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LncRNA LINC00628 overexpression inhibits the growth and invasion through regulating PI3K/Akt signaling pathway in osteosarcoma

R. HE[1], J.-X. WU[2,3], Y. ZHANG[1], H. CHEN[1], L. YANG[1]

[1]Center for Joint Surgery, Southwest Hospital, Third Military Medical University, Chongqing (Army Medical University), China
[2]Department of Pathology, Chongqing Medical University, Chongqing, China
[3]Center for Molecular Medicine Testing, Chongqing Medical University, Chongqing, China

Abstract. – OBJECTIVE: Osteosarcoma (OS) is the most common primary malignancy, mainly arising from the metaphysic of the long bones of adolescents and young adults. Although osteosarcoma has been studied widely, the underlying molecular mechanism remains unclear. Increasing evidence shows that abnormal long non-coding RNAs (LncRNAs) expression is involved in tumorigenesis. The aim of this study was to identify the detailed role of LncRNA LINC00628 in osteosarcoma.

MATERIALS AND METHODS: The relative mRNA expression level of LINC00628 in adjacent tissues, osteosarcoma tissues with or without metastasis and osteosarcoma cell lines were detected by qRT-PCR. Overall survival curves for two groups defined by high and low expression level of LINC00628 in osteosarcoma patients. The cell proliferation, invasion and migration in osteosarcoma cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected. The cell cycle distribution and apoptosis rate in osteosarcoma cells after transfection with lncRNA- NC or lncRNA-LINC00628 were measured using the Flow cytometry analysis. The relative protein expression level of p-PI3K, p-Akt, P53 and Bcl-2 in osteosarcoma cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by Western blot.

RESULTS: LINC00628 expression was significantly decreased in osteosarcoma tissues compared with adjacent tissues. Meanwhile, osteosarcoma tissues with metastasis were significantly associated with a low expression level of LINC00628 and the low expression level of LINC00628 has a lower overall survival rate. LINC00628 expression was increased in osteosarcoma cell lines after transfection with lncRNA-LINC00628 and the cell proliferation, invasion and migration in osteosarcoma cells after transfection with lncRNA-LINC00628 were significantly inhibited. Moreover, the cell cycle was arrested in G0/G1 phase and the apoptosis rate was increased in osteosarcoma cells after transfection with lncRNA-LINC00628. Mechanistically, the relative protein expression level of p-PI3K, p-Akt and Bcl-2 were significantly increased and the relative expression of P53 was significantly decreased in osteosarcoma cells after transfection with lncRNA-LINC00628.

CONCLUSIONS: LINC00628 expression was decreased in osteosarcoma. The overexpression of LINC00628 inhibited the proliferation, invasion and migration and promoted cell apoptosis in osteosarcoma cells through the inactivation of PI3K/Akt signaling pathway. This lncRNA may be involved in the development and progression of osteosarcoma.

Key Words:
LncRNA LINC00628, Osteosarcoma, Proliferation, Apoptosis, PI3K, Akt, P53, Bcl-2.

Introduction

Osteosarcoma is the most common primary malignancy, mainly arising from the metaphysic of the long bones of adolescents and young adults[1,2]. Osteosarcoma is a biologically heterogeneous disease that evolves in the background of various genetic and epigenetic alterations[3]. The development of osteosarcoma from normal epithelial cells to malignant carcinomas is believed to be a multistage process involving genetic changes, leading to the activation of oncogenes and inactivation of tumor suppressor genes[4,5]. A large number of oncogenes and

Corresponding Author: Liu Yang, MD; e-mail: jointsurgury@163.com

tumor suppressor genes have been reported to be responsible for the development of osteosarcoma, but the molecular mechanisms underlying the migration and invasion of advanced osteosarcoma remains unclear[6,7]. Therefore, there is a great need to understand the underlying mechanisms of osteosarcoma progression for the treatment of osteosarcoma.

Long non-coding RNAs (LncRNAs) are a class of RNAs that have more than 200 nucleotides and have the ability to code proteins in animals and plants[8,9]. They are highly conserved among species and play important roles in various physiological and pathological processes including cancers[10,11]. Many lncRNAs are highly tissue-specific and important for cell development and differentiation. As such, the aberrant expression of lncRNAs can lead to cellular dedifferentiation, oncogenesis, cancer metastasis and tumor invasion[12]. An increasing number of lncRNAs were shown to be involved in growth and metastasis of osteosarcoma, including lncRNA-MALAT1, lncRNA-H19, lncRNA-HOTAIR, lncRNA-ATB, lncRNA-CCAT1, lncRNA-ANCR, lncRNA-CRNDE, and lncRNA-UCA1[13-15]. However, the detailed mechanisms of lncRNAs are still need to explore.

