miR-342-3p suppresses cell migration and invasion in preeclampsia by targeting platelet-derived growth factor receptor α

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Abstract. miR-342-3p expression was increased in the placentas of women with preeclampsia (PE) according to previous examinations; the mechanism underlying the development and progression of PE requires further investigation. The present study aimed to explore the mechanism and functionality of microRNA (miR)-342-3p in trophoblastic cells. The expression of miR-342-3p and platelet-derived growth factor receptor α (PDGFRA) in the placentas of 30 patients with PE and 30 normal controls was detected. In addition, HTR8/SVneo cells were transfected with miR-342-3p mimics, small interfering RNA (siR)-PDGFRA or their corresponding negative controls; then the proliferation, migration, invasion and the distribution of the cell cycle of these cells were analyzed. Additionally, a dual-luciferase reporter assay was performed. According to these analyses, the expression of miR-342-3p was significantly increased, while that of PDGFRA was significantly lower in the PE group compared with the normal group. Transfection with miR-342-3p mimics led to a significant decrease in cell proliferation, migration and invasion, and also affected the cell cycle. Furthermore, miR-342-3p mimics reduced the expression of PDGFRA; miR-342-3p overexpression also reduced the mRNA and protein levels of BCL-2 and Caspase-3. In addition, transfection of siR-PDGFRA exhibited similar effects to those of miR-342-3p mimics. Finally, PDGFRA was reported to be a direct target of miR-342-3p. In conclusion, miR-342-3p was proposed to inhibit the proliferation, migration, invasion and G1/S phase transition of HTR8/SVneo cells by suppressing PDGFRA. Our findings suggest that miR-342-3p may be a novel clinical indicator or prognostic marker for PE.

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Abbreviations: PE, preeclampsia; miRNA, microRNA; MSCs, mesenchymal stem cells; PDGFRA, platelet-derived growth factor receptorα; EVT, extravillous trophoblast; MAPK, mitogen-activated protein kinase

Key words: miRNA-342-3p, PDGFRA, PE

Introduction

Preeclampsia (PE) is a serious obstetric complication, and poses a serious threat to pregnant women and fetuses (1). The incidence of PE around the world is 2-8% (2). At present, PE is one of the main causes of maternal mortality. The pathogenesis of PE is not fully understood; thus, as an effective treatment for PE, pregnancies may be terminated. At present, PE is considered to be associated with dysfunction of the placenta (3), endothelial dysfunction (4) and abnormal increases in the apoptosis of trophoblasts (5). Of note, increased migration and invasion of trophoblastic cells, and decreased apoptosis have been hypothesized as potential therapeutic strategies for the treatment of PE; however, further investigation is required.

MicroRNAs (miRNAs/miRs) regulate the expression of their target genes in a negative manner. Numerous studies have shown that miRNAs are associated with cell migration, apoptosis, differentiation and proliferation (6-9). It was reported that the expression profiles of miRNAs in PE were markedly diverse in umbilical cord blood, maternal serum, placental samples and mesenchymal stem cells (MSCs) (10-14). miR-342-3p is one of the most highly expressed miRNAs in placentas from patients with PE (15), but its biological mechanism in PE remains unknown. miR-342-3p has been proposed to inhibit cell migration in cervical cancer (16), and suppress cell invasion and metastasis in lung cancer (17). Additionally, miR-342-3p may inhibit the progression of hepatocellular carcinoma through the nuclear factor-'B pathway (18). These findings suggest that miR-342-3p may serve vital roles in trophoblastic cell proliferation, migration and invasion in PE.

Gene expression profiling revealed that the expression levels of platelet-derived growth factor receptor α (PDGFRA) were decreased in PE patients compared with the normal group (19), yet the mechanism of PDGFRA in PE remains

unclear. TargetScan, microcosm and miRanda analyses identified PDGFRA as one of the putative target genes for miR-342-3p (20). Further study is needed to determine the association between miR-342-3p and PDGFRA in PE.

In the present study, we investigated the roles of miR-342-3p and PDGFRA in the placental tissues of patients with PE and in HTR8/SVneo cells. In our research, miR-342-3p was reported to reduce the migration and invasion of trophoblastic cells by suppressing PDGFRA. This suggested that miR-342-3p may be associated with the pathology of PE.

Materials and methods

Tissue collection. A total of 30 placentas were obtained from patients with PE and healthy controls who underwent cesarean section from January 2013 to September 2017. The age range of the patients was 23-39 years (mean age, 28.63±2.24 years). The diagnosis of PE was conducted as previously reported (21). The clinical data of patients was present in Table I. Patients with PE were characterized by high blood pressure and a high protein content in the urine. Tissues were quickly snap-frozen in liquid nitrogen during surgery and stored at -80˚C until use. Written informed consent was obtained from each patient. The exclusion criteria for the two groups included: Patients with essential hypertension or kidney disease, a history of drug or alcohol abuse half year prior to providing written informed consent. In addition, the patients with PE were pathologically analyzed by two specialists.

Cell culture. HTR8/SVneo cells were acquired from the American Type Culture Collection (ATCC). Cells were cultured in RPMI-1640 (Labdel Comércio de Produtos para Laboratório) and 10% fetal bovine serum (Labdel Comércio de Produtos para Laboratório) and 100 streptomycin mg/ml, 100 penicillin U/ml, in a humidified chamber at 37˚C with 5% CO_2.

