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MicroRNA-1-3p inhibits the growth and metastasis of ovarian cancer cells by targeting DYNLT3

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Abstract. – OBJECTIVE: The purpose of this study was to explore the role of microRNA-1-3p in the progression of ovarian cancer (OVC) and its possible molecular mechanisms.

PATIENTS AND METHODS: For the purpose of exploring the specific mechanism of the oncogene dynein light chain Tctex-type 3 (DYNLT3) in OVC, bioinformatics techniques were applied to predict miRNAs that might bind to DYNLT3, and then microRNA-1-3p was selected. After measuring the expression levels of microRNA-1-3p and DYNLT3 in 60 pairs of OVC tissue samples, the Pearson correlation analysis was used to calculate the expression correlation of microRNA-1-3p and DYNLT3. In addition, Dual-Luciferase reporting assay was used to verify the combination of the two in OVC cells. Furthermore, microRNA-1-3p NC, microRNA-1-3p mimics, and microRNA-1-3p mimics+ DYNLT3-OE (overexpression) were transfected into ES-2 and SKOV-3 cells, respectively. Subsequently, real-time quantitative polymerase chain reaction (qPCR) was performed to examine microRNA-1-3p level in each group of cells, followed by cell counting kit-8 (CCK-8), 5-Ethynyl-2'-deoxyuridine (EdU) test, and transwell assay to verify the impact of microRNA-1-3p on the proliferation, migration ability, and invasiveness of OVC cells. Finally, the mRNA and protein levels of DYNLT3 were examined by qPCR and Western blot in OVC, respectively.

RESULTS: Bioinformatics prediction results showed that a total of three possible miRNAs bound to the oncogene DYNLT3. Then, microRNA-1-3p was selected for further validation. qPCR results revealed that microRNA-1-3p was down-regulated in OVC tissues and cells, while DYNLT3 was up-regulated in OVC tissues. In addition, Pearson correlation analysis indicated that microRNA-1-3p was negatively correlated with DYNLT3 expression, and the Dual-Luciferase reporter assay confirmed that microRNA-1-3p was able to bind directly to the 3'-UTR of DYNLT3. Besides, microRNA-1-3p-mimics transfection remarkably decreased the mRNA and protein expressions of DYNLT3. On the contrary, transfection of microRNA-1-3p-mimics remarkably inhibited the proliferation, migration ability, and invasiveness of OVC cells. Moreover, the transfection of microRNA-1-3p-mimics+DYNLT3-OE partially reversed the inhibitory effect of microRNA-1-3p-mimics on the proliferative, migrate ability, and invasiveness of OVC cells.

CONCLUSIONS: MicroRNA-1-3p is under expressed either in OVC tissues or in cell lines, and overexpression of microRNA-1-3p may inhibit proliferative and migrate ability and invasiveness of OVC cells by modulating DYNLT3, which make microRNA-1-3p a potential therapeutic target for OVC.

Key Words:
Ovarian cancer, MicroRNA-1-3p, DYNLT3, Cell proliferation, Cell migration.

Introduction

Ovarian cancer (OVC) is the second most common cause of death related to malignant tumors of the female reproductive system, as most patients are found to have advanced tumors and are prone to metastasis and recurrence after treatment[1]. The main treatment for ovarian cancer is surgery combined with chemotherapy with paclitaxel and platinum drugs. Although the diagnosis and treatment level of OVC development has improved in recent years, the 5-year survival rate is only 30% while the fatality rate is still rising, and one of the main reasons is the lack of reliable early diagnosis and treatment targets[2]. Therefore, it is of great significance to study the diagnostic and therapeutic markers closely related to the progression of OVC and its mechanism of action.

MicroRNA (miRNA) is a kind of short non-coding single-stranded RNAs with a length of about 22 nt, which mainly regulates the expression of target genes at the post-transcrip-

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tional level, and is thought to be closely related to the occurrence and progression of tumors in recent years[3]. MiRNA binds to the 3'-untranslated region (3'-UTR) of target gene mRNA and regulates its transcription, stability, and protein translation. Several studies have shown that the expression disorder of miRNA promotes the occurrence and development of human tumors[4]. MicroRNA-92a and microRNA-144 can be used as biomarkers for diagnostic screening of colorectal cancer and can be helpful for further classification[5]. MicroRNA-196b promotes the migration ability and invasiveness of HCC cells by targeting FOXP2 and is correlated with the staging and prognosis of HCC patients[6]. Differential miRNA expression levels were examined to diagnose and predict bladder cancer[7]. These findings reveal that microRNAs play a key part in the development of tumorigenesis and deserve further exploration.

