Int J Clin Exp Pathol 2020;13(5):869-879
www.ijcep.com /ISSN:1936-2625/IJCEP0096320

Original Article

The overexpression of lncRNA MEG3 inhibits cell viability and invasion and promotes apoptosis in ovarian cancer by sponging miR-205-5p

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Received April 29, 2019; Accepted July 22, 2019; Epub May 1, 2020; Published May 15, 2020

Abstract: Purpose: Ovarian cancer is a common and fatal cancer in women. The long non-coding RNA (lncRNA) MEG3 was reported to affect the cellular processes of ovarian cancer, but the mechanisms remain unclear. Here, we aimed to explore the potential regulatory mechanism of MEG3 in ovarian cancer. Materials and methods: A reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was conducted to analyze the expression levels of MEG3 and miR-205-5p in tissues and cell lines. An MTT assay was utilized to determine the cell viability of ovarian cancer SKOV-3 and OVCAR-8 cells. A flow cytometry analysis was employed to disclose the ovarian cancer cell apoptosis. The migration and invasion of SKOV-3 and OVCAR-8 cells were examined using a Transwell assay. A bioinformatics analysis indicated miR-205-5p as a direct target of MEG3, and a luciferase reporter assay was conducted to validate the interaction between MEG3 and miR-205-5p. Results: MEG3 was significantly down-regulated, while miR-205-5p was up-regulated in ovarian cancer tissues and cell lines. The overexpression of MEG3 and the knockdown of miR-205-5p inhibited cell viability, migration and invasion but promoted the apoptosis rate in ovarian cancer cells. MiR-205-5p was identified as a downstream gene of MEG3 and is negatively regulated by MEG3. The introduction of miR-205-5p reversed the up-regulation of MEG3-mediated suppression effects on cell viability, migration and invasion and increased cell apoptosis in ovarian cancer cells. Conclusion: The overexpression of lncRNA MEG3 inhibits cell proliferation and cell invasion and promotes apoptosis in ovarian cancer by sponging miR-205-5p.

Keywords: MEG3, ovarian cancer, cell viability, apoptosis, migration and invasion, miR-205-5p

Introduction

Ovarian cancer is the 7th most common cancer and the 8th most common cause of cancer death among women in the world, and its 5-year survival rate is lower than 45% [1]. Ovarian cancer derives from the fallopian tubes, the ovarian surface, or from inclusion cysts in the ovarian parenchyma [2]. Because of the lack of explicit early symptoms and diagnostic markers, most patients are diagnosed at the advanced-stages of ovarian cancer, which leads to the high mortality of this disease [3]. Therefore, it is urgently needed to identify specific biomarkers and clarify the mechanisms of ovarian cancer metastasis and invasion to advance effective therapeutic strategies.

Long non-coding RNAs (lncRNAs) are a group of non-coding RNAs (ncRNAs) consisting of more than 200 nucleotides (nt) [4]. Although they lack the potential to code proteins, lncRNAs exert key functions in different biological processes, especially tumorigenesis and tumor development [5]. In different kinds of cancers, lncRNAs may function as tumor facilitators or suppressors [6]. For example, lncRNA CASC9 is highly expressed in ovarian cancer tissues and cell lines, promotes ovarian cancer cell proliferation and migration, and invasion *in vitro,* and accelerates tumor growth *in vivo* [7]. LncRNA GIHCG is up-regulated in ovarian cancer tissues, and promotes the cell cycle and colony formation abilities of ovarian cancer cells by regulating microRNA-429 [8]. In contrast, ln-

cRNA GAS5 expression is clearly decreased in ovarian cancer, and acts as a tumor suppressor by triggering inflammasome formation [9]. The expression of lncRNA TUBA4B is significantly reduced in epithelial ovarian cancer tissue specimens, and the exogenous overexpression of TUBA4B blocks the proliferation of ovarian cancer cells [10].

Located on human chromosome 14q32, the lncRNA maternally expressed 3 gene (MEG3) is an imprinted gene that encodes lncRNA-MEG3 RNA [11]. MEG3 functions as a tumor repressor in certain human cancers, such as gliomas [12], gallbladder cancer [13], bladder urothelial carcinoma [14], and breast cancer [15], as well as in ovarian cancer [16]. Regrettably, the functional role of MEG3 in ovarian cancer has been elusive.

MicroRNAs (miRNAs), composed of approximately 22 nucleotides, are associated with cellular processes, such as inflammation, cell-cycle regulation, proliferation, differentiation, apoptosis, and migration by blocking the translation and stability of messenger RNAs (mRNAs) [17]. Large quantities of miRNAs have been reported to be involved in the prognosis, chemoresistance, and metastasis/relapse of ovarian cancer, for example miR-200c, miR-152, miR-21, and miR-221 [18, 19]. MiR-205-5p is down-regulated in certain types of human cancer, such as colon cancer [20], oral squamous cell carcinoma (OSCC) [21], prostatic carcinoma [22] and renal cell carcinoma [23], but it is up-regulated in ovarian cancer [24]. Herein, we tried to investigate the impact of miR-205-5p on ovarian cancer progression *in vitro*.

In the current study, we determined the expression levels of MEG3 and miR-205-5p in ovarian cancer tissues and cell lines and the functional effects of MEG3 and miR-205-5p on ovarian cancer cellular processes. The potential molecular mechanism was initially explored.