Cell transfection. The cell line was transfected with miR-342-3p mimics and the negative control (Thermo Fisher Scientific, Inc., cat. no. 4464058.) at a concentration of 100 nmol/l. The cells were transfected using Lipofectamine™ 2000 (Invitrogen; Thermo Fisher Scientific, Inc.). The duration between transfection and subsequent analysis was 48 h. The sequence of the miR-342-3p mimics was 5'-GAAACUGGGCUCAAGGUGAGGGGUGCUAUCUGUGAUUGAGGGACAUGGUUAAUGGAAUUGUCUCACACAGAAAUCGCACCCGUCACCUUGGCCUACUUA-3'.

Knockdown of PDGFRA in the cell line. Small interfering RNAs (siRs) against PDGFRA (siRPDGFRA) and the control (scramble) were purchased from Santa Cruz Biotechnology, Inc. HTR8/SVneo cells were transfected with 20 µM siRPDGFRA or scramble siRNA utilizing Lipofectamine® 2000 (Invitrogen; Thermo Fisher Scientific, Inc.), according to the manufacturer's protocols.

Reverse transcription-quantitative PCR (RT-qPCR). Total RNA was extracted from tissues and cells utilizing TRIzol reagent (Thermo Fisher Scientific, Inc.). For detecting mRNAs, a PrimeScript™ RT reagent kit (Takara Bio, Inc., cat. no. RR047A) was used for RT; the experiment was performed as follows: Three times at 37˚C, 15 min for each time; and inactivation at 85˚C for 5 sec. RT was performed for miRNAs using an Mir-X™ miRNA First-Strand Synthesis kit (Takara Bio, Inc, cat. no. 638313) according to the manufacturer's protocols. qPCR was performed using an SYBR® qRT-PCR kit (Clontech Laboratories, Inc.) for mRNAs and miRNAs under the following thermocycling conditions: 94˚C for 4 min, followed by 40 cycles of 94˚C for 30 sec and 60˚C for 60 sec. The sequences of primers employed were presented in Table II. Relative miRNA expression levels were standardized to that of small nucleolar RNA U6, whereas that for relative mRNA expression was normalized to the expression levels of β-actin using the $2^{-\Delta\Delta Cq}$ method (22).

Western blot analysis. Cells were collected 48 h after transfection and prepared for lysis in radioimmunoprecipitation assay buffer (BioVision, Inc.). Protein concentration was determined via a bicinchoninic acid assay. Protein (50 µg/lane) was separated via 8% SDS-PAGE. Separated proteins were transferred to polyvinylidene fluoride membranes (EMD Millipore). The membranes were blocked with 5% fat-free milk powder for 2 h at room temperature, and then incubated with primary antibodies against PDGFRA (1:1,000; Santa Cruz Biotechnology, Inc., cat. no. sc-338), anti-BCL-2 (1:1,000; Abcam, cat. no. ab59348), anti-Caspase-3 (1:500; Abcam, cat. no. ab13847) and β-actin antibody (1:1,000; Santa Cruz Biotechnology, Inc., cat. no. sc-47778) at 4˚C overnight. Subsequently, the membranes were incubated with horseradish peroxidase-conjugated antimouse IgG (H+L) (1:10,000; Invitrogen; Thermo Fisher Scientific, Inc., cat. no. 62-6520) or anti-rabbit IgG (1:5,000; Invitrogen; Thermo Fisher Scientific, Inc., cat. no. 65-6122) antibody for 1 h at room temperature. The membranes were developed utilizing an ECL kit (Pierce; Thermo Fisher Scientific, Inc.) and visualized with X-ray film. Protein expression levels were standardized to those of β-actin. Data was analyzed by Quantity One version 4.62 software (Bio-Rad Laboratories, Inc.).

Cell proliferation analysis. To analyze cell proliferation, a Cell Counting Kit-8 (CCK-8) assay was conducted using a CCK-8 proliferation assay kit (Dojindo Molecular Technologies, Inc.) at 0, 12, 24 and 48 h following transfection, according to the manufacturer's protocols. Cells were transfected with mimics or negative control (ctrl group), or treated with Lipofectamine 2000 without miRNA molecules in the mock group. Cells ($1x10^5$) were seeded in 96-well plates for analysis. Then, 100 µl CCK-8 reagent was added to the well; at 2 h later, the absorbance was measured at 450 nm with a microplate reader.

Transwell invasion and migration assay. Cell invasion was investigated based on the capacity of the cells invade through the 8 mm pores of polycarbonate membranes. Briefly, HTR8/SVneo cells ($1.0x10^5$ cells/well) transfected with siRPDGFRA or scramble were placed in the upper chamber, and 600 µl of RPMI1640 medium with 10% fetal bovine serum was placed in the lower chamber. After incubating for 1 day under standard conditions at 37˚C, the cells on the upper surface that had not migrated were removed with a sterile cotton swab. Migrated cells were stained with 0.1% crystal violet for 5 min at room temperature and analyzed under a light microscope in 5 random fields (magnification, x200). The techniques used in

Table I. Clinical information of patients enrolled in the present study.

Variable	Control (n=30)	PE (n=30)	P-value
Age (years)	28.83±2.42	28.63±2.24	0.741
Gestational age (weeks)	38.67±0.55	36.07±0.78	<0.0001
Systolic pressure (mmHg)	113.03±9.02	156.67±5.80	<0.0001
Diastolic pressure (mmHg)	67.70±7.26	95.80±3.21	<0.0001
Proteinuria (g/24 h)	N/A	3.55±0.86	N/A

PE, preeclampsia.

Table II. Primers for reverse transcription-quantitative polymerase chain reaction.