Dynein light chain Tctex-type 3 (DYNLT3) is a member of the cytoplasmic dynamic protein light chain Tctex family. DYNLT3 mainly plays a regulatory role in mitosis and meiosis, as well as chromosome binding[8,9]. DYNLT3 may promote the proliferation, migration, and invasion abilities of OVC cells by affecting the levels of ki-67 and Ezrin protein, so as to play a pro-cancer role[10]. Furthermore, high expression of DYNLT3 was further confirmed to be associated with the overall survival and progression-free survival in patients with OVC through the bioinformatics database. Therefore, it was believed that finding effective methods to inhibit the expression of DYNLT3 gene is very promising for gene therapy of OVC. In recent years, the silencing effect of miRNA in human tumors has been widely explored. MicroRNA-1-3p, as an oncogene, has been reported in bladder cancer for the first time[11]. It was found that DYNLT3 was the target gene of microRNA-1-3p in OVC. The purpose of this study was to explore the effect of microRNA-1-3p/DYNLT3 axis on the proliferation, migration ability, and invasiveness of OVC cells by detecting the expression of microRNA-1-3p in OVC tissues and cell lines.

Patients and Methods

Clinical Sample Collection

60 pairs of OVC tissues and adjacent normal ones were retained from hospitalized patients from January 2016 to December 2018. All tissue samples were examined and confirmed by our pathologists. The investigation was approved by the Ethics Committee of the Hospital. All patients had signed informed consent form prior to surgery. The collected samples were immediately stored in liquid nitrogen at –80°C. This work was conducted in accordance with the Declaration of Helsinki.

Cell Culture and Transfection

The human normal ovarian epithelial cell line (IOSE80) and human OVC cell lines (OC3, HO-8910, ES-2, SKOV-3) were all purchased from the Shanghai Cell Bank of the Chinese Academy of Sciences (Shanghai, China), fetal bovine serum (FBS) from Gibco (Rockville, MD, USA), Roswell Park Memorial Institute-1640 (RPMI-1640), and Dulbecco's Modified Eagle's Medium/F12 (DMEM/F12) and liposome Lipofectamine 2000 from Invitrogen (Carlsbad, CA, USA). IOSE80 and SKOV-3 cells were cultured in DMEM/F12 medium containing 10% FBS and 1% penicillin/streptomycin at 37°C in a humidified incubator containing 5% CO_2,, while OC3, HO-8910, and ES-2 cells were cultured in RPMI-1640 medium containing 10% FBS and 1% penicillin/streptomycin. Normal control group (NC group), microRNA-1-3p-mimics group, and microRNA-1-3p-mimics+DYNLT3-OE group were set in this experiment. Cells with better viability in log phase growth were plated into a six-well plate. When cell density reached 30%-40%, transfection was performed using Lipofectamine 2000 kit following the instructions. The microRNA NC, microRNA-1-3p-mimics and DYNLT3 overexpression plasmids (pcDNA3.1-DYNLT3) were all purchased from Gene Pharma (Shanghai, China).

Quantitative Real Time-Polymerase Chain Reaction (qRT-PCR)

Total RNA was extracted in one step by TRIzol reagent (Invitrogen, Carlsbad, CA, USA) and then reversely transcribed into complementary deoxyribose nucleic acid (cDNA) using PrimeScript reverse transcription kit (TaKaRa, Otsu, Shiga, Japan). Then, qPCR was performed using SYBR® Premix Ex Taq™ (TaKaRa, Otsu, Shiga, Japan) and StepOne Plus Real-time PCR System (Applied Biosystems, Foster City, CA, USA). The relative gene expression levels were quantified by $2^{-\Delta\Delta}$Ct method, with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and U6 as internal reference, respectively. The primer sequences are listed below: microRNA-1-3p

F: 5'-TGGAATGTAAAGAAGTATGTAT-3'; R: 5'-CGCTTCACGAATTTGCGTG-3'; DYNLT3 F: 5′-TGCGACGAGGTTGGCTTCAA-3′, R: 5′-TGCAGTCCACTGGTTGATGTT-3′; U6, F: 5'-CTCGCTTCGGCAGCACATA-3', R: 5'-CGCTTCACGAATTTGCGTG-3'; GADPH, F: 5'-AGCCACATCGCTCAGACAC-3', R: GCCCAATACGACCAAATCC-3'.

Dual-Luciferase Reporting Assay

The DYNLT3 Luciferase reporter vector containing the binding sites to microRNA-1-3p was constructed by Guangzhou Ruibo Biotechnology Co., Ltd. (Guangzhou, China). The 3′-UTR sequence of the DYNLT3 gene and the mutated 3'-UTR sequence were cloned into the p-GL3.0 plasmid to construct a Dual-Luciferase reporter vector, namely DYNLT3-WT 3'-UTR, DYNLT3-MUT 3'-UTR. The vector was co-transfected with microRNA-1-3p-mimics, and the fluorescence value was detected with a Dual-Glo Luciferase Assay System after 48 h of routine culture. The experiment was repeated three times.

Cell Counting Kit-8 (CCK-8) Assay

After 24 h of transfection, SKOV-3 and ES-2 cells (1×10^3 cells/well) were plated in 96-well culture plates. The cells were cultured for 6 h, 24 h, 48 h, and 72 h, respectively, and then added with 10 μL of CCK-8 reagent (RiboBio, Guangzhou, China). After incubation for 2 h, the optical density (OD) value of each well was measured in the microplate reader at 450 nm absorption wavelength.