LncRNA LINC00628 locates in the second intron of PLEKHA6 (pleckstrin homology domain containing A6) in chromosome 1q32.1, the mature RNA of which is 1290bp and has a ploy A tail and is discovered in many tumor formations[16]. It was shown to be down-regulated in human gastric cancer and worked as a tumor suppressor by long-range modulation of the expression of cell cycle related genes[16]. However, the underlying mechanisms of LINC00628 expression abnormality in osteosarcoma remain to be uncovered. We investigated the role of LINC00628 in osteosarcoma. The relative mRNA expression level of LINC00628 in adjacent tissues, osteosarcoma tissues with or without metastasis and osteosarcoma cell lines, was detected. The cell proliferation, invasion, migration, cell cycle distribution and apoptosis rate in osteosarcoma cells after transfection with lncRNA- NC or lncRNA-LINC00628 were measured. We validated that LINC00628 was decreased and overexpression of LINC00628 significantly inhibited proliferation, invasion, and migration and promoted the cell apoptosis in osteosarcoma cells through the inactivation of PI3K/Akt signaling pathway.

Materials and Methods

Human Tissues, Cell Lines, and Transfection

A total of 80 osteosarcoma tissue samples and the matched adjacent non-cancerous tissue samples from osteosarcoma patients underwent clinical surgeries were acquired at the Department of Orthopedics, The First Affiliated Hospital of Chongqing Medical University during 2012 to 2013. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (Chongqing, China). The patients or their legal guardian provided written informed consents to the surgical procedures and gave permission to use resected tissue specimens for research purposes. Meanwhile, the patients with preoperative history of radiotherapy, chemotherapy, and positive surgical margins were excluded in our study. The patients' clinical data were collected and 49 osteosarcoma patients with lymph node metastasis and 31 osteosarcoma patients without lymph node metastasis. All the collected tissues were immediately frozen in liquid nitrogen and stored at -80°C before RNA isolation. The normal osteoblast cells (NHOst) and osteosarcoma cell lines of HOS, MG-63, SOSP-9607 and U2OS were acquired from the Cell Bank of the Chinese Academy of Sciences (Shanghai, China). The normal human osteoblast cell line was grown in Dulbecco's Modified Eagle Medium (DMEM):F12 (Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (FBS) and osteosarcoma cell lines were grown in Dulbecco's modified Eagle's medium (DMEM; Invitrogen, Carlsbad, CA, USA) supplemented with 10% fetal bovine serum (FBS; HyClone, South-Logan, UT, USA). All the cells were maintained under the recommended culture conditions and incubated at 37°C in a humidified environment with 5% CO_2. LncRNA-LINC00628 and its negative control (lncRNA-NC) were purchased from RiboBio Biotech (Guangzhou, China). Osteosarcoma cells were seeded at a density of 10^5 per well in 96-well plates, grown for 24 h to reach 30-50% confluence, and then transfected with lncRNA-LINC00628 or lncRNA-NC using Lipofectamine 2000 Transfection Reagent (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's instructions. The up-regulated expression efficacy was confirmed by qRT-PCR and Western blotting analysis.

RNA Extraction and Quantitative Reverse-Transcriptase Polymerase Chain Reaction (qRT-PCR)

Total RNAs was severally extracted from tumor tissues and controls using a TRIzol kit (Invitrogen, Carlsbad, CA, USA). cDNA was subsequently synthesized from total RNA using an Omniscript RT kit (Qiagen, Valencia, CA, USA) according to the manufacturer's protocol. RT-PCR reaction was conducted on the Mastercycler® ep realplex EP (Eppendorf 2S, Hamburg, Germany). 25 μl reaction mixture contained 1 μl of cDNA from samples, 12.5 μl of 2 X Fast EvaGreen™ qPCR Master Mix, 1 μl primers (10 mM), and 10.5 μl of RNase/DNase-free water. The Ct value was defined as the cycle number at which the fluorescence intensity reached a certain threshold where amplification of each target gene was within the linear region of the reaction amplification curves. GAPDH was used as an internal control for all the tissues and cultured cells. Relative mRNA expression of LINC00628 was calculated using the 2-ΔΔCt method. Primers used were as following: LINC00628 forward, 5'- AGAGCGAGCAGGATGAGATAGT-3' and reverse, 5'- GTGAGCAAGGAAGTTGACAGTG -3'; GAPDH forward, 5'- GAAGGTGAAGGTCGGAGTC -3', and reverse, 5'- GAAGATGGTGATGGGATTTC -3'. All experiments were performed three times independently, and the average was used for comparison.

