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Original Article

lncRNA MALAT1 promotes chondrocyte proliferation by inhibiting MiR-127-5p

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Abstract: Objective: To investigate the effect of MALAT1 on the biological function of chondrocytes and its molecular mechanism. Methods: One hundred and two patients with osteoarthritis surgery in Ningbo No. 6 Hospital were selected as the research group (RG), and 69 patients with femoral neck fracture surgery were enrolled as the control group (CG). The cartilage tissue culture cells were removed, and PCR analysis was performed to measure the expression levels of MALAT and miR-127-5p in the serum and chondrocyte cell lines of the two groups of patients. The correlation between serum MALAT expression and clinical pathological features and prognosis in patients with osteoarthritis was analyzed. In addition, the biological function of MALAT on osteoarthritis chondrocytes was determined *in vitro*, and the regulatory relationship between MALAT and miR-127-5p in osteoarthritis was explored. Results: MALAT was highly expressed in the serum of patients with osteoarthritis, while miR-127-5p was lowly expressed, with a negative correlation between the two. Through Cox analysis, it was found that high expression of MALAT1, age, housework, family history of osteoarthritis, history of knee trauma, damp and dark living environment and obesity were independent factors affecting the prognosis of patients with osteoarthritis. Overexpression of miR-127-5p silenced MALAT1 to inhibit the proliferation and invasion of osteoarthritis chondrocytes, but increased the rate of apoptosis. After co-transfection with MALAT1-inhibitor+miR-127-5p-mimc, the proliferation and invasion of chondrocytes were markedly inhibited, and the apoptosis rate was clearly increased. Inhibition of MALAT1 could improve the expression of miR-127-5p, thereby reducing the proliferation and invasion ability of chondrocytes in osteoarthritis, but significantly increasing the rate of apoptosis. Conclusion: MALAT1 promoted osteoarthritis chondrocyte proliferation and prevented apoptosis by targeting miR-127-5p.

Keywords: MALAT1, miR-127-5p, osteoarthritis, chondrocytes, biological function

Introduction

As a common joint disease found in the clinic, osteoarthritis is also the major cause of joint pain and patient disability [1]. The aging of the population also increases the risk of osteoarthritis [2]. Osteoarthritis affects the structural integrity of articular cartilage, resulting in hypertrophic chondrocytes, biomechanical damage or permanent cartilage damage [3]. The effective treatment of bones and joints and the slowing down of disease progression depend on early detection and diagnosis [4]. At present, the gold standard for clinical diagnosis of osteoarthritis is X-ray imaging. However, due to the degeneration of articular cartilage, X-ray cannot directly see the tissue for diagnosis in the early stage of osteoarthritis, so early diagnosis and behavioral intervention are needed to prolong the health and quality of life of patients with osteoarthritis [5]. Therefore, here we elucidated the relevant mechanisms of osteoarthritis and sought for new potentially highly sensitive, specific and reliable mechanisms to improve the prognosis of patients with osteoarthritis.

Non-coding RNA is considered clinically as a major player in the pathogenesis of diseases such as cancer [6], among which MALAT1 is one of the most abundantly expressed lncRNAs, with altered expression levels in a variety of cancers [7]. MALAT1 is also highly conserved across species and widely expressed in human tissues [8]. In addition, it is found to be involved in the occurrence of a variety of cancers, such

as the induction of invasion, migration and tumor growth in pancreatic cancer, cervical cancer, lung cancer and colorectal cancer [9, 10]. There is also evidence showing that MALAT1 not only participates in various physiological processes, including synaptic formation, myogenesis and epigenetic modification of gene expression, but also plays a key role in a variety of pathological conditions [11]. For example, in the study of Gao G C et al. [12], MALAT1 blocked the activation of JNK signaling pathway to reduce the IL-1β-induced chondrocyte inflammation, and inhibited the apoptosis of chondrocytes and the degradation of extracellular matrix. As to miR-127-5p, it has an overlapping gene structure, which plays a role in embryogenesis, tumor germination, and lung development. Apart from that, it is reported to be lower expressed in osteoarthritis cartilage tissue than normal tissue, and can promote the occurrence and development of osteoarthritis by regulating the expression of MMP-13 [13]. Studies have shown that lncRNAs can act as a sponge for miRNAs, thereby reducing the regulatory effect of mRNA [14]. According to Liang J et al. [15], miR-127-5p was the direct target gene of MALAT1, and the binding of MALAT1 to miR-127-5p could inhibit the expression of miR-127-5p and promote the proliferation of chondrocytes through the PI3K/AKt pathway.

Therefore, this study was designed to explore the effect of MALAT1 regulation of miR-127-5p on cell biological function in patients with osteoarthritis, aiming to provide a new therapeutic target for patients with osteoarthritis.