Gene	Primer sequence (5'→3')
Hsa-miR-342-3p stem-loop primer	GCGCGTGAGCAGGCTGGAGAAATTAACCACGCGCACGGGT
Hsa-miR-342-3p forward primer	TCTCACACAGAAATCGC
Hsa-miR-342-3p reverse primer	GAGCAGGCTGGAGAA
U6 forward primer	GCTTCGGCAGCACATATACTAAAT
U6 reverse primer	CGCTTCACGAATTTGCGTGTCAT
PDGFRA forward primer	TTGAAGGCAGGCACATTTACA
PDGFRA reverse primer	GCGACAAGGTATAATGGCAGAAT
BCL-2 forward primer	CCGTTGGCCCCCGTTGCTTT
BCL-2 reverse primer	CTGGCGGAGGGTCAGGTGGA
Caspase-3 forward primer	CTCGGTCTGGTACAGATGTCGATG
Caspase-3 reverse primer	GGTTAACCCGGGTAAGAATGTGCA
β-actin forward primer	TGGCACCCAGCACAATGAA
β-actin reverse primer	CTAAGTCATAGTCCGCCTAGAAGCA

Hsa, homo sapiens; miR, microRNA; BCL-2, B-cell lymphoma 2; PDGFRA, platelet-derived growth factor receptor α.

the Transwell invasion assay were based on the cell migration assay; however, Matrigel was used.

Cell cycle assay. The cell cycle was analyzed via flow cytometry. After 48 h post-transfection, HTR8/SVneo cells were trypsinized in chilled PBS, fixed in 70% ethanol for 24 h at -20˚C, and then stained with propidium iodide for 10 min on ice. The samples were calculated using a flow cytometer and CellQuest Pro version 5.1 software (BD Biosciences).

miRNA target prediction and dual-luciferase reporter assay. TargetScan (version 6.0; http://www.targetscan.org/vert_60/), microcosm (version 1.1; https://tools4mirs.org/software/mirna_databases/microcosm-targets/) and miRanda (version August 2010; http://www.microrna.org/microrna/home.do) were used to predict miRNAs that could potentially target PDGFRA and identify possible binding regions. The fragment of the human PDGFRA with [wild type (wt)] or without [mutant (mut)] the miR-342-3p binding site at the 3'-untranslated region (3'-UTR) was cloned and inserted into the pGL3-basic luciferase report plasmid (Promega Corporation) to generate the luciferase reporter vectors, PDGFRA 3'-UTR-wt and PDGFRA 3'-UTR-mut. 293T cells (American Type Culture Collection) were treated in 96-well plates at 5,000 cells per well and incubated for 24 h at 37˚C with 5% CO_2 prior to transfection. Then, miR-342-3p mimics or miR-negative control was transfected into 293T cells using Lipofectamine 2000 with 100 ng of PDGFRA 3'-UTR-wt or PDGFRA 3'-UTR-mut, or 10 ng of pRL-TK *Renilla* plasmid (Promega Corporation). Following incubation for 48 h, the luciferase activities were determined with a Dual Luciferase Reporter System (Promega Corporation); *Renilla* luciferase was used for normalization.

Statistical analysis. SPSS 19.0 (IBM Corp.) was employed for statistical analysis. Data were presented as the mean ± standard deviation, and an independent samples t-test was conducted for comparisons between two groups; analysis was performed in a two-tailed manner. Cell viability was analyzed by one-way analysis of variance with a Student-Newman-Keuls post hoc test. P<0.05 was considered to indicate a statistically significant manner.

Results

Analysis of tissue samples. The clinical information of patients was presented in Table I. Compared with the control group, patients with PE exhibited significantly higher systolic pressure and diastolic pressure, notable