Cell Proliferation Assay

Cell proliferation was assessed by the CCK-8 assay. Briefly, MG-63 and U2OS cells were seeded at a density of 10^3 per well in 96-well plates and transfected with lncRNA-LINC00628 or lncRNA-NC, respectively. 10 μL CCK-8 solution (Dojindo Laboratories, Shanghai, China) was added to each well and then cells were incubated for additional 10 min before proceeding to detection of absorbance at 405 nm. All experiments were performed in triplicate.

Cell Invasion and Migration Assays

In invasion and migration assays, 1.0×10^5 cells/ml of MG-63 and U2OS cells were prepared after transfection with lncRNA-LINC00628 or lncRNA-NC, respectively. The cell migration and invasion capacity were determined using transwell assay (Corning, Corning, NY, USA). Transfected cells were resuspended in serum-free medium. Then, 200 μl cell suspensions were seeded into the upper chamber with a porous membrane coated with (for the transwell invasion assay) or without (for the migration assay) Matrigel (BD Biosciences, San Diego, CA, USA). Complete medium was added to the bottom wells of the chambers. After migrate for 24 h or to invade for 48 h, the number of migratory and invasive cells was counted in five randomly selected high-power fields under a microscope. The presented data represent three individual wells.

Cell Cycle Analysis and Apoptosis Analysis

MG-63 and U2OS cells were seeded into six-well plates with a concentration of 3×10^5 cells/well after being transfected with lncRNA-LINC00628 or lncRNA-NC, respectively. Afterwards, cells were collected with low-speed centrifugation (1000 rpm, 5 min) at 4°C and cell pellets were re-suspended in 1 ml of PBS solution, fixed with 75% of ice-cold ethanol and stored at -20°C for two days. Prior to flow cytometry (FCM) analysis, cells were lysed, centrifuged and re-suspended in propidium iodide (PI, Sigma-Aldrich, St. Louis, MO, USA) staining buffer containing 50 μl/ml of PI and 250 μl/ml of RNase A. Finally, the cell mixture was incubated at 4°C for 30 min in the dark environment to detect cell cycle and stained with 5 μ L of annexin V-FITC to detect apoptosis by fluorescence activated cell sorting (FACS) technique (Beckman, Germany). All experiments were performed in triplicate.

Western Blot Assay

Cells were lysed in lysis buffer in the presence of aprotinin, leupeptin, phenylmethanesulfonyl fluoride (PMSF) (Sigma-Aldrich, St. Louis, MO, USA) and phosphatase inhibitor cocktails II and III (Sigma-Aldrich, St. Louis, MO, USA). Proteins were quantized by Bradford method. Then, 50 mg of total protein extracts were fractionated by 10% sodium dodecyl sulfate-polyacrylamide gel electrophoresis and transferred to polyvinylidene difluoride (PVDF) membranes (GE Healthcare, Piscataway, NJ, USA). The membrane was incubated with the following primary antibodies: anti-p-PI3K, anti-p-Akt, anti-P53, anti-Bcl-2 (Santa Cruz Bio-Technology, Santa Cruz, CA, USA), and anti- GAPDH antibody (Cell Signaling Technology, Danvers, MA, USA). Binding of the primary antibody was detected using an enhanced chemiluminescence kit (ECL Amersham, Little Chalfont, UK). Each sample was in triplicate.

Statistical Analysis

All the data were expressed as mean ± SD (standard deviation, SD) and all the statistical analysis was performed using SPSS statistical software package (SPSS Inc., Chicago, IL, USA). Patient survival and their differences were determined by Kaplan-Meier method and log-rank test. Paired and unpaired two-tail Student's *t*-test were applied to test the results. $p < 0.05$ was considered statistically significant.

Results

LINC00628 Expression Was Decreased in Osteosarcoma Tissues and Associated with the Metastasis and Poor Prognosis of Cancer

In order to detect the expression level of LINC00628 in osteosarcoma, the relative mRNA expression level of LINC00628 in adjacent tissues and osteosarcoma tissues with or without metastasis were analyzed by qRT-PCR. LINC00628 expression was significantly decreased in osteosarcoma tissues compared with adjacent tissues (Figure 1A). Furthermore, the relationship of the LINC00628 and osteosarcoma development was studied. Osteosarcoma tissues with metastasis was significantly associated with a low expression level of LINC00628 (Figure 1B) and the low expression level of LINC00628 has a lower overall survival rate by Kaplan-Meier method and log-rank test (Figure 1C).