Materials and methods

Cell source

The cartilage tissues of 102 patients with osteoarthritis who underwent knee arthroplasty in Ningbo No. 6 Hospital from March 2018 to June 2019 were selected as the RG, and 69 cases of femoral neck fracture without osteoarthritis or rheumatoid arthritis were collected as the CG. This study was approved by the Medical Ethics Committee of Ningbo No. 6 Hospital, and all the patients signed the informed consent form. Serum from patients in the RG and CG was collected, and all tissues were frozen in liquid nitrogen and stored at -80°C for subsequent experiments. Prior to this study, patients had not been treated for cancer.

Source of instruments and reagents

High-speed refrigerated centrifuge (Sichuan Shuke Instrument Co., Ltd., Chengdu, China, article No.: LG-25M-1), UV spectrophotometer (Spectral Technology Co., Ltd., Dongguan, China, article No.: SPCC), flow cytometer (Beamdiag Biotechnology Co., Ltd., Changzhou, China, article No.: 1026), fluorescence inverted microscope (Coslan Scientific Co., Ltd., Guangzhou, China, article No.: Axio Observer), CO_2 constant temperature incubator (Zeonwo Instrument Co., Ltd., Shanghai, China, article No.: Y021), microplate reader (Delica Biotechnology Co., Ltd., Beijing, China, article No.: 21261000), Real-time quantitative PCR instrument (Huafeng Biotechnology Co., Ltd., Guangzhou, China, article No.: EQ-03), gel imaging system (Chundu Biotechnology Co., Ltd., Wuhan, China, article No.: CD-11257-ML), high-pressure moist heat sterilizer (PKUCare Industrial Park Technology Co., Ltd., Beijing, China, article No.: G180DS); DMEM, bovine fetal serum (Gibco, USA, 1142802, 10010023), D-hanks solution (Python Biotechnology Co., Ltd., Guangzhou, China, article No.: AAPR26-4-250), qRT-PCR and Reverse Transcription Kit (TransGen Biotechnology, Beijing, China, AQ141-01, AQ141-01), CCK-8 Kit (Bestbio, article No.: BB-4202), Plasmid Extraction Kit (North Connaught Biotechnology Co., Ltd., Shanghai, China, article No.: d6942-01), AnnexinV-FITC (Kemin Biotechnology Co., Ltd., Shanghai, China, DXT-130-097-928), Transwell kit (Biogenius Biotechnology Co., Ltd., Shanghai, China, Transwell), flow cytometry Instrument (BD Corporation, USA, FACS Canto II), multi-functional microplate reader (BioTek Botten, USA, DLK-0001622). All primers were designed and synthesized by Shanghai Sangon Biotechnology Co., Ltd.

Isolation and culture of chondrocytes

The chondrocytes were isolated by two-step enzymatic digestion and then cultured, with the steps as follows: the cartilage was placed in a sterile petri dish and rinsed several times with PBS buffer, and the tissue was cut into pieces with scissors. Then 0.25% trypsin was used to fully digest it, placed in a 37°C incubator for oscillation incubation for 38 min to remove and discard the supernatant. After that, it was rinsed with D-hanks, digested with type II col-

lagen of 2 mg/ml and put in an incubator at 37°C for a 6-hour oscillating incubation. Then it was taken out to discard the supernatant before rinsing it with D-hanks. After washing, the chondrocytes were centrifuged until they were spherical, easy to suspend and not easy to adhere to the wall to ensure that they were primary chondrocytes. The steps of passage experiment: the primary chondrocytes were put into 10% bovine fetal serum DMEM high glucose medium, and all the cells were cultured in 37°C incubator (5% CO_2). Subculture was performed after primary cells were re-digested. Cells from 2-3 passages were used for experiments.

PCR detection

The total RNA was extracted from the cells using TRIzol kit, and the integrity, purity and concentration of the total RNA were detected by an UV spectrophotometer. MALAT1 and miR-127-5p reverse transcription were performed strictly according to the kit instructions. The PCR reaction system was as follows: 2 × Talent qPCR PreMix: 10 μl, upstream and downstream primers: 1.25 μl each, cDNA: 100 ng, and water was added to 20 μl. PCR reaction conditions: pre-denaturation at 94°C for 30 s, denaturation at 94°C for 5 s, annealing at 60°C for 30 s, totaling 40 cycles. GADPH was set as the internal reference for MALAT1, U6 as the internal reference for miR-127-5p, and the data was analyzed by $2^{-\Delta\Delta ct}$.

WB detection

The total protein was extracted from cultured cells by RIPA lysis method and placed in a centrifuge tube at 4°C and 1500 × g for 10 min. Then the supernatant was collected as the protein sample, and the concentration was determined by BCA method. The protein concentration was adjusted to 4 μg/μL, separated by 12% SDS-PAGE electrophoresis, and then ionized and transferred to 0.22 μm PVDF membrane. Then it was blocked with 5% skim milk for 2 h, then we added IGF-1, β-actin primary antibody 1:1000 and it was sealed at 4°C overnight. After that, the primary antibody was washed and the horseradish peroxidase-labeled goat anti-rabbit secondary antibody (1:5000) was added, incubated at 37°C for 1 h, and rinsed 3 times with PBS, 5 min each. Then the excess liquid on the membrane was blotted with filter paper, and then developed by ECL. The protein bands were scanned and the grayscale values were analyzed in Quantity One software, with GAPDH as the internal reference.

