ORIGINAL ARTICLE

Annals of Agricultural and Environmental Medicine
www.aaem.pl

Role of lncRNA SNHG7 in osteogenic differentiation of bone marrow mesenchymal stem cells

Wei Wang[1,A,C-F], **Jing Liu**[2,A,E-F], **Yanning Luo**[2,A-B,F] ✉

[1] *Department of Hand and Foot Microsurgery, Lianshui County People's Hospital, China*
[2] *Department of Hand and Foot Microsurgery, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, China*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Wei Wang, Jing Liu, Yanning Luo. Role of lncRNA SNHG7 in osteogenic differentiation of bone marrow mesenchymal stem cells. Ann Agric Environ Med. doi:10.26444/aaem/218949

Abstract

Introduction and Objective. Bone marrow mesenchymal stem cells (BMSCs), as an ideal cell source for bone regeneration, are crucial in the osteogenic differentiation. The aim of the article is to explore the effects of lncRNA SNHG7 on osteogenic differentiation and its regulation of miR-214-5p.

Materials and Method. Alkaline phosphatase (ALP), osterix, runt-related transcription factor 2 (RUNX2), and osteocalcin (OCN) were measured to assay the regulating function of lncRNA SNHG7 in osteogenic differentiation in human BMSCs (HBMCs). Late osteogenic markers were assayed by a quantitative real-time polymerase chain reaction (qRT-PCR) and an ALP Activity Assay Kit. The dual-luciferase reporter assay was used to identify the binding relationship between lncRNA SNHG7 and miR-214-5p, or miR-214-5p and BMP2.

Results. LncRNA SNHG7 was upregulated in osteogenic differentiation of HBMSCs and was time-dependent. Overexpression of lncRNA SNHG7 increased the level of ALP, RUNX2, osterix, and OCN. LncRNA SNHG7 targeted and negatively regulated miR-214-5p. When lncRNA SNHG7 was inhibited, miR-214-5p was upregulated. The downregulation of osteogenic markers (OCN, osterix, and RUNX2) caused by suppressing lncRNA SNHG7 was reversed by transfecting the miR-214-5p inhibitor. Additionally, the BMP2 was reduced by overexpressing lncRNA SNHG7, and the regulating effects of lncRNA SNHG7 on BMP2 were reversed by overexpressing miR-214-5p.

Conclusions. LncRNA SNHG7 could increase the level of BMP2 via downregulating miR-214-5p to promote osteogenic differentiation in HBMSCs. LncRNA SNHG7 may be a promoting factor of the osteogenic differentiation of HBMSCs after being upregulated.

Key words

BMP2, osteogenic differentiation, miR-214-5p, LncRNA SNHG7, human bone marrow mesenchymal stem cells

INTRODUCTION

Due to their osteogenic differentiation capacity and immunomodulatory properties, BMSCs have been widely investigated as a potential cell-based therapy for bone defects and diseases characterized by bone loss, such as osteoporosis [1]. The BMSCs are an ideal cell source for bone regeneration [2]. BMSCs with a significant function for multi-differentiation are reported to treat skeletal diseases and traumas. It has been reported that the reduction of osteogenic differentiation capacity of BMSCs can promote the occurrence of osteomyelitis with bone defects [3], and the differentiation of BMSCs can facilitate the correction of bone imbalance and alleviate osteoporosis. The differentiation of BMSCs is essential to the complication of lumbar spinal fusion with autogenous bone graft [4]. The osteogenic differentiation in BMSCs has extensive applications in the repair of defects in the oral maxillofacial bone, which is widely considered [5]. With the clinical application in BMSCs, the study of the osteogenic differentiation in BMSCs is paramount for treating disease [6].

The osteogenic differentiation in BMSCs is regulated by multiple signalling pathways, which is considered a complex process [7]. The noncoding RNAs (ncRNAs) could regulate the osteogenic differentiation in BMSCs. Additionally, long non-coding RNAs (lncRNAs) are widely considered to participate in osteogenic differentiation in BMSCs [8]. Recently, lncRNA HOTAIRM1 has been identified as a regulator for the osteogenic differentiation, and negatively regulates miR-152-3p [9]. The study of lncRNAs in promoting osteogenic differentiation is promising and has potential for clinical treatment. MiRNAs are also widely considered to participate in the BMSCs differentiation, and influence mRNA degradation and mRNA translation. Many miRNAs were identified to play an important role in bone regeneration. MiR-214-5p regulated osteoclast formation to affect OVX-induced bone resorption in mice [10].

Recently, lncRNA SNHG7 has been reported to promote the differentiation of human dental pulp stem cells (hDPSCs) [11]. The hDPSCs and human BMSCs (hBMSCs) both have strong abilities to become bone-forming cells. They play important roles in repairing bone tissue and maintaining spine health [12]. Despite the function of lncRNA SNHG7

✉ Address for correspondence: Yanning Luo, Department of Hand and Foot Microsurgery, Huangshi Central Hospital, Affiliated Hospital of Hubei Polytechnic University, China
E-mail: luoyanninglyn@163.com

Received: 22.01.2026; accepted: 06.03.2026; first published: 01.04.2026

having been reported in hDPSCs, its regulated function has not been clarified in the osteogenic differentiation of hBMSCs. Therefore, an investigation of the regulated function of lncRNA SNHG7 in hBMSCs for osteogenic differentiation was undertaken.

MATERIALS AND METHOD

Cell culture and treatment. hBMSCs was purchased from the American Type Culture Collection (ATCC, USA; Catalog No. PCS-500-012). These cells were isolated from healthy human bone marrow and were used at passages 3-6 for all experiments. And the cells were cultured in mesenchymal stem cell growth medium 2 (Merck KGaA, Shanghai, China), which was supplemented with 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin under the conditions with 5% CO_2 at 37 °C.