5-Ethynyl-2′-Deoxyuridine (EdU) Assay

EdU cell proliferation assay (RiboBio, Guangzhou, China): ES2 and SKOV-3 cells in the NC group, microRNA-1-3p-mimics group and microRNA-1-3p-mimics+DYNLT3-OE group were treated with 100 μL of 50 μmol EdU medium for 2 h. After discarding the medium, the cultured cells fixed with 50 μL of 4% paraformaldehyde for 30 min at RT, and then stained with 1×Apollo for 30 min. Thereafter, an appropriate amount of 1× Hoechst 33342 reaction solution was prepared and added to each well. After incubation for 30 min, photographs were taken using a fluorescence microscope (Nikon, Tokyo, Japan) and the percentage of EdU positive cells was examined.

Transwell Cell Migration Assay

To determine cell migration capacity, transwell chamber was used (Corning, Corning, NY, USA) for mobility assays. The cells were seeded with 100 μL of serum-free medium at density of 3×10^4 in the upper layer of transwell chamber, which was placed in a 24-well plate. 600 μL of complete medium was added in the plate, and culture was maintained for 24 h. Next, the cells of the outer layer were collected, and cell fixation was carried out for 5 min using 4% formalin, and then fixed in 100% methanol for 20 min. Then, the cells were stained with crystal violet for 15 minutes at RT, washed twice with phosphate-buffered saline (PBS). After that, the cells in the upper layer of the chamber were scraped off with a wet cotton swab. Next, the transwell chamber was photographed under a microscope, and 5 independent fields were randomly selected each time.

Transwell Cell Invasion Assay

The upper transwell chamber was added with 100 μL of diluted Matrigel gel (Corning, Corning, NY, USA) and allowed to incubate for 1 h. ES-2 and SKOV-3 cells were transfected for 24 h, and then trypsinized to prepare a cell suspension of 2×10^8/L. Then, the upper chamber was added with 100 μL of cell suspension, while the lower chamber was filled with 600 μL of 10% fetal bovine serum complete medium, and cultured for 48 h. After erasing the non-invasive cells on the upper chamber with a cotton swab, the cells on the other side were fixed with formaldehyde. Finally, the crystal violet was used to stain cells for 15 min, and the number of cells in the chamber surface was observed under a microscope, and the experiment was repeated 3 times.

Western Blot Assay

At 24 h after transfection, the cells of each group were lysed with radioimmunoprecipitation assay (RIPA) cell lysate (Beyotime, Shanghai, China). Protein samples were separated by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE), transferred to polyvinylidene difluoride (PVDF) membrane (Millipore, Billerica, MA, USA), and blocked with 5% skim milk powder for 1 h at RT. Next, primary antibodies were added for incubation overnight at 4°C shaker. Then, the membrane was rinsed 3 times with Tris-Buffered Saline and Tween-20 (TBST) and incubated with second antibody for 1 h at RT. After that, the protein samples on the membrane were finally developed and analyzed with enhanced chemiluminescence (ECL) luminescence kit (Thermo Fisher Scientific, Waltham, MA, USA).

Statistical Analysis

Data were shown as mean ± standard deviation, the *t*-test was used for differences between groups, and Pearson correlation analysis was used for bivariate analysis. The experiment adopted a bilateral *p*-value of less than 0.05 as the validity criterion of the experimental results. All experimental analyses were performed using Statistical Product and Service Solutions (SPSS) 21.0 software (IBM, Armonk, NY, USA). GraphPad Prism 7.0 (San Diego, CA, USA) software was used to perform related statistical analysis mapping.

Results

MicroRNA-1-3p is a Potential Regulatory Gene of DYNLT3 and is Underexpressed in OVC Tissue Samples and Cell Lines

First, bioinformatics methods were used to predict miRNAs that may be targeted for binding to DYNLT3. As a result, hsa-microRNA-1-3p, hsa-microRNA-125b-5p, and hsa-microRNA-125a-5p were found as common part among the three databases (DIANA TargetBase 8.0, http://carolina.imis.athena-innovation.gr, TargetScan Human 7.2, http://targetscan.org/cgi-bin/targetscan/vert_72, and starBase 2.0, http://starbase.sysu.edu.cn/agoClipRNA.php?source=mRNA) (Figure 1A). Hence, these miRNAs were then validated by literature review on PubMed, which indicated that both microRNA-125b-5p and microRNA-125a-5p have been explored in OVC and have been shown to be down-regulated. Therefore, microRNA-1-3p was chosen for further study. Subsequently, qPCR revealed that microRNA-1-3p was also remarkably under expressed in both OVC tissues (Figure 1B) and cells (Figure 1C). At the same time, DYNLT3 level in OVC tissues was found remarkably higher than that in adjacent normal tissues (Figure 1D). Besides, the Pearson correlation analysis showed that microRNA-1-3p was in negative correlation with DYNLT3 gene