CCK-8 for cell proliferation

Cells were collected 24 hours after transfection, adjusted to $4*10^6$ cells, and inoculated on 96-well plates, in which 100 μl of cell suspension was added. After culture for 24 h, 48 h, 72 h and 96 h, 10 μL CCK8 solution and 90 μL basal medium (DMEM) were added to each well, and the cells were cultured at 37°C for 2 hours. Then, the OD value of each group of cells was measured using a microplate reader at 450 nm.

Transwell method for cell invasion

Cells were collected 24 hours after transfection, adjusted to $5*10^4$, and inoculated on 6-well plates. Then it was rinsed with PBS twice and then inoculated in the upper chamber where 200 μL DMEM culture medium was added, and 500 mL DMEM (containing 20% FBS) was added to the lower chamber. After culture at 37°C for 48 h, the substrates and cells that did not pass through the membrane surface of the upper chamber were wiped, washed with PBS for 3 times, fixed with paraformaldehyde for 10 min, and washed with double distilled water for 3 times. After drying, the cells were stained with 0.5% crystal violet, and the cell invasion was observed by a microscope.

Apoptosis detection

After digestion with 0.25% trypsin, the transfected cells were washed twice with PBS, and mixed with 100 μL binding buffer to prepare a suspension of $1*10^6$ cells/mL. Next was the successive addition of Annexin V-FITC and PI before incubating it at room temperature for 5 min shielded from light. Finally, the FC500MCL flow cytometry system was used for detection, and the experiment was repeated for 3 times to get the average value.

Target gene detection

Potential target prediction for MALAT1 was performed by starbase3.0. MALAT1 was cloned into pmirGLO dual luciferase target expres-

sion vector using Lipofectamine™2000 kit. PmirGLO-MALAT1-3'UTR wild type (Wt) and pmirGLO-MALAT1-3'UTR mutant (Mut) were established and transferred into the downstream of the luciferase reporter gene for sequencing identification. The plasmids that were correctly sequenced were then co-transfected with miR-127-5p-mimics or miR-NC into osteoarthritis chondrocytes.

Statistical methods

In this study, the collected data was analyzed using SPSS 20.0, and the illustrations were performed by GraphPad 7. An independent t-test was employed for inter-group comparisons, and one-way ANOVA was adopted for multi-group comparisons. Post pairwise comparison was performed by LSD-t, and repeated measurement ANOVA was utilized for multi-time expression analysis. ROC was used to plot the diagnostic value of MALAT1 in osteoarthritis. Pearson correlation coefficient was applied to analyze the correlation between miR-127-5p and MALAT1 expression levels in serum and tissue of patients, Log-rank test for analysis, and Cox regression analysis for the prognosis of the patients. P<0.05 indicated a statistically significant difference.

Results

Diagnosis of MALAT1 and miR-127-5p expression in the serum of patients with osteoarthritis

The results of qRT-PCR showed the different expression levels of MALAT1 and miR-127-5p in the serum of the two groups, that is, MALAT1 was higher and miR-127-5p was lower in the RG than in the CG (P<0.05). We further provided the ROC curve for the diagnosis of osteoarthritis by serum MALAT1 and miR-127-5p. The results showed that the AUC, sensitivity and specificity of serum MALAT1 in the diagnosis of osteoarthritis were 0.898, 83.33% and 84.06% respectively, while the AUC of serum MALAT1 in the diagnosis of osteoarthritis was 0.897, the sensitivity was 82.35%, and the specificity was 82.61%. Pearson test analysis demonstrated that the expression of MALAT1 and miR-127-5p was negatively correlated in the serum of patients with osteoarthritis (P<0.05) (**Table 1**; **Figure 1**).

Relationship between MALAT1 and clinicopathological characteristics in patients with osteoarthritis

Through multivariate Cox regression analysis of pathological data and serum MALAT1 expression in patients with osteoarthritis, we found that high expression of MALAT1, age, housework, family history of osteoarthritis, history of knee trauma, damp and dark living environment and obesity were independent factors affecting the prognosis of patients with osteoarthritis (**Tables 2**, **3**).

Effects of MALAT1 expression in transfected chondrocytes on cell biological function in patients with osteoarthritis

The expression of MALAT1 in transfected osteoarthritis chondrocytes was detected, and the expression of MALAT1 in the MALAT1-inhibitor group was remarkably lower than that in the si-NC after transfection (P<0.05). The detection of cell proliferation, invasion and apoptosis after transfection revealed that the ability of proliferation and invasion in MALAT1-inhibitor group was much lower, and the apoptosis rate was dramatically higher than those in the si-NC group (P<0.05) (**Figure 2**).