Osteogenic medium was used for the osteogenic differentiation of hBMSCs. The medium included 10 mM β-glycerol, phosphate, 50 μg/mL ascorbic acid, and 100 mM dexamethasone (Beyotime, Shanghai, China). The cells were cultured in the medium for 7, 14, and 21 days for assaying expression level, and for 7 days to evaluate the cell function. Fresh medium was replaced for the cells every day.

Transfection of cells. The shRNA targeting lncRNA SNHG7, miR-214-5p mimics, miR-214-5p inhibitor, and negative control were obtained by Ribobio (Guangzhou, China). The overexpression plasmids (oe-SNHG7) were constructed by sequence of human lncRNA SNHG7 into the pcDNA3.1 vector (Ribobio, Guangzhou, China). For cell transfection, hBMSCs were seeded into 24-well plates at a density of 4×10^4 cells per well, and cultured overnight to reach approximately 70–80% confluence. For each well, 1 μg of plasmid DNA (shRNA or overexpression plasmid) or 50 nM of oligonucleotides (mimics or inhibitor) was diluted in Opti-MEM medium and mixed with Lipo6000 transfection reagent (Beyotime, Shanghai, China), according to the manufacturer's instructions. The transfection complexes were added to the cells and incubated for 48 h in growth medium. Following transfection, the medium was replaced with osteogenic medium to induce differentiation. Transfection efficiency was validated by quantitative reverse transcription polymerase chain reaction (qRT-PCR).

Alkaline phosphatase (ALP) activity assay. For the detection of ALP activity the Alkaline Phosphatase Assay Kit (Beyotime, Shanghai, China) was used. Briefly, the induced hBMSCs were washed twice with ice-cold phosphate-buffered saline (PBS) and then lysed in cell lysis buffer (Cell Signaling Technology, USA) without phosphatase inhibitors. The lysates were collected by scraping, sonicated on ice, and centrifuged at 12,000 × g for 10 min at 4 °C to remove debris. The supernatant was collected for subsequent analysis. Induced cells were lysed with cell lysis buffer without inhibitors and added the chromogenic substrate solution to the cell lysate and incubated for 30 min at 37 °C. For the ALP activity measurement, 50 μL of each cell lysate supernatant was mixed with 50 μL of chromogenic substrate solution (p-nitrophenyl phosphate) in a 96-well plate and incubated at 37 °C for 30 min in the dark. To generate a calibration curve, 98 μL ALP Assay Buffer was added to 2 μL 4-MU (50mM), mixed well, and prepared into 100 μL of a 1 mM concentration 4-MU standard solution. 1 mM 4-MU standard solutions of 0, 0.2, 0.5, 1, 2, 5, 10, and 20 μL were added to the standard wells of a 96 well plate, and supplemented to 20 μL with ALP Assay Buffer. Absorbance at the excitation wavelength of 360 nm and the emission wavelength of 450 nm was immediate?. The final data was expressed as fold changes to the control group.

qRT-PCR. After collecting the total RNA by using the RNeasy Mini Kit (Beyotime, Shanghai, China), the RNA was transcribed into cDNA through the BeyoRT II First Strand cDNA Synthesis Kit (Beyotime, Shanghai, China). Then, BeyoFast SYBR Green One-Step qRT-PCR Kit (Beyotime, Shanghai, China) on an ABI7500 system was used to perform qRT-PCR amplification reaction. Supplementary Table 1 lists all primers.

Bioinformatics analysis. The StarBase database (https://rnasysu.com/encori/) was used to predict the binding site between lncRNA SNHG7 and miR-214-5p.

Dual-luciferase reporter assay. The wild-type (wt) or mutated-type (mut) sequences of lncRNA SNHG7 (5'-AGUGCUGUUUACAG CUGUCCGU-3') or BMP2 (5'-GGUUCCUAAGGAHHACG UGUCCGUC-3'), which contained the binding sites of miR-214-5p or not, were constructed. The sequence was then cloned into the dual-luciferase reporter vector pmirGLO to construct wt-SNHG7/BMP2 and mut-SNHG7/BMP2. The hBMSCs were cultured in the 24-well plates, and transfected the constructed wt-SNHG7/BMP2, mut-SNHG7/BMP2, and miR-214-5p mimic/mimic NC into the cells using the lipo6000 transfection reagent at 25 °C for 48 h. Finally, the luciferase activity was assayed by the Dual Luciferase Reporter Gene Assay Kit (Beyotime, Shanghai, China).

RNA pulldown assay. For the RNA pulldown assay, 3′-biotinylated miR-214-5p (Bio-miR-214-5p) or a 3′-biotinylated negative control miRNA (Bio-NC) was transfected into cultured hBMSCs. After a transfection period of 48 h, cells were harvested and lysed. The cell lysate was then incubated with streptavidin-coated agarose beads to capture biotin-tagged miRNAs and their associated RNA-binding partners. Following incubation, the bead complexes were isolated through centrifugation and subjected to stringent washing steps to remove non-specifically bound materials. Finally, RNA was purified from the pulldown material, and the specific enrichment of SNHG7 was quantitatively measured using qRT-PCR assay.

Statistical analysis. All statistical analyses were obtained using GraphPad 9.0 software. One-way ANOVA followed by Tukey's *post hoc* test, and two-way ANOVA with Bonferroni *post hoc* test were employed for comparisons among multiple groups. Each cell experiment was repeated 3 times, and the data shown as mean ± standard deviation (SD). Additionally, error bars depicted SD, and the P-value<0.05 was considered significant.

