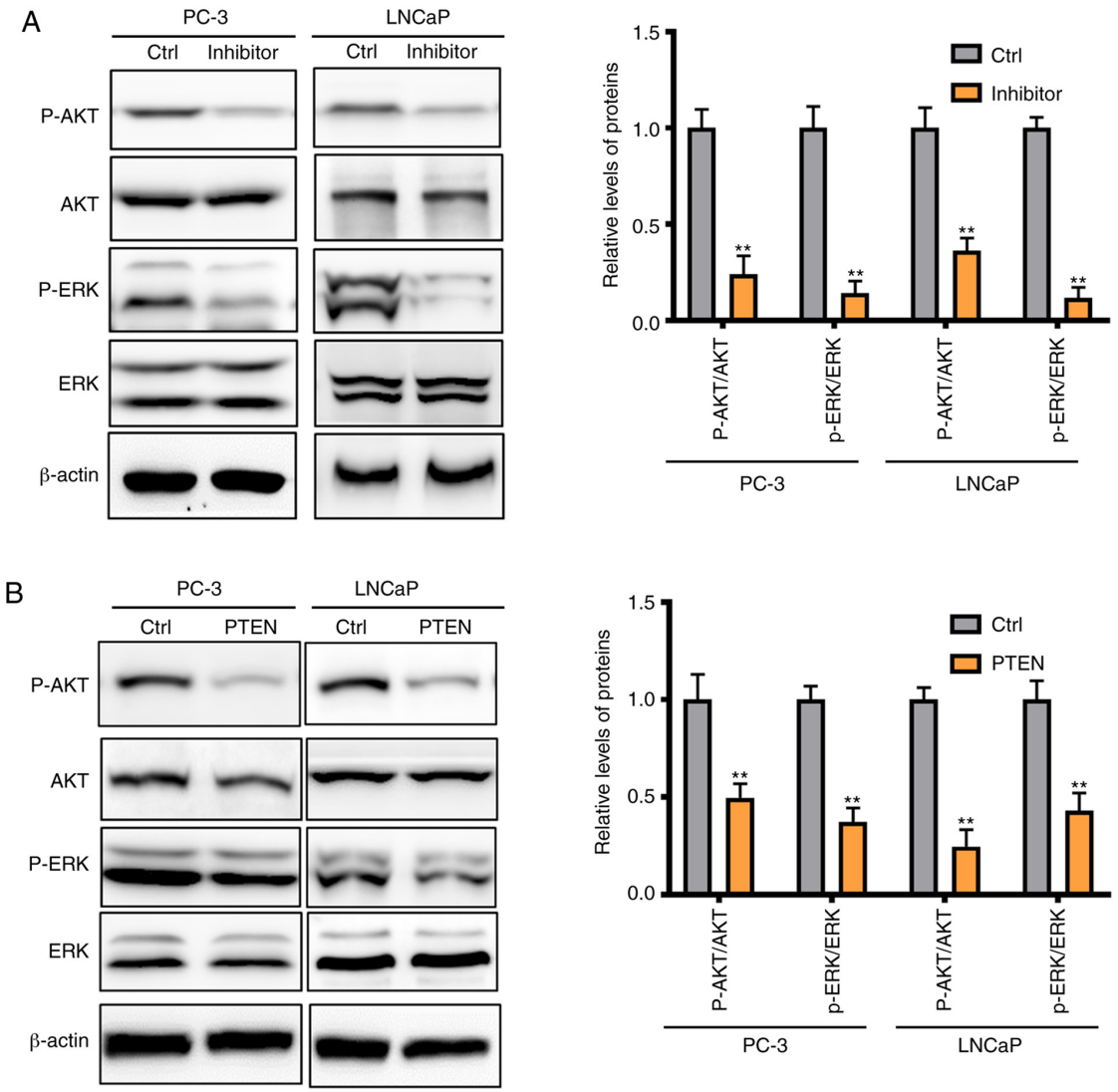

Figure 5. Silencing miRNA-1297 or overexpressing PTEN inhibits the ARK/ERK signaling pathway. (A and B) Following transfection of the miRNA-1297 inhibitor or the PTEN-overexpression plasmid, the p-AKT, AKT, p-ERK and ERK levels in PC-3 and LNCaP cells were measured by Western blotting. Untransfected PC-3 and LNCaP cells served as the control group. **P<0.01 vs. control group. PTEN, phosphatase and tensin homolog.

