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Effect of lncRNA MALAT1 on rats with myocardial infarction through regulating ERK/MAPK signaling pathway

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Abstract. – OBJECTIVE: To explore the effect of the long non-coding ribonucleic acid (lncRNA) metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) on rats with myocardial infarction (MI) by regulating the extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK) signaling pathway.

MATERIALS AND METHODS: The Sprague-Dawley (SD) rat model of MI was established, and lncRNA MALAT1 was overexpressed using pcDNA-MALAT1 plasmids (MALAT1 group, n=10) and silenced using RNA interference technique (siMALAT1 group, n=10). The Sham group (n=10) was also set up. The transfection efficiency of lncRNA MALAT1 in rats was detected *via* Reverse Transcription-Polymerase Chain Reaction (RT-PCR). 2 weeks after the successful modeling, the cardiac function indexes were measured through magnetic resonance imaging (MRI) and echocardiography (ECG). The myocardial tissue injury was observed *via* hematoxylin-eosin (HE) staining, and the apoptosis of myocardial tissues was detected *via* terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay. Moreover, the levels of the serum inflammatory factors were detected *via* enzyme-linked immunosorbent assay (ELISA), the messenger RNA (mRNA) expressions of Collagen I and III, the apoptosis, the and pathway genes were detected *via* RT-PCR. The expressions of ERK/MAPK pathway-related proteins in myocardial tissues were detected *via* Western blotting.

RESULTS: The expression of lncRNA MALAT1 was remarkably increased in the MALAT1 group but evidently declined in the siMALAT1 group ($p<0.05$), indicating the successful transfection. The fractional shortening (FS, %) and ejection fraction (EF, %) were significantly restored in siMALAT1 group ($p<0.05$), suggesting that the silence of MALAT1 can improve the cardiac function after acute MI. The results of the HE staining and TUNEL assay manifested that siMALAT1 group had milder myocardial injury and decreased apoptosis compared with MALAT1 group. In the MALAT1 group, the mRNA expressions of Collagen I and III, Caspase3, ERK2, and MAPK were remarkably increased ($p<0.05$), while the mRNA expression of Bcl-2 was remarkably decreased ($p<0.05$). The above expressions had the opposite trends in siMALAT1 group. Besides, the protein expressions of ERK2 and MAPK in MALAT1 group were significantly increased ($p<0.05$).

CONCLUSIONS: The downregulation of lncRNA MALAT1 can significantly improve the cardiac function after MI in SD rats mainly by inhibiting the ERK/MAPK pathway.

Key Words:
LncRNA MALAT1, ERK/MAPK signaling pathway, Myocardial infarction, Rats, Apoptosis, Inflammation.

Introduction

Acute myocardial infarction (AMI) is a severe cardiovascular disease with the highest morbidity and mortality rates in the world, characterized by myocardial ischemia or persistent ischemia and hypoxia[1]. In AMI, the myocardium fails to perform normal systolic and diastolic functions, and the coronary blood flow is blocked, sharply declined, or forced to interrupt, seriously affecting the normal myocardial function, and leading to severe myocardial ischemia[2,3]. AMI is mainly caused by the decline and obstruction of blood flow due to coronary stenosis, resulting in spot-like rupture of coronary arteries, which will cause various secondary reactive diseases and even necrosis in the severe stage[4]. AMI is characterized by acute onset, serious consequences once it occurs, high mortality rate, and rapid development, seriously threatening people's health[5]. The complexity of the myocardial infarction (MI) has been understood in detail through in-depth research. The MI-induced characteristic changes in metabolism and ultrastructure cause irreversible

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damages. The myocardial ischemia/reperfusion is an important goal for the treatment of MI, and it may lead to cell death[6]. With the continuous innovation of the basic research and the advancement of clinical practice, the therapeutic regimens for MI patients have been gradually improved in the last few decades.

