miRNA-181a Inhibits the Proliferation, Migration, and Epithelial–Mesenchymal Transition of Lens Epithelial Cells

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PURPOSE. MicroRNA-181a (miR-181a) is thought to be involved in posterior capsule opacification (PCO). This study investigated the role of miR-181a in the proliferation, migration, and epithelial–mesenchymal transition (EMT) of lens epithelial cells (LECs).

METHODS. The expression of miR-181a was detected in human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts by quantitative RT-PCR (qRT-PCR). The proliferation of SRA01/04 cells transfected with miR-181a mimics was analyzed by MTT assays and bromodeoxyuridine (BrdU)-incorporation assays. The migration of SRA01/04 cells was evaluated by wound-healing assays and Transwell migration. Luciferase reporter assays were used to validate the regulation of a putative target of miR-181a.

RESULTS. The expression of miR-181a is decreased in human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts. A significant decrease in proliferation was observed in SRA01/04 cells transfected with miR-181a mimics. The overexpression of miR-181a inhibited the migration ability of LECs. Downregulation of fibronectin, Slug, and cyclooxygenase-2 (COX-2) expression and upregulation of E-cadherin expression were induced in human PCO-attached LECs transfected with miR-181a mimics and miR-181a-overexpressing LECs obtained from patients with anterior polar cataracts. Furthermore, luciferase assays using a reporter carrying a putative miR-181a target site in the 3’ untranslated region of c-Met, Slug, and COX-2 revealed that miR-181a directly targets c-Met, Slug, and COX-2.

CONCLUSIONS. These data reveal that miR-181a can inhibit the proliferation, migration, and EMT of LECs and suggest that the restoration of miRNA-181a expression may be a potential novel therapeutic target for the prevention and treatment of posterior capsule opacification.

Keywords: lens epithelial cells, proliferation, migration, epithelial–mesenchymal transition, miR-181a
miRNA-181a in the Treatment of PCO

MicroRNAs (miRNAs) are small noncoding RNAs consisting of 22 nucleotide base pairs, which could regulate gene expression at the posttranscriptional level by binding to the 3′ untranslated regions (UTRs) of target mRNAs, resulting in mRNA either translational repression or transcript degradation. Evidence also indicates that some miRNAs play a role in regulating lens differentiation, cataractogenesis, and PCO. Specifically, we previously reported that the expression of miR-26b is downregulated in human PCO-attached LECs and that miR-26b can inhibit the proliferation, migration, and EMT of LECs. MicroRNA-181a (miR-181a) belongs to the miR-181s family, which includes four highly conserved mature miR-181s (miR-181a, miR-181b, miR-181c, and miR-181d). Recent findings indicate that miR-181a is a multifunctional miRNA that participates in many biological processes, such as apoptosis, cell proliferation, and cellular invasion, and functions as a tumor suppressor. Furthermore, a recent study has shown that miR-181a expression is downregulated in human PCO tissues when comparing the miRNA profile in human PCO tissues with that of normal-attached LECs; however, the mechanism for dysregulation of miR-181a expression in PCO has not been reported to date. Therefore, the aim of the present study was to explore the ability of miR-181a to affect the PCO. In this study, we present the first evidence demonstrating that miR-181a can inhibit the proliferation, migration, and EMT of LECs by directly silencing c-Met, Slug, and COX-2.

Materials and Methods

Patient Lens Epithelial Cell Collection and Culture

Fresh lens capsules with adherent LECs were obtained during cataract surgery from 46 patients with the clinical diagnosis of nuclear or anterior polar cataracts. The ages of the patients ranged from 42 to 86 years. The study was approved by the Ethics Committee of Beijing Shijitan Hospital, Capital Medical University, Beijing, People’s Republic of China, and the study was performed in accordance with the Declaration of Helsinki. Each participant received detailed information and provided informed consent before being included in the study. In brief, after injecting viscoelastic agent into the anterior chamber, continuous curvilinear capsulorrhexis was performed. The anterior capsules were carefully removed with forceps and spread onto tissue culture dishes with the epithelium side up. Then, a single drop of FBS was placed on the epithelial surface to allow for adequate adherence of the tissue to the dish. Dulbecco’s modified Eagle’s medium (DMEM) supplemented with 20% FBS was added, and the cells were incubated at 37°C for 48 hours, the culture medium was replaced with fresh medium of each well reached 90% confluence, and the confluent monolayers of the SRA01/04 cells were scratched.