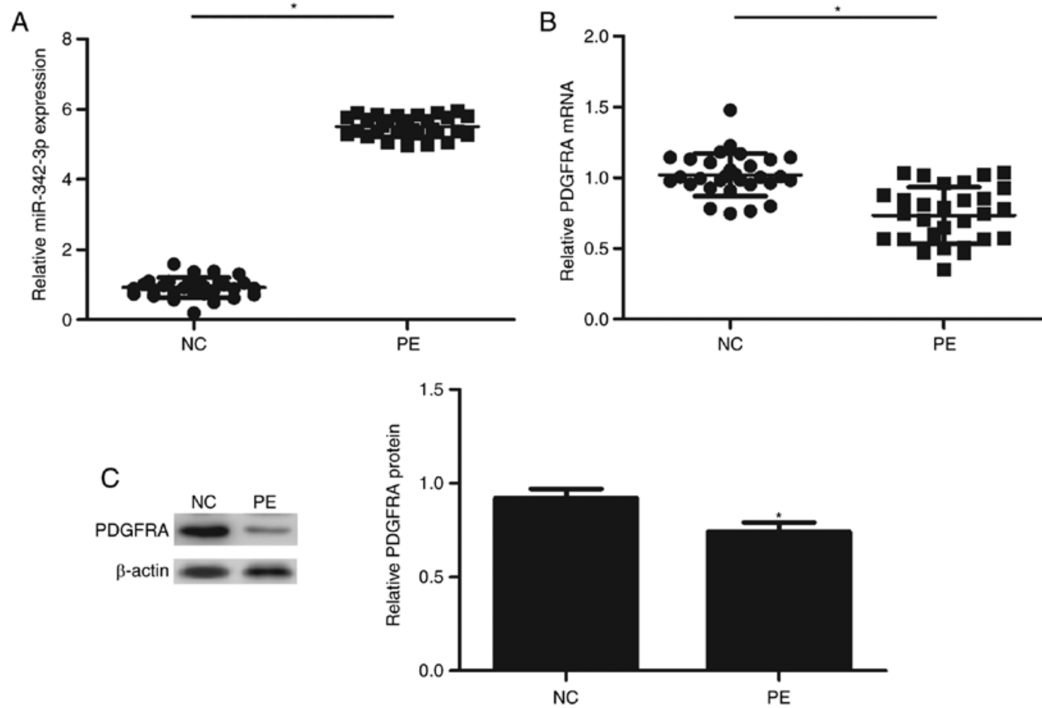

Figure 1. Expression of miR-342-3p and PDGFRA in the placental tissues from patients with PE and healthy controls. (A) miR-342-3p expression was upregulated in in the PE group. (B) PDGFRA was significantly downregulated in the PE group at the (B) mRNA and (C) protein levels. *P<0.05 vs. NC. miR, microRNA; NC. NC, negative control; PE, preeclampsia; PDGFRA, plateletderived growth factor receptor α.

proteinuria and a significantly shorter duration of gestation (P<0.0001).

Expression levels of miR-342-3p and PDGFRA in the two patient groups. The expression of miR-342-3p and PDGFRA was analyzed in tissues via RT-qPCR. As presented in Fig. 1, miR-342-3p was significantly upregulated in the PE group compared with the control group (P<0.01; Fig. 1A). On the contrary, the expression of PDGFRA was significantly decreased in patients with PE compared with the control (P<0.01; Fig. 1B and C).

miR-342-3p may affect cell proliferation and the cell cycle. Additionally, to explore the role of miR-342-3p, we performed a CCK-8 assay to determine the effects of miR-342-3p on cell proliferation. After 48 h, we confirmed that transfection of miR-342-3p mimics into cells significantly increased miR-342-3p expression compared with the control group (P<0.01; Fig. 2A). Furthermore, RT-qPCR and western blotting were conducted to investigate the effects of miR-342-3p on PDGFRA in a cell line. Overexpression of miR-342-3p resulted in a significant decrease in the expression of PDGFRA at the mRNA (P=0.001; Fig. 2B) and protein levels (P=0.006; Fig. 2D) compared with the control. Cell proliferation was significantly inhibited (P=0.006; Fig. 2E) after transfection with miR-342-3p mimics compared with the control. In addition, the effects of miR-342-3p on the cell cycle of HTR-8/SVneo cells were analyzed via flow cytometry. The results demonstrated that the percentage of HTR-8/SVneo cells in G1 phase significantly increased from 59.66±3.75% prior transfection to 66.94±2.39% at 48 h post-transfection (P=0.047; Fig. 3A). The percentage of cells in S phase was significantly reduced from 24.79±1.87% prior transfection to 21.07±1.36% following transfection (P=0.049; Fig. 3A).

miR-342-3p suppresses cell migration and invasion. Additionally, Transwell migration and invasion assays were conducted. As presented in Fig. 4, transfection with miR-342-3p mimics significantly inhibited cell migration (P=0.027; Fig. 4A) and invasion (P=0.022; Fig. 4B) compared with the control group.

miR-342-3p may affect the expression of BCL-2 and Caspase-3 in cells. Transfection with miR-342-3p mimics significantly reduced the mRNA (*P*=0.017; Fig. 5A) and protein expression (P=0.035; Fig. 5C and E) levels of BCL-2. On the contrary, overexpression of miR-342-3p significantly increased the mRNA (P=0.001; Fig. 5B) and protein expression (P=0.001; Fig. 5D and E) levels of Caspase-3.

siR-PDGFRA exhibits similar effects to miR-342-3p mimics. PDGFRA knockdown was performed in cells to its effects in PDGFRA in HTR-8/SVneo cells. After 48 h post-transfection, the mRNA and protein expression levels of PDGFRA were significantly decreased by 43.7±3.2% (P=1.56×10^{-4}; Fig. 2C) and 47.0±5.0% (P=3.08×10^{-4}; Fig. 2F), respectively, compared with the control. Additionally, PDGFRA knockdown significantly increased the percentage of HTR-8/SVneo cells in G1 phase from 56.63±1.40% prior to knockdown to 66.30±4.07% at 48 h following siR-PDGFRA transfection (P=0.018; Fig. 3B) compared with the control. Furthermore, cell proliferation (P=0.023; Fig. 2G), migration (P=0.01; Fig. 4C) and invasion (P=0.003; Fig. 4D) were significantly inhibited following PDGFRA knockdown compared with the control.