Long non-coding ribonucleic acids (lncRNAs) have been recognized as important regulatory factors in such cellular process as cell proliferation, differentiation, and cell identity establishment[7]. The expression of lncRNAs is often deregulated in cancer[8,9]. The functions of lncRNAs remain unclear, but some lncRNAs interact with transcription factors and chromatin regulators to regulate the expression of specific genes. The biological importance and specificity of lncRNAs in human diseases such as cancer and cardiovascular disease have been confirmed in some studies[10,11]. The high-throughput sequencing and microarray-based genomic research focus on the potential effects of lncRNAs on the pathological processes of the cardiovascular diseases, such as AMI, myocardial ischemia/reperfusion injury, heart failure, and hypertension[12]. Recently, it is reported that the expression of the metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) in peripheral blood cells of 414 AMI patients is higher than that in 86 healthy volunteers, which is considered as an important predictor of the left ventricular dysfunction[13]. MALAT1 located on chromosome 13 is involved in the activation of the hypoxia pathway. However, there is limited evidence about the role of MALAT1 in AMI and its regulatory mechanism[14]. The mitogen-activated protein kinase (MAPK) subfamilies, such as p38, and c-Jun N-terminal kinase (JNK), lead to inflammation, apoptosis, and cell death. The pro-survival kinase regulates cell differentiation and proliferation, promotes cell survival, and protects tissues[15]. Yu et al[16] have shown that the activation of the extracellular signal-regulated kinase 1 (ERK1)/ERK2 and inhibition on p38/MAPK maintain the cytoskeletal structure and protect against myocardial injury by reducing oxidative stress and inflammation. Therefore, the relative activity of these pro-apoptotic and pro-survival kinase pathways will determine the cell survival or death. ERK1/2, involved in regulating a variety of vital processes, including MI and ventricular remodeling, is an important signal transduction pathway in myocardial regulation and plays an important role in the occurrence and development of MI[17,18]. Currently, it is important to clarify the role of MALAT1 in the development of MI, and further study its underlying mechanism of action, which may help understand the pathogenesis of disease, and provide a theoretical foundation for the subsequent research on MI.

In the current study, the rat model of MI was established and MALAT1 was overexpressed and silenced. The cardiac function indexes, the levels of serum inflammatory factors, and apoptosis were detected. Moreover, the messenger RNA (mRNA) and protein expressions of apoptosis genes and ERK/MAPK pathway-related genes were measured, so as to confirm whether the up-regulation or down-regulation of MALAT1 is able to suppress the ERK/MAPK pathway, thus exerting a protective effect in MI.

Materials and Methods

Reagents and Instruments

The main reagents and instruments were: Interleukin-1 (IL-1) and IL-6 enzyme-linked immunosorbent assay (ELISA) kits (Sbjbio, Nanjing, China), RIPA lysis buffer (Beyotime, Shanghai, China), loading buffer, protease inhibitor, and bicinchoninic acid (BCA) protein concentration assay kit (Biosharp, Hefei, China), β-actin and secondary antibodies (Univ-Bio, Shanghai, China), primary antibodies (CST), tissue homogenizer (Haimen Aiband Laboratory Equipment Co., Ltd., Haimen, China), electrophoresis apparatus (Bio-Rad, Hercules, CA, USA), microplate reader (Thermo Fisher Scientific, Waltham, MA, USA), 2500 gel imager (Bio-Rad, Hercules, CA, USA), quantitative Polymerase Chain Reaction (qPCR) instrument (7900 Fast, Applied Biosystems, Foster City, CA, USA), and TRIzol reagent, diethyl pyrocarbonate (DEPC)-treated water, SuperScript III RT kit and Sybr qPCR Mix (ABI, Applied Biosystems, Foster City, CA, USA).

Animal Modeling

This study was approved by the Animal Ethics Committee of Xiangtan Central Hospital Animal Center. A total of 30 male Sprague-Dawley (SD) rats weighing 220-280 g were purchased and fed adaptively for 1 week. Then, 20 SD rats were randomly selected, and the permanent ligation of left anterior descending coronary artery was performed aseptically to establish the rat model of AMI. LncRNA MALAT1 was overexpressed through the transfection of pcDNA-MALAT1 plasmids (MALAT1 group, n=10) obtained from GeneCopoeia using Lipofectamine 2000 reagent (Invitrogen, Carlsbad, CA, USA) according to the instructions, while it was knocked out using RNA interference technique (siMALAT1 group, n=10). The Sham group (n=10) was also set up. To deeply study the role of lncRNA MALAT1 in MI rats, the transfection efficiency of lncRNA MALAT1 in rats was detected *via* Reverse Transcription-Polymerase Chain Reaction (RT-PCR), so as to prepare for the subsequent study of the molecular mechanism of lncRNA MALAT1 in MI.