Effects of miR-127-5p expression in transfected chondrocytes on cell biological function in patients with osteoarthritis

The expression of miR-127-5p in the transfected miR-127-5p-mimc group was found to be clearly higher than that in the miR-NC group (P<0.05). The proliferation, invasion and apoptosis of the transfected cells showed that the proliferation and invasion ability of the miR-127-5p-mimc group was noticeably lower than that of the miR-NC group, and the apoptosis rate was significantly elevated (P<0.05) (**Figure 3**).

Gene identification of MALAT1

We predicted the potential target of MALAT1 by starbase3.0, and found that there were target binding sites between miR-127-5p and MALAT1. Then, we detected the activity of double luciferase and noticed that the luciferase activity of MALAT1-3'UT Wt decreased notably after overexpression of miR-127-5p (P<0.05), but had no effect on the lucifera-

Table 1. Relationship between MALAT1 and clinicopathological characteristics of patients with osteoarthritis

Diagnostic indexes	AUC	95% CI	Standard error	Cut-off value	Sensitivity (%)	Specificity (%)
MALAT1	0.898	0.852-0.945	0.024	1.418	83.33	84.06
miR-127-5p	0.897	0.852-0.944	0.023	0.915	82.35	82.61

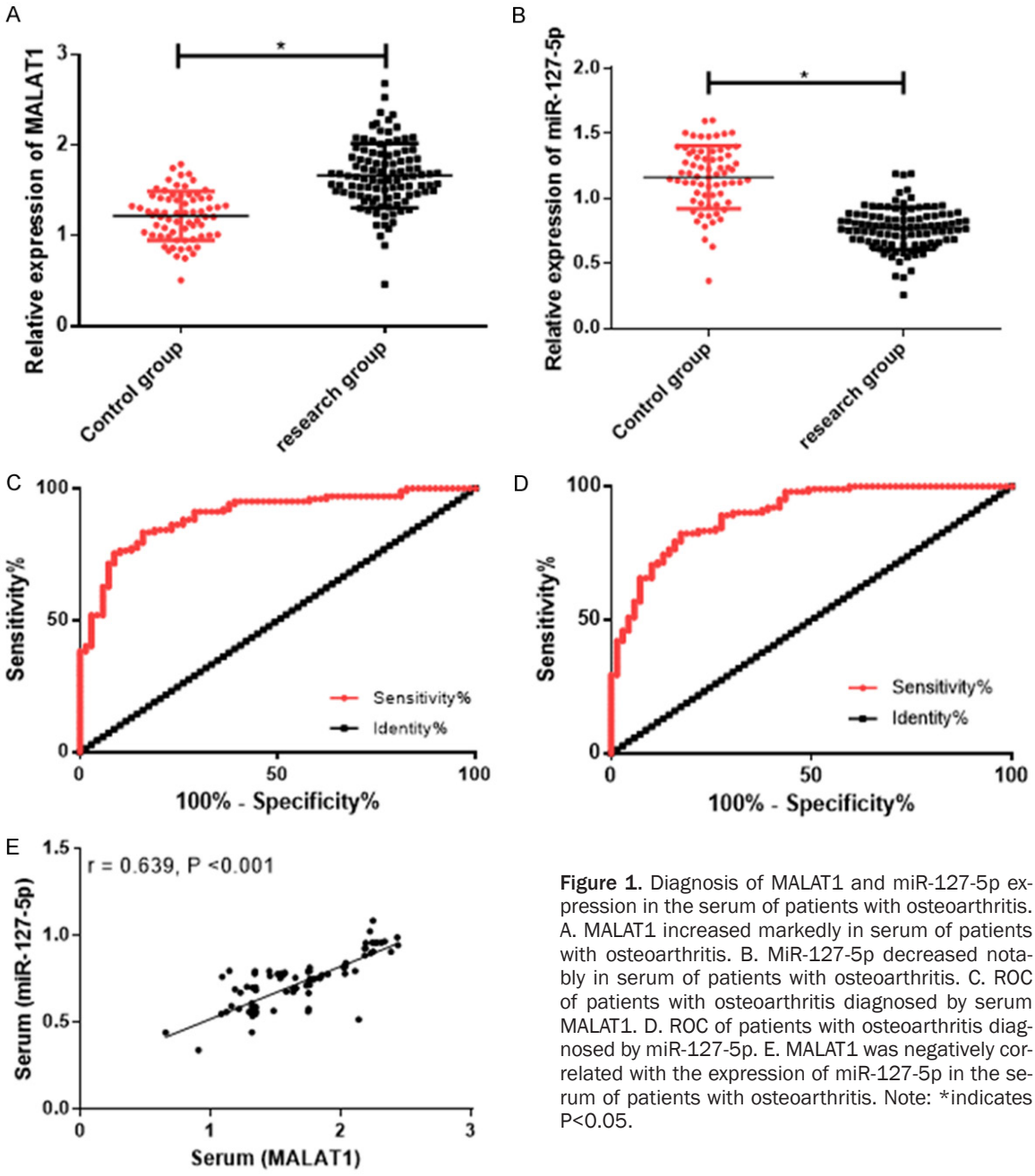

Figure 1. Diagnosis of MALAT1 and miR-127-5p expression in the serum of patients with osteoarthritis. A. MALAT1 increased markedly in serum of patients with osteoarthritis. B. MiR-127-5p decreased notably in serum of patients with osteoarthritis. C. ROC of patients with osteoarthritis diagnosed by serum MALAT1. D. ROC of patients with osteoarthritis diagnosed by miR-127-5p. E. MALAT1 was negatively correlated with the expression of miR-127-5p in the serum of patients with osteoarthritis. Note: *indicates P<0.05.