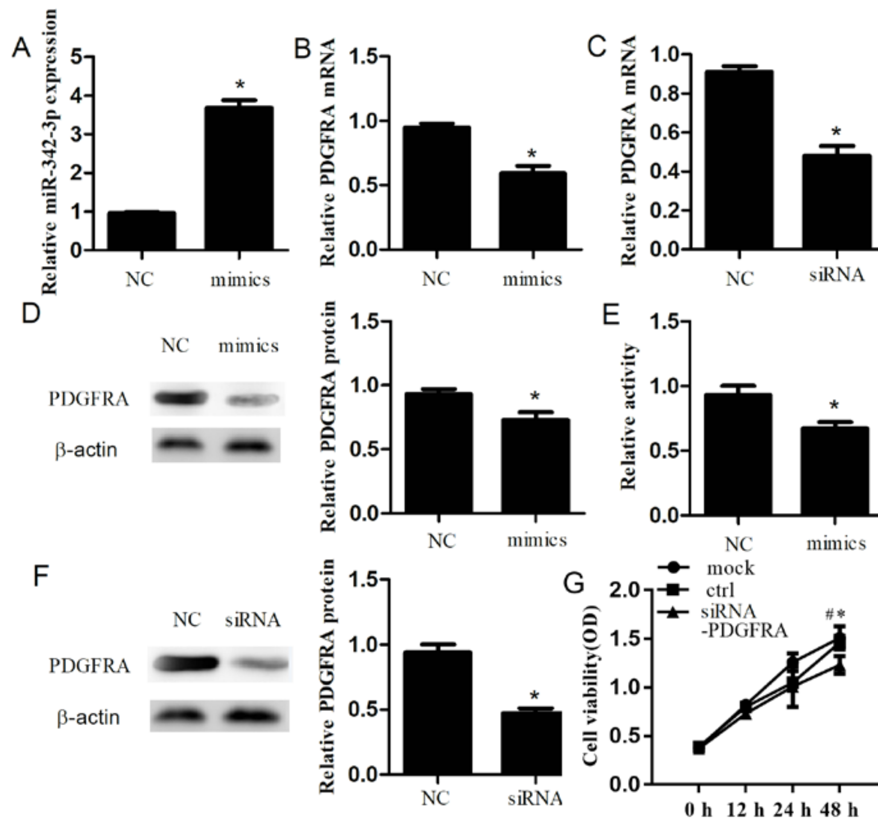

Figure 2. miR-342-3p regulates the proliferation of HTR-8/SVneo cells via PDGFRA. (A) Fold change in miR-342-3p expression in HTR-8/SVneo cells transfected with miR-342-3p mimics. (B) PDGFRA mRNA expression in HTR-8/SVneo cells decreased following transfection with miR-342-3p mimics. (C) Alterations in the mRNA expression levels of PDGFRA in HTR-8/SVneo cells 48 h after transfection with siRNA-PDGFRA and siRNA-NC. (D) Alterations in the protein expression levels of PDGFRA in HTR-8/SVneo cells transfected with miR-342-3p mimics or NC. (E) miR-342-3p mimics transfection reduced the proliferation of HTR-8/SVneo cells. (F) Alterations in the protein expression levels of PDGFRA in HTR-8/SVneo cells 48 h post-transfection with siRNA-PDGFRA or siRNA-NC. *P<0.05 vs. NC. (G) siRNA-PDGFRA suppressed the proliferation of HTR-8/SVneo cells. *P<0.05 vs. mock; #P<0.05 vs. ctrl group. Ctrl, control; miR, microRNA; NC. NC, negative control; OD, optical density; PDGFRA, platelet-derived growth factor receptor α; siRNA, small interfering RNA.

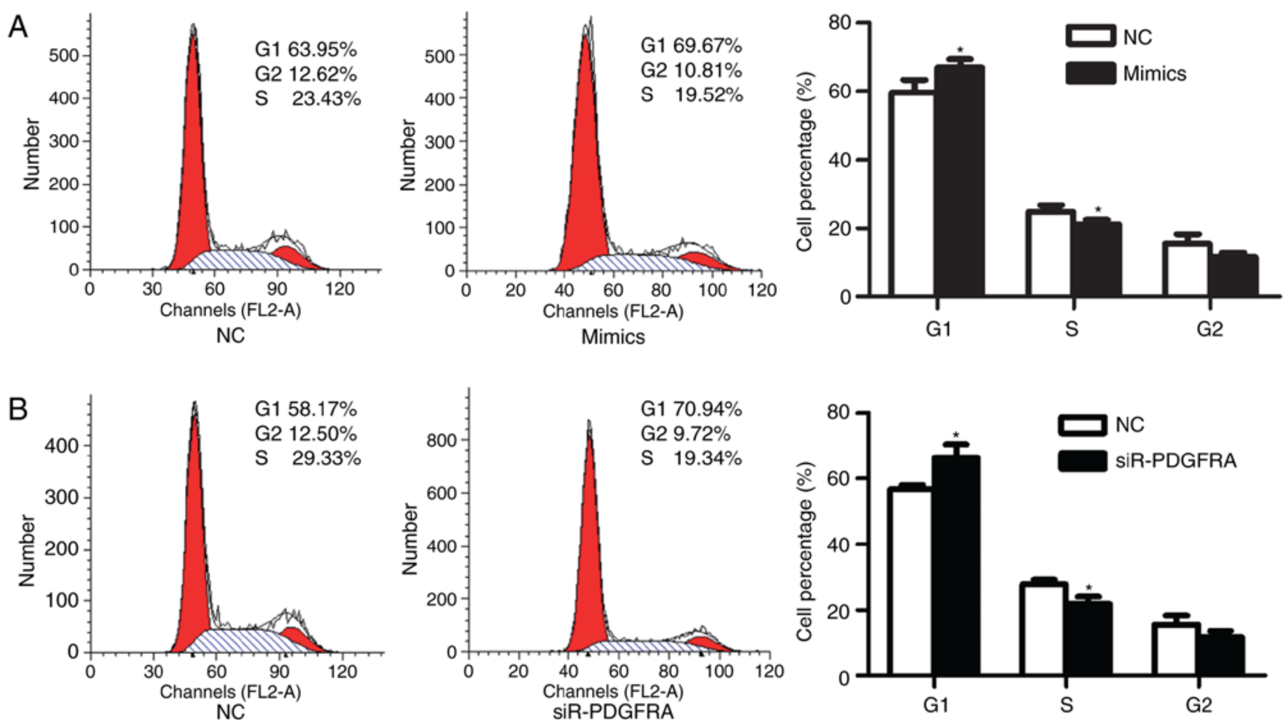

Figure 3. Effects of miR-342-3p mimics and siR-PDGFRA on the cell cycle of HTR8/SVneo cells. (A) Overexpression of miR342-3p inhibited G1/S phase transition. (B) Knockdown of PDGFRA promoted G1 phase arrest. *P<0.05 vs. NC. NC, negative control; PDGFRA, platelet-derived growth factor receptor α.