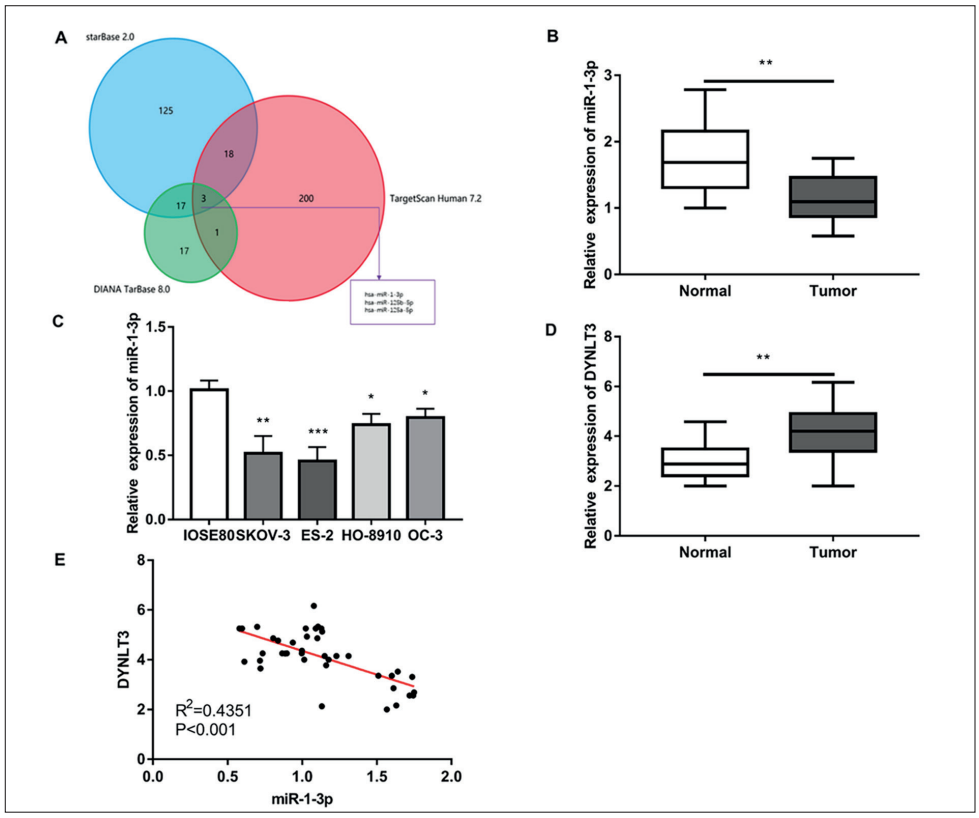

Figure 1. In ovarian cancer, miR-1-3p expression is down-regulated and DYNLT3 expression is up-regulated. **A,** MiRNAs that may bind to DYNLT3 are predicted by bioinformatics methods. **B,** Relative expression levels of miR-1-3p in 60 pairs of ovarian cancer tissues and adjacent normal tissues are detected by RT-qPCR. **C,** Expression level of miR-1-3p in ovarian cancer cell lines is analyzed by RT-qPCR. **D,** Relative expression levels of DYNLT3 in 60 pairs of ovarian cancer tissues and adjacent normal tissues are detected by RT-qPCR. **E,** Pearson correlation analysis shows that miR-1-3p is negatively correlated with DYNLT3 gene expression level **p*<0.05, ***p*<0.01, ****p*<0.001.

expression (Figure1E), indicating that DYNLT3 expression was likely to be affected by microRNA-1-3p.

MicroRNA-1-3p can Regulate the Gene and Protein Expression Level of DYNLT3 in OVC Cells

The above results indicate that microRNA-1-3p may have a regulatory relationship with DYNLT3 in OVC tissues and cells, so the binding of the two was further observed using Dual-Luciferase reporting technology. First, the bioinformatics database predicted that DYNLT3 might be the target gene of microRNA-1-3p (Figure 2A). Then, transfection of microRNA-1-3p-mimics in OVC cell lines ES2 and SKOV3 was found to enhance microRNA-1-3p expression (Figure 2B). Subsequently, the Dual-Luciferase reporter gene assay showed that in ES2 and SKOV3 cells, the Luciferase activity of the DYNLT3-WT 3'UTR group was significantly reduced after transfection of miR-1-3p-mimics compared to miRNA-NC, whereas the Luciferase activity in the DYNLT3-MUT 3'UTR group was not significantly different (Figure 2C, 2D), suggesting that microRNA-1-3p can bind to the 3'-UTR of the DYNLT3 gene. Subsequently, qPCR results verified a significant decrease in the mRNA expression level of DYNLT3 in OVC cells