se activity of MALAT1-3'UTR Mut (P>0.05). PCR results exhibited that miR-127-5p expression in osteoarthritis chondrocytes was significantly down-regulated after transfection with MALAT1-mimics in rescue experiments, while it was significantly up-regulated after transfection with MALAT1-inhibitor (P<0.05) (**Figure 4**).

Table 2. Relationship between MALAT1 and clinicopathological characteristics in patients with osteoarthritis

Factors	n	MALAT1		T value	*P* value
		High expression group (n=51)	Low expression group (n=51)		
Age (years)				4.638	0.031
≥60	61	44 (72.13)	17 (27.87)		
<60	41	21 (51.22)	20 (48.78)		
Gender				0.421	0.517
Male	69	35 (50.72)	34 (49.28)		
Female	33	19 (57.58)	14 (42.42)		
Housework				6.628	0.010
A little or none	23	17 (29.31)	41 (70.69)		
Most	46	24 (54.55)	20 (45.45)		
Family history of osteoarthritis				16.820	<0.001
Yes	56	41 (73.21)	15 (26.79)		
No	46	15 (32.61)	31 (67.39)		
History of knee trauma				7.222	0.007
Yes	57	38 (66.67)	19 (33.33)		
No	45	18 (40.00)	27 (60.00)		
Damp and dark living environment				10.360	0.001
Yes	42	29 (69.05)	13 (30.95)		
No	60	22 (36.67)	38 (63.33)		
Physical exercise				0.503	0.478
Yes	59	26 (44.07)	33 (55.93)		
No	43	22 (51.16)	21 (48.84)		
Obesity				7.067	0.008
Yes	63	47 (74.60)	16 (25.40)		
No	39	19 (48.72)	20 (51.28)		

Table 3. Cox regression analysis

Factors	Univariate Cox			Multivariate Cox		
	P value	HR	95% CI	*P* value	HR	95% CI
Age	0.022	0.182	1.042-2.364	0.001	1.864	1.632-2.129
Gender	0.664	1.116	0.685-1.232			
Housework	0.038	1.245	0.486-2.469	0.030	1.004	0.023-2.008
Family history of osteoarthritis	0.048	1.815	1.012-4.120	<0.001	4.678	2.339-9.356
History of knee trauma	0.033	1.116	0.681-1.83	0.016	3.092	1.546-6.184
Damp and dark living environment	<0.001	6.151	2.773-13.644	0.017	2.462	1.231-4.924
Physical exercise	0.179	1.965	0.983-3.930			
Obesity	0.034	1.435	0.718-2.870	0.005	3.128	1.564-6.256

Rescue experiment

Cell biological function was detected by co-transfection of osteoarthritis chondrocytes with MALAT1-inhibitor+miR-127-5p-mimcs. The results showed that the proliferation, invasion and apoptosis of cells transfected with MALAT1-inhibitor+miR-127-5p-mimcs were not different from those of transfected si-NC cells, while the proliferation, invasion and apoptosis of cells transfected with MALAT1-inhibitor were greatly enhanced, and the apoptosis rate was notably declined (**Figure 5**).

Discussion

Osteoarthritis, which can occur in any joint, is a disease that causes swelling, pain and stiff-