LINC00628 Expression Was Decreased in Osteosarcoma Cell Lines

In order to detect the expression level of LINC00628 in osteosarcoma cell lines, the relative expression level of LINC00628 in osteosarcoma cell lines, including NHOst, HOS, MG-63, SOSP-9607 and U2OS were detected by qRT-PCR. The results showed that the relative mRNA expression levels of LINC00628 were significantly decreased in osteosarcoma cell lines, compared with NHOst cell line (Figure 2).

LINC00628 Expression Was Increased in Osteosarcoma Cell Lines After Transfection with lncRNA-LINC00628

In order to investigate the role of LINC00628 in osteosarcoma carcinogenesis, lncRNA-LINC00628 was introduced into osteosarcoma cells. The relative mRNA expression level of LINC00628 in MG-63 and U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by qRT-PCR. The results showed that the relative mRNA expression levels of LINC00628 were obviously increased in osteosarcoma cell lines after transfection with lncRNA-LINC00628, compared with transfection with lncRNA-NC (Figures 3A and 3B).

The Cell Proliferation, Invasion and Migration in Osteosarcoma Cells Were Inhibited After Transfection with lncRNA-LINC00628

To determine whether LINC00628 suppressed the proliferation, migration and invasion potential of osteosarcoma cells, MG-63 and U2OS cells were transfected with lncRNA- NC or lncRNA-LINC00628, followed by the proliferation, invasion and migration of those cells were analyzed, respectively. As expected, the results showed that up-regulation of LINC00628 significantly suppressed

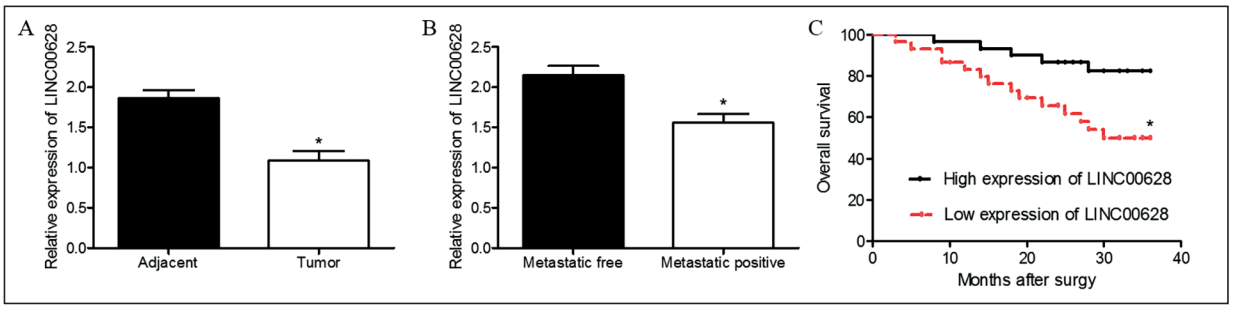

Figure 1. LINC00628 expression was decreased in osteosarcoma tissues and associated with the metastasis and poor prognosis of cancer. ***(A)*** The relative mRNA expression level of LINC00628 in adjacent tissues and osteosarcoma tissues. ***(B)*** The relative mRNA expression level of LINC00628 in osteosarcoma tissues with or without metastasis. ***(C)*** Overall survival curves for two groups defined by high and low expression level of LINC00628 in osteosarcoma patients. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with the control group).

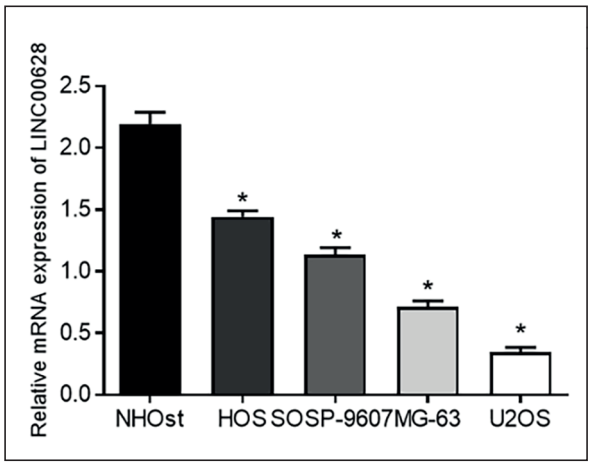

Figure 2. LINC00628 expression was decreased in osteosarcoma cell lines. The relative mRNA expression level of LINC00628 in osteosarcoma cell lines were detected by qRT-PCR. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with FHC group).

the proliferation in MG-63 and U2OS cells at 72 h and 96 h (Figures 4A and 4B). These data suggested that up-regulation of LINC00628 inhibited the proliferation in osteosarcoma cells. Invasion and migration activities of MG-63 and U2OS cells after transfected with lncRNA- NC or lncRNA-LINC00628 were measured with the Transwell. The results demonstrated that up-regulation of LINC00628 inhibited the invasion (Figures 5A) and migration (Figures 5B) in osteosarcoma cell lines compared with lncRNA- NC group. These data suggest that overexpression of LINC00628 suppressed proliferation and motility of osteosarcoma cells.