Materials and methods

Clinical specimens

The current study was approved by the Ethics Committee of Pudong New Area People's Hospital Affiliated to Shanghai Health University. 20 pairs of ovarian cancer tissues and corresponding adjacent tissues were obtained from 20 women diagnosed with ovarian cancer. Written informed consents were obtained from all patients. All samples were frozen in liquid nitrogen at once and conserved at -80°C until used.

Cell culture and transfection

A normal ovarian epithelial cell line and 4 ovarian cancer cell lines (SKOV-3, OVCAR-3, OVCAR-5, and OVCAR-8) were purchased from the American Type Culture Collection (ATCC, Manassas, VA, USA). The above cell lines were maintained in Roswell Park Memorial Institute 1640 Medium (RPMI1640; Gibco, Grand Island, NY, USA) containing 10% fetal bovine serum (FBS; HyClone, Logan, UT, USA) n a 5% CO_2 humidified incubator (Thermo Fisher Scientific, Waltham, MA, USA) at 37°C.

The pcDNA 3.1 plasmid was purchased from Thermo Fisher Scientific. The pcDNA 3.1-MEG3 plasmid, si-MEG3 and its negative control si-NC, miR-205-5p mimics (miR-205-5p) and its negative control miR-NC mimics (miR-NC), miR-205-5p inhibitor and its negative control miR-NC inhibitor were synthesized by (GenePharma Co. Ltd. Shanghai, China). The above plasmids or oligonucleotides were transfected into SK-OV-3 and OVCAR-8 cells using Lipofectamine™ 3000 reagent (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's instructions. At 48 h post-transfection, the cells were collected for further investigation.

Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay

Total RNA was extracted from ovarian cancer tissues and para-carcinoma tissue and a normal ovarian epithelial cell line and 4 ovarian cancer cell lines the utilizing TRIzol reagent (Life Technologies, Grand Island, NY, USA). A total of 500 ng RNA was subjected to reverse transcription to synthesize cDNA with a RevertAid RT Reverse Transcription kit (Thermo Fisher Scientific). For the mRNA detection, qPCR was performed using a SYBR Master Mix (Applied Biosystems, Foster City, CA, USA). For the miRNA expression detection, qPCR was performed using a TaqMan reverse transcription kit and TaqMan MicroRNA Assays (Thermo Fisher Scientific). qPCR was performed on StepOnePlus™ Real-time PCR Systems (Applied Biosystems). GAPDH and U6 were used as the negative controls for MEG3 and miR-205-5p, separately. The primers used in this study were: MEG3, 5'-GCCCTAGGGGAGTGACTACA-3' (forwa-

rd) and 5'-ACTCGGGACATACCTGCTCT-3' (reverse); GAPDH, 5'-GAAGGTGAAGGTCGGAGTC-3 (forward) and 5'-GAAGGTGAAGGTCGGAGTC-3' (reverse); miR-205-5p, 5'-CCTTCATTCCACCGGAGT-3' (forward) and 5'-GTCCAGTTTTTTTTTTTTTTTTCAGACT-3' (reverse); U6, 5'-CTCGCTTCGGCAGCACATA-3 (forward) and 5'-AACGATTCACGAATTTGCGT-3' (reverse). The relative expression of MEG3 and miR-205-5p were evaluated using the threshold cycle $2^{-\Delta\Delta Ct}$ method.

MTT assay

Transfected SKOV-3 and OVCAR-8 cells (~4 × 10^3 per well) were seeded in 96-well plates and maintained at 37°C for 24 h, 48 h, and 72 h. Then MTT solution (Sigma-Aldrich, St. Louis, MO, USA) was added to the medium and incubated for another 4 h at 37°C. After removal of the supernatant, 150 μL dimethyl sulfoxide (DMSO, Sigma-Aldrich) was added into the well. The absorbance of each well at 490 nm was measured with a microplate reader (Bio-Rad, Hercules, CA, USA).

Cell apoptosis assay

A flow cytometry analysis was employed to quantify the cell apoptotic rates by using an Annexin V-FITC/PI apoptosis detection kit (BioVision, Milpitas, CA, USA). Transfected SKOV-3 and OVCAR-8 cells were washed twice with phosphate buffered saline (PBS) and re-suspended in 200 μL binding buffer. Next, 10 μL Annexin V-FITC and PI were added and the cell suspension was incubated at room temperature for 10 min away from light. The cell apoptosis was determined using a flow cytometer (FACScan; BD Biosciences), and the data were analyzed using CellQuest software (BD Biosciences).

Transwell assay

For the invasion assay, transfected SKOV-3 and OVCAR-8 cells were cultured to confluence (>90%) in 24-well dishes. Then the transfected cells (~3 × 10^4) were re-suspended in 200 μL RPMI1640 medium (without serum) and placed into the upper chamber (8 μm pore size; BD Biosciences, San Jose, CA, USA), which were pre-coated with Matrigel (BD Biosciences). An RPMI1640 medium containing 5% FBS was added to the lower chamber. After 24 h of incubation, the cells remaining on the upper membrane and that had invaded through the membrane were stained with 0.1% crystal violet at room temperature for 15 min, them photographed with an optical microscope (Olympus, Tokyo, Japan). The stained cells were dissolved in 10% acetic acid quantified by measuring the absorbance at 595 nm using a microplate reader.