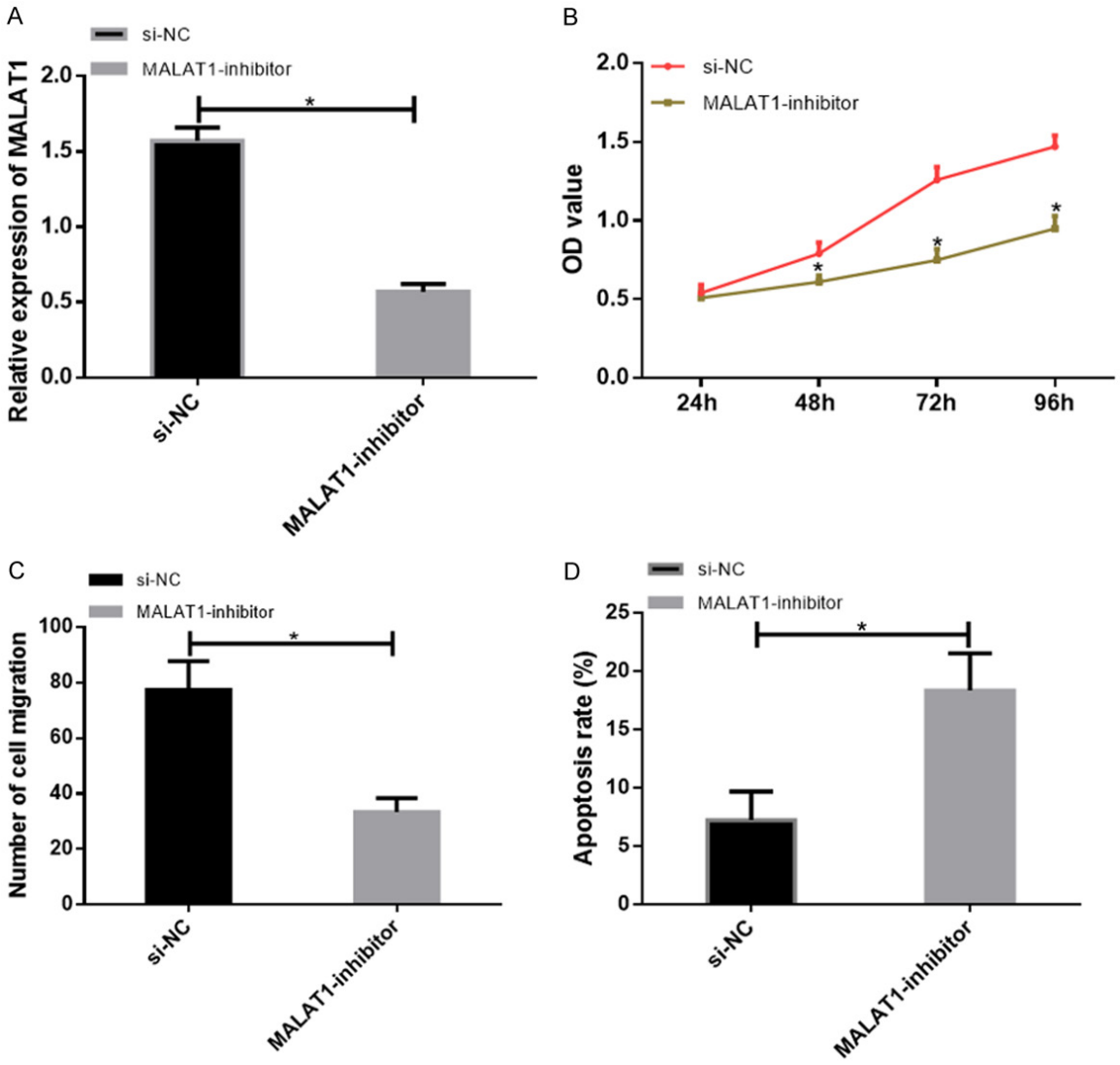

Figure 2. Effects of MALAT1 expression in transfected chondrocytes on cell biological function in patients with osteoarthritis. A. Expression of MALAT1 in osteoarthritis chondrocytes after transfection. B. Proliferation of osteoarthritis chondrocytes after transfection. C. Invasion of osteoarthritis chondrocytes after transfection. D. Apoptosis of osteoarthritis chondrocytes after transfection. Note: *indicates $P<0.05$.

ness in patients' joints, and the symptoms worsen over time [16, 17]. It is a challenging disease in the clinic, and its treatment options are limited. The traditional drug therapy can only relieve pain but cannot reverse cartilage damage [18]. Moreover, the poor self-repair ability of cartilage and lack of characteristic diagnostic biomarkers make this disease more complicated [19, 20]. Therefore, finding biomarkers that affect the prognosis of osteoarthritis is of great significance for improving the prognosis of patients with osteoarthritis.

LncRNA has been shown to play an important role in the pathological states of many cancers, and can influence tumor progression by interacting with DNA, RNA and proteins, regulating cell cycle and immune response [21, 22]. MALAT1 is a conserved lncRNA, which produces marked effects on maintaining the undifferentiated states of hematopoietic stem cells and the activation of B cells [23]. In the study of Xiao X et al. [24], MALAT1 could promote the expression of alkaline phosphatase, osteocalcin and other specific markers in osteoblasts by inhibiting the expression and activity of miR-204. However, it is unclear whether MALAT1 can regulate the biological function of chondrocytes in osteoarthritis by targeting miR-127-5p. Therefore, this study firstly analyzed the expres-

