European Review for Medical and Pharmacological Sciences 2019; 23: 8175-8185

LncRNA PART1 modulates chondrocyte proliferation, apoptosis, and extracellular matrix degradation in osteoarthritis *via* regulating miR-373-3p/SOX4 axis

Y.-J. ZHU, D.-M. JIANG

Department of Orthopedics, The First Affiliated Hospital of Chongqing Medical University, No. 1 Friendship Road, Yuanjiagang, Chongqing, China

Abstract. – OBJECTIVE: Osteoarthritis (OA) is a common disease in articular cartilages. It has been reported that long non-coding RNAs (lncRNAs) play an important role in various pathological processes of OA. However, the role of PART1 in OA development is unclear.

PATIENTS AND METHODS: The expression levels of PART1 and miR-373-3p were detected in cartilage tissues and chondrocytes using quantitative Real Time-Polymerase Chain Reaction (qRT-PCR). Cell proliferation was assessed by Cell Counting Kit-8 (CCK-8) assay. Cell apoptosis was determined by flow cytometry and Western blot assay. The expression of extracellular matrix (ECM)-related proteins was examined by Western blot assay. Expression of SRY-related high-mobility group box 4 (SOX4) was measured by qRT-PCR or Western blot assay. The interactions among PART1, miR-373-3p, and SOX4 were predicted using starBase v2.0 database and confirmed by Dual-Luciferase reporter assay and RNA immunoprecipitation (RIP) assay.

RESULTS: PART1 and SOX4 were up-regulated while miR-373-3p was down-regulated in OA cartilage tissues and chondrocytes. PART1 silencing hindered cell proliferation and ECM degradation, and triggered cell apoptosis in OA chondrocytes. PART1 modulated SOX4 expression by targeting miR-373-3p. Inhibition of miR-373-3p restored the regulation of cell proliferation, ECM degradation, and apoptosis induced by interfering PART1. Upregulation of SOX4 restored the effects on OA progression induced by inhibiting PART1.

CONCLUSIONS: PART1 promoted OA progression by regulating miR-373-3p/SOX4 axis, providing an effective therapeutic target for osteoarthritis.

Key Words:
PART1, MiR-373-3p, SOX4, Osteoarthritis, Chondrocyte.

Introduction

Osteoarthritis (OA) is a degenerative joint disease often occurring in the elderly[1]. OA features degenerative changes in articular cartilage and secondary bone hyperplasia[2]. At present, few studies have been conducted on the molecular mechanism of OA pathogenesis. Khan and Haqqi[3] have found that some non-coding RNAs (ncRNAs) are molecular regulators of OA occurrence and development. Therefore, investigating new non-coding RNAs in OA progression is pivotal for OA treatment. Long non-coding RNAs (lncRNAs), a type of ncRNAs, contain more than 200 nucleotides in length[4]. Accumulating evidence[5] implicated that the dysregulation of lncRNAs occupied an important position in the progression of various tumors. In addition, Chen et al[6] have revealed that lncRNAs regulated a variety of biological processes of OA, including degradation of extracellular matrix (ECM) and inflammatory responses. For instance, lncRNA MALAT1 induced OA deterioration by regulating the degradation of the cartilage matrix via targeting the miR-150-5p/AKT3 axis[7]. Chen et al[8] indicated that lncRNA maternally expressed gene 3 (MEG3) modulated chondrocytes proliferation, apoptosis, and ECM degradation by sponging miR-93 and regulating TGFBR2 expression in OA. Moreover, lncRNA TNFSF10 facilitated OA progression[9] via sponging miR-376-3 and upregulating FGFR1 expression. However, the underlying molecular mechanism of lncRNA prostate androgen-regulated transcript-1 (PART1) in the progression of OA is unclear.

MicroRNAs (miRNAs) are highly conserved short noncoding RNAs consisting of 18-25 nu-

Corresponding Author: Dianming Jiang, MD; e-mail: fuhuyueoruzc@163.com

cleotides[10]. MiRNAs play a key role in OA by regulating gene expression associated with cartilage development and regulating OA-related pathology, including inflammation, apoptosis, and autophagy[11]. For instance, miR-204 and miR-211 maintained homeostasis in mesenchymal joint cells to prevent the progression of osteoarthritis[12]. MiR-320c suppressed osteoarthritis development by inhibiting the typical Wnt signaling pathway[13]. Knockdown of miR-495 inhibited chondrocyte apoptosis and induced chondrocyte proliferation by directly targeting chemokine ligand 4 and regulating the NF-κB signaling pathway in osteoarthritis[14]. Upregulation of miR-449a contributed to the degradation of chondrocyte ECM in osteoarthritis[15]. However, the functional role of miR-373-3p in OA progression requires further investigation. Therefore, we studied the effects of lncRNA PART1 on chondrocyte proliferation, apoptosis, and extracellular matrix degradation in OA, and further investigated the potential mechanism of lncRNA PART1 in OA progression.

Patients and Methods

Tissue Specimens

The cartilage tissues were acquired from patients with OA (n=35) and patients without OA (n=15). All cartilage samples were obtained from the Department of Orthopedics at The First Affiliated Hospital of Chongqing Medical University (Chongqing, China). The research was approved by the Ethics Committee of the Department of Orthopedics at The First Affiliated Hospital of Chongqing Medical University (Chongqing, China). Written informed consents were signed by all participants.

Cell Culture

Chondrocytes were isolated from cartilage tissues as previously reported[16]. Briefly, at 37°C, cartilage tissues were digested with 0.25% trypsin for 30 min, followed by 0.2% type II collagenase for 4 h. Chondrocytes were incubated in Dulbecco's Modified Eagle's Medium (DMEM; Gibco, Rockville, MD, USA) supplemented with 10% fetal bovine serum (FBS; Gibco, Rockville, MD, USA) at 37°C with 5% CO_2.