SRA01/04 Cell Culture

The human lens epithelial cell line SRA01/04 was obtained from the Cancer Institute and Hospital, Chinese Academy of Medical Sciences (Beijing, China). The method for SRA01/04 cell culture has been described in detail previously. In brief, cells were routinely cultured in Eagle’s minimum essential medium (Life Technologies Corp., Gibco/Brl, Grand Island, NY, USA) with 10% FBS in a 5% CO2 humidified atmosphere at 37°C. Cells were passaged at approximately 80% confluence.

Transfection

The method for cell transfection has been previously described in detail. In brief, miR-181a mimics and the scrambled control microRNA were obtained from GenePharma (Shanghai, China). For 1 × 10⁶ cells, 0.4 nmol microRNA mimics or miR-181a control mimic were mixed with 15 μL GenePORTER transfection reagent (GTS, Inc., San Diego, CA, USA) and transfected into the cells. After 6 hours, the supernatant was removed, and fresh medium was added.

Quantitative RT-PCR (qRT-PCR)

The qRT-PCR method has been described in detail previously. The primers are as follows: miR-181a sense, 5′-CGGCTCGAGCAAAATATGTTAACTCTTAC-3′; miR-181a antisense, 5′-GGCGGTCGACTTCTTTAATATTAAAACTTG-3′; E-cadherin sense, 5′-GTCATCAAGGGAATGCA-3′; E-cadherin antisense, 5′-TGATCGGTACCTGATGACAAA-3′; fibronectin sense, 5′-AGCGGAATCTACCTAGGCAAT-3′; fibronectin antisense, 5′-GGTTTGGTGATCATACCTT3′.

MTT Cell Proliferation Assay

The method for the MTT cell proliferation assay has been described in detail previously. In brief, the optical density value of each well was measured at 570 nm using a μQuant Universal Microplate Spectrophotometer (Bio-Tek Instruments, Winooski, VT, USA).

Cell Proliferation Detected by 5-Bromodeoxyuridine (BrdU) Incorporation Assay

The method for the BrdU incorporation assay has been described in detail previously. In brief, cells (5 × 10⁵) were plated into 96-well plates in 10% FBS/DMEM in the presence of miR-181a mimics or scrambled control microRNA. After 24, 48, and 72 hours, the culture medium was replaced with fresh medium. The cells were labeled with 10 μM 5-bromo-2′-deoxyuridine (BrdU; Sigma-Aldrich Corp., St. Louis, MO, USA) for 2 hours. After the cells were fixed in 0.4% paraformaldehyde for 20 minutes and washed with PBS, they were incubated in 1.5 M HCl for 10 minutes. Then, the cells were washed with PBS and incubated with mouse anti-BrdU-fluorescein isothiocyanate (Roche, Indianapolis, IN, USA) for 2 hours. The cells were washed four times with PBS. Then, the cells were incubated with the secondary antibody (Jackson ImmunoResearch Laboratories, West Grove, PA, USA) for 1 hour and washed with PBS. Finally, the cells were counterstained with 4′,6-diamino-2-phenylindole (DAPI, 1 μg/mL; Invitrogen, Carlsbad, CA, USA), mounted, and examined, and then counted using fluorescence light microscopy (BX50; Olympus, Inc., Tokyo, Japan).

Wound-Healing Assay

The method of wound-healing assay has been described in detail previously. In brief, SRA01/04 cells were seeded in a 24-well plate (1 × 10⁵ cells/well). After 24 hours of transfection with microRNA mimics or miR-181a control mimics, the cell density of each well reached 90% confluence, and the confluent monolayers of the SRA01/04 cells were scratched.
with a sterile, 20-μL pipette tip. Wounded monolayers were washed with PBS to remove detached cells and debris, and fresh medium was added to each well. The wounds in each well were photographed at 0, 24, 48, and 72 hours. The length of the remaining wound in each image was measured five times using Imagej software (http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). The data were quantified based on the percentage of average gap (AG); the wound at 0 hours was considered 100% AG. The results were analyzed in triplicate.