Determination of Cardiac Function

After the routine feeding for 4 weeks in each group, the left ventricular function was detected through magnetic resonance imaging (MRI) and echocardiography (ECG). The rats in each group were fixed in the supine position and received ECG (probe frequency: 10 MHz) according to the instructions of the instrument, and the ejection fraction (EF), the left ventricular end-diastolic diameter (LVEDd), the left ventricular end systolic diameter (LVESd), and fractional shortening (FS) were recorded.

Detection of Levels of Serum Inflammatory Factors Via ELISA

After 4 mL of venous blood was aseptically collected from the caudal vein, it was placed in a test tube containing no anticoagulant, placed at room temperature for 30 min, and centrifuged at 2000 g for 10 min. Then, the separated serum was collected to detect the levels of the serum inflammatory factors interleukin-8 (IL-8), IL-6, and IL-1β using the ELISA kits according to the instructions and actual conditions. Finally, the absorbance in each group was detected using a microplate reader.

Hematoxylin-Eosin (HE) Staining

After anesthesia with pentobarbital, the rats in each group were aseptically sacrificed, and the heart tissues were separated, immersed in formalin for 7 d, washed with running water for 24 h, dehydrated with gradient alcohol, and routinely prepared into tissue sections (5 μm in thickness). After deparaffinization, the sections were hydrated with ethanol in a decreasing concentration and baked dry, followed by HE staining, dehydration with alcohol in an increasing concentration, transparentization with xylene, and sealing. Finally, the sections were observed under a light microscope.

TUNEL Apoptosis Assay

The paraffin sections prepared were examined to detect myocardial apoptosis according to the instructions of the TUNEL apoptosis assay kit (Roche, Basel, Switzerland). After labeling reaction using the fluorescence developer, the sealed sections were fixed, rinsed, and infiltrated with 0.1% Triton X-100. The FITC-labeled TUNEL-positive cells were observed under a fluorescence microscope, and counted in 10 fields of view.

Quantitative RT-PCR (qRT-PCR)

After anesthesia with pentobarbital, the rats in each group were aseptically sacrificed, and the heart tissues were separated and washed. Then, the total RNA was extracted using TRIzol reagent from myocardial tissues, and the RNA purity and concentration were detected. The primer amplification was performed using the 20 μL system (2 μL of cDNA, 10 μL of mix, 2 μL of primer, and 6 μL of ddH_2O, for a total of 40 cycles). The RNA was reversely transcribed into complementary deoxyribose nucleic acid (cDNA) (note the use of isopropanol), and stored in an ultra-low temperature refrigerator to prevent degradation. Then, PCR was performed: pre-denaturation at 95°C for 2 min, 94°C for 20 s, 60°C for 20 s, and 72°C for 30 s, for a total of 40 cycles. The expression levels of the target genes were detected *via* qRT-PCR, and the mRNA expression in myocardial tissues was calculated using the $2^{-\Delta\Delta Ct}$ method (Table I).

Western Blotting

After anesthesia with pentobarbital, the rats in each group were aseptically sacrificed, and the heart tissues were separated, cut into pieces and added with lysis buffer, followed by tissue homogenization. After the protein was extracted, the total protein concentration in myocardial tissues in each group was detected using the BCA protein concentration assay kit. Then, the protein samples were prepared using protein and 5 × Buffer (1:4) at 98°C for 6 min. 10% separation gel and 5% spacer gel were also prepared for protein loading and electrophoresis, and the protein was transferred onto a polyvinylidene difluoride (PVDF) membrane (Millipore, Billerica, MA, USA), sealed with bovine serum albumin (BSA) at room temperature, incubated with the primary antibody (1:1500) in a box overnight and incubated again with the secondary antibody for 1 h.