RESULTS

Upregulation of lncRNA SNHG7 in osteogenic differentiation of HDFs. RUNX2, osterix, and OCN [13] are considered as the osteoblast-associated factors, which present the osteogenic differentiation in hBMSCs to a certain extent. In this the expressions of RUNX2, osterix, and OCN in hBMSCs induced by osteogenic differentiation were assayed. The results showed that the expression of these genes increased over time as osteogenesis progressed (Fig. 1A-C). The expression of SNHG7 was upregulated in osteogenic differentiation, and was also time-dependent (1.9-fold at 7 days, 2.5-fold at 14 days, and 2.9-fold at 21 days increase, compared to control hBMSCs at 0 day) (Fig. 1D). It was therefore speculated that SNHG7 also has the potential to promote osteogenic differentiation.

Upregulation of lncRNA SNHG7 promoted osteogenic differentiation in hBMSCs. To identify the speculation and clarify the cell function of lncRNA SNHG7 in osteogenic differentiation, an attempt was made to inhibit or overexpress lncRNA SNHG7. After transfecting sh-SNHG7 plasmids in hBMSCs, the expression of lncRNA SNHG7 was significantly downregulated when compared with sh-NC (Fig. 2A). The oe-SNHG7 vector was used to transfect hBMSCs, which led to upregulation of lncRNA SNHG7 (7.8-fold increase compared to vector) (Fig. 2B). ALP, osterix, and RUNX2 were the early osteogenic markers and OCN the late osteogenic marker. After inhibiting lncRNA SNHG7, the activity of ALP became weakened, but the opposite function was performed by overexpressing lncRNA SNHG7 (Fig. 2C). The expression of RUNX2, OCN, and osterix were assayed. Results showed that the expressions of RUNX2, OCN, and osterix were reduced after inhibiting lncRNA SNHG7 compared with sh-NC (Fig. 2D-F). Moreover, overexpression of lncRNA SNHG7 increased the levels of RUNX2, OCN, and osterix (Fig. 2D-F). In brief, the upregulation of lncRNA SNHG7 promoted osteogenic differentiation in hBMSCs.

LncRNA SNHG7 targeted miR-214-5p. Recently, lncRNAs were identified as being essential in bone regeneration and bone tissue engineering by miRNAs [14]. StarBase v2.0 was used to predict that miR-214-5p was the target of lncRNA SNHG7. The binding sites are shown in Figure 3A.

The expression of miR-214-5p decreased over time, as osteogenesis progressed (Fig. 3B). Firstly, the transfection