**Transwell Migration Assay**

The method of Transwell migration assay has been described in detail previously. In brief, SRA01/04 cells were seeded into the inner chamber of tissue culture inserts (Transwell Assay System; Corning, High Wycombe, UK) of 24-well plates. Cells transfected with microRNA mimics or miR-181a control mimics at a density of 5 × 10^5 cells/mL were added to the upper polycarbonate membrane insert and allowed to migrate through the 8-μm pores, and in the lower well, 300 μL DMEM with 20% FBS was used as chemoattractant. After 48 hours of incubation at 37°C in 5% CO2, the membranes were fixed with 10% formaldehyde and stained with hematoxylin. The cells that had migrated to the bottom of the insert were counted five times in random microscope fields.

**Western Blot Analysis**

The method used for Western blot analysis has previously been described in detail. The primary antibodies are anti-c-Met, anti-Slug, anti-cyclin-dependent kinase 2 (CDK2), anti-CDK4, anti-CDK6, anti-E-cadherin, anti-fibronectin, anti-actin (all from Cell Signaling Technology, Beverly, MA, USA), and anti-COX-2 (Santa Cruz Biotechnology, Santa Cruz, CA, USA).

**Luciferase Assay**

The method of luciferase assay has been described in detail previously. In brief, the 3’-UTRs of c-Met, Slug, and COX-2 containing the predicted miR-181a binding or mutant sites were amplified by PCR using the following primers: c-Met sense 5'-TGGAGCTCTGAGAATAATGAGGGCTTCT-3'; c-Met antisense, 5'-TGAGTCGACTTCTGGGAGGCTTGAG-3'; Slug sense 5'-ATATCGAGATGCAAATAAAGTGCCAAAGG-3'; Slug antisense, 5'-ATATCGAGATGCAAATAAAGTGCCAAAGG-3'; COX-2 sense 5'-CGGGTTACCGTTGCTACATGGA-3'; COX-2 antisense, 5'-GCCTGAGGCTGTTTTGTTGCTG-3'; mutant c-Met sense 5'-CTATGACCTACCTGATGAAAGGCG-3'; mutant Slug sense 5'-GCCACCGCGAATCTGCTGCCGTTAAAAGAATTTATCGAGGAAAGATTTATGAGGAAAGGCTTCT-3'; mutant Slug antisense, 5'-CTAGCTCTGTCGAGTGCCTCTCCG-3'; mutant COX-2 sense 5'-GTTATGAAATATAGAAGC-3'; mutant COX-2 antisense, 5'-GACGAAAAGACGTCAAAACT-3'; fragments were subcloned into the Not I and Xho I sites in the 3’-UTR of Renilla luciferase of the psiCHECK-2 psiCHECK-2 reporter vector (psiCHECK-2; Promega, Madison, WI, USA). The psiCHECK-2/c-Met 3’-UTR or psiCHECK-2/c-Met 3’-UTR mutant, psiCHECK-2/Slug 3’-UTR or psiCHECK-2/Slug 3’-UTR mutant, and psiCHECK-2/COX-2 3’-UTR or psiCHECK-2/COX-2 3’-UTR mutant reporter plasmids (200 ng) were cotransfected with the miR-181a mimics or miR-181a control mimics into SRA01/04 cells (60% confluence). After 48 hours, the cells were lysed, and reporter activity was assessed using the Dual-Luciferase Reporter Assay System (Promega, Madison, WI, USA) in accordance with the manufacturer’s protocols.

**Statistical Analysis**

All experiments were performed at least three times. Quantitative data are presented as the mean ± SE and were analyzed by 1-way ANOVA or Student’s t-test. A P value of <0.05 was considered statistically significant.

**Results**

**Expression of miR-181a Is Decreased in Human PCO-Attached LECs and LECs Obtained From Patients With Anterior Polar Cataracts**

To investigate the involvement of miR-181a in PCO development, we analyzed the level of miR-181a in human PCO-attached LECs and normal-attached LECs by qRT-PCR. MicroRNA-181a expression was significantly decreased in human PCO-attached LECs compared with normal-attached LECs (3.8-fold, P < 0.01) (Fig. 1A). The expression levels of EMT markers were also determined in human PCO-attached LECs and normal-attached LECs by qRT-PCR (Figs. 1B, 1C). Downregulation of E-cadherin and upregulation of fibronectin expression were detected in human PCO-attached LECs.