Table I. Sequences of primers for RT-PCR

Genes	Primer sequences
Linc00961	Forward: 5'- GCAGAATGCCATGGTTTCCC -3' Forward: 5'-CTGTTCTGGATGGGAGCGAA-3' Reverse: 5'-ACAGTCACCACGAACAGCAC-3'
miR-367	Forward: 5'-TTCTCCGAACTTTGCACGTTT-3' Reverse: 5'-ACGTGACACGTTCGGAGAATT-3'
Cyclin D1	Forward: 5'-AGCTGTGCATCTACACCGAC-3' Reverse: 5'-TGTGAGGCGGTAGTAGGACA-3'
Bax	Forward: 5'-GCGACTGATGTCCCTGTCTC-3' Reverse: 5'-AAAGATGGTCACGGTCTGCC-3'
Bcl-2	Forward: 5'-CTCCCACAGACTCTGTAAG-3' Reverse: 5'-GCATTACCTGGGGCTGTAATT-3'
Caspase3	Forward: 5'-ATTTGGAACCAAAGATCATACA-3' Reverse: 5'-CTGAGGTTTGCTGCATCGAC-3'
β-actin	Forward: 5'-CCAAGGCCAACCGCGAGAAGAT-3' Forward: 5'-AGGGTACATGGTGGTGCCGCCA-3'
U6	Forward: 5'-CGCTTCGGCAGCACATATACT-3' Forward: 5'-CGCTTCACGAATTTGCGTGTC-3'

After the ECL solution was added, the protein bands were scanned and quantified using the Odyssey scanner, and the level of protein to be detected was corrected using β-actin. The Western blotting bands were quantified using Image Lab software (Bio-Rad, Hercules, CA, USA).

Statistical Analysis

The Statistical Product and Service Solutions (SPSS) 19.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis of raw data. The data were expressed as mean ± standard deviation ($\overline{\chi}$±s), and p<0.05 or p<0.01 suggested the statistically significant difference. The bar graph was plotted using the GraphPad Prism 5.0 (La Jolla, CA, USA).

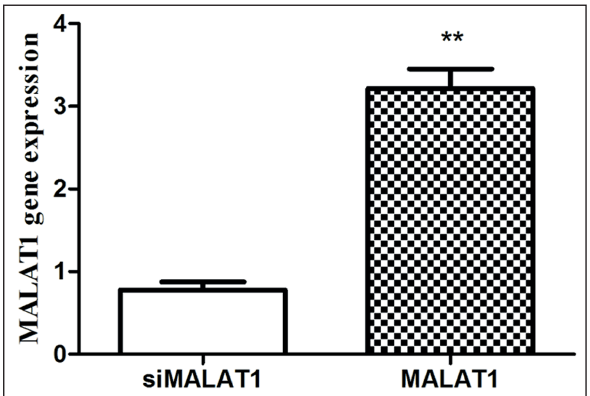

Figure 1. Transfection efficiency of lncRNA MALAT1. The expression of serum lncRNA MALAT1 is significantly higher in the MALAT1 group than that in the siMALAT1 group (p<0.01). **p<0.01: There is a statistically significant difference.

Results

Transfection Efficiency of LncRNA MALAT1 in Each Group

To verify the transfection efficiency of lncRNA MALAT1, the level of serum lncRNA MALAT1 was detected *via* RT-PCR in the two groups. As shown in Figure 1, the expression of the serum lncRNA MALAT1 was significantly higher in MALAT1 group than that in the siMALAT1 group (p<0.01).

Cardiac Function Indexes in Rats

In MALAT1 group, FS and EF were evidently lower, while LVEDd and LVESd were evidently larger than those in the Sham group (p<0.05). The above indexes had the opposite trends in siMALAT1 group (Table II), indicating that the rat model of MI was established successfully.