The Cell Cycle Was Arrested and the Apoptosis Rate Was Increased in Osteosarcoma Cells After Transfection with lncRNA-LINC00628

The cell cycle distribution and apoptosis rate in MG-63 and U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628 were measured using the Flow cytometry analysis to study the functional mechanism of LINC00628 in osteosarcoma. These data suggested that osteosarcoma cell cycle was prominently shifted from S phase and G2/M phase to G0/G1 phase, cell percentage in G0/G1 phase was significantly increased and cell percentage in S phase was significantly decreased and promoted cell apoptosis after transfection with lncRNA-LINC00628 (Figures 6A and 6B). The results showed that up-regulation LINC00628 arrested cell cycle in G0/G1 phase to induce cell apoptosis in osteosarcoma.

The Activation of PI3K/Akt Signaling Pathway in Osteosarcoma Cells Were Inhibited After Transfection with lncRNA-LINC00628

In order to study the mechanism of up-regulation LINC00628 arrested cell cycle in G0/G1 phase to induce cell apoptosis in osteosarcoma. The relative protein expression level of p-PI3K, p-Akt, P53 and Bcl-2 in MG-63 and U2OS

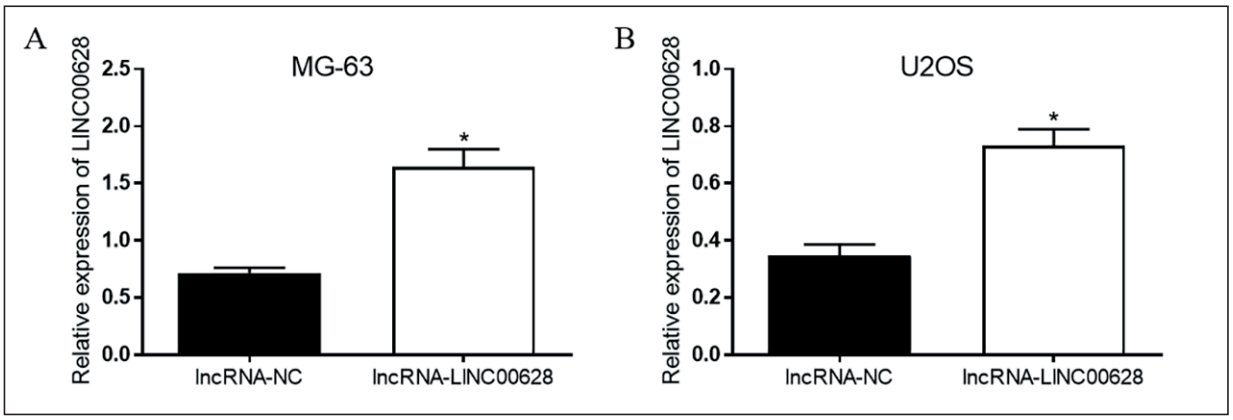

Figure 3. LINC00628 expression was increased in osteosarcoma cell lines after transfection with lncRNA-LINC00628. ***(A)*** The relative mRNA expression level of LINC00628 in MG-63 cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by qRT-PCR. ***(B)*** The relative mRNA expression level of LINC00628 in U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by qRT-PCR. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with lncRNA- NC group).