As for the migration assay, the procedure was analogous, except that cells were seeded in the upper part of the chamber without Matrigel.

Luciferase reporter assay

The online software miRcode (http://www.mircode.org/) and miRBase (http://www.mirbase.org/) were utilized to predict the downstream gene of MEG3, and we found that miR-205-5p can directly bind with the 3'-untranslated region (3'-UTR) of MEG3. The 3'-UTR sequence of MEG3 was amplified and cloned into the psi-CHECK-2 luciferase reporter vector (Promega Corp., Madison, WI, USA) to synthesize MEG3 wt, and the mutant of the 3'-UTR of MEG3 was subcloned into the vector to synthesize MEG3 mut. The SKOV-3 and OVCAR-8 cells were co-transfected with miR-205-5p mimics and MEG3 wt or MEG3 mut. Lipofectamine™ 2000 reagent. 48 h later, the co-transfected cells were collected and the relative luciferase activity was measured using the Dual-Luciferase Reporter Assay System (Promega).

Statistical analysis

All the experiments were performed three times, and all the data were presented as the mean ± SD (standard deviation). All statistical analyses were conducted utilizing SPSS 19.0 statistical software (SPSS, Chicago, IL, USA). A one-way analysis of variance (ANOVA) was used to analyze the differences among the data in the various groups. $P < 0.05$ was considered statistically significant.

Results

MEG3 expression is decreased in ovarian cancer tissues and cell lines

To clarify the effect of MEG3 on the progression of ovarian cancer, we initially measured the expression level of MEG3 in ovarian cancer tissues and in the corresponding adjacent tissues using an RT-qPCR assay. The data revealed that the MEG3 expression was decreased in the

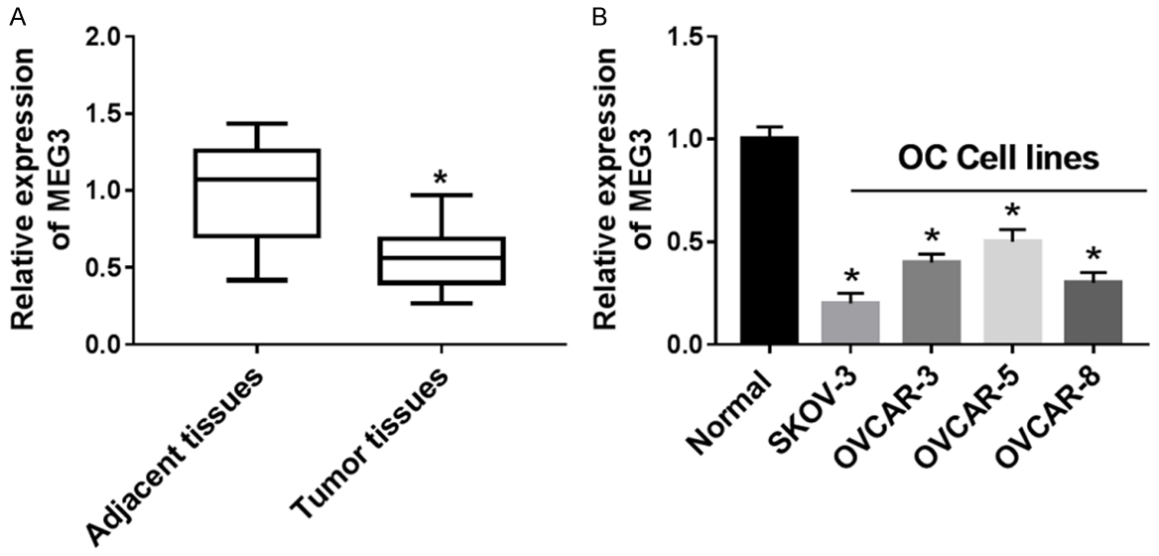

Figure 1. MEG3 expression was decreased in ovarian cancer tissues and cell lines. A. The expression levels of MEG3 in 20 pairs of ovarian cancer tissues and corresponding adjacent tissues were measured using RT-qPCR. $^{*}P < 0.05$ compared to adjacent tissues. B. The MEG3 expression in a normal ovarian epithelial cell line and in 4 ovarian cancer cell lines (SKOV-3, OVCAR-3, OVCAR-5 and OVCAR-8) was also determined using RT-qPCR. $^{*}P < 0.05$ compared to normal ovarian epithelial cells.

ovarian cancer tissues compared with the expression in the adjacent tissues (**Figure 1A**). An RT-qPCR assay was also employed to examine MEG3 expression in a normal ovarian epithelial cell line and in 4 human ovarian cancer cell lines (SKOV-3, OVCAR-3, OVCAR-5, and OVCAR-8). The MEG3 expression was also reduced in all the above human ovarian cancer cell lines (**Figure 1B**).

Overexpression of MEG3 significantly inhibits cell viability, migration and invasion and promotes apoptosis in ovarian cancer cells

To figure out the functional role of MEG3 on ovarian cancer cells, pc-MEG3 was transfected into SKOV-3 and OVCAR-8 cells. As shown in **Figure 2A**, the MEG3 expression in the SKOV-3 and OVCAR-8 cells was distinctly increased after transfection. An MTT assay demonstrated that the up-regulation of MEG3 effectively inhibited the cell viability of the SKOV-3 and OVCAR-8 cells (**Figure 2B** and **2C**). A flow cytometry analysis was conducted to disclose the effects of MEG3 on ovarian cancer cell apoptosis. The apoptosis rate of SKOV-3 and OVCAR-8 cells transfected with pc-MEG3 was strikingly higher than it was in the cells transfected with Vector (**Figure 2D**). A Transwell assay indicated that the exogenous introduction of MEG3 distinctly hindered cell migration and the invasion rate in SKOV-3 and OVCAR-8 cells (**Figure 2E** and **2F**).