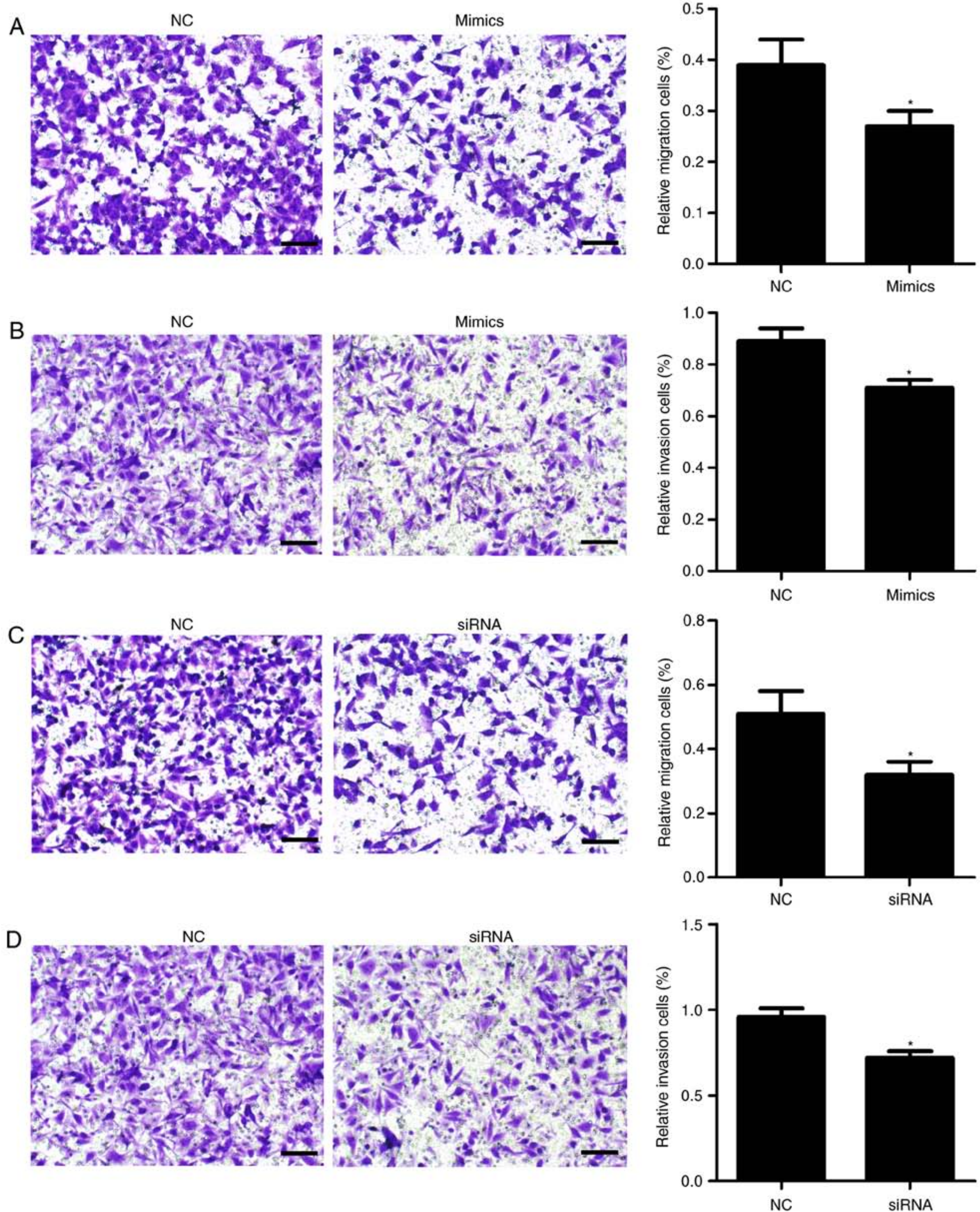

Figure 4. Effects of miR-342-3p mimics and siR-PDGFRA on the migration and invasive abilities of HTR8/SVneo cells. (A) Overexpression of miR-342-3p inhibited cell migration. Scale bar, 100 μm. (B) Overexpression of miR-342-3p suppressed cell invasion. Scale bar, 100 μm. (C) Downregulation of PDGFRA inhibited cell migration. Scale bar, 100 μm. (D) Downregulation of PDGFRA suppressed cell invasion. Scale bar, 100 μm. *P<0.05 vs. NC. NC, negative control; PE, preeclampsia; PDGFRA, platelet-derived growth factor receptor α; siRNA, small interfering RNA.

PDGFRA is a direct target of miR-342-3p. As presented in Fig. 6A, bioinformatics analysis indicated that the 3'-UTR of PDGFRA has a target sequence for miR-342-3p. Transfection with miR-342-3p mimics significantly decreased the luciferase activity of cells possessing PDGFRA 3'-UTR-wt compared with the control (P<0.01), while transfection with miR-342-3p mimics had no significant effects on the luciferase activity of cells possessing PDGFRA 3'-UTR-mut (Fig. 6B). These findings indicated that PDGFRA is likely to be a target of miR-342-3p.