Cell Transfection

Chondrocytes were inoculated into 6-well plates. Then, cell transfection was performed using Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA) when cells confluence reached approximately 70%. The vectors and oligonucleotides used were as follows: small interfering RNA (siRNA) against PART1 (si-PART1#1 and si-PART1#2), the negative control siRNA (si-NC), miR-373-3p mimic (miR-373-3p), the mimic control (miR-NC), miR-373-3p inhibitor (anti-miR-373-3p), and SRY-related high-mobility group box 4 (SOX4) overexpression vector (pcDNA-SOX4). All sequences were synthesized by GenePharma (Shanghai, China).

Quantitative Real-Time PCR (qRT-PCR)

Total RNA was isolated from cartilage and chondrocytes using TRIzol reagent (Invitrogen, Carlsbad, CA, USA). Subsequently, RNA was reversely transcribed to cDNA using High-capacity cDNA Reverse Transcription kit (Applied Biosystems, Foster City, CA, USA). Then, the mRNA expression was detected using SYBR Green PCR Master Mix (Thermo Fisher Scientific, Waltham, MA, USA). Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) or U6 were used as internal control. The primer sequences were listed below: PART1-Forward: 5'-GCTGCACTGGAACAACACAG-3', PART1-Reverse, 5'-TCAGGGTAGGCCAGCAGTAT-3'; miR-373-3p-Forward: 5'-GAAGTGCTTCGATTTTGCC-3', miR-373-3p-Reverse, 5'-GAATACCTCGGACCCTGC-3'; SOX4-Forward: 5'-AGCGACAAGATCCCTTTCATTC-3', SOX4-Reverse, 5'-CGTTGCCGGACTTCACCTT-3'; GAPDH-Forward: 5'-AGCCACATCGCTCAGACA-3', GAPDH-Reverse, 5'-GCCCAATACGACCAAATCC-3'; U6-Forward: 5'-CTCGCTTCGGCAGCACA-3', U6-Reverse, 5'-AACGCTTCACGAATTTGCGT-3'.

Cell Counting Kit-8 (CCK-8) Assay

CCK-8 solution (Dojindo Laboratories, Kumamoto, Japan) was used to evaluate cell viability. The cells (3.0×10^3) were seeded into 96-well plate. After incubation for 24 h, 48 h, 72 h, and 96 h, the CCK-8 solution was dropped to each well. After 2 h of incubation, the OD value was detected at 450 nm with a Microplate Reader (Bio-Rad, Hercules, CA, USA).

Flow Cytometry

Cell apoptosis was detected using Annexin V-FITC/propidium iodide (PI) Apoptosis Detection kit (Invitrogen, Carlsbad, CA, USA). Briefly, OA chondrocytes were seeded into six-well plate and cleaned with cold phosphate-buffered saline (PBS) twice. Then, cells were stained with Annexin V-FITC and PI for 15 min. At last, the apop-

totic rate was monitored by Attune NxT Flow Cytometer (Thermo Fisher Scientific, Waltham, MA, USA).

Western Blot Assay

After cells were lysed using RIPA buffer (Invitrogen, Carlsbad, CA, USA), equal amounts of protein samples were separated by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), and then transferred onto polyvinylidene difluoride (PVDF) membranes (Millipore, Billerica, MA, USA). The membranes, once blocked with 5% skim milk for 2 h, were incubated with primary antibodies at 4°C overnight, followed by secondary antibody (1:4,000; Abcam, Cambridge, MA, USA) for 2 h at 37°C. The intensity was detected by enhanced chemiluminescence (ECL) reagents (Millipore, Billerica, MA, USA). The primary antibodies were purchased from Abcam (Cambridge, MA, USA) with a ratio of 1:1000. Antibodies were as follows: B-cell lymphoma-2 (Bcl-2) antibody, Bcl-2 Associated X (Bax) antibody, Cleaved-cas-3 antibody, matrix metalloproteinase-13 (MMP13) antibody, type II Collagen (COL2) antibody, Aggrecan antibody, SOX4 antibody, and GAPDH.

Dual-Luciferase Reporter Assay

The sequences of PART1 or SOX4 3'UTR containing wild-type or mutant binding site of miR-373-3p were inserted into pmirGLO vector (Promega, Madison, WI, USA) to form WT-PART1, MUT-PART1, SOX4 3'UTR-WT or SOX4 3'UTR-MUT, respectively. Then, the corresponding vector and miR-373-3p or miR-NC were cotransfected into chondrocytes using Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA). The luciferase activity was detected using Dual-Luciferase Reporter Kit (Promega, Madison, WI, USA).

RNA Immunoprecipitation (RIP) Assay

RIP assay was carried out using Magna RNA Immunoprecipitation Kit (Millipore, Billerica, MA, USA). Briefly, OA chondrocytes were transfected with miR-373-3p or miR-NC. After collecting cell lysates, they were incubated with magnetic beads containing Anti-Ago2 or Anti-IgG. Finally, the enrichment of PART1 and miR-373-3p was measured by qRT-PCR.

Statistical Analysis

GraphPad Prism 7.0 software (GraphPad, La Jolla, CA, USA) was executed to analyze all data. The data were represented by mean ± standard deviation. Student's *t*-test or one-way analysis of variance (ANOVA) was carried out for significant analysis. All experiments were repeated three times independently.