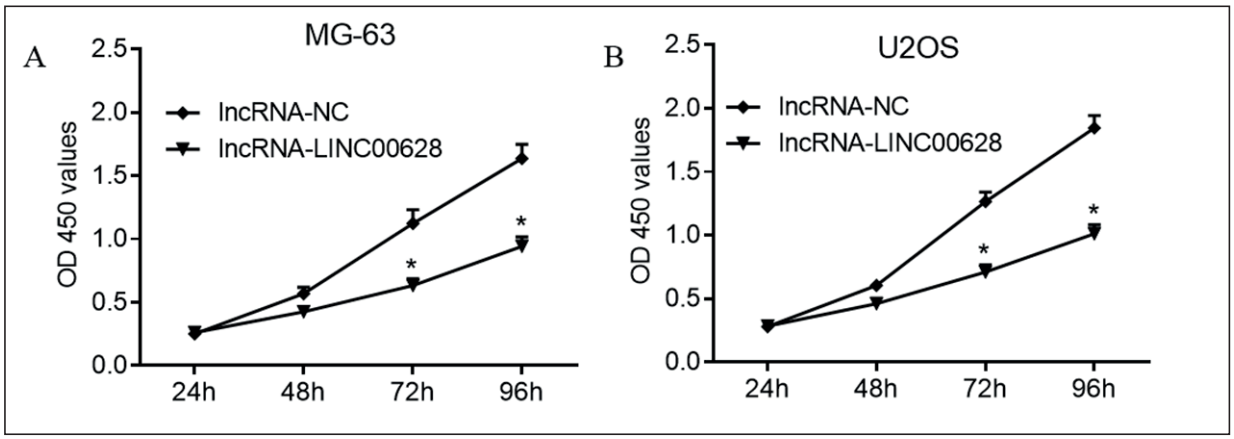

Figure 4. The cell proliferation in osteosarcoma cells was inhibited after transfection with lncRNA-LINC00628. ***(A)*** The CCK8 assay was used to detect MG-63 cells proliferation rate after transfection with lncRNA- NC or lncRNA-LINC00628. ***(B)*** The CCK8 assay was used to detected U2OS cells proliferation rate after transfection with lncRNA- NC or lncRNA-LINC00628. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with lncRNA- NC group).

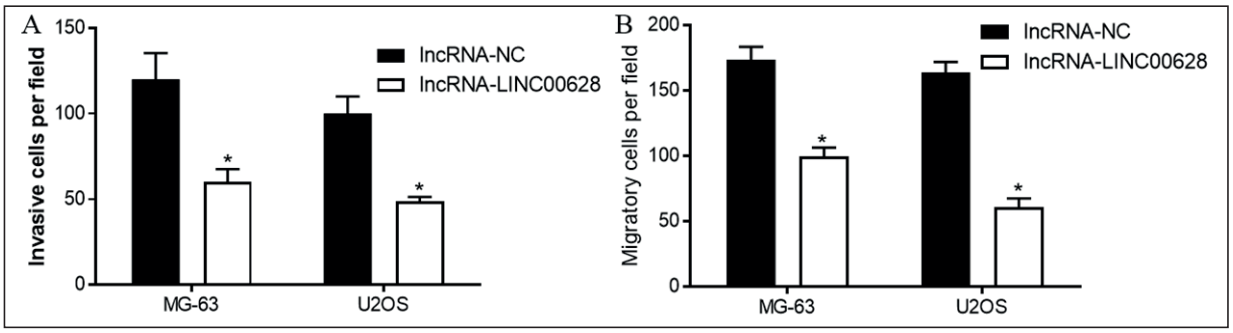

Figure 5. The cell invasion and migration in osteosarcoma cells were inhibited after transfection with lncRNA-LINC00628. ***(A)*** The invasion assay was used to detect the invasion activities of MG-63 and U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628. ***(B)*** The migration assay was used to detect the migration activities of MG-63 and U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628. All assays were performed in duplicates and data were Mean ± SD (*p < 0.05 compared with lncRNA- NC group).

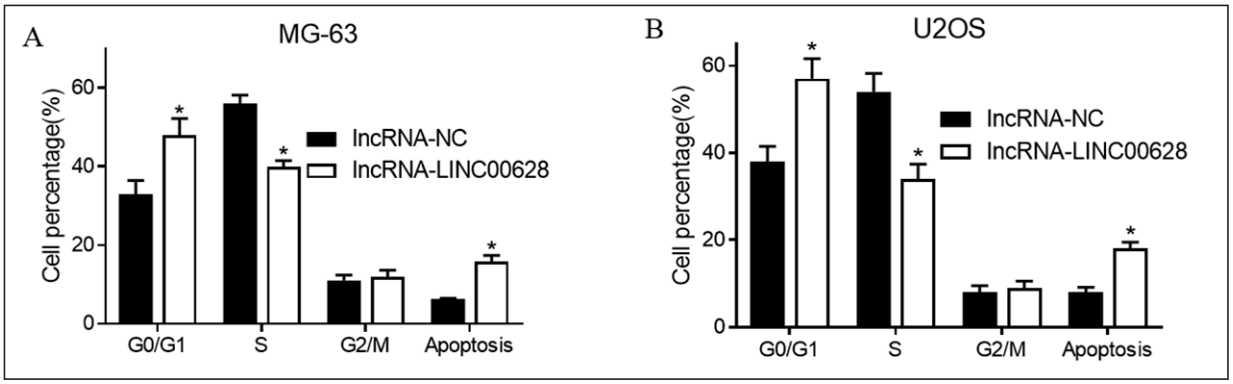

Figure 6. The cell cycle was arrested and the apoptosis rate was increased in osteosarcoma cells after transfection with lncRNA-LINC00628. ***(A)*** The cell cycle distribution and apoptosis rate in MG-63 cells after transfection with lncRNA- NC or lncRNA-LINC00628 were measured using the Flow cytometry analysis. ***(B)*** The cell cycle distribution and apoptosis rate in U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628 were measured using the Flow cytometry analysis. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with lncRNA- NC group).

cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by Western blot. Mechanistically, the relative protein expression level of p-PI3K, p-Akt and Bcl-2 were significantly increased and the relative expression of P53 was significantly decreased in osteosarcoma cells after transfection with lncRNA-LINC00628 (Figures 7A and 7B). It suggested that up-regulation of LINC00628 inhibited the proliferation, invasion and migration and promoted cell apoptosis in osteosarcoma cells through the inactivation of PI3K/Akt signaling pathway.