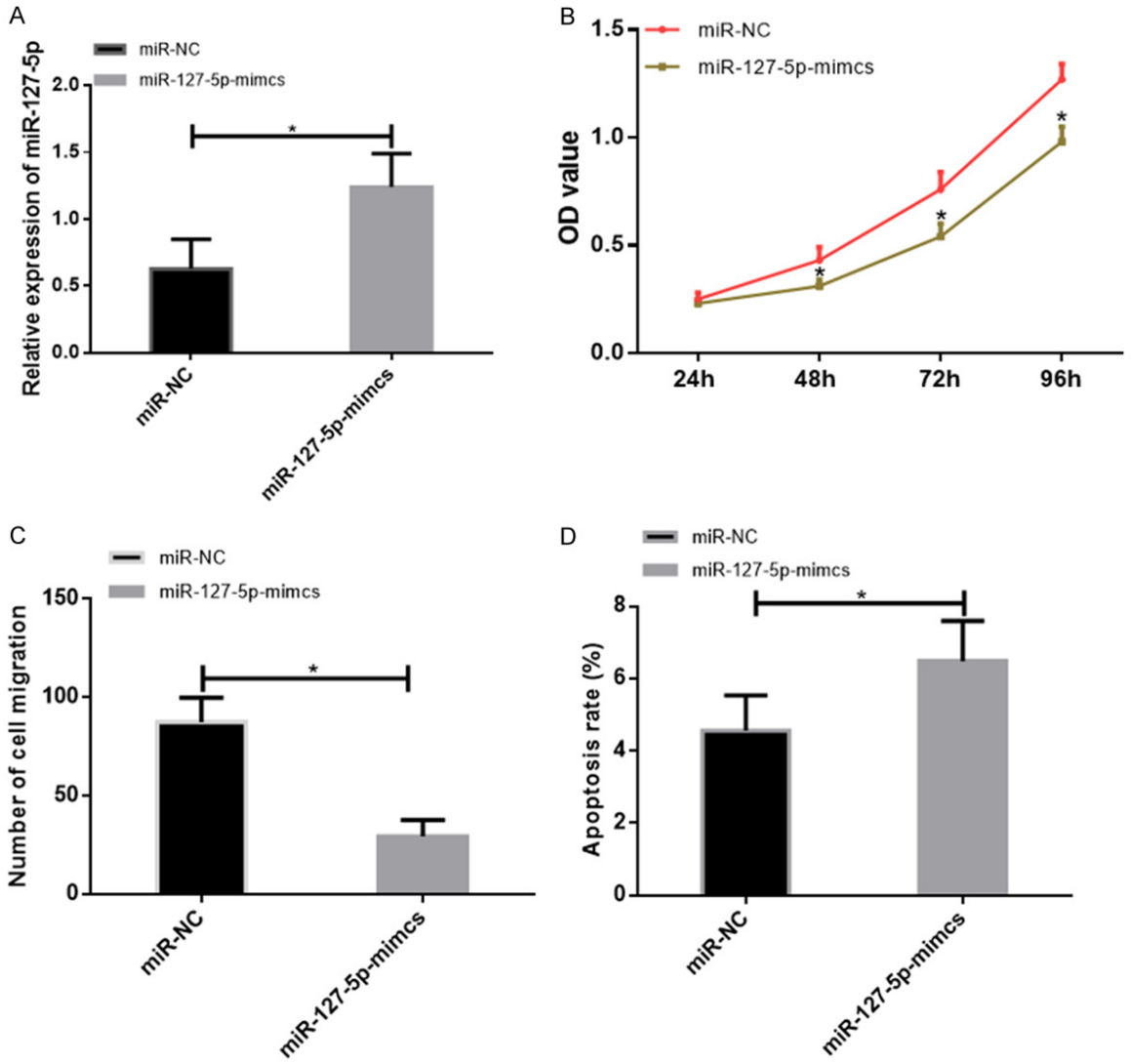

Figure 3. Effects of miR-127-5p expression in transfected chondrocytes on cell biological function in patients with osteoarthritis. A. Expression of miR-127-5p in osteoarthritis chondrocytes after transfection. B. Proliferation of osteoarthritis chondrocytes after transfection. C. Invasion of osteoarthritis chondrocytes after transfection. D. Apoptosis of osteoarthritis chondrocytes after transfection. Note: *indicates $P<0.05$.

sion of MALAT1 and miR-127-5p in osteoarthritis, and observed the clinical value of detecting osteoarthritis in both groups. The results showed that the serum expression of MALAT1 in the RG was remarkably higher than that in the CG, while miR-127-5p was significantly lower. According to the ROC curve analysis, the AUC value of MALAT1 was 0.898 and that of miR-127-5p was 0.897, indicating that both of them enjoyed higher diagnostic efficacy for osteoarthritis. Further Pearson correlation analysis revealed that MALAT1 was negatively correlated with miR-127-5p expression in the serum of patients with osteoarthritis. We then analyzed the relationship between the pathological data of patients with osteoarthritis and MALAT1 through Cox, and found that high MALAT1 expression, age, housework, family history of osteoarthritis, history of knee trauma, damp and dark living environment, and obesity were independent factors influencing the prognosis of patients with osteoarthritis. In a study by Palazzo C et al. [25], age, gender, diet, joint factors, and genetic factors are all risk factors for osteoarthritis, which is similar to the results of this study. We hypothesized that MALAT1 and miR-127-5p were involved in the development of osteoarthritis, which was fur-