Results

PART1 Was Highly Expressed in OA Cartilage Tissues and OA Chondrocytes

First, the expression of PART1 was detected using qRT-PCR in 35 patients with OA and 15 normal patients. The results exhibited that the expression level of PART1 was dramatically elevated in cartilage tissues of OA patients compared with normal group (Figure 1A). Additionally,

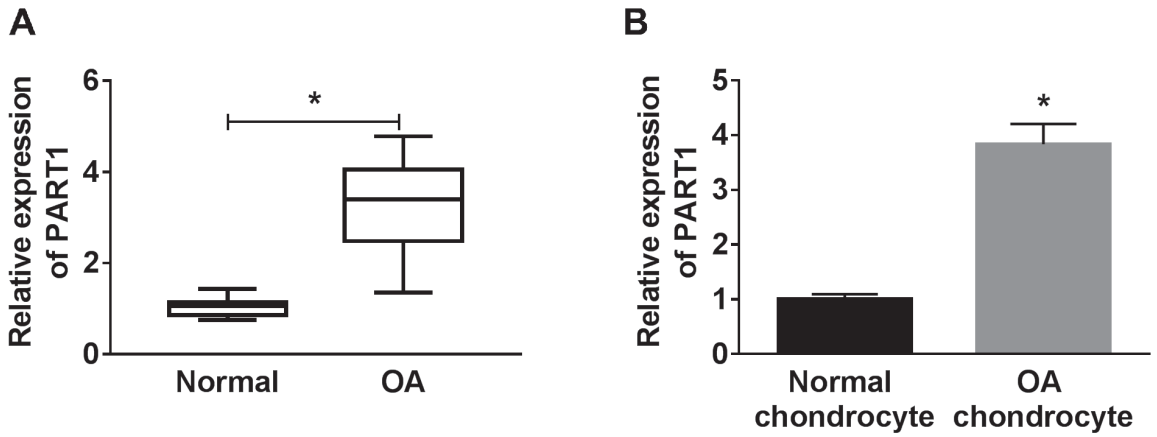

Figure 1. PART1 was upregulated in OA cartilage tissues and OA chondrocytes. **A**, Expression level of PART1 was detected in cartilage tissues of normal patients and OA patients by qRT-PCR. **B**, Expression level of PART1 was measured in normal chondrocytes and OA chondrocytes using qRT-PCR. *$p < 0.05$.

normal chondrocytes and OA chondrocytes were isolated by enzymatic digestion. The results of qRT-PCR revealed that the expression of PART1 in OA chondrocytes was distinctly higher than that in normal chondrocytes (Figure 1B). These results hinted that PART1 might play a critical role in OA development.

Knockdown of PART1 Inhibited Cell Proliferation and ECM Degradation, and Promoted Cell Apoptosis in OA Chondrocytes

To investigate the effect of PART1 on the progression of osteoarthritis, PART1 was down-regulated in OA chondrocytes by transfection of si-PART1. The results showed that PART1 expression was markedly reduced in OA chondrocytes transfected with si-PART1#1 or si-PART1#2 compared with si-NC group, and si-PART1#1 had higher knockdown efficiency (Figure 2A). CCK-8 assay revealed that suppression of PART1 remarkably decreased the viability of OA chondrocytes compared to control group (Figure 2B). Furthermore, inhibition of PART1 significantly increased the apoptosis rate of OA chondrocytes in comparison with si-NC group (Figure 2C). Similarly, Western blot assay suggested that PART1 silencing strikingly reduced the protein level of Bcl-2 and enhanced the protein levels of Bax and Cleaved-cas-3 in OA chondrocytes (Figure 2D). In addition, the expression levels of ECM-related proteins (MMP13, COL2, and Aggrecan) were detected by Western blot analysis. The results disclosed that the protein level of MMP13 was evidently down-regulated, and the protein levels of COL2 and Aggrecan were apparently upregulated in OA chondrocytes after PART1 suppression (Figure 2E). All these data indicated that depletion of PART1 suppressed cell proliferation and ECM degradation, and facilitated cell apoptosis in OA chondrocytes.

PART1 Was a Sponge of MiR-373-3p in OA Chondrocytes

To explore the underlying mechanism of PART1 in OA progression, online database starBase2.0 was applied to predict the target miRNAs of PART1. The prediction exhibited that PART1 contained the complementary binding sites of miR-373-3p (Figure 3A). Dual-Luciferase reporter assay demonstrated that miR-373-3p mimic conspicuously reduced the luciferase activity of WT-PART1 reporter but did not affect the luciferase activity of MUT-PART1 reporter (Figure 3B). RIP assay was performed to further verify the interaction between PART1 and miR-373-3p, and the results suggested that PART1 and miR-373-3p were significantly enriched in Ago2 antibody complex compared with anti-IgG group (Figure 3C). Furthermore, the expression of miR-373-3p was measured in OA chondrocytes transfected with si-NC, si-PART1#1 or si-PART1#1+anti-miR-373-3p, respectively. The results of qRT-PCR showed that suppression of PART1 resulted in a significant increase of miR-373-3p expression, while the increase was reversed after transfection with anti-miR-373-3p (Figure 3D). The expression of miR-373-3p was strikingly decreased in OA cartilage tissues and OA chondrocytes (Figure 3E and 3F). Moreover, the expression levels of PART1 and miR-373-3p were negatively correlated in OA cartilage tissues (Figure 3G). These data demonstrated that miR-373-3p was a direct target of PART1 in OA chondrocytes.

PART1 Promoted OA Progression Via Regulating MiR-373-3p

To explore the effect of miR-373-3p on the progression of osteoarthritis, OA chondrocytes were transfected with si-NC, si-PART1#1 or si-PART1#1+anti-miR-373-3p, respectively. The results revealed that PART1 interference notably reduced the viability of OA chondrocytes, whereas this effect was restored after the inhibition of miR-373-3p (Figure 4A). Additionally, knockdown of PART1 distinctly increased the apoptosis rate of OA chondrocytes, and this effect was reverted after transfection with anti-miR-373-3p (Figure 4B). Consistently, suppression of PART1 led to an evident decrease in Bcl-2 expression and a conspicuous increase in the levels of Bax and Cleaved-cas-3, while the protein levels were recovered by down-regulating miR-373-3p (Figure 4C). Furthermore, PART1 interference dramatically reduced the protein level of MMP13 and significantly enhanced the protein levels of COL2 and Aggrecan, but the protein levels were restored after inhibition of miR-373-3p (Figure 4D). All these data elucidated that inhibition of miR-373-3p restored the regulation of cell proliferation, ECM degradation, and apoptosis induced by interfering PART1.