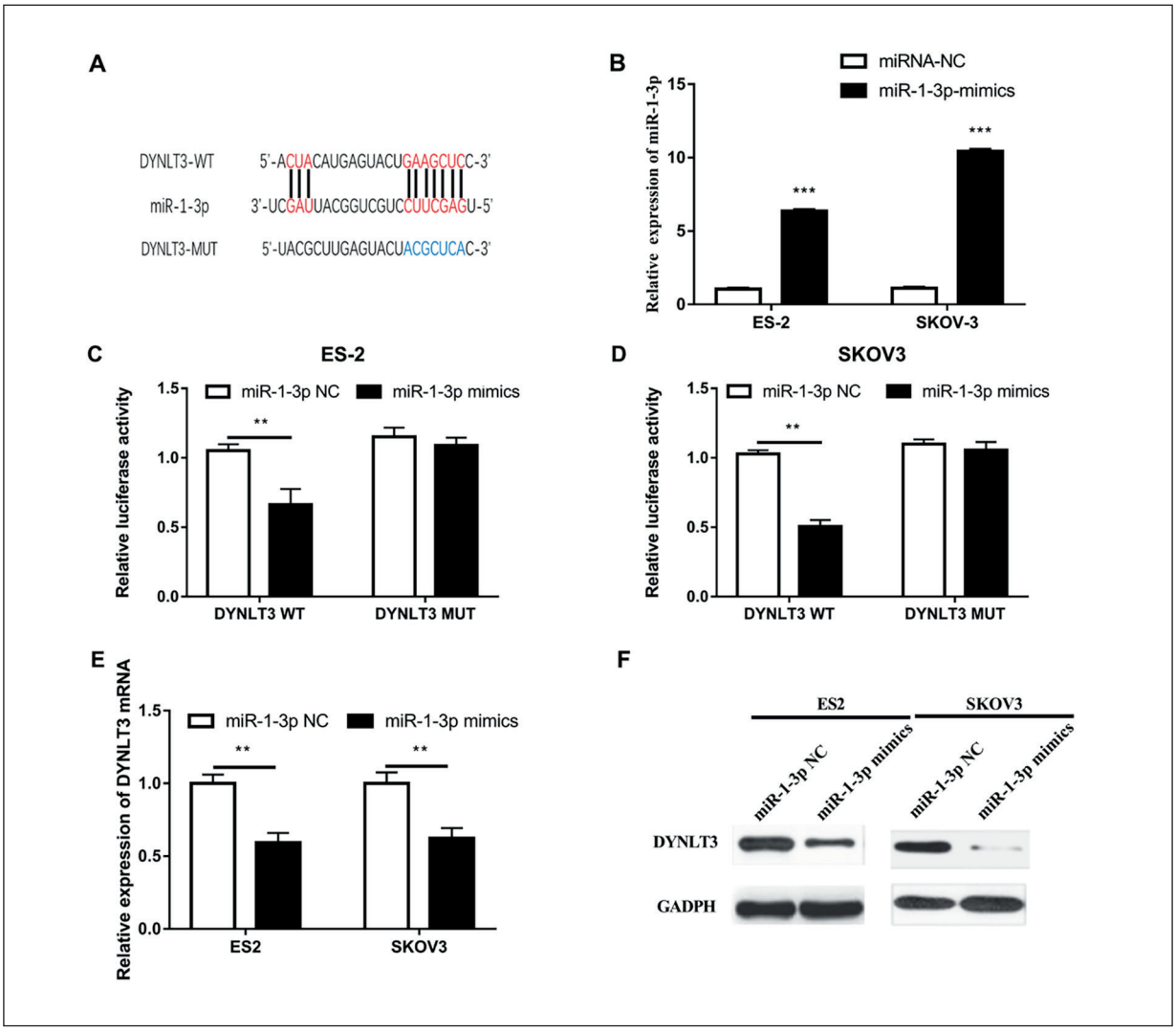

Figure 2. DYNLT3 is the target gene for miR-1-3p. **A,** Bioinformatics method predicts the binding site of miR-1-3p to DYNLT3.**B,** Transfection of miR-1-3p-mimics in ovarian cancer cell lines ES2 and SKOV3 increases the expression level of miR-1-3p. **C, D,** Binding relationship of miR-1-3p to DYNLT3 is examined by Dual-Luciferase reporter assay in ES2 and SKOV3 cells. **E-F,** Expressions of DYNLT3 mRNA and protein after transfection of miR-1-3p-mimics and miRNA-NC in ovarian cancer ES-2 and SKOV-3 cell lines $^{**}p<0.01$, $^{***}p<0.001$.

transfected with microRNA-1-3p-mimics (Figure 2E), and Western blot results also showed a downward trend in DYNLT3 protein level (Figure 2F). These results indicate that microRNA-1-3p can regulate the transcription and translation levels of the key oncogenic gene DYNLT3 by binding to its 3'-UTR region.