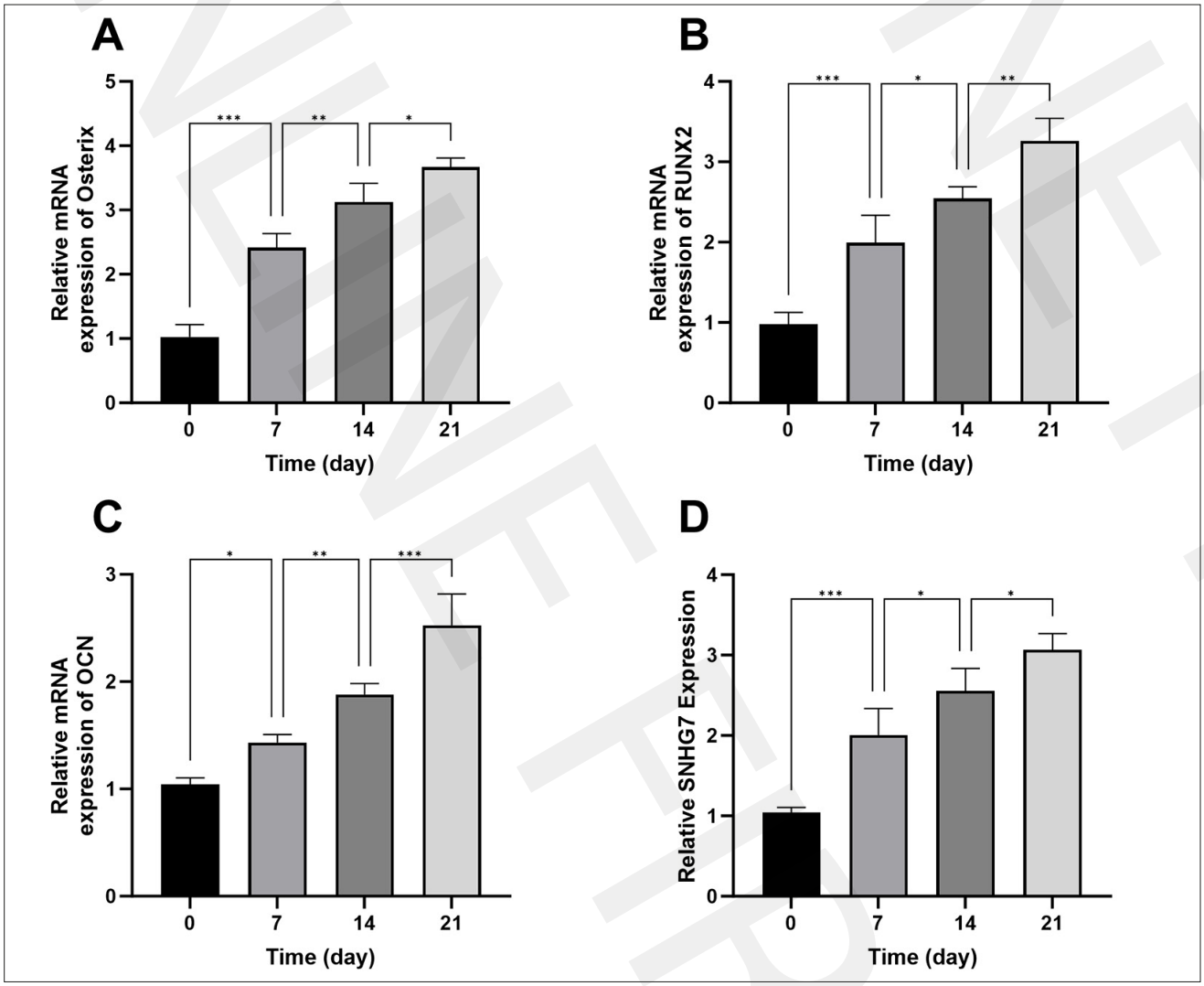

Figure 1. Upregulation of lncRNA SNHG7 during osteogenic differentiation. (A) Relative mRNA of osterix. (B) Relative mRNA of RUNX2. (C) Relative mRNA of OCN. (D) lncRNA SNHG7 time-dependently increased in osteogenic differentiation.
*P< 0.05; **P< 0.01; ***P< 0.001; tested by one-way ANOVA with Tukey's test for multiple comparisons in grouped analyses

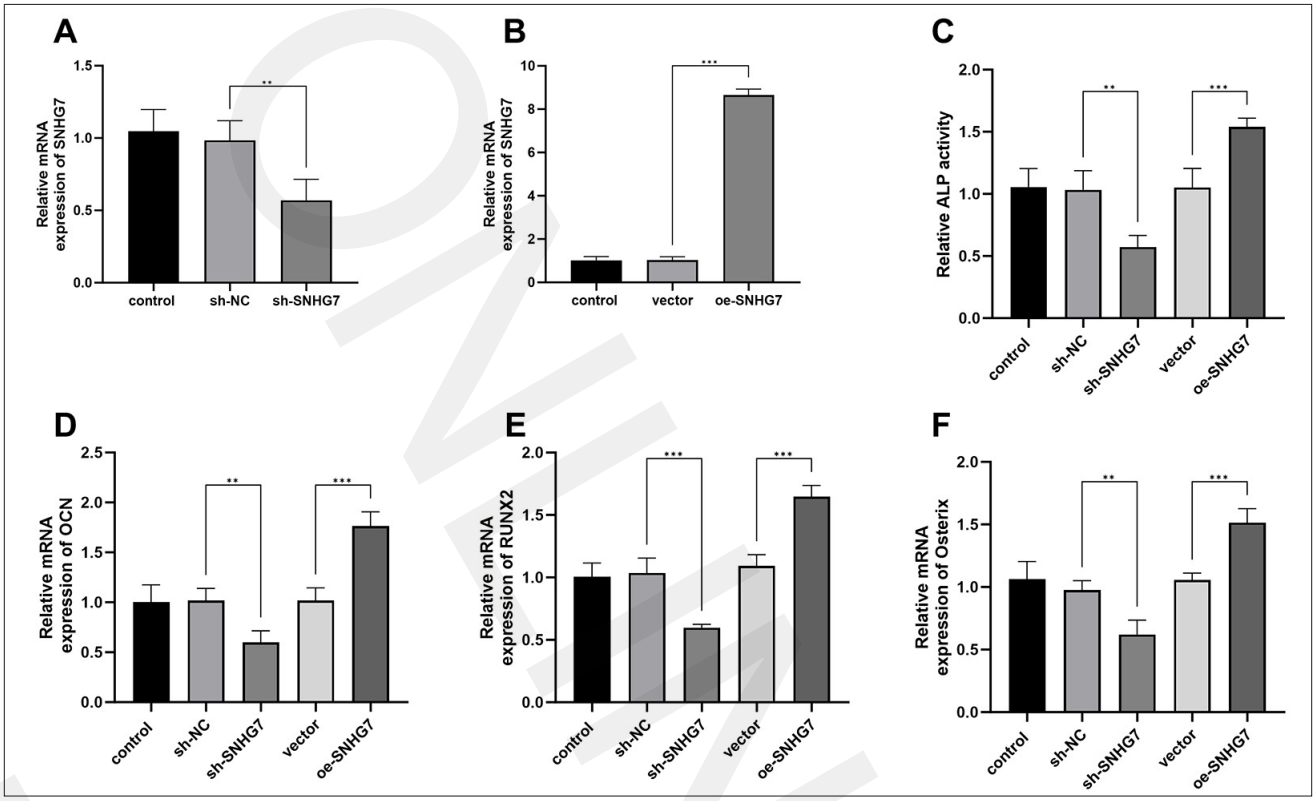

Figure 2. Regulated function of lncRNA SNHG7 for osteogenic differentiation. (A) Relative expression of lncRNA SNHG7 after inhibiting lncRNA SNHG7. (B) Relative expression of lncRNA SNHG7 after overexpressing lncRNA SNHG7. (C) Activity of ALP after inhibiting or overexpressing lncRNA SNHG7. (D) Relative mRNA levels of OCN after inhibiting or overexpressing lncRNA SNHG7. (E) Relative mRNA levels of RUNX2 after inhibiting or overexpressing lncRNA SNHG7. (F) Relative mRNA levels of Osterix after inhibiting or overexpressing lncRNA SNHG7.
**P< 0.01; ***P< 0.001; tested by one-way ANOVA with Tukey's test for multiple comparisons in grouped analyses