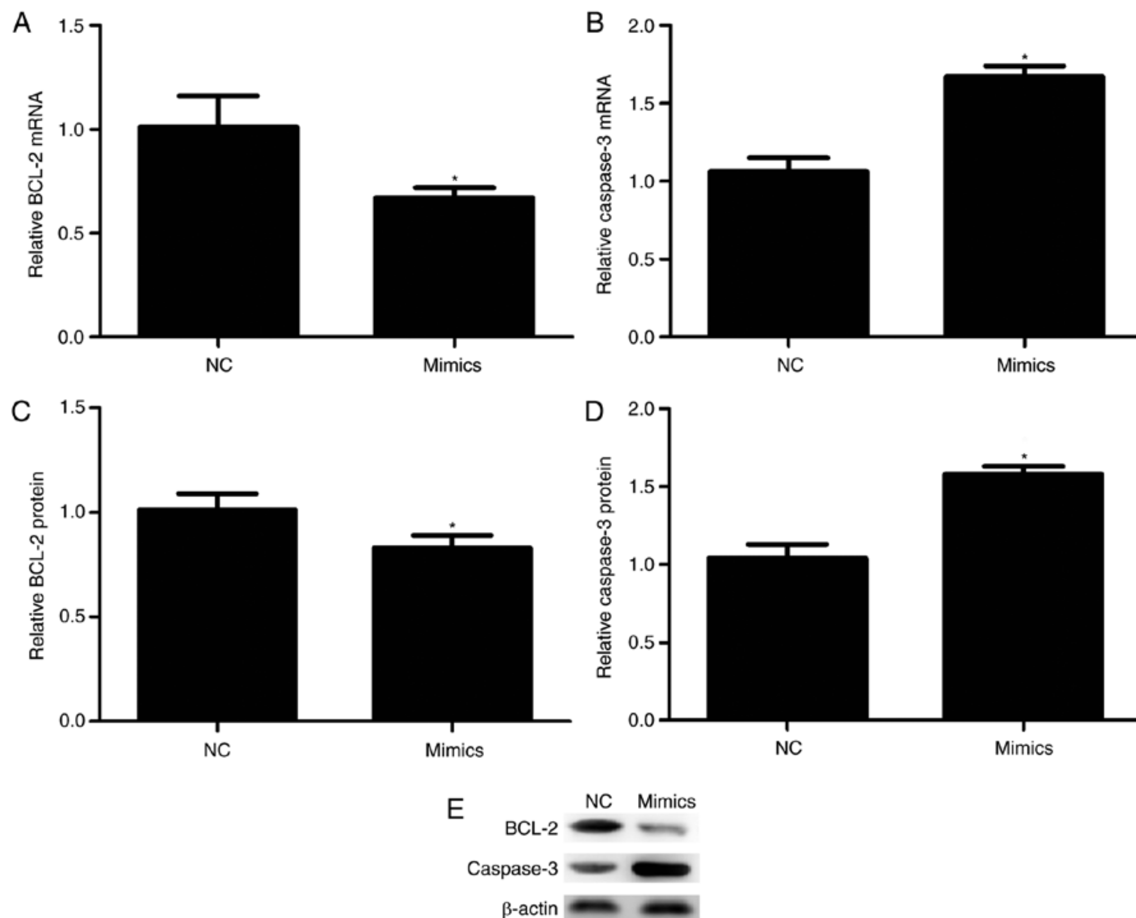

Figure 5. Effects of transient overexpression of miR-342-3p on the expression of BCL-2 and Caspase-3 in HTR-8/SVneo cells. (A) mRNA expression levels of BCL-2 in the two transfection groups. (B) mRNA expression levels of Caspase-3 in the two transfection groups. (C) The protein expression levels of BCL-2 in the two transfection groups. (D) The protein expression levels of Caspase-3 in the two transfection groups. (E) Western blot gel of BCL-2, Caspase-3 and β-actin expression. *P<0.05 vs. NC. BLC-2, B-cell lymphoma 2; NC, negative control; PDGFRA, platelet-derived growth factor receptor α.

Discussion

In the first trimester of pregnancy, extravillous trophoblasts (EVTs) with an invasive phenotype serve an important role in the formation of the maternal-fetal interface (23). At present, the importance of incomplete EVT invasion and subsequent abnormal remodeling of the spiral arteries was highlighted in the etiology of PE; these processes are modulated by a variety of inflammatory and immune cells (23). The migration ability of trophoblasts is important in deep placentation for the normal and healthy development of the fetus (23). Incomplete trophoblast migration and invasion could lead to insufficient deep placentation, which has been associated with PE (23). Reduced trophoblast proliferation has been reported to serve an important role in the development of PE (24).