MicroRNA-1-3p can Affect the Proliferation of OVC Cells

MicroRNA-1-3p-mimics+DYNLT3-OE, microRNA-1-3p-mimics and miRNA-NC were transfected in ES2 and SKOV3 cells, respectively, and microRNA-1-3p level was detected using qPCR. The results revealed that compared with miRNA-NC, microRNA-1-3p-mimics remarkably enhanced the expression of microRNA-1-3p, which was partially reversed by transfection of microRNA-1-3p-mimics+DYNLT3-OE group (Figure 3A). In addition, CCK8 assay detected a significant decrease in the cell proliferation ability after overexpression of microRNA-1-3p, which was also reversed by transfection of microRNA-1-3p-mimics+DYNLT3-OE (Figure 3B,

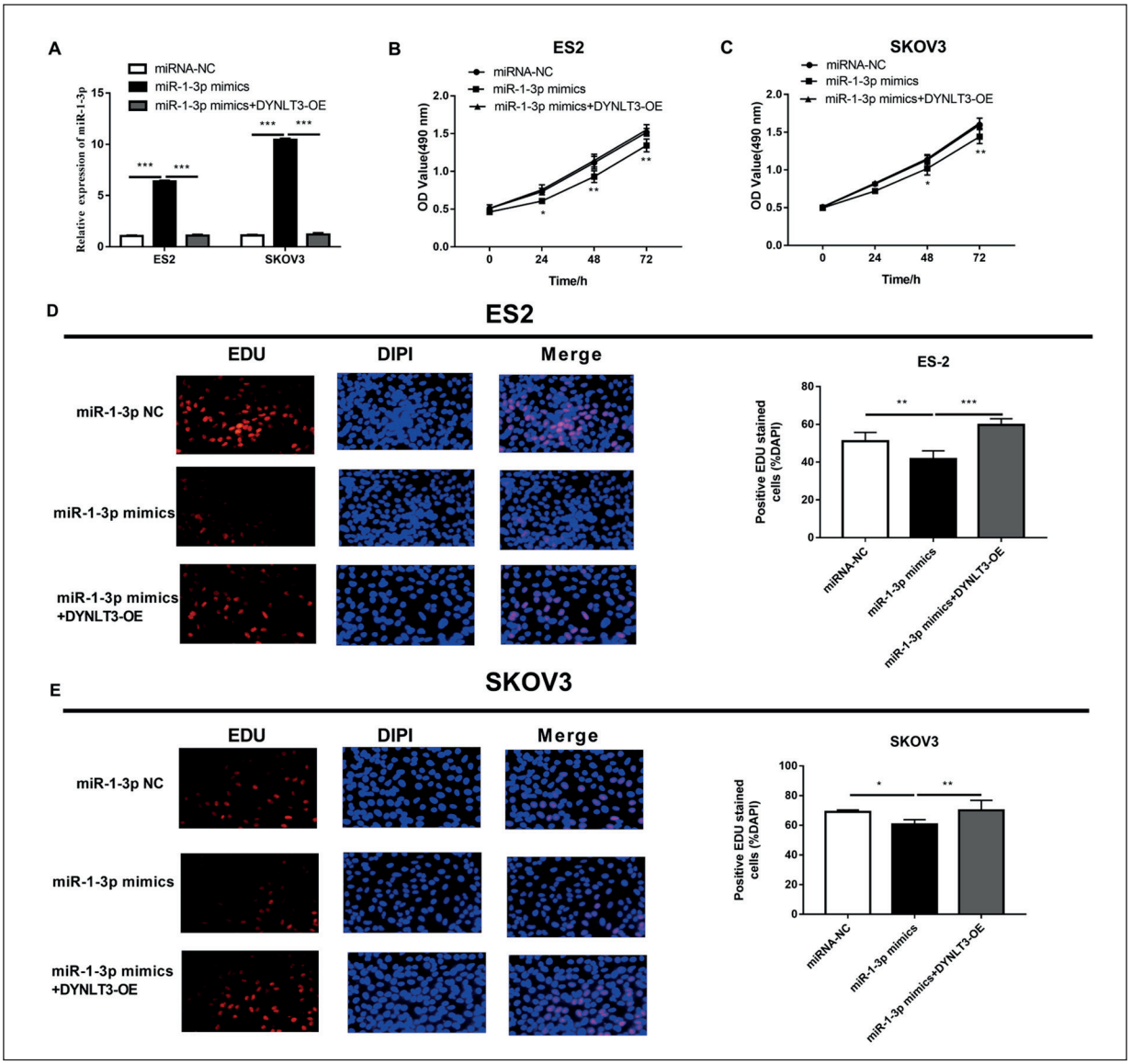

Figure 3. MiR-1-3p inhibits the proliferative capacity of ovarian cancer cells by targeting DYNLT3. **A,** Transfection of miR-1-3p-mimics+DYNLT3-OE, miR-1-3p-mimics and NC in ES-2 and SKOV-3 cell lines, followed by RT-qPCR for detection of miR-1-3p expression Happening. **B, C,** The CCK-8 assay detects changes in cell proliferation capacity after overexpression of miR-1-3p and DYNLT3 in ES-2 and SKOV-3 cell lines. **D, E,** The EDU assay detects changes in cell proliferation capacity after overexpression of miR-1-3p and DYNLT3 in ES-2 and SKOV-3 cell lines (magnification: 20×) *p<0.05, **p<0.01, ***p<0.001.