Detection Results of Cytokines in Each Group

The levels of inflammatory factors IL-8, IL-6, and IL-1β were detected, and it was found that they were significantly increased in MALAT1 group compared with those in the other two

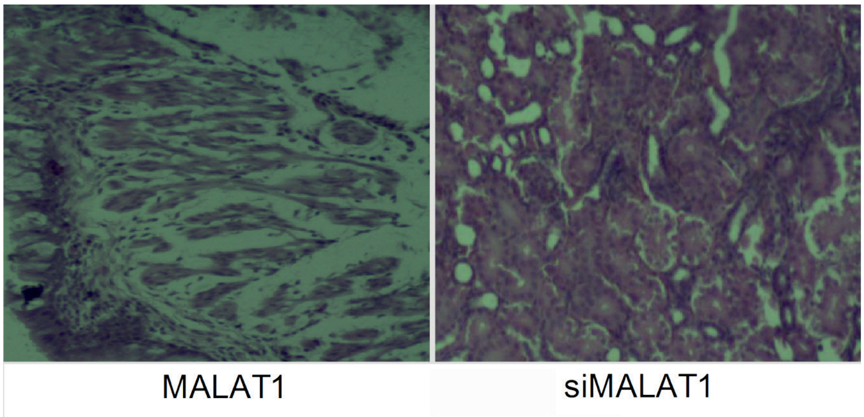

Figure 2. HE staining of heart. **A,** MALAT1 group (×10). **B,** siMALAT1 group (×10). The myocardial cells are disorderly arranged and the muscle fibers are thickened in the MALAT1 group. In the siMALAT1 group, the myocardial injury almost cannot be observed.

Table II. Cardiac function indexes in rats detected *via* MRI & ECG.

Group	LVEDd (mm)	LVESd (mm)	EF (%)	FS (%)
Sham group	3.58±0.89	4.10±0.23	65.2±3.1	58.6±3.7
MALAT1 group	8.74±0.18[a]	7.89±0.21[a]	45.7±3.3[a]	36.9±2.1[a]
siMALAT1 group	5.01±0.21[b]	5.29±0.61[b]	59.9±2.0[b]	50.6±1.1[b]

Note: In the MALAT1 group, FS and EF are evidently lower, while LVEDd and LVESd are evidently larger than those in the Sham group. [a]$p<0.05$ *vs*. Sham group, [b]$p<0.05$ *vs*. MALAT1 group.

Table III. Levels of inflammatory factors (mg/L).

Group	IL-8	IL-6	IL-1β
Sham group	40.58±1.86	64.69±1.20	50.2±3.4
MALAT1 group	180.45±2.18[a]	201.46±1.26[a]	141.6±3.7[a]
siMALAT1 group	72.14±1.23[b]	84.14±1.63[b]	80.4±2.2[b]

Note: Levels of inflammatory factors. The levels of the inflammatory factors are significantly increased in the MALAT1 group compared with those in the other two groups, while they significantly decline in the siMALAT1 group ($p<0.05$). [a]$p<0.05$ *vs*. Sham group, [b]$p<0.05$ *vs*. MALAT1 group.

groups, while they significantly declined in siMALAT1 group ($p<0.05$) (Table III), suggesting that a large number of inflammatory factors are produced during MI, which further indicate the development of MI.

HE Staining Results

The results of HE staining (Figure 2) showed that the myocardial cells were disorderly arranged and the muscle fibers were thickened in the MALAT1 group (Figure 2A). In the siMALAT1 group, the myocardial cells were orderly arranged with normal structure and muscle fibers, and the myocardial injury almost could not be observed (Figure 2B).

Myocardial Apoptosis

According to the results of TUNEL staining (Figure 3), there was almost no myocardial apoptosis in the Sham group, a large number of apoptotic cells in the MALAT1 group, and a significantly decrease of myocardial apoptosis in the siMALAT1 group, indicating that the silence of MALAT1 can protect myocardial cells from injury.