MEG3 directly targeted miR-205-5p and counter-regulated miR-205-5p expression

The MiRCode and miRBase websites were utilized to predict the downstream gene of MEG3 and showed that wild type MEG3 contains a binding site for miR-205-5p (**Figure 3A**). A luciferase reporter assay was conducted to further validate the interaction between MEG3 and miR-205-5p. The luciferase activity of the SKOV-3 and OVCAR-8 cells co-transfected with MEG3 wt and miR-205-5p mimic was markedly decreased, but no obvious change was observed in the luciferase activity of the cells co-transfected with the MEG3 mut and miR-205-5p mimic (**Figure 3B**, **3C**). An RT-qPCR assay exhibited that the overexpression of MEG3 down-regulated miR-205-5p expression, and the knockdown of MEG3 elevated miR-205-5p expression (**Figure 3D**).

MiR-205-5p was up-regulated in ovarian cancer tissues and cell lines

To investigate the expression levels of miR-205-5p in ovarian cancer tissues and cell lines, an RT-qPCR assay was performed. We found that miR-205-5p expression in ovarian cancer

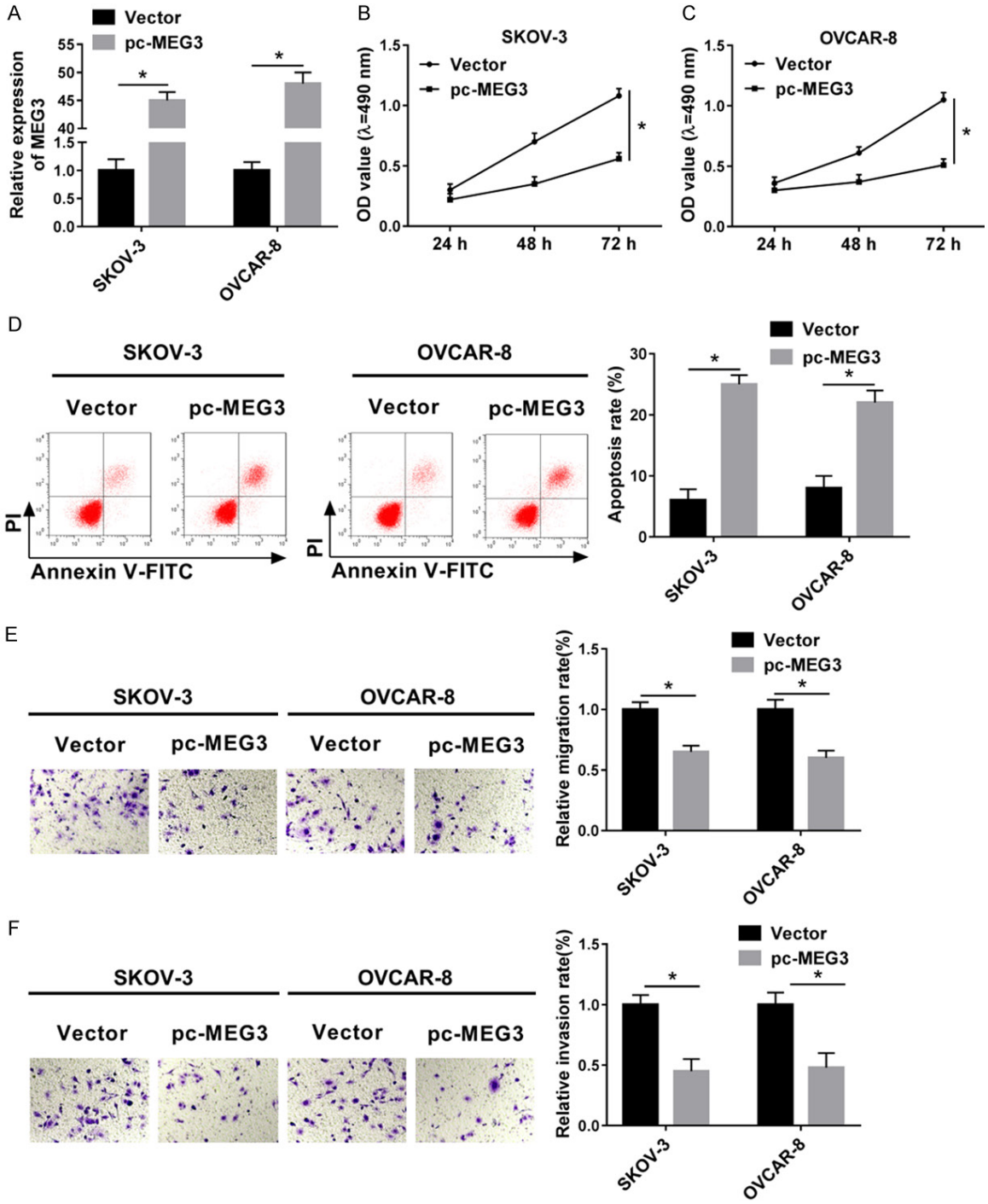

Figure 2. The overexpression of MEG3 significantly inhibited cell viability, migration and invasion but promoted apoptosis in ovarian cancer cells. SKOV-3 and OVCAR-8 cells were transfected with pc-MEG3 or a vector. A. RT-qPCR was utilized to determine the transfection efficiency. B, C. MTT assay for SKOV-3 and OVCAR-8 cells after transfection for 24 h, 48 h and 72 h. D. Flow cytometry analysis for SKOV-3 and OVCAR-8 cells after transfection. E. The relative migration rate of SKOV-3 and OVCAR-8 cells after transfection. F. The relative invasion rate of SKOV-3 and OVCAR-8 cells after transfection. $^{*}P < 0.05$ compared to cells transfected with the vector.