3C). At the same time, the results of EdU revealed that microRNA-1-3p overexpression remarkably decreased the proportion of OVC cells in the proliferative phase, while transfection of microRNA-1-3p-mimics+DYNLT3-OE remarkably increased that (Figure 3D, 3E). These results indicate that upregulation of microRNA-1-3p is able to reduce the proliferative capacity of OVC cells, while overexpression of DYNLT3 can reverse the inhibitory effect of microRNA-1-3p.

MicroRNA-1-3p can Affect the Migration Ability and Invasiveness Ability of OVC Cells

To explore the function of microRNA-1-3p, microRNA-1-3p-mimics+DYNLT3-OE, microRNA-1-3p-mimics, and miRNA-NC were transfected in ES-2 and SKOV-3, respectively, followed by transwell cell migration assay to detect cell migration ability. After 24 h, it was found that the cell migration rate of microRNA-1-3p-mimics group was remarkably lower than that of miRNA-NC group, but cells in microRNA-1-3p-mimics+DYNLT3-OE group showed a significant increase in cell migration compared to the microRNA-1-3p-mimics group (Figure 4A, 4B). At the same time, changes in cell invasive ability were determined using the transwell method. Under the same culture conditions, OVC cells were plated in the transwell chamber, and the number of OVC cells transfected with microRNA-1-3p-mimics passed through the transwell membrane were much less than that of cells in control group, where-