the gene expression resulting in alteration of cell behaviors, including cell apoptosis, proliferation, invasion and migration. Therefore, screening the miRNA, which serves as the regulator of PTEN, is of great significance for the treatment of PC. In the present study, the results of Targetscan revealed that miRNA-1297 may bind to PTEN via four binding sites. miRNA-1297 was reported to serve a role in various cancer types. For instance, miRNA-1297 promoted cell proliferation via targeting PTEN in germ cell tumors (23). miRNA-1297 also exerted a promotive effect on cervical carcinoma progression via targeting PTEN (33). Furthermore, miRNA-1297 was confirmed as a contributor toward oral squamous cell carcinoma progression via regulating PTEN (34). The present study revealed that miRNA-1297 was overexpressed in PC tissues. Furthermore, miRNA-1297 was upregulated in patients with stage III/IV PC, compared with those with stage I/II PC. The patients with higher miRNA-1297 level also had lower survival rates. These findings demonstrated that miRNA-1297 also acted as an oncogene that is involved in the progression of PC. The present study further investigated the miRNA-1297 level in different PC cell lines. It was found that miRNA-1297 level was significantly upregulated in all the cancer cells, particularly in PC-3 cells and LNCaP cells. The results indicated that miRNA-1297 was overexpressed in the hormone-sensitive PC LNCaP cell line and the hormone-insensitive PC cell lines, PC-3, VCaP and DU145. Subsequently, the experiments were performed using LNCaP (left supraclavicular lymph node derived, early stage of PC) and PC-3 (bone derived, poorly differentiated) cell lines, for the representation of different types and stages of PC. The miRNA-1297 expression in hormone-insensitive VCaP and DU145 cells was also upregulated, indicating that miRNA-1297 expression may serve a role in bone and brain metastases of PC. However, further research may be required. Taken together, the results of the present study revealed that miRNA-1297 served a broader role in different prostate cancer cells and may be a promising therapeutic target.

Cell proliferation and invasion are of great importance for cancer progression and numerous previous studied have reported that they are regulated by miRNA (35-38). The results

of the present study indicated that silencing miRNA-1297 inhibited cell migration and invasion in PC-3 cells and LNCaP cells. This suggested that miRNA-1297 was involved in PC cell migration and invasion.

PTEN was reported to be the directive target of miRNA-1297 in numerous cancer types (23,33,34). In the present study, the four binding sites predicted by Targetscan were confirmed via Luciferase Reporter Assay. The miRNA-1297 level was negatively associated with the PTEN level in patients with PC and silencing miRNA-1297 may upregulate PTEN in PC cells. In addition, overexpression of PTEN in PC cells significantly suppressed the cell migration and invasion. Based on these results, we hypothesized that miRNA-1297 was involved in the progression of PC via targeting PTEN. MMP-2, MMP-9, E-cadherin and N-cadherin were the metastasis-associated proteins which served important roles in the metastasis of PC (39). The results of the present indicated that miRNA-1297-silencing and PTEN-overexpression inhibited PC cell migration via suppressing MMP-2, MMP-9 and N-cadherin expression. These results were also consistent with those of previous reports (39,40).

The AKT/ERK pathway was highly expressed in PC and associated with an unfavorable prognosis (41,42). Additionally, previous studies confirmed that the AKT/ERK pathway was suppressed by PTEN (43-45). In the present study, the phosphorylation level of AKT and ERK were inhibited following silencing of miRNA-1297. These changes to the AKT and ERK pathway may be attributed to the upregulation of PTEN. These findings suggested that the AKT/ERK pathway was the downstream pathway of miRNA-1297/PTEN axis. Taken together, these results suggested that miRNA-1297-silencing restrained cell migration and invasion via blockage of the AKT/ERK pathway by targeting PTEN.

There are certain limitations to the present study. To begin with, only the miRNA-1297-silenced model was used and the overexpression of miRNA-1297 was not tested in the experiments. Furthermore, the role of miRNA-1297 was not further investigated in DU145 and VCaP cell lines. More cell models and more cell lines should be used in future studies.

In conclusion, miRNA-1297 was found to be overexpressed in PC tissues and associated with the progression of PC. Silencing miRNA-1297 was confirmed to inhibit cell migration and invasion via blocking of the AKT/ERK pathway by targeting PTEN. These findings provided evidence of developing a novel strategy for the treatment of PC in the future.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

LW conceived and designed the experiments, performed the experiments, analyzed the data, contributed reagents/materials/analytical tools, wrote the manuscript, prepared figures and tables, and reviewed drafts of the paper. JG performed the experiments, analyzed the data and prepared figures and tables. YZ performed the experiments. SK conceived and designed the experiments, and reviewed drafts of the paper. LW and SK confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of North China University of Science and Technology affiliated Hospital (approval no. 2016-0311).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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