SOX4 Was a Target of MiR-373-3p

Bioinformatics database starBase v2.0 was used to predict the targets of miR-373-3p, and SOX4 was selected as a candidate gene (Figure 5A). Dual-Luciferase reporter assay was per-

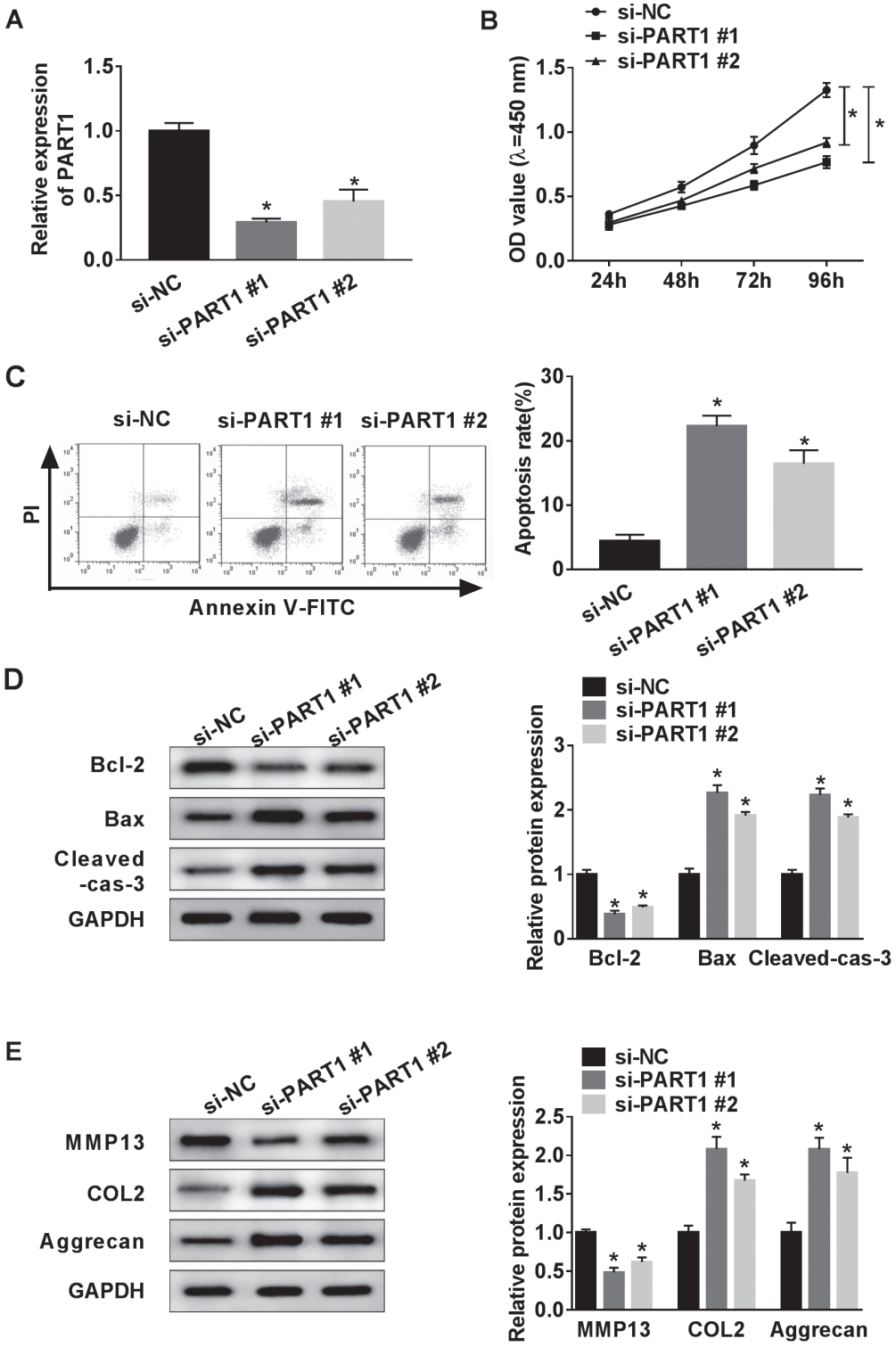

Figure 2. Knockdown of PART1 inhibited cell proliferation and ECM degradation, and promoted cell apoptosis in OA chondrocytes. **A-E**, OA chondrocytes were transfected with si-NC, si-PART1#1 or si-PART1#2, respectively. (A) The expression of PART1 was examined by qRT-PCR. **B**, Viability of OA chondrocytes was estimated by CCK-8 assay. **C**, Flow cytometry was conducted to monitor the apoptosis rate of OA chondrocytes. **D**, Protein levels of apoptosis-related proteins (Bcl-2, Bax, and Cleaved-cas-3) were detected by Western blot assay. **E**, Protein levels of ECM-associated proteins (MMP13, COL2, and Aggrecan) were tested using Western blot assay. *$p < 0.05$.