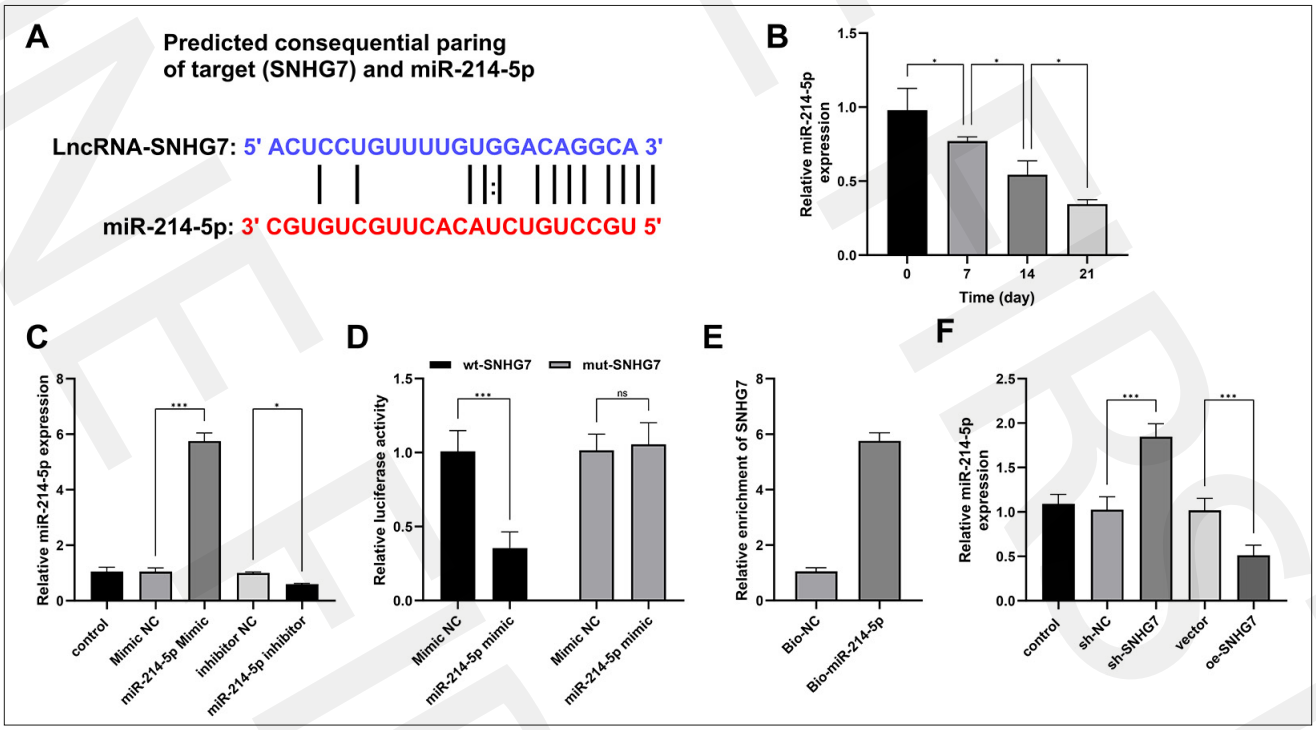

Figure 3. LncRNA SNHG7 targeted miR-214-5p. (A) StarBase prediction of the shared binding sites between lncRNA SNHG7 and miR-214-5p. (B) MiR-214-5p decreased time-dependently in osteogenic differentiation. Significance was tested by one-way ANOVA with Tukey's test. (C) Expression of miR-214-5p after transfection with mimic or inhibitor. Significance tested by one-way ANOVA with Tukey's test. (D) Results of a dual-luciferase reporter assay about lncRNA SNHG7 targeting miR-214-5p. Significance was tested by two-way ANOVA with Bonferroni's *post-hoc* test. (E) Expression of SNHG7 using qRT-PCR in hBMSCs samples pulled down by biotinylated miR-214-5p or negative control (NC). Significance tested by t test. (F) Expression of miR-214-5p after inhibiting or overexpressing SNHG7. Significance tested by one-way ANOVA with Tukey's test.
ns – no significance; *P< 0.05; ***P< 0.001