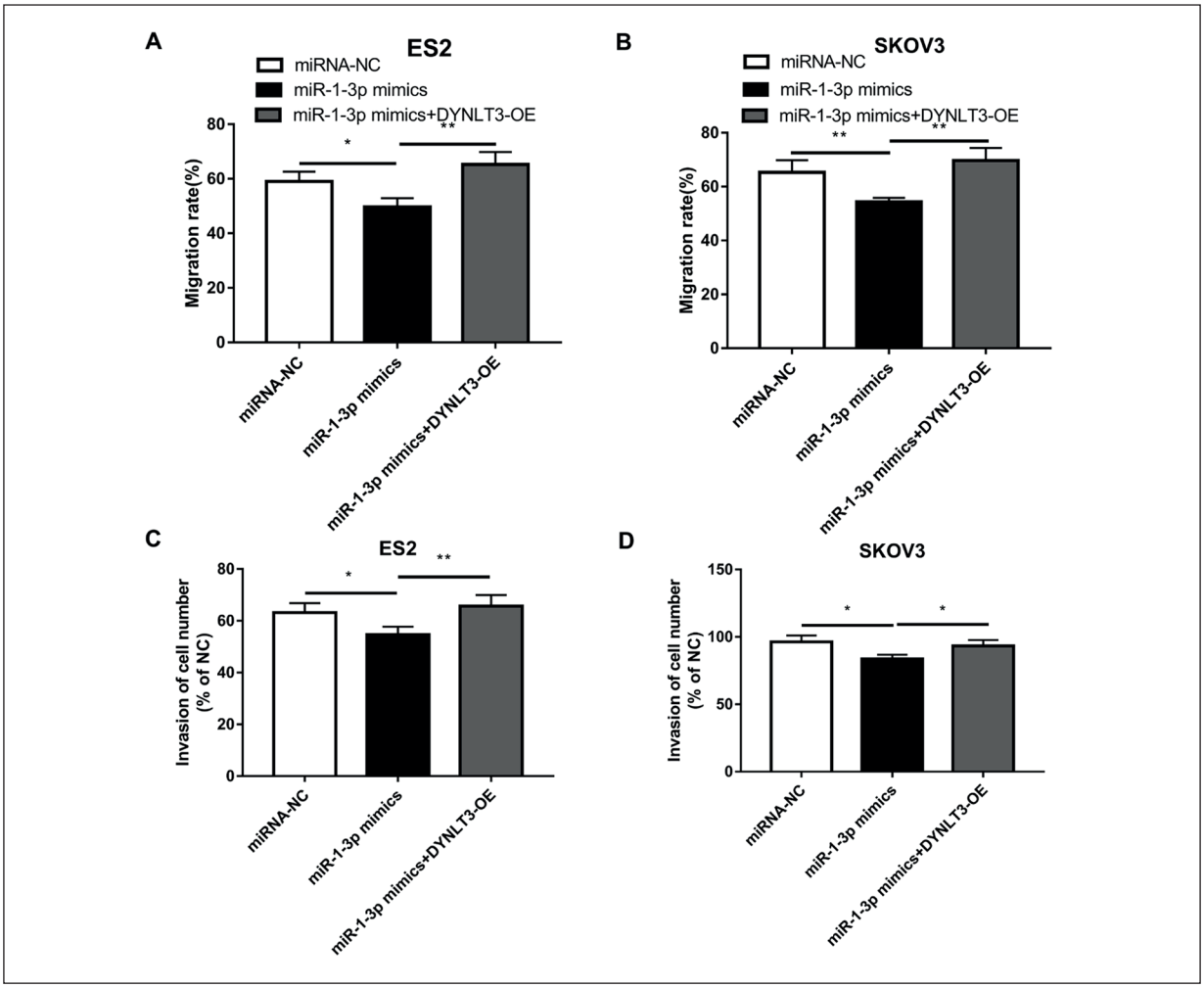

Figure 4. MiR-1-3p inhibits the migration and invasion of ovarian cancer cells by targeting DYNLT3. **A, B,** Transwell cell migration assay is used to assess changes in migration capacity of ES-2 and SKOV-3 cells transfected with miR-1-3p-mimics+DYNLT3-OE, miR-1-3p-mimics and miR-1-3p-NC. **C, D,** Invasion cell invasion assay is used to detect changes in invasive ability of ES-2 and SKOV-3 cells transfected with miR-1-3p-mimics+DYNLT3-OE, miR-1-3p-mimics and miR-1-3p-NC *p<0.05, **p<0.01.

as the treatment of microRNA-1-3p-mimics+-DYNLT3-OE significantly elevated the number (Figure 4C, 4D). The results demonstrated that microRNA-1-3p was capable of attenuating the migration ability and invasiveness of OVC cells *in vitro*, which, however, could be restored by the overexpression of DYNLT3.

Discussion

Most patients with OVC seek medical treatment due to abdominal mass or ascites, and most patients are found to be in advanced stage of OVC, which owns the highest mortality rate in the female reproductive system[12]. At present, tumor recurrence and chemotherapy resistance have become an urgent problem to be solved in the clinical treatment of OVC. Therefore, it is important to explore the occurrence and development mechanism of OVC and find new therapeutic targets to improve the prognosis and survival rate of OVC patients. Currently, the molecular regulation mechanism of miRNA has been researched in-depth, and the relationship between miRNA and OVC progression has been continuously reported. A variety of microRNAs have been reported[13] to be abnormally expressed in OVC and play an important part in its cell growth, migration ability, and invasiveness as oncogenes or tumor suppressor genes. Of note, Yu et al[14] have shown that miRNA-21 in OVC promotes the occurrence and development of OVC by regulating the expression of PTEN gene. In addition, Wang et al[15] have found that microRNA-19a negatively regulates the expression of PTEN and promotes the growth of OVC cells. Above researches indicate that there are multiple regulatory mechanisms of miRNA that affect the occurrence and development of OVC, and further studies are needed.

MicroRNA-1-3p is a small non-coding microRNA that regulates gene expression by regulating translation inhibition or mRNA cleavage[16] and participates in gene regulation of various human cancers, such as liver cancer, breast cancer, and bladder cancer[17-19]. However, the mechanism of microRNA-1-3p in OVC still needs to be further explored. In this study, the expression of microRNA-1-3p in OVC tissues and cell lines was remarkably down-regulated compared with normal paracancerous tissues and normal ovarian epithelial cells, suggesting that microRNA-1-3p may participate in the incidence and development of OVC. The novelty of this work was that we further explored the biological function of microRNA-1-3p in OVC. We found that after microRNA-1-3p was overexpressed in ES-2 and SKOV-3 cell lines, the proliferation, migration, and invasion abilities of OVC cells were remarkably reduced. DYNLT3 overexpression reversed the activity, migration ability, and invasiveness of OVC cells, suggesting that microRNA-1-3p may be involved in the progression of OVC mainly by inhibiting the proliferation, migration, and invasion abilities of OVC cells.

DYNLT1 and DYNLT3 are two members of dynein light chain Tctex family, which are mainly involved in antivesicular transport, spindle localization in mitosis, and axon transport[20]. DYNLT participates in the occurrence and development of various tumors[21]. DYNLT1 has been shown to be associated with the progression of liver cancer. Shao et al[22] have shown that DYNLT3 can be one of the candidate oncogenes for salivary adenoid cystic carcinoma. Meanwhile, DYNLT3 promotes proliferation, migration ability, and invasiveness of OVC cells[10]. In this research, through bioinformatics methods and Dual-Luciferase reporter gene experiments, microRNA-1-3p could complement DYNLT3 in OVC. Further investigations showed that the expression of microRNA-1-3p was decreased in OVC cell lines, while the DYNLT3 level was remarkably up-regulated. After the overexpression of microRNA-1-3p in OVC cell lines, the expressions of DYNLT3 mRNA and protein were remarkably reduced. We found that microRNA-1-3p may target DYNLT3, thus inhibiting the proliferation, migration ability, and invasiveness of OVC cells, as well as inhibiting the progress of OVC.

Conclusions

In summary, we demonstrated that the expression of microRNA-1-3p was decreased in OVC tissues and cell lines, and microRNA-1-3p overexpression could remarkably inhibit the proliferative activity, migrate ability, and invasiveness of OVC cells. The mechanism may be that microRNA-1-3p targets to interfere with the expression of DYNLT3, thereby inhibiting the incidence and development of OVC. This study provides a new direction for the exploration of the incidence, development, and treatment of OVC.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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