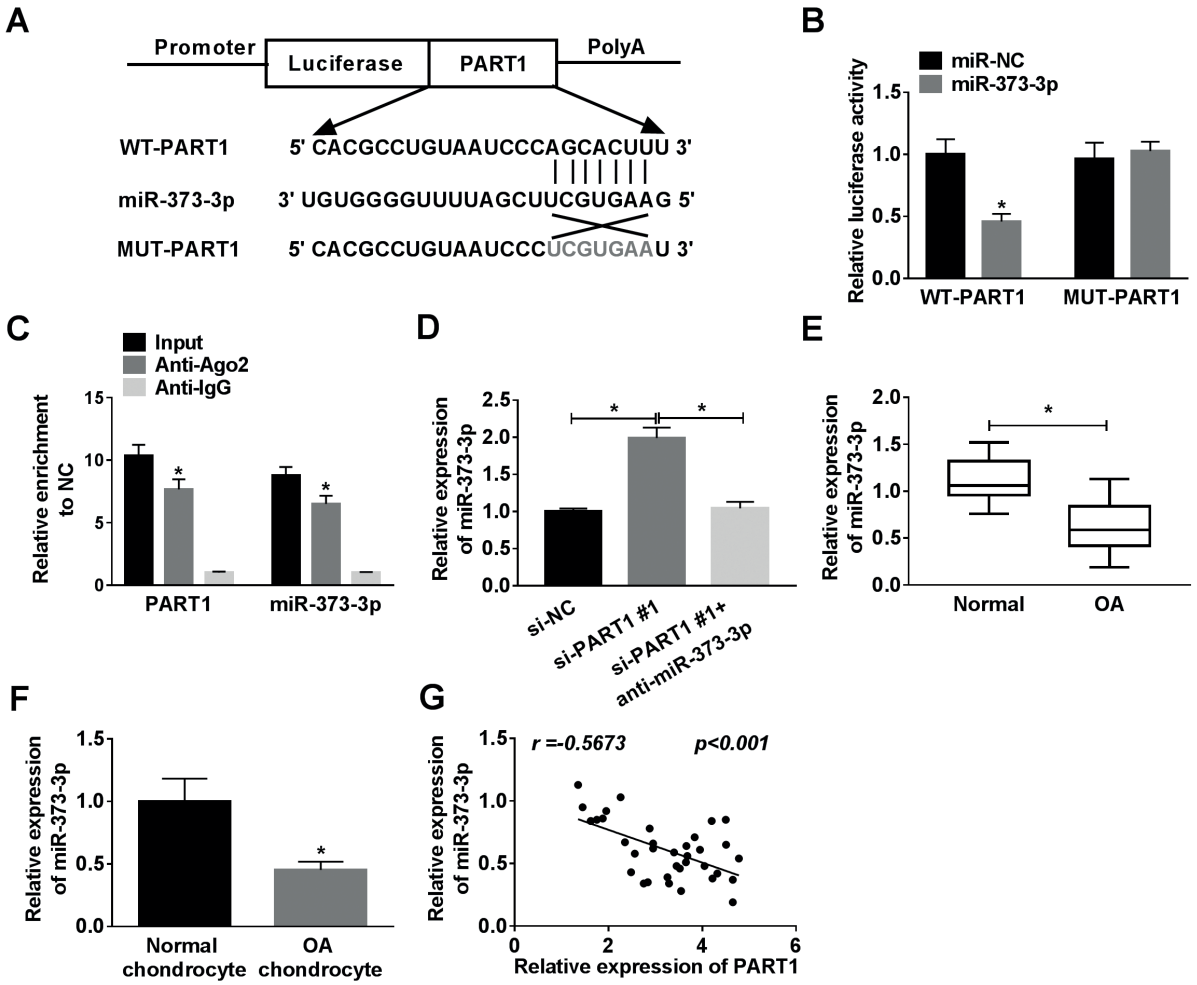

Figure 3. PART1 was a sponge of miR-373-3p in OA chondrocytes. **A**, Predicted binding sites for PART1 and miR-373-3p were exhibited. **B**, Luciferase activity was evaluated in OA chondrocytes cotransfected with WT-PART1 or MUT-PART1 and miR-NC or miR-373-3p mimic using dual-luciferase reporter assay. **C**, RIP assay was utilized to confirm the correlation between PART1 and miR-373-3p. **D**, Level of miR-373-3p was measured in OA chondrocytes transfected with si-NC, si-PART1#1 or si-PART1#1+anti-miR-373-3p, respectively. **E** and **F**, Expression level of miR-373-3p was examined in cartilage tissues and chondrocytes. **G**, Spearman was used to test the relationship between PART1 and miR-373-3p in OA cartilage tissues. $*p < 0.05$.

formed to confirm whether miR-373-3p directly targeted SOX4. The results exhibited that mature miR-373-3p significantly decreased the luciferase activity of SOX4 3'UTR-WT reporter, but did not affect the luciferase activity of SOX4 3'UTR-MUT reporter (Figure 5B). Moreover, the expression of SOX4 was substantially upregulated in OA cartilage tissues compared with normal group (Figure 5C). The correlation between miR-373-3p and SOX4 was negative in OA cartilage tissues (Figure 5D). The mRNA and protein levels of SOX4 were remarkably elevated in OA chondrocytes compared with normal chondrocytes (Figure 5E and 5F). Then, the expression of SOX4 was measured in OA chondrocytes transfected with miR-NC or miR-373-3p. The results of qRT-PCR and Western blot revealed that upregulation of miR-373-3p obviously reduced the mRNA and protein levels of SOX4 (Figure 5G and 5H). Altogether, these data manifested that SOX4 directly interacted with miR-373-3p in OA chondrocytes.

PART1 Promoted OA Progression Via Regulating SOX4

To investigate the relationship among PART1, miR-373-3p, and SOX4, OA chondrocytes were transfected with si-NC, si-PART1#1, si-PART1#1+anti-miR-373-3p or si-PART1#1+pcD-

NA-SOX4, respectively. The results showed that the depletion of PART1 apparently decreased the mRNA expression of SOX4, while SOX4 expression was recovered after transfection with anti-miR-373-3p or pcDNA-SOX4 (Figure 6A). In addition, depletion of PART1 substantially reduced the protein expression of SOX4, whereas miR-373-3p inhibition or SOX4 overexpression