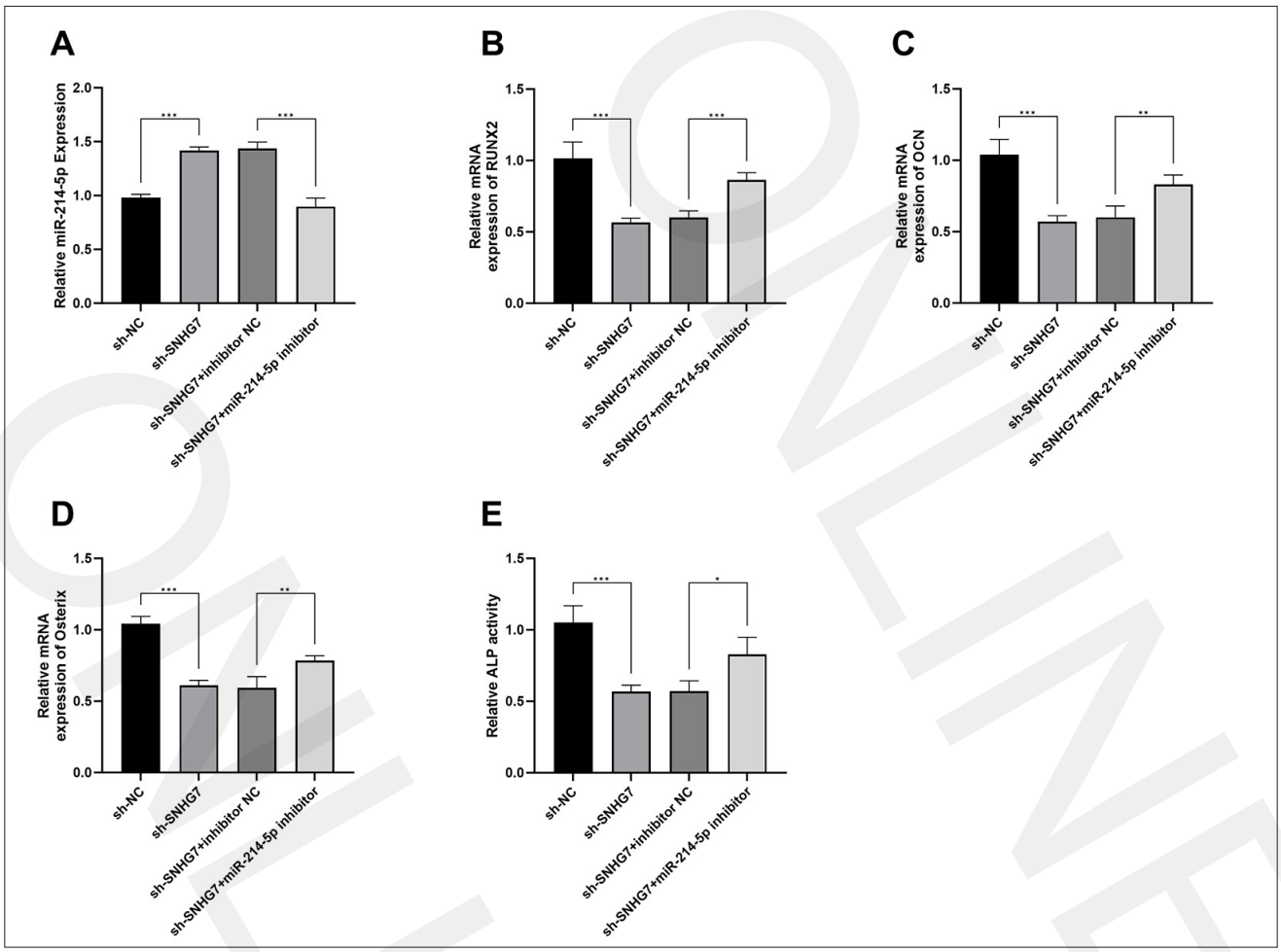

Figure 4. LncRNA SNHG7 downregulates miR-214-5p in osteogenic differentiation. (A) Co-transfected efficiency of sh-SNHG7 and miR-214-5p inhibitor. (B) Inhibiting miR-214-5p reversed the expression level of RUNX2 by inhibiting lncRNA SNHG7. (C) Inhibiting miR-214-5p reversed the expression level of OCN by inhibiting lncRNA SNHG7. (D) Inhibiting miR-214-5p reversed the expression level of Osterix by inhibiting lncRNA SNHG7. (E) Inhibiting miR-214-5p reversed the function by inhibiting lncRNA SNHG7 in the expression of ALP activity.
*P< 0.05; **P< 0.05; ***P< 0.001; tested by one-way ANOVA with Tukey's test for multiple comparisons in grouped analyses

efficiency of the mimics/inhibitors of miR-214-5p was verified, and the expression of miR-214-5p was upregulated after transfecting the mimics, but inhibitors decreased the expression of miR-214-5p (Fig. 3C). Next, the binding relationship of lncRNA SNHG7 and miR-214-5p was identified by a dual-luciferase reporter assay. Luciferase activity decreased in hBMSCs with co-transfection of miR-214-5p mimic and wt-SNHG7, but there was no significant difference in luciferase activity in hBMSCs co-transfected with miR-214-5p mimic and mut-SNHG7 (Fig. 3D). Pull-down assay further verified that SNHG7 directly bound to miR-214-5p because a significant amount of SNHG7 was measured in miR-214-5p-biotinylated hBMSCs (Fig. 3E). The expression of miR-214-5p increased after inhibiting SNHG7 (Fig. 3F). However, when SNHG7 we overexpressed, the expression of miR-214-5p decreased (Fig. 3F).

LncRNA SNHG7 downregulated miR-214-5p to osteogenic differentiation in hBMSCs. In a previous study, miR-214 participated in osteogenic differentiation which was mentioned [25]. The current study further explored the mechanism of miR-214-5p in osteogenic differentiation. Firstly, the co-transfected efficiency of sh-SNHG7 and miR-214-5p was verified (Fig. 4A). Then, the effect of lncRNA SNHG7 on the negative regulation of miR-214-5p for osteogenic differentiation in hBMSCs was explored. After inhibiting lncRNA SNHG7, the expression of osteogenic

Supplementary Table 1. Sequences of primers for qRT-PCR sequence

Primers for qRT-PCR	Sequences (5′-3′)
lncRNA SNHG7 (Forward)	AAATGTCAGCAGTGCCAGTG
lncRNA SNHG7 (Reverse)	GATGGGGTTTCAGGCAGTTG
GAPDH (Forward)	GTCTCCTCTGACTTCAACAGCG
GAPDH (Reverse)	ACCACCCTGTTGCTGTAGCCAA
miR-214–5p (Forward)	TGCCTGTCTACACTTGCTGTGC
miR-214–5p (Reverse)	GGTGCAGGGTCCG AGGTAT
U6 (Forward)	CTCGCTTCGGCAGCACA
U6 (Reverse)	AACGCTTCACGAATTTGCGT
Osterix (Forward)	GCAGCTAGAAGGGAGTGGTG
Osterix (Reverse)	AAGCCTTGCCATACACCTTG
RUNX2 (Forward)	GGTACCAGATGGGACTGTGG
RUNX2 (Reverse)	TCGTTGAACCTTGCTACTTGG
OCN (Forward)	ATGAGAGCCCTCACACTCCT
OCN (Reverse)	CAAGGGGAAGAGGAAAGAAG
BMP2 (Forward)	TGCAGGAAAGTGAATGATGG
BMP2 (Reverse)	TGATGAGGGCCACGAGATA