tissues was apparently elevated, compared with the levels in the adjacent tissues (**Figure 4A**). Additionally, the expression level of miR-205-5p was significantly enhanced in the ovarian cancer SKOV-3 and OVCAR-8 cells, compared to the normal cells (**Figure 4B**). A Pearson

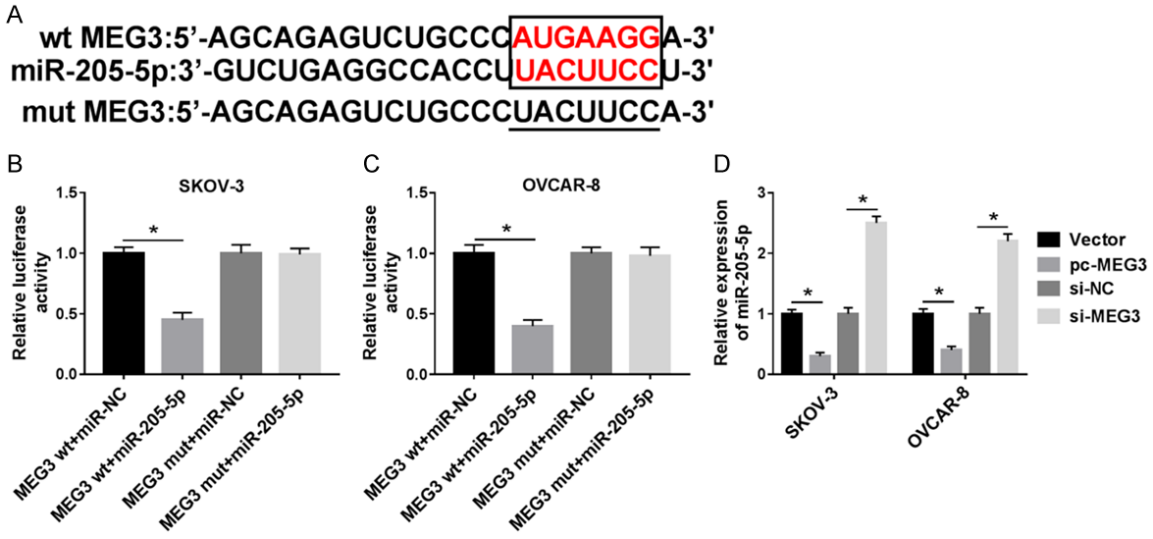

Figure 3. MEG3 directly targeted miR-205-5p and counter-regulated miR-205-5p expression. A. The putative binding site between miR-205-5p and MEG3 is marked in red. B, C. Luciferase reporter assays for SKOV-3 and OVCAR-8 cells co-transfected with MEG3 wt or MEG3 mut plasmid, with miR-205-5p mimic or miR-NC, $^{*}P < 0.05$ compared to cells co-transfected with MEG3 wt and miR-NC. D. The expression of miR-205-5p in SKOV-3 and OVCAR-8 cells after transfection. $^{*}P < 0.05$ compared to cells transfected with Vector. $^{*}P < 0.05$ compared to cells transfected with si-NC.

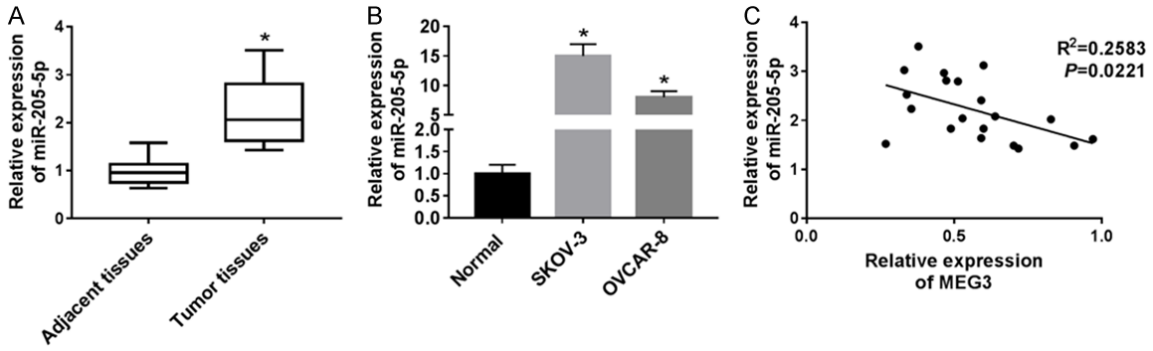

Figure 4. MiR-205-5p was up-regulated in ovarian cancer tissues and cell lines. A. The miR-205-5p expression in 20 pairs of ovarian cancer tissues and related adjacent tissues was evaluated by RT-qPCR. $^{*}P < 0.05$ compared to adjacent tissues. B. The miR-205-5p expression in a normal ovarian epithelial cell line and 2 ovarian cancer cell lines (SKOV-3 and OVCAR-8) was also tested by RT-qPCR. $^{*}P < 0.05$ compared to normal ovarian epithelial cells. C. Correlation analysis between miR-205-5p and miR-205-5p in ovarian cancer tissues, $P = 0.0221$, $R^2 = 0.2583$.