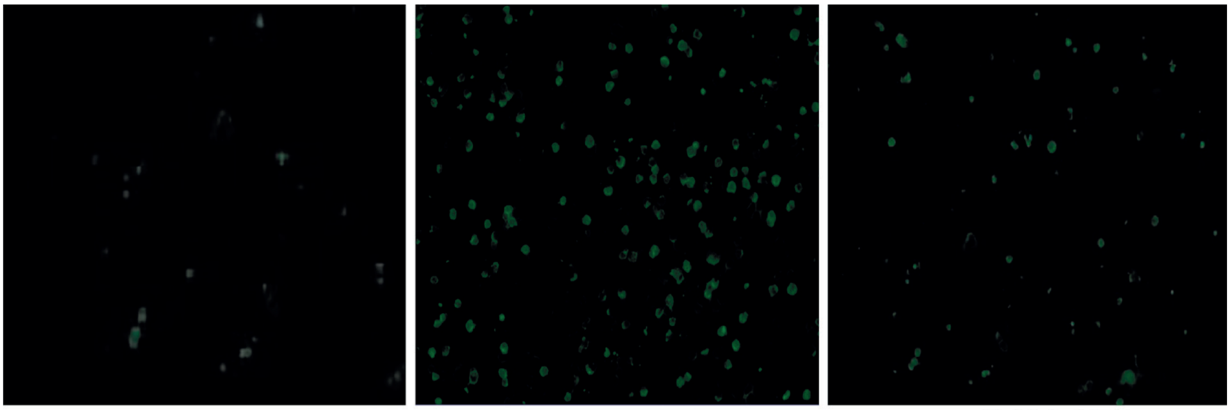

Figure 3. Apoptosis detected *via* TUNEL staining. There is almost no myocardial apoptosis in the Sham group (×40), a large number of apoptotic cells in the MALAT1 group (×40), and remarkably decreased myocardial apoptosis in the siMALAT1 group (×40).

Expressions of Key Infarction Genes, Apoptosis, and Pathway Genes Detected Via RT-PCR

According to the results of RT-PCR (Figure 4), in the siMALAT1 group, the mRNA expressions of Caspase3, MAPK, ERK2, Collagen I and III were remarkably decreased (p<0.05), while the mRNA expression of Bcl-2 was remarkably increased (p<0.05). The above expressions had the opposite trends in MALAT1 group. The above findings demonstrate that the silence of MALAT1 inhibits the occurrence of MI.

Western Blotting Results

As shown in Figure 5, the protein levels of MAPK and ERK2 remarkably declined in siMALAT1 group (p<0.05), while they were remarkably increased in the MALAT1 group, suggesting that the silence of MALAT1 prevents the occurrence of MI by inhibiting the levels of MAPK and ERK2.

Discussion

In the severe stage, AMI will cause a variety of secondary reactive diseases, which will pose the economic burden on individuals and families, as well as social burden, and harm the development of social pension benefits. Therefore, an early accurate diagnosis is the key to a successful treatment and prognosis improvement, and the risk of cardiovascular events is reduced through percutaneous coronary intervention and postoperative drug maintenance. The early administration of statins[19] is significant progress in the prevention and treatment of cardiovascular diseases, which brings good news to patients and their families. However, the long-term drug administration will cause liver and kidney dysfunction, hindering the treatment and prognosis of patients, for this reason, further research is needed. Vausort et al[13] have reported that MALAT1 plays a regulatory role in MI and serves as an important predictor of left ventricular dysfunction. However, there is limited evidence about the role of MALAT1 in AMI and its regulatory mechanism. In the present study, the rat model of MI was established and MALAT1 was silenced and overexpressed. Moreover, whether MALAT1 plays a role in MI was further observed, and the pathogenesis of MI was studied, so as to find the potential therapeutic methods. The established model could well simulate the physiological process of human MI, so it was used as the object of study. To verify the transfection efficiency of lncRNA MALAT1, the level of the serum lncRNA MALAT1 was detected *via* RT-PCR in the two groups. The results showed that the expression of the serum lncRNA MALAT1 was significantly higher in the MALAT1 group than that in the siMALAT1 group, suggesting the successful transfection. In the MALAT1 group, FS and EF were evidently lower, while LVEDd and LVESd were evidently larger than those in the Sham group. Moreover, it was found in HE staining that the muscle fibers were thickened and there was evident myocardial fibrosis in the MALAT1 group, demonstrating that the rat model of MI was successfully established.