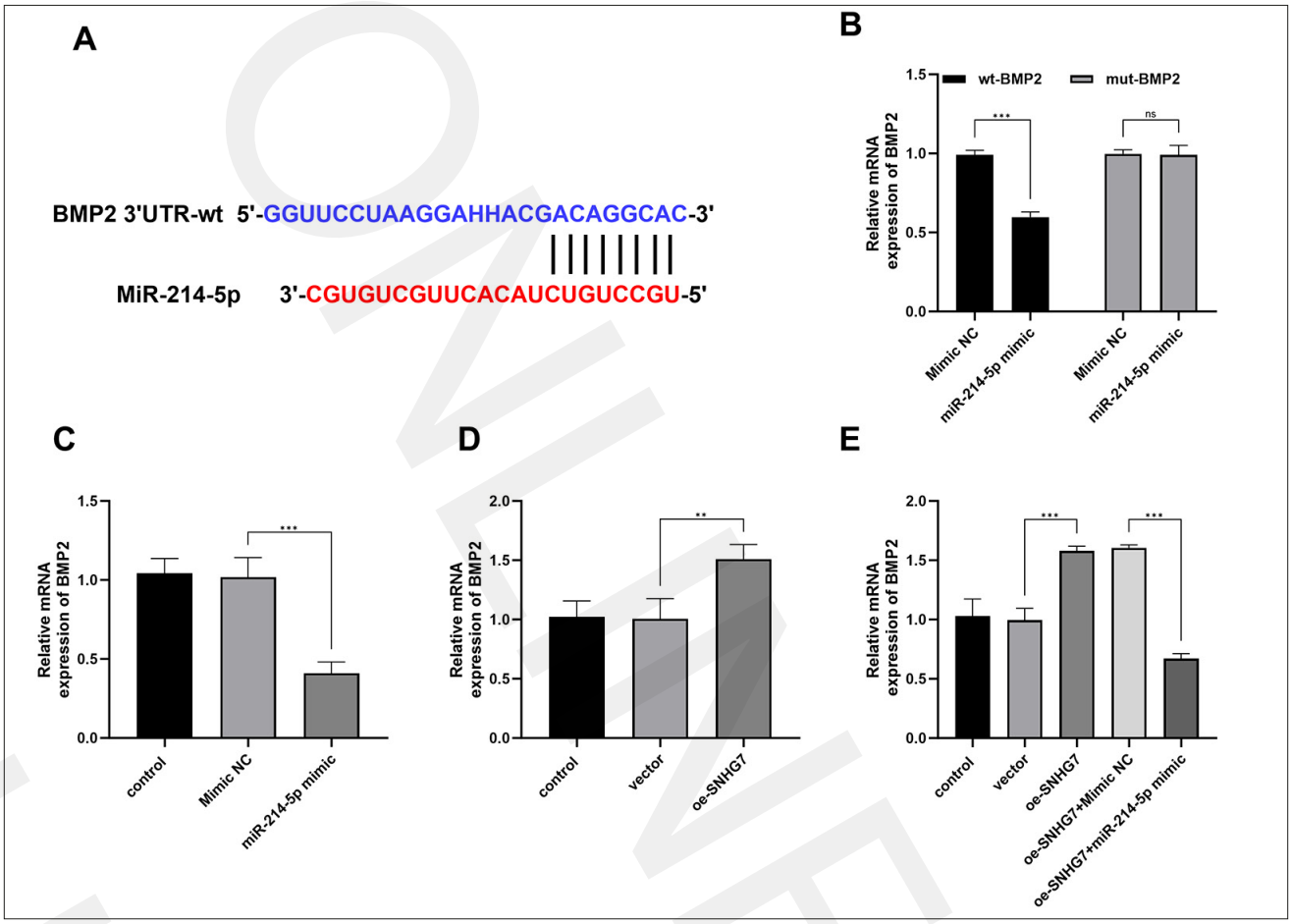

Figure 5. LncRNA SNHG7 upregulated BMP2 by inhibiting miR-214-5p. (A) Binding site of miR-214-5p and BMP2. (B) Luciferase activity assay. Significance was tested by two-way ANOVA with Bonferroni's *post-hoc* test. (C) Relative mRNA of BMP2 decreased after overexpressing miR-214-5p. Significance tested by one-way ANOVA with Tukey's test. (D) Relative mRNA of BMP2 increased after overexpressing lncRNA SNHG7. Significance tested by one-way ANOVA with Tukey's test. (E) Overexpressing miR-214-5p reversed the effects of lncRNA SNHG7 overexpression on BMP2. Significance was tested by one-way ANOVA with Tukey's test.
ns – no significance; $^{**}P < 0.01$, $^{***}P < 0.001$

markers (OCN, osterix, and RUNX2) decreased significantly. Interestingly, the function of inhibiting lncRNA SNHG7 was reversed after inhibiting miR-214-5p (Fig. 4B-D). Additionally, the reduced activity of ALP due to inhibiting lncRNA SNHG7 was alleviated by inhibiting miR-214-5p (Fig. 4E).

LncRNA SNHG7 regulated BMP2 via miR-214-5p. BMP2 participates in postnatal skeletal homeostasis and provides the osteogenic signal that is required for the reparative ability of bone [15]. It has been reported that miR-214-5p negatively regulates BMP2 [16]. This study attempted to investigate the regulated function of lncRNA SNHG7 on BMP2 via miR-214-5p in hBMSCs. Firstly, the binding site of BMP2 and miR-214-5p was shown (Fig. 5A). Luciferase activity decreased in hBMSCs after co-transfecting miR-214-5p mimic and wt-BMP2, but no significant difference was observed in hBMSCs co-transfected with miR-214-5p mimic and mut-BMP2 (Fig. 5B). The level of BMP2 was reduced by overexpressing miR-214-5p compared with mimic negative control (Fig. 5C). Additionally, to investigate the regulated mechanism between lncRNA SNHG7 and BMP2, overexpressing lncRNA SNHG7 upregulated the level of BMP2 by 1.5-fold (Fig. 5D). Interestingly, overexpressing miR-214-5p could reverse the increase of BMP2 caused by overexpressing lncRNA SNHG7 (Fig. 5E).