Discussion

The qRT-PCR validation results showed that LINC00628 was significantly decreased in osteosarcoma cell lines, HOS, MG-63, SOSP-9607 and U2OS, compared with the normal osteoblast cells, NHOst. LINC00628 expression was significantly decreased in osteosarcoma tissues compared with the paired adjacent normal tissues. In addition, the expression level of LINC00628 in osteosarcoma with lymph node metastasis was decreased compared with osteosarcoma without lymph node metastasis and the low expression level of LINC00628 has a lower overall survival rate. Statistical analyses revealed that down-regulated expression of LINC00628 was significantly correlated with tumor progression in osteosarcoma patients. Furthermore, up-regulated expression of LINC00628 suppressed cell proliferation, invasion and migration in MG-63 and U2OS cells. Moreover, osteosarcoma cell cycle was prominently shifted from S phase and G2/M phase to G0/G1 phase, cell percentage in G0/G1 phase was significantly increased and cell

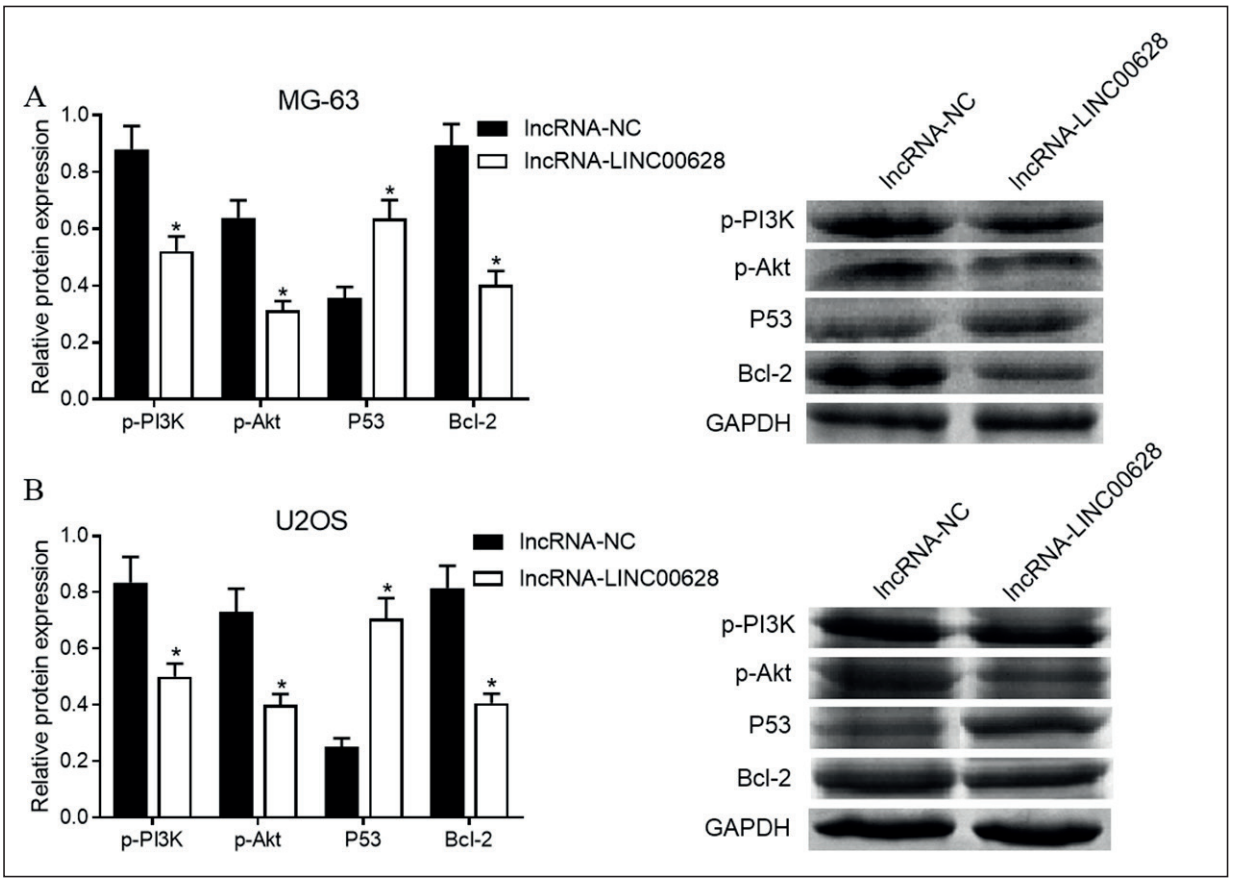

Figure 7. The activation of PI3K/Akt signaling pathway in osteosarcoma cells were inhibited after transfection with lncRNA-LINC00628. ***(A)*** The relative protein expression level of p-PI3K, p-Akt, P53 and Bcl-2 in MG-63 cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by Western blot. ***(B)*** The relative protein expression level of p-PI3K, p-Akt, P53 and Bcl-2 in U2OS cells after transfection with lncRNA- NC or lncRNA-LINC00628 were detected by Western blot. All assays were performed in duplicates and data were Mean ± SD (*$p < 0.05$ compared with lncRNA- NC group).

percentage in S phase was significantly decreased and promoted cell apoptosis after transfection with lncRNA-LINC00628, which showed up-regulation LINC00628 arrested cell cycle in G0/G1 phase to induce cell apoptosis. Mechanistically, the relative protein expression level of p-PI3K, p-Akt and Bcl-2 were significantly increased and the relative expression of P53 was significantly decreased in osteosarcoma cells after transfection with lncRNA-LINC00628. In summary, these data suggested that LINC00628 could be exploited for designing novel strategies against osteosarcoma metastasis and might serve as a tumor suppressor in osteosarcoma and provide novel target for the treatment in the future.

Recent investigations[17,18] have indicated that many lncRNAs have been shown to aberrantly express in human cancers. Accumulating evidence has showed is important for specific binding and meaningful secondary structures involved in multiple gene regulatory networks[19-21]. Scholars[22,23] have reported lncRNAs with biological functions associated with the proliferation, metastasis, invasion, migration and apoptosis in human cancer cells. In