Several studies[20] on MALAT1-knockout mice and endothelial cell model showed that MALAT1 can regulate serum amyloid A-3 and further inhibit cells from secreting inflammatory factors IL-6, IL-1, and NF-κB. There are reports demonstrating that MALAT1 is involved in the improvement of renal function in diabetic rats after treatment, and that the expressions of the pro-inflammatory cytokines IL-6, IL-1, and NF-κB decline after the expression level of MALAT1 which is significantly down-regulated in renal tissues[21]. The inflammatory cytokines participate and play an indispensable role in left ventricular remodeling after AMI, so the anti-inflammatory therapy can improve ventricular remodeling and cardiac function in MI rats. In the present study, the levels of inflammatory factors IL-8, IL-6, and IL-1β were detected, and it was found that they were evidently increased in the MALAT1 group compared with those in the other two groups, while they evidently declined in the siMALAT1 group. This finding was consistent with the above studies, and suggested that the silence of MALAT1 can inhibit the excessive production of inflammatory cytokines, prevent it from causing irreversible damage to cells, and resist inflammatory injury. Studies have revealed that apoptosis is involved in the injury in MI, which can respond to the invasion into cells and rapidly initiate the apoptotic reflex in the case of a fatal threat, so it can be used as an important guide for clinical diseases, such as tumors and myocardial apoptosis. In addition, apoptosis is regulated by apoptosis-related genes and proteins, including Bcl-2 and Caspase3. In this report, the expression level of apoptotic gene Caspase3 was remarkably higher, while that of anti-apoptotic gene Bcl-2 was remarkably lower in the MALAT1 group. According to the results of TUNEL staining, there was almost no myocardial apoptosis in Sham group, a large number of apoptotic cells in the MALAT1 group, and a remarkable decrease

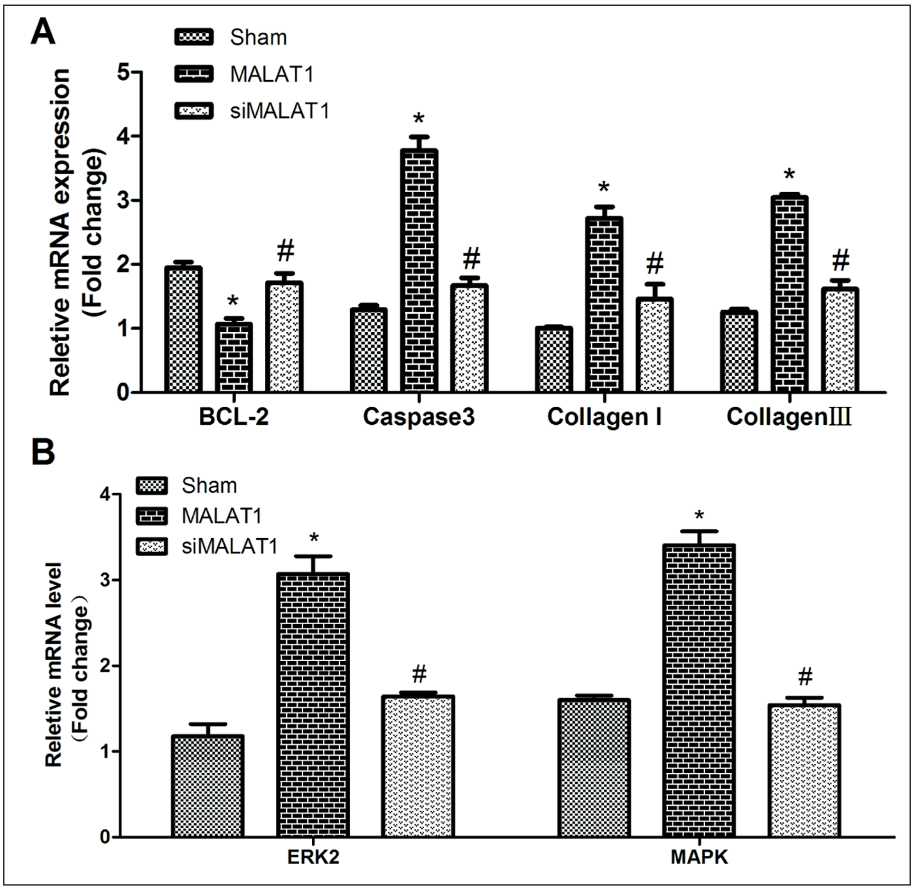

Figure 4. Gene expression levels. In the siMALAT1 group, the mRNA expressions of Caspase3, MAPK, ERK2, Collagen I and III are remarkably decreased (p<0.05), while the mRNA expression of Bcl-2 is remarkably increased (p<0.05). *p<0.05 vs. Sham group, #p<0.05 *vs.* MALAT1 group.