During the formation of anterior polar cataracts, LECs can transdifferentiate and proliferate into mesenchyme-like cells or myofibroblasts through the EMT. To investigate the involvement of miR-181a in anterior polar cataract development, we determined the level of miR-181a in LECs obtained from patients with anterior polar cataracts and nuclear cataracts by qRT-PCR. MicroRNA-181a expression was significantly decreased in LECs obtained from patients with anterior polar cataracts compared with patients with nuclear cataracts (3.2-fold, P < 0.01) (Fig. 1D). Downregulation of E-cadherin and upregulation of fibronectin expression were also detected in the LECs obtained from patients with anterior polar cataracts (Figs. 1E, 1F).

**miR-181a Inhibits the Proliferation and Migration of SRA01/04 Cells**

MicroRNA-181a was downregulated in human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts, suggesting a potential role in the biological properties of LECs. MicroRNA-181a expression was significantly higher in the SRA01/04 cells transfected with miR-181a mimics compared with the cells transfected with miR-181a control mimics, as shown by qRT-PCR (26.4-fold, P < 0.01) (Fig. 2A). In addition, miR-181a control expression was significantly higher in the SRA01/04 cells transfected with miR-181a control mimics (Fig. 2B). As shown in Figure 2C, the overexpression of miR-181a inhibited SRA01/04 cell growth at 24, 48, and 72 hours after miR-181a mimics transfection, as determined by the MTT assay (P < 0.01). Furthermore, to confirm that the effects of miR-181a on cell proliferation were not related with high expressed levels of microRNA, the overexpression of miR-498 did not affect SRA01/04 cell growth at 24, 48, and 72 hours after miR-498 mimics transfection (Supplementary Fig. S1). Additionally, SRA01/04 cells were immunostained for BrdU (Fig. 2D, red), and their nuclei were stained with DAPI (Fig. 2D, blue). The BrdU assay revealed that the overexpression of miR-181a inhibited SRA01/04 cell growth at 24, 48, and 72 hours after transfection (P < 0.05, Figs. 2D, 2E).

To confirm the effects of miR-181a on cell migration, SRA01/04 cells were transfected with miR-181a mimics or miR-181a control mimics. After 48 hours of incubation, SRA01/04 cells transfected with miR-181a mimics demonstrated reduced
migration across the polycarbonate membrane compared with the control cells (Fig. 2F). Additionally, the wound-healing assay revealed that the miR-181a–overexpressing cells moved slower than the SRA01/04 cells transfected with the miR-181a control mimics and the mock SRA01/04 cells (Figs. 2G, 2H).

**miR-181a Downregulated c-Met Expression and Other Cell Cycle–Related Proteins via Regulation of c-Met**

The c-Met and cell cycle–related proteins have been found to be associated with the proliferation, protein synthesis, and migratory responses of LECs.8–10,28 To investigate the mechanism through which miR-181a affects LEC proliferation, we evaluated the expression of c-Met and other cell cycle–related proteins in SRA01/04 cells transfected with miR-181a mimics and the mock SRA01/04 cells (Figs. 2G, 2H).

To determine whether miR-181a inhibits LEC proliferation by downregulating c-Met and its downstream molecules, we altered the expression level of c-Met using specific small interfering RNA (siRNA) in SRA01/04 cells (Fig. 4B). Western blot analysis revealed that the expression levels of CDK2, CDK4, and CDK6 were significantly decreased in the c-Met siRNA-transfected cells compared with the c-Met control siRNA-transfected cells and the mock SRA01/04 cells (Fig. 3B).

We used miRanda to search for the 3′-UTR sequences of the miRNAs encoding c-Met, CDK2, CDK4, and CDK6 and found that only the c-Met mRNA contained a seed sequence for miR-181a, which suggests that miR-181a binds directly to its 3′-UTR (Fig. 3C). To test this proposal, we performed a luciferase reporter assay to verify that miR-181a directly targets c-Met (Fig. 3D).