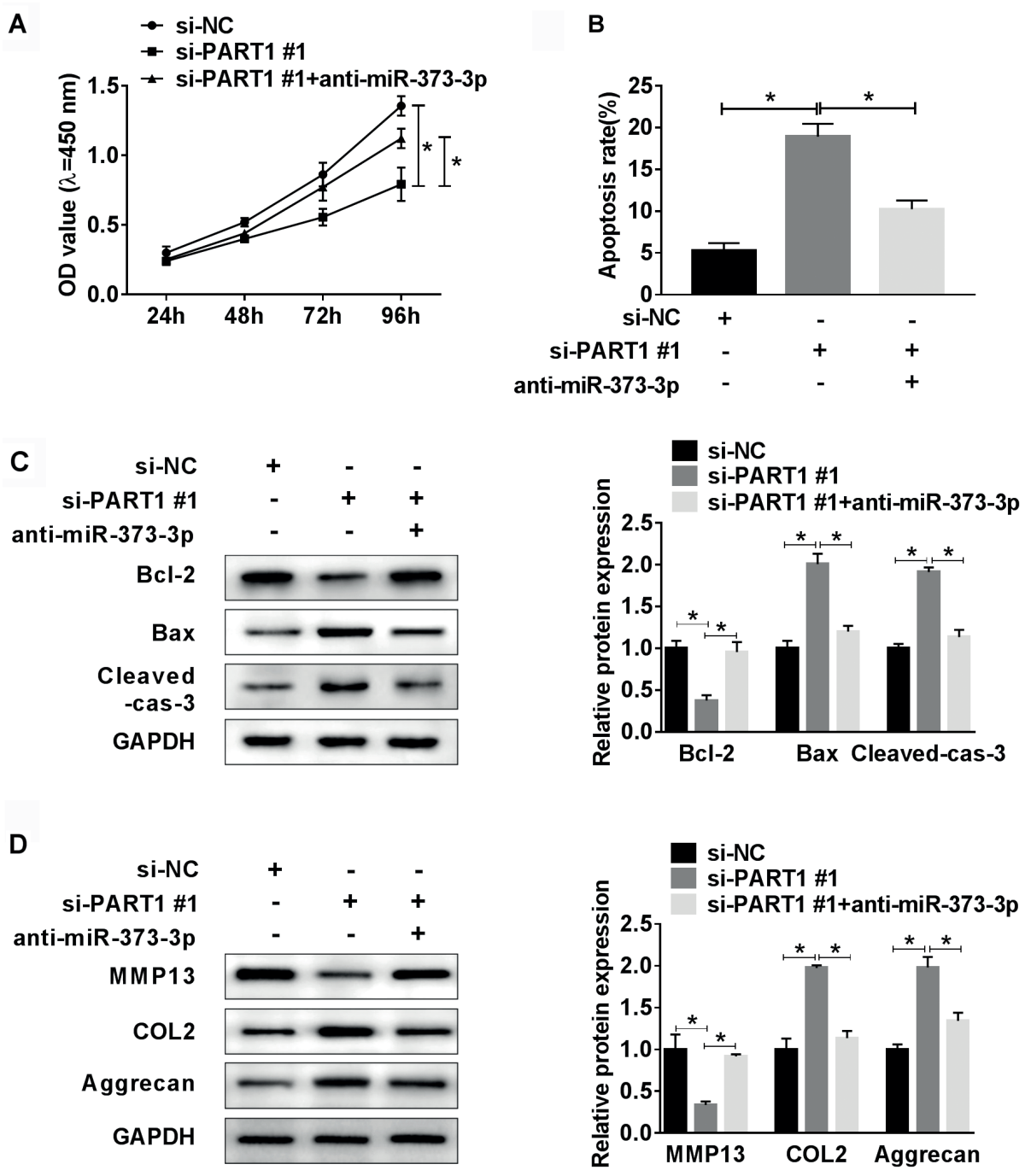

Figure 4. PART1 promoted OA progression via regulating miR-373-3p. **A-D**, OA chondrocytes were transfected with si-NC, si-PART1#1 or si-PART1#1+anti-miR-373-3p, respectively. **A**, CCK-8 assay was used to measure the viability of OA chondrocytes. **B**, Apoptosis rate of OA chondrocytes was monitored by flow cytometry. **C**, Protein levels of apoptosis-related proteins (Bcl-2, Bax and Cleaved-cas-3) were tested using Western blot assay. **D**, Protein levels of ECM-associated proteins (MMP13, COL2, and Aggrecan) were detected by Western blot assay. *$p < 0.05$.