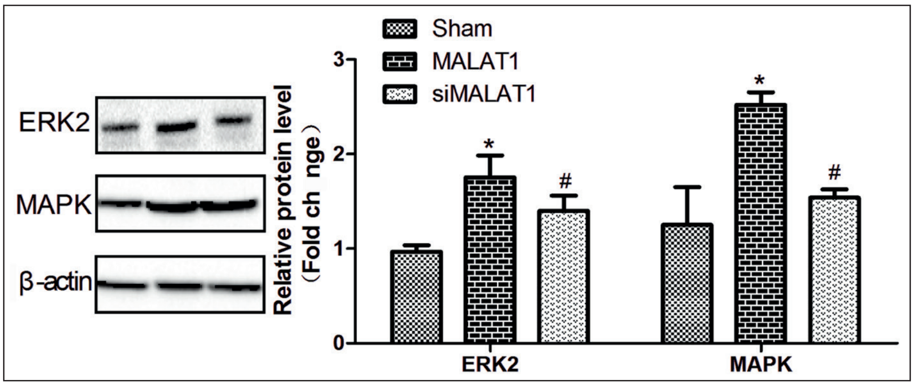

Figure 5. Protein expression. The protein levels of MAPK and ERK2 remarkably decline in the siMALAT1 group, while they are remarkably increased in the MALAT1 group. *$p<0.05$ *vs.* Sham group, $^{\#}p<0.05$ *vs.* MALAT1 group.

of myocardial apoptosis in the siMALAT1 group, indicating that the silence of MALAT1 can protect myocardial cells from injury. Similar results were also obtained previously[22,23].

Many genes and proteins can indicate the occurrence and development of MI, including Collagen and Check1. Check1 is a key molecule for regulating mitosis of myocardial cells, whose increased expression can promote the occurrence of MI. Collagen I and Collagen III are important components of the expression of the myocardial cells, and their expressions will be remarkably elevated once MI occurs[24]. In RT-PCR of this study, the mRNA levels of Collagen I and III were significantly increased in the MALAT1 group, while they were significantly decreased in the siMALAT1 group, demonstrating that the silence of MALAT1 suppresses the expressions of MI genes. The MAPK family includes ERK, p38 MAPK, etc. There are many reports about the activation of ERK in heart tissues, and whether MI is related to the regulation of ERK and MAPK remains to be further studied. According to Thomas et al[25], the targeted inhibition on p38 MAPK can reduce myocardial apoptosis and improve myocardial performance after ischemia-reperfusion injury. Moreover, the activation of the ERK1/2 signal is considered as one of the major components of the risk pathway for MI[26]. In RT-PCR of this study, it was also observed that the mRNA levels of MAPK and ERK2 were remarkably decreased in the siMALAT1 group, while they had the opposite trends in the MALAT1 group. Similar changes were also found in the protein assay, suggesting that the silence of MALAT1 prevents the occurrence of MI by inhibiting the levels of MAPK and ERK2, which is consistent with the above studies. To sum up, we clarified that MALAT1 is involved in the occurrence of MI through the ERK/MAPK signaling pathway. In the future, more *in vitro* experiments, such as immunofluorescence, flow cytometry, and electrophoretic mobility shift assay, can be performed from multiple levels and perspectives, hoping to provide an important theoretical and experimental basis for subsequent related research.

Conclusions

It was found in a series of *in vivo* animal experiments and gene/protein assays that the silence of MALAT1 may regulate the development of MI in rats by inhibiting the ERK/MAPK signaling pathway, and MALAT1 can serve as an indicator molecule for MI. The results in the present study provide an experimental basis and some theoretical base for the treatment of MI and the effect of MALAT1 on ERK/MAPK signaling pathway.

Conflicts of interest

The authors declare no conflicts of interest.

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