**miR-181a Inhibits the EMT of Human PCO-Attached LECs and LECs Obtained From Patients With Anterior Polar Cataracts via Regulation of Slug and COX-2**

To determine the potential ability of miR-181a to downregulate fibronectin and upregulate E-cadherin, human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts were transfected with miR-181a mimics or miR-181a control mimics. When comparing the human PCO-attached LECs to normal-attached LECs, the expression of E-cadherin was decreased, and the expression of fibronectin, Slug, and COX-2 was increased in the PCO-attached LECs, as shown by Western blot analysis (Fig. 4A). However, a downregulation of fibronectin, Slug, and COX-2 expression and an upregulation of E-cadherin expression were observed in the miR-181a–overexpressing human PCO-attached LECs. As shown in Figure 4B, the expression of E-cadherin was decreased, and the expression of fibronectin, Slug, and COX-2 was increased in LECs obtained from patients with anterior polar cataracts. Furthermore, a downregulation of...
Figure 2. MicroRNA-181a inhibited proliferation and migration of SRA01/04 cells. (A) MicroRNA-181a expression was significantly increased in the SRA01/04 cells transfected with miR-181a mimics compared by qRT-PCR with the SRA01/04 cells transfected with miR-181a mimics control (2640-fold, \( P < 0.01 \)). (B) MicroRNA-181a control expression was significantly higher in the SRA01/04 cells transfected with miR-181a control mimics (2580-fold, \( P < 0.01 \)). (C) MTT assay results revealed that overexpression of miR-181a inhibited SRA01/04 cell growth at 24, 48, and 72 hours compared with the SRA01/04 cells transfected with miR-181a control mimics and mock SRA01/04 cells. (D) The SRA01/04 cells labeled with BrdU

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were induced in miR-181a–overexpressing LECs obtained from patients with anterior polar cataracts. We used miRanda to search for the 3′-UTR sequences of the mRNAs encoding E-cadherin, fibronectin, Slug, and COX-2 and found that Slug and COX-2 mRNA contained a seed sequence for miR-181a, which suggests that miR-181a binds directly to these 3′-UTRs (Figs. 4C, 4E). To test this proposal, we performed a luciferase reporter assay to verify that miR-181a directly targets Slug and COX-2 (Figs. 4D, 4F).

**DISCUSSION**

Posterior capsule opacification is the most common postoperative complication of cataract surgery that causes vision loss; its incidence is 30% to 50% in adults and 100% in children who receive surgery.1 Although PCO is known to be associated with wrinkling/contraction of the posterior capsule and the pathologic progression of postoperative residual LECs, including proliferation, migration, and EMT, the mechanism underlying this process is not yet clearly understood. MicroRNAs affect essential biological processes such as metabolism, cell

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**FIGURE 3.** Introduction of miR-181a downregulated c-Met expression and other cell cycle–related proteins. (A) SRA01/04 cells were transfected with miR-181a mimics or miR-181a control mimics. Cell lysates were prepared and used for Western blot analysis of c-Met, CDK2, CDK4, and CDK6. β-actin was used as a loading control. Overexpression of miR-181a, which suggests that miR-181a binds directly to these 3′-UTRs (Figs. 4C, 4E). To test this proposal, we performed a luciferase reporter assay to verify that miR-181a directly targets Slug and COX-2 (Figs. 4D, 4F).

**FIGURE 4.** The region of the c-Met mRNA 3′-UTR predicted to be targeted by miR-181a. (D) Dual-luciferase report assays were performed on SRA01/04 cells. The luciferase activity of wild-type (WT) reporter transfectsed with miR-181a mimics was significantly decreased compared with miR-181a mimics control (P < 0.01). However, the luciferase reporter activity was not inhibited by miR-181a mimics when the seeding sites were mutated (P > 0.05). Results are statistically significant (**P < 0.01). Error bars denote SEM.
MicroRNA-181a inhibited the EMT of human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts via regulation of Slug and COX-2. (A) Western blot analysis detected downregulated E-cadherin and upregulated fibronectin, Slug, and COX-2 in human PCO-attached LECs compared with that of normal-attached LECs. However, the expression of E-cadherin was increased and the expression of fibronectin, Slug, and COX-2 was decreased in human PCO-attached LECs transfected with miR-181a mimics. (B) The expression of E-cadherin was downregulated, and the expression of fibronectin, Slug, and COX-2 was increased in LECs obtained from patients with anterior polar cataracts, by Western blot analysis. However, downregulation of fibronectin, Slug, and COX-2 and upregulation of E-cadherin were induced in miR-181a–overexpressing LECs obtained from patients with anterior polar cataracts. (C, E) The region of the Slug and COX-2 mRNA 3′-UTR predicted to be targeted by miR-181a. (D, F) Dual-luciferase report assays were performed on SRA01/04 cells. The luciferase activity of WT reporter transfected with miR-181a mimics was significantly decreased compared with miR-181a mimics control. However, the luciferase reporter activity was not inhibited by miR-181a mimics when the seeding sites were mutated (P > 0.05). Dual-luciferase reporter assay verified that miR-181a directly targets Slug and COX-2. Results are statistically significant (*P < 0.05, **P < 0.01). Error bars denote SEM.
proliferation, migration, differentiation, and development, and EMT by negatively regulating the translation and stability of their target miRNAs. In this study, we discovered that miR-181a expression was downregulated in human PCO-attached LECs and LECs obtained from patients with anterior polar cataracts, which implies a potential role in PCO and anterior polar cataracts.