analysis indicated that the expression level of miR-205-5p in ovarian cancer tissues was inversely correlated with MEG3 expression (**Figure 4C**).

Knockdown of miR-205-5p blocked cell viability, migration and invasion and promoted apoptosis in ovarian cancer cells

To explore the effect of miR-205-5p on ovarian cancer cells, we constructed SKOV-3 and OVCAR-8 cells with miR-205-5p down-regulated through transfection with an miR-205-5p inhibitor. RT-qPCR was used to detect the transfection efficiency (**Figure 5A**). An MTT assay indicated that the knockdown of miR-205-5p clearly hindered the cell viability of the SKOV-3 and OVCAR-8 cells (**Figure 5B**, **5C**). A flow cytometry analysis revealed that the reduction of miR-205-5p expression facilitated the apoptosis rate of the SKOV-3 and OVCAR-8 cells, compared with the rate in the cells transfected with the miR-NC inhibitor (**Figure 5D**). A Transwell assay demonstrated that the knock-

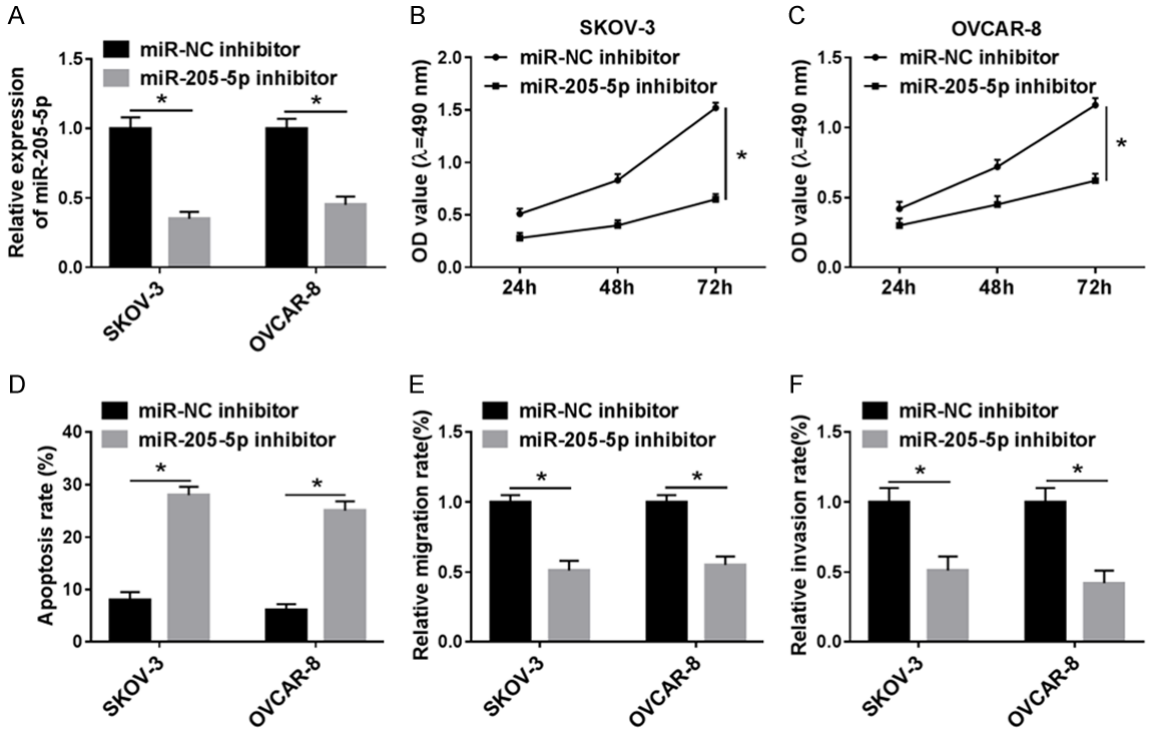

Figure 5. The knockdown of miR-205-5p blocked cell viability, migration, and invasion and promoted apoptosis in ovarian cancer cells. SKOV-3 and OVCAR-8 cells were transfected with miR-205-5p inhibitor or miR-NC inhibitor. A. An RT-qPCR assay was conducted to test the transfection efficiency. B, C. The MTT assay for the SKOV-3 and OVCAR-8 cells after transfection for 24 h, 48 h, and 72 h. D. Flow cytometry analysis for SKOV-3 and OVCAR-8 cells after transfection. E. The relative migration rate of SKOV-3 and OVCAR-8 cells after transfection. F. The relative invasion rate of SKOV-3 and OVCAR-8 cells after transfection. $^{*}P < 0.05$ compared to cells transfected with miR-NC inhibitor.

down of miR-205-5p evidently inhibited the migration and invasion rate of the SKOV-3 and OVCAR-8 cells (**Figure 5E**, **5F**).