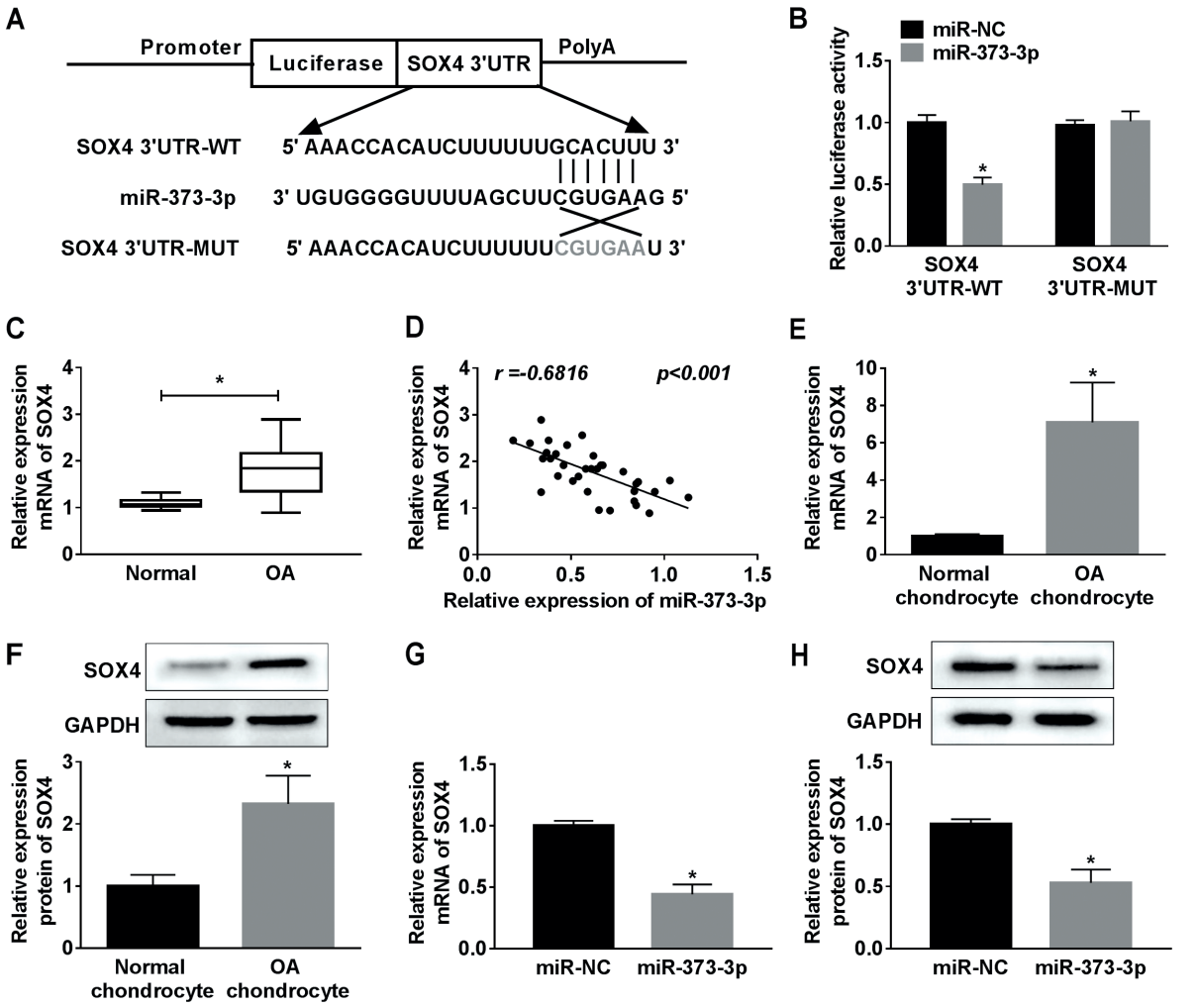

Figure 5. SOX4 was a target of miR-373-3p in OA chondrocytes. **A**, Putative binding sites for miR-373-3p and SOX4 3'UTR were showed. **B**, Dual-luciferase reporter assay was applied to analyze the luciferase activity in OA chondrocytes cotransfected with SOX4 3'UTR-WT or SOX4 3'UTR-MUT and miR-NC or miR-373-3p mimic. **C**, Expression of SOX4 was detected in cartilage tissues of normal patients and OA patients by qRT-PCR. **D**, Correlation between miR-373-3p and SOX4 in OA cartilage tissues was analyzed. **E** and **F**, mRNA and protein levels of SOX4 were tested in normal and OA chondrocytes by qRT-PCR and Western blot. **G** and **H**, mRNA and protein levels of SOX4 were detected in OA chondrocytes transfected with miR-NC or miR-373-3p mimic. *$p < 0.05$.

restored the effect (Figure 6B). These results indicated that PART1 regulated SOX4 expression via sponging miR-373-3p.

Furthermore, OA chondrocytes were transfected with si-NC, si-PART1#1 or si-PART1#1+p-cDNA-SOX4 to explore the role of SOX4 in OA progression. CCK-8 assay suggested that overexpression of SOX4 recuperated the inhibition of cell viability induced by PART1 knockdown (Figure 6C). Additionally, flow cytometry exhibited that upregulation of SOX4 relieved the promotion of cell apoptosis induced by PART1 silencing (Figure 6D). In the meantime, PART1 knockdown evidently decreased the protein level of Bcl-2 and conspicuously increased the protein levels of Bax and Cleaved-cas-3, while this effect was reverted by upregulating SOX4 (Figure 6E). In addition, PART1 knockdown strikingly inhibited the protein expression of MMP13 and markedly facilitated the protein levels of COL2 and Aggrecan, whereas this effect was recovered after transfection with pcDNA-SOX4 (Figure 6F). Taken together, these data demonstrated that overexpression of SOX4 restored the regulation of cell proliferation, ECM degradation, and apoptosis induced by down-regulating

PART1.

Discussion

The main pathological feature of OA is cartilage damage. The degradation of chondrocyte ECM and apoptosis of chondrocytes are the important causes of osteoarthritis[17]. Some studies[18,19] have suggested that abnormally expressed lncRNAs were closely associated with many pathological processes of OA. Wang et al[20] found that FOXD2-AS1 was overtly upregulated in cartilage of OA patients and promoted the progression of OA via targeting miR-27a-3p and upregulating TLR4 expression. Fan et al[21] showed that lncRNA DANCR triggered OA progression by sponging miR-577 and inducing SphK2 expression. Sun et al[22] revealed that lncRNA PART1 induced cell proliferation and hindered apoptosis in prostate cancer by modulating toll-like receptor pathways. Hu et al[23] observed that knockdown of PART1 restrained cell proliferation in bladder cancer. In this study, PART1 was conspicuously upregulated in OA cartilage tissues and OA chondrocytes. Furthermore, PART1 knockdown impeded proliferation and ECM degradation, and expedited apoptosis of OA chondrocytes.

Increasing evidence indicated that miRNAs occupied a crucial position in OA development. Chen and Wu[24] revealed that miR-103 impeded proliferation and formation of chondrocytes by