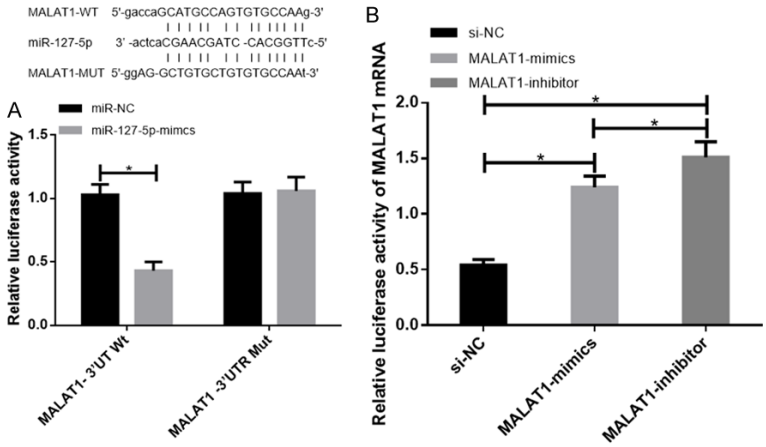

Figure 4. Gene identification of MALAT1. A. The results of dual-Luciferase Reporter (DLR) assay showed that there were binding sites and relative luciferase activity between MALAT1 and miR-127-5P. B. Relative protein expression of MALAT1 in transfected osteoarthritis chondrocytes. Note: *indicates P<0.05.

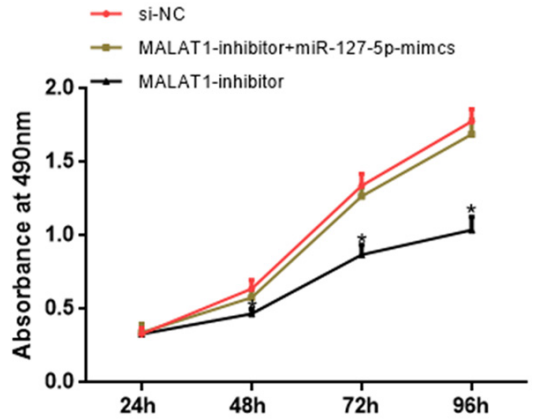

Figure 5. Rescue experiment. Changes in biological function of osteoarthritis chondrocytes after cotransfection with MALAT1-inhibitor+miR-127-5p-mimcs. The MALAT1-inhibitor+miR-127-5p-mimcs group did not differ markedly in cell proliferation compared with the si-NC group, while it differed significantly with the MALAT1-inhibitor group concerning the proliferation ability of cells.

ther verified by cell biology experiments. Through the detection of MALAT1 and miR-127-5p in chondrocytes of osteoarthritis, we found that the expression of MALAT1 in chondrocytes increased while the expression of miR-127-5p decreased. Subsequently, we transfected MALAT1-inhibitor and miR-127-5p-mimc plasmids into chondrocytes and found that after transfection, the proliferation and invasion ability of MALAT1 cells were inhibited, while the apoptosis rate of cells was significantly increased, indicating that down-regulation of MALAT1 expression could not only inhibit the proliferation and invasion ability of cells, but also improve the apoptosis rate. Furthermore, transfection of miR-127-5p also inhibited cell proliferation and invasion, and promoted apoptosis, suggesting that MALAT1 and miR-127-5p could be potential targets for the treatment of osteoarthritis. Then we conducted a rescue experiment to explore the relationship between MALAT1 and miR-127-5p. It turned out that the proliferation, invasion and apoptosis of osteoarthritis chondrocytes in the MALAT1-inhibitor+miR-127-5p-mimcs group were not significantly different from those in the si-NC group, while the proliferation, invasion of chondrocytes increased and the apoptosis rate decreased compared with the MALAT1-inhibitor group, suggesting a certain regulatory relationship between the two. Therefore, we further verified the regulatory relationship between MALAT1 and miR-127-5p by DLR. The results showed that overexpressed miR-127-5p markedly lowered the luciferase activity of MALAT1-3UT Wt, but it had no effect on the luciferase activity of MALAT1-3'UTR Mut. Besides, the transfection of MALAT1-mimicsdramatically down-regulated miR-127-5p expression in chondrocytes, while the transfection of MALAT1-inhibitor led to remarkably up-regulated expression of miR-127-5p. All these indicate that there was a targeted regulatory relationship between MALAT1 and miR-127-5p, that is, inhibition of MALAT1 could improve the expression of miR-127-5p, thus reducing the proliferation and invasion ability of osteoarthritis chondrocytes and increasing the rate of apoptosis.

Although this study confirmed that MALAT1 can inhibit miR-127-5p-mediated cell proliferation, there is still room for improvement. Such as the lack of tumor formation experiments in nude mice, and further verification to validate whether MALAT1 is consistent with cell experiments *in vivo* still need to be addressed. Therefore in future research, we will carry out more basic

studies to verify the results of this study by analyzing more potential mechanisms of MALAT1 through biological information.

In summary, MALAT1 promotes proliferation of osteoarthritis chondrocytes and prevents apoptosis by targeting miR-127-5p.

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Disclosure of conflict of interest

None.

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