Up-regulation of miR-205-5p reversed the pc-MEG3-mediated suppression impact on cell viability, migration, and invasion, as well as promotion on apoptosis in ovarian cancer cells

To figure out whether MEG3 exerted its function by directly targeting miR-205-5p in ovarian cancer cells, some rescue experiments were performed. An RT-qPCR assay revealed that the miR-205-5p mimic reversed the inhibitory effect of pc-MEG3 on miR-205-5p expression in SKOV-3 and OVCAR-8 cells (**Figure 6A**). The overexpression of MEG3 inhibited the cell viability of SKOV-3 and OVCAR-8 cells, but the miR-205-5p mimic weakened the reduction of cell viability of the two cell lines (**Figure 6B** and **6C**). As for apoptosis, the up-regulation of MEG3 reinforced the apoptosis rate of the SKOV-3 and OVCAR-8 cells, but the impact could be abolished by the miR-205-5p mimic (**Figure 6D**). As shown in **Figure 6E**, **6F**, the gain of MEG3 blocked the migration and invasion of the SKOV-3 and OVCAR-8 cells, but the introduction of miR-205-5p effectively rescued the suppression of migration and invasion of the SKOV-3 and OVCAR-8 cells induced by pc-MEG3.

Discussion

Ovarian cancer is a frequent tumor of the female reproductive system, and its mortality rate is the highest among gynecological malignant tumors [25]. While great advances have been made in ovarian cancer surgery, chemotherapy, and radiotherapy, the therapeutic effect is still often insufficient [7]. Therefore, more effort is required to disclose the molecular mechanism underlying ovarian cancer progression.

In recent years, more and more lncRNAs, including MEG3, have been identified and proved

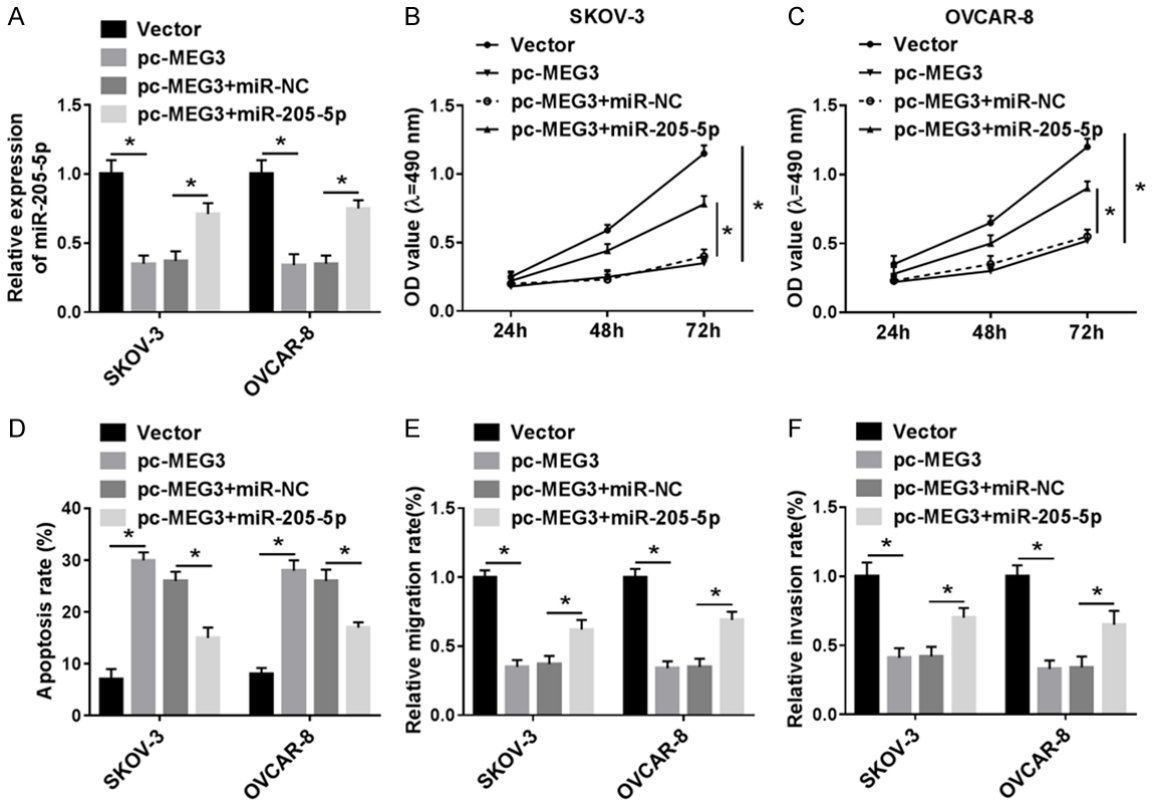

Figure 6. The up-regulation of miR-205-5p reversed the pc-MEG3-mediated suppression impact on cell viability, migration, and invasion, as well as promoting apoptosis in ovarian cancer cells. SKOV-3 and OVCAR-8 cells were transfected with pc-MEG3 or co-transfected with miR-205-5p mimic. A. The miR-205-5p expression in the SKOV-3 and OVCAR-8 cells after transfection was measured by RT-qPCR assay. B, C. The MTT assay for SKOV-3 and OVCAR-8 cells after transfection. D. Flow cytometry analysis for SKOV-3 and OVCAR-8 cells after transfection. E. The relative migration rate of SKOV-3 and OVCAR-8 cells after transfection. F. The relative invasion rate of SKOV-3 and OVCAR-8 cells after transfection. $^{*}P < 0.05$ compared to cells transfected with Vector. $^{*}P < 0.05$ compared to cells co-transfected with pc-MEG3 and miR-NC.