osteosarcoma, the functions and molecular mechanisms of many lncRNAs have not been well characterized. Therefore, the identification of osteosarcoma-associated lncRNAs and investigation of their molecular and biological functions are urgent. LncRNA LINC00628 is a newly discovered LncRNA and its role in human gastric cancer was shown in previous literature [16]. LINC00628 negatively regulated its neighboring gene LRRN2 expression, however, its inhibitory effects on gastric cancer progression mainly depended on regulating cell cycle related genes [16]. In our study, LINC00628 expression was significantly decreased in osteosarcoma tissues and cell lines. The low expression level of LINC00628 has a lower overall survival rate and up-regulation of LINC00628 inhibited cell proliferation, invasion and migration. The results indicated that LINC00628 can affect the growth and mobility in osteosarcoma.

PI3K/Akt signaling pathway plays important roles in the progression of osteosarcoma[24-26]. PI3K is activated by oncogenes, and activated PI3K promoted cancer cell growth and invasion [27]. Akt, a downstream effector of PI3K, is implicated in various cellular processes, including cell proliferation, cell invasion, metabolism and EMT [28]. It has been reported that the activation of Akt enhances the EMT, down-regulates E-cadherin transcription, and increases cancer cell migration and invasion[29]. PI3K/Akt signaling pathway activation is associated with higher invasive and migratory capacities in human osteosarcoma cells[30,31]. Thus, blocking this pathway may be a good way for the treatment of osteosarcoma. In our study, the cell cycle was arrested in G0/G1 phase and the apoptosis rate was increased in osteosarcoma cells after transfection with lncRNA-LINC00628. Mechanistically, the relative protein expression level of p-PI3K, p-Akt and Bcl-2 was significantly increased and the relative expression of P53 was significantly decreased in osteosarcoma cells after transfection with lncRNA-LINC00628. These data showed that the overexpression of LINC00628 inhibited the proliferation, invasion and migration and promoted cell apoptosis in osteosarcoma cells through the inactivation of PI3K/Akt signaling pathway and PI3K/Akt pathway is involved in osteosarcoma cells death.

Conclusions

We demostrated that LINC00628 expression was decreased in osteosarcoma. The overexpression of LINC00628 inhibited the proliferation, invasion and migration and promoted cell apoptosis in osteosarcoma cells through the inactivation of PI3K/Akt signaling pathway. The study indicated that LINC00628 may be a biomarker for the prognosis of osteosarcoma patients.

Acknowledgements

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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