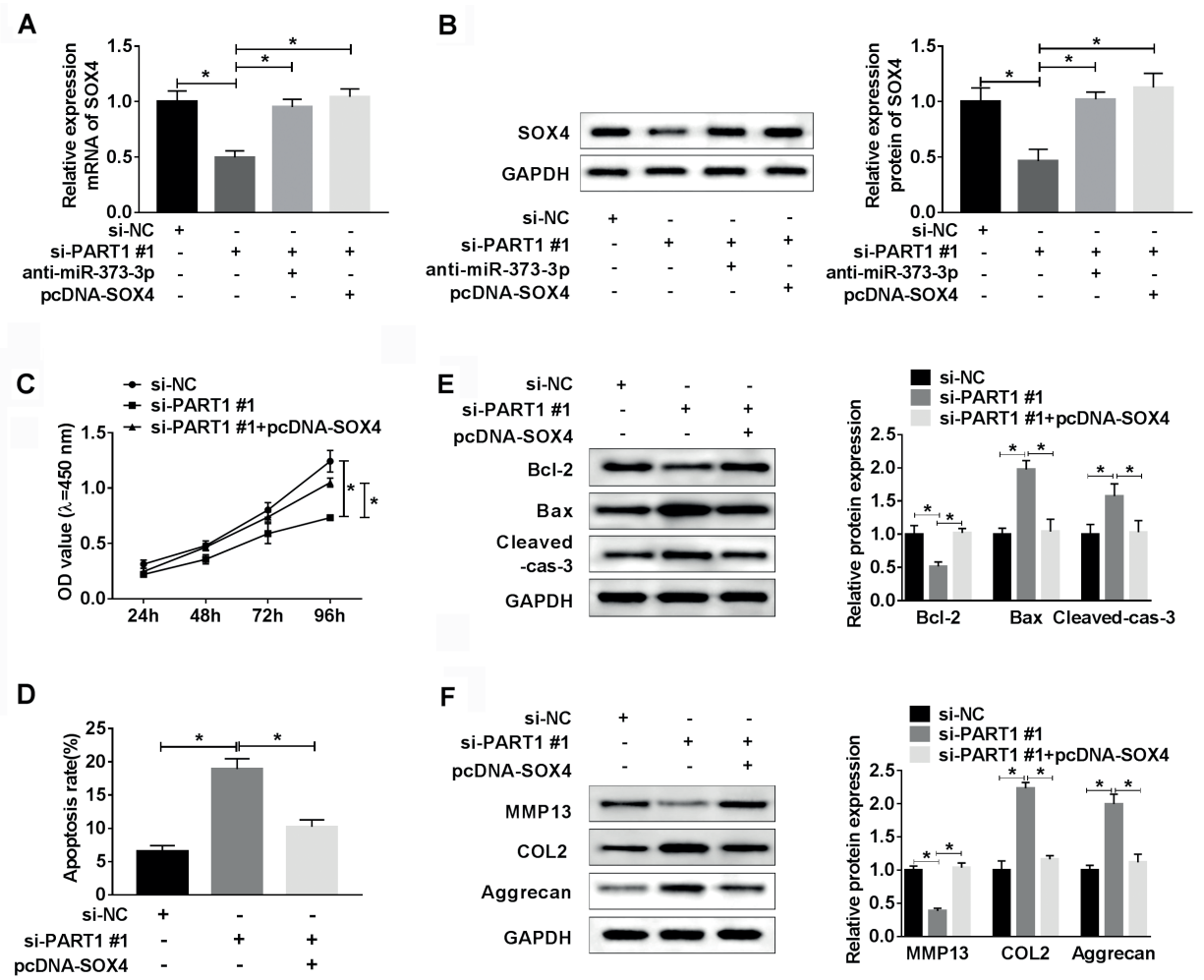

Figure 6. PART1 promoted OA progression via regulating SOX4. **A** and **B**, mRNA and protein levels of SOX4 were measured in OA chondrocytes transfected with si-NC, si-PART1#1, si-PART1#1+anti-miR-373-3p or si-PART1#1+pcDNA-SOX4, respectively. **C-F**, OA chondrocytes were transfected with si-NC, si-PART1#1 or si-PART1#1+pcDNA-SOX4, respectively. **C**, CCK-8 assay was carried out to evaluate the viability of OA chondrocytes. **D**, Flow cytometry was applied to estimate the apoptosis rate of OA chondrocytes. **E** and **F**, Western blot analysis was performed to detect the protein levels of apoptosis-related proteins and ECM-related proteins. *$p < 0.05$.

down-regulating Sox6 expression. Conversely, miR-31 facilitated chondrocyte proliferation and migration via targeting C-X-C motif chemokine ligand 12[25]. We utilized starBase2.0 to predict that miR-373-3p was a target of PART1. Researchers[26,27] have suggested that miR-373 expression was inhibited in OA chondrocytes. MiR-373 restrained chondrocyte proliferation and inflammatory response by upregulating P2X7 receptor expression[26,28]. The present research showed that miR-373-3p was conspicuously down-regulated in OA cartilage tissues and OA chondrocytes. PART1 directly targeted miR-373-3p in OA chondrocytes. Additionally, the inhibition of miR-373-3p restored the regulation of cell proliferation, ECM degradation, and apoptosis induced by interfering PART1.

Sun et al[29] demonstrated that SOX4 contributed to ECM degradation. Takahata et al[30] suggested that SOX4 induced cartilage degradation in osteoarthritis by upregulating ADAMTS4 and ADAMTS5. SOX4 promoted proliferation and chondrogenesis of synovium-derived mesenchymal stem cells[31]. In the present study, PART1 regulated SOX4 expression by acting as a sponge of miR-373-3p. SOX4 expression was substantially higher in patients with OA than that in normal patients. Likewise, SOX4 was highly expressed in OA chondrocytes. Meanwhile, overexpression of SOX4 restored the regulation of cell proliferation, ECM degradation, and apoptosis induced by down-regulating PART1.

Conclusions

In summary, PART1 could modulate SOX4 expression via targeting miR-373-3p in chondrocytes. Furthermore, PART1 occupied an important position in modulating chondrocyte proliferation, apoptosis, and ECM degradation in osteoarthritis by regulating the miR-373-3p/SOX4 axis. Our results might provide potential therapeutic targets for osteoarthritis treatment.

Conflicts of interest

The authors declare no conflicts of interest.

Declarations

Ethics Approval and Consent to Participate

This investigation was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University. The methods used in this study were performed in accordance with relevant guidelines and regulations. Written consent was obtained from the participants or guardians of participants under 16 years old.

Availability of Data and Materials

All original data and materials are available from the corresponding author upon request.

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