to be involved in the regulation of many biological processes in ovarian cancer progression, such as cell cycle arrest, apoptosis, metastasis, and cell proliferation [26]. In non-small cell lung cancer (NSCLC), lncRNA MEG3 participates in tumorigenesis and development by regulating BRCA1, B-cell lymphoma-2 (Bcl-2) and BCL2-associated X (Bax) expression by competitively binding to microRNA-7-5p. The exogenous overexpression of MEG3 promotes the apoptosis of lung cancer cells [27]. An earlier study illustrated that the overexpression of MEG3 repressed cell proliferation and the cell cycle but elevated the cell apoptosis of bladder urothelial carcinoma cells *in vitro* and suppressed tumor growth *in vivo* as well. MEG3 exerts its function as a tumor suppressor by regulating miR-96 along with TPM1 [14]. Jin and his colleagues reported that the up-regulation of MEG3 inhibits gallbladder cancer cell proliferation and invasion and leads to cell apoptosis and decreased tumorigenicity in nude mice [13]. Xu *et al*. pointed out that lncRNA MEG3 inhibits cell proliferation and migration but facilitates autophagy in glioma U251 cells by up-regulating Sirt7 and participates in hampering the PI3K/AKT/mTOR pathway [28]. LncRNA MEG3 is down-regulated in prostate cancer tissues and cells, and can decrease the proliferation, migration, and invasion abilities in prostate cancer cells by regulating miR-9-5p and its targeting gene QKI-5 [29]. In epithelial ovarian carcinoma (EOC), MEG3 acts as a tumor suppressor in EOC via meditating ATG3 activity and inducing autophagy [30]. In the current study, MEG3 expression was reduced in ovarian cancer tissues and cell lines, which is consistent with a previous study [16]. Our investigation revealed that the exogenous introduction of MEG3 apparently inhibited cell viability, migra-

tion, and invasion but promoted apoptosis in ovarian cancer SKOV-3 and OVCAR-8 cells. The above results demonstrated the antineoplastic effect of MEG3 in ovarian cancer. Though researchers have indicated that MEG3 restrained cell proliferation, elevated apoptosis, and blocked cell cycle progression by positively regulating PTEN [16], we tried to find another potential mechanism.

The online tools miRCode and miRBase were utilized to screen out the candidate target miRNAs of MEG3, and they indicated that MEG3 contains a binding site for miR-205-5p. This target relationship was initially confirmed in our study. The ectopic expression of miRNAs is involved in the occurrence and progression of human tumors, including ovarian cancer [31]. A growing body of evidence reveals that miRNAs could function as tumor suppressor genes or oncogenes in ovarian cancer, which are likely to be used as diagnosis and prognosis biomarkers and for cancer therapies [32]. For instance, miR-205-5p, miR-21-5p and miR-141-3p were up-regulated in urine samples of the two most prevalent urological malignancies, bladder cancer and prostate cancer, and these oncogenic microRNAs have the potential to be specific biomarkers for the identification of the two malignancies [33]. The overexpression of miR-205 in NSCLC cells promotes tumor cell proliferation *in vitro* and blood vessel formation *in vivo* [34]. On the other hand, miR-205-5p serves as a tumor inhibitor. In colon cancer, the up-regulation of miR-205-5p blocked the epithelial to mesenchymal transition in tumor cells, which may prolong the survival time of patients and elevate the efficiency of the therapeutic impact in advanced-stage patients [20]. MicroRNA-205-5p directly targets metalloproteinases-2 (TIMP-2) to repress OSCC cell migration and invasion [21]. In this study, we observed that miR-205-5p was up-regulated in ovarian cancer tissues and cell lines, which was consistent with a former study [24]. Moreover, miR-205-5p expression was negatively regulated by MEG3. The knockdown of miR-205-5p blocked cell viability, migration and invasion while promoting apoptosis in ovarian cancer cells. Additionally, a gain of miR-205-5p reversed the pcMEG3-mediated suppression impact on cell viability, migration, and invasion, and promoted apoptosis in ovarian cancer cells.

In summary, we found the down-regulation of MEG3 and the up-regulation of miR-205-5p in ovarian cancer tissues and cell lines. Clearly, miR-205-5p expression was counter-regulated by MEG3 and inversely correlated with MEG3 expression. Both the introduction of MEG3 and the silencing of miR-205-5p significantly inhibited cell viability, migration, and invasion in ovarian cancer cells and facilitated the apoptosis of ovarian cancer cells. MiR-205-5p was identified as a downstream gene of MEG3, and a rescue experiment revealed that miR-205-5p could reverse the MEG3-mediated effects on cellular processes in ovarian cancer cells. In conclusion, the overexpression of lncRNA MEG3 inhibits cell proliferation and cell invasion and promotes apoptosis in ovarian cancer via sponging miR-205-5p.

Disclosure of conflict of interest

None.

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