Within a few hours after cataract extraction surgery, proliferation of the remaining LECs may begin. Concurrently, the majority of anterior LECs that reside on the internal surface of the anterior lens capsule migrate to the previously cell-free posterior capsule. Thus, inhibition of LEC proliferation and migration may be an effective strategy in preventing PCO. The MET proto-oncogene encodes the receptor tyrosine kinase (RTK) c-MET. In the canonical HGF/c-MET signaling pathway, c-MET dimerizes and autophosphorylates upon ligand binding, which, in turn, creates active docking sites for proteins that mediate the downstream signaling, resulting in activation of the mitogen-activated protein kinase (MAPK), phosphoinositide-3 kinase (PI3K), and Rac1-Cdc42 pathways. Previous studies have demonstrated that LECs normally express c-Met and that this expression is upregulated after mechanical trauma. Therefore, the autocrine feedback system may regulate normal LECs and modulate the epithelial migration and growth that is associated with the development of PCO. Hence, the HGF/c-Met signaling pathway has been shown to be involved in LECs proliferation and migration.

A large number of studies have shown that microRNAs affect essential biological processes such as metabolism, cell proliferation, migration, differentiation, and development by regulating c-MET. Consistent with previous studies, our study demonstrated that miR-181a inhibits the proliferation and migration of SRA01/04 cells, using MTT, BrdU incorporation, wound-healing, and Transwell migration assays. Furthermore, miR-181a downregulated c-Met expression via regulation of c-Met mRNA. The expression levels of cell cycle–regulatory proteins were determined to investigate the mechanism underlying the antiproliferative activity of miR-181a inhibition. Our study revealed that cell cycle–related molecules, including CDK2, CDK4, and CDK6, were downregulated in miR-181a–transfected LECs. Cyclin-dependent kinases are the catalytic subunits of a family of mammalian heterodimeric serine/threonine kinases that have been implicated in controlling cell-cycle progression and transcription. CDK2, CDK4, and CDK6 are all members of the CDK family, which are essential for controlling the G1/S phase transition. Consequently, to determine whether miR-181a inhibits LEC proliferation by downregulating c-Met and its downstream molecules, we altered the expression level of c-Met using specific siRNA in SRA01/04 cells. Using a c-Met knockdown approach, we demonstrated that the expression levels of CDK2, CDK4, and CDK6 were significantly decreased in c-Met siRNA-transfected cells compared with c-Met control siRNA–transfected cells and mock SRA01/04 cells. This finding suggests that miR-181a regulates the proliferation of LECs by negatively regulating c-Met and thereby also regulates its downstream molecules.

Increasing evidence indicates that the LECs of anterior subcapsular cataracts and anterior polar cataracts are trans-differentiated into fibroblast-like cells and produce a large amount of extracellular components that are not normally present in the lens capsules. Previous studies have demonstrated that EMT not only plays a role in the trauma. Therefore, the autocrine feedback system may be involved in LECs proliferation and migration.

The HGF/c-Met signaling pathway has been shown to be involved in LECs proliferation and migration.

In summary, the current study provides new insights regarding the ability of miRNA-181a to inhibit the proliferation, migration, and EMT of LECs. MicroRNAs are believed to have potential therapeutic value for many diseases. These data indicate that miR-181a may have important clinical consequences in the treatment of PCO by directly silencing c-Met, Slug, and COX-2.

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