The importance of miRNAs in PE has been reported. The transient upregulation of miR-136 could induce the apoptosis of MSCs, and affect the formation and development of capillaries (25). miR-125b may be associated with the occurrence of PE by targeting sphingosine-1-phosphate lyase 1 (26). In addition, miR-128a could be involved in the pathogenesis of PE by means of initiating apoptosis (27). miR-195 was associated with the pathogenesis of PE by targeting the activin receptor type-2B (28). In the present study, the expression of miR-342-3p was upregulated in the placentas of patients with

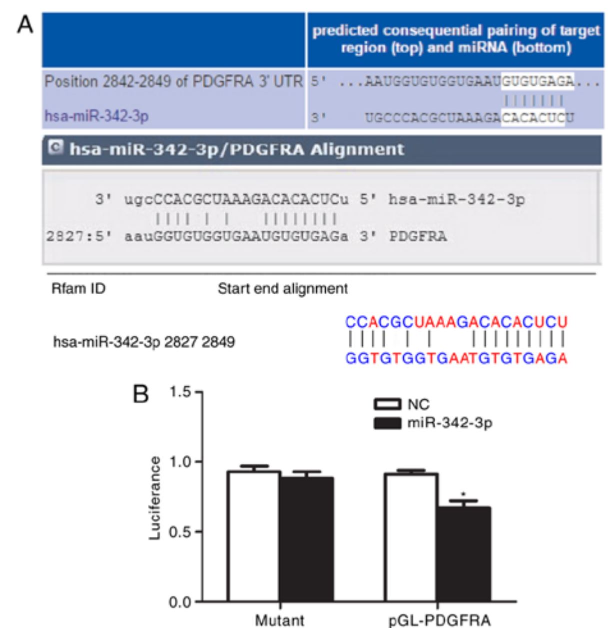

Figure 6. PDGFRA is a direct target of miR-342-3p. (A) Binding site for miR-342-3p within the 3' UTR of PDGFRA. Lines represent the targeting sites between the seed sequence of miR-342-3p and the UTR of PDGFRA. (B) Luciferase activities of the different groups. *P<0.05 vs. NC. hsa, *homo sapiens*; PDGFRA, platelet-derived growth factor receptor α; miR, microRNA; NC, negative control; UTR, untranslated region.

PE; the transient overexpression of miR-342-3p decreased cell proliferation, migration and invasion. Overexpression of miR-342-3p also inhibited G1/S phase transition; the expression of BCL-2 was decreased while that of Caspase-3 had increased, which suggested miR-342-3p may serve a role in the proliferation, migration, invasion and the cell cycle of trophoblastic cells. miR-342-3p may play a key role in the pathogenesis of PE.

In the field of obstetrics, miR-342-3p was downregulated in intrauterine growth restriction pregnancies if the gestational weeks was <34 weeks (29). In addition, miR-342-3p was reported to be increased in the plasma in pregnancies with severe PE (30), which was in line with our outcomes. miR-342-3p has been suggested to target certain genes, including Forkhead box protein M1, RAP2B, member of RAS oncogene family, IκB kinase, transforming growth factor-β activated kinase 1 binding protein (TAB)2, TAB3, anterior gradient 2, astrocyte elevated gene-1, T-lymphoma invasion and metastasis-inducing protein 1, E2F transcription factor 1 and C-terminal binding protein 2 (16-18,31-36). We revealed PDGFRA to be a novel direct target of miR-342-3p in trophoblastic cells. In our study, PDGFRA expression in the placental tissues of patients with PE was decreased, whereas that of miR-342-3p was increased. In addition, the expression of PDGFRA decreased following transfection with miR-342-3p mimics in cells; siR-PDGFRA transfection appeared to exhibit similar effects to those of miR-342-3p mimics. Furthermore, the results of the dual-luciferase assay indicated a direct connection between miR-342-3p and PDGFRA. Collectively, these findings suggest PDGFRA as a direct target of miR-342-3p in PE.

PDGFRA is a type III receptor tyrosine kinase that regulates cell proliferation, differentiation, adhesion and survival. Ligand binding activates the kinase, stimulating cellular signaling proteins, including mitogen-activated protein kinases (MAPKs), signal transducers and activators of transcription and phosphatidylinositol-3 kinases (37). High expression of PDGFRA has been detected in various cancers, such as breast cancer (38), ovarian cancer (37), gastrointestinal stromal tumors (39) and melanoma (40). These findings indicate that PDGFRA is associated with various physiological and pathological processes, such as cell survival, migration and wound healing. In our study, PDGFRA was determined to promote cell proliferation, migration and invasion, and affected the cell cycle in trophoblastic cells. Increases in PDGFRA expression could induce cell proliferation, and activate the AKT and MAPK signal pathways. On the contrary, these pathways were suppressed in response to reductions in PDGFRA expression (41); further investigation into the mechanism underlying the roles of PDGFRA in PE is required.

Our study has certain limitations. Only 30 cases of PE placentas and 30 normal placentas were employed for histological analysis. In the future, a larger sample size is required to validate our findings. In addition, *in vitro* experiments were performed; however, further insight from investigations may be obtained by conducted *in vivo* research in rats or mice as models. The present study aimed to determine the mechanism underlying incomplete trophoblastic invasion in PE. However, endothelial dysfunction is also one of the major causes of PE (4), yet this was not explored in our study this paper; thus, this should be investigated in the future.

In conclusion, our research demonstrated that miR-342-3p was upregulated and PDGFRA expression was decreased in PE. Functional experiments showed that miR-342-3p could affect the proliferation, migration, invasion and cell cycle of trophoblastic cells by targeting PDGFRA. The present study proposed that miR-342-3p may be a novel clinical indicator or prognostic marker for PE.

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Availability of data and materials

The datasets used during the present study are available from the corresponding author on reasonable request.

Authors' contributions

XY analyzed and interpreted the patient data, and was a major contributor in writing the manuscript. FG performed the statistical analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee in the First Hospital of China Medical University agreed our research. Written informed consent for participation in the study or use of their tissues was obtained from all participants.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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