DISCUSSION

The differentiation of BMSCs, which are precursor stem cells of osteoblasts and adipocytes, plays an essential role in bone balance [17]. Non-coding RNAs were considered to be key regulators in bone formation based on the verified regulation of noncoding RNAs in the differentiation and function of osteoblasts. Recently, many lncRNAs have obtained gained more attention in the osteogenic differentiation process of BMSCs, such as lncH19, LINC00707, lncRNA DANCR, and lncRNA HOX [7]. LncRNA SNHG7 has been identified to participate in the osteogenic differentiation of hDPSCs [11]. Both the hDPSCs and hBMSCs have a strong ability to become bone-forming cells, and play important roles in repairing bone tissue and maintaining spine health. In this study, it was also found that lncRNA SNHG7 increased with osteogenic-induced time for osteogenic differentiation in hBMSCs, and inhibiting lncRNA SNHG7, decreased the level of RUNX2, osterix, and OCN. Runx2 is crucial for chondrocyte maturation and drives multipotent mesenchymal cells to become osteoblasts [18]. Osterix, as a potential osteogenic key marker, plays an important regulatory role in the stimulation of osteoblast differentiation [19]. OCN is also essential for maintaining muscle health, improving exercise performance, and aiding tissue repair. These results show that lncRNA SNHG7 may prevent osteoblast differentiation and bone tissue repair.

MiRNAs are known regulators of cell functions, and the functions of osteoblasts and osteoclasts are affected via aberrant expression of relevant miRNAs [20]. Several miRNAs have been identified that were significant in osteoblast differentiation. The expression of miR-2861 is enhanced by increasing histone deacetylase 5 (HDAC5)-mediated, which identified the significant function of miR-2861 in osteoblast differentiation [21]. MiRNA-15b decreased Smurf1 to protect the RUNX2 protein from proteasome degradation [22]. In the current study, starBase v2.0 was used to predict the targets of SNHG7, and further identified that miR-214-5p was targeted and negatively regulated by it, which was identified by luciferase activity assay. MiR-214-5p was identified as being downregulated and participating in osteogenic differentiation. Additionally, its upregulation could decrease the level of RUNX2, osterix, and OCN, indicating the risk function of miR-214-5p for osteoblast differentiation. It has also been reported that the in LOC100506178/miR-214-5p/BMP2 pathway regulates hBMSC differentiation into osteoblasts and promotes bone formation, in which miR-214-4p was downregulated. Additionally, the upregulation of miR-214-5p inhibited ALP activity and the expression of Runx2 and OCN, which are essential in osteogenic differentiation [23].

The level of BMP2 is widely considered to be important for the skeleton [21], and belongs to the transforming growth factor-beta superfamily. Recently, many studies have indicated the significance of BMP2 in promoting osteogenic differentiation and Smad pathway activity [24]. A number of studies identified that lncRNAs and miRNAs can regulate the expression of BMP2, and LncRNA MSC-AS1 could upregulate BMP2, which promoted osteogenic differentiation [25]. A negative regulation of BMP2 from miR-214-5p in osteogenic differentiation has also been reported [15]. Based on a previous study, in the presented study, experiments were conducted to explore the regulated mechanism and binding relationship of miR-214-5p and BMP2. Consistent with expectations, the same conclusion was obtained, that miR-214-5p can target and negatively regulate BMP2. Building upon this finding, the function of lncRNA SNHG7 in regulating BMP2 expression was investigated further, which resulted in the identification of the regulation of lncRNA SNHG7 for BMP2, which meant that overexpressing lncRNA SNHG7 led to an increase in BMP2 level. Additionally, it was found that the increase of BMP2 by overexpressing lncRNA SNHG7 was reversed by overexpressing miR-214-5p. Therefore, this demonstrated that lncRNA SNHG7 may regulate BMP2 by miR-214-5p to promote osteogenic differentiation in hBMSCs from the above results. While hBMSCs provided a relevant model, the *in vitro* system cannot fully recapitulate the complex *in vivo* microenvironment. Future validation using appropriate animal models of bone loss to confirm the physiological relevance of the SNHG7/miR-214-5p axis is needed.

CONCLUSION

The study demonstrated that as osteogenesis progressed, lncRNA SNHG7 increased over time. LncRNA SNHG7 could promote the formation of bone in hBMSCs. Mechanistically, lncRNA SNHG7 may increase the level of BMP2 by regulating miR-214-5p in hBMSCs.

REFERENCES

1. Bajada S, Mazakova I, Richardson JB, Ashammakhi N. Updates on stem cells and their applications in regenerative medicine. J Tissue Eng Regen Med. 2008;2(4):169–83. http://doi.org/10.1002/term.83
2. Matsushita Y, Ono W, Ono N. Bone regeneration via skeletal cell lineage plasticity: All hands mobilized for emergencies: Quiescent mature skeletal cells can be activated in response to injury and robustly participate in bone regeneration through cellular plasticity. Bioessays. 2021;43(1):e2000202. http://doi.org/10.1002/bies.202000202
3. Wen HJ, Zhu SY, Yang HG, Guo FY. Investigation on the molecular mechanism of SPA interference with osteogenic differentiation of bone marrow mesenchymal stem cells. Sci Rep. 2024;14(1):15600. http://doi.org/10.1038/s41598-024-66502-2
4. Liu B, Gan W, Jin Z, et al. The Role of miR-34c-5p in Osteogenic Differentiation of Bone Marrow Mesenchymal Stem Cells. Int J Stem Cells. 2021;14(3):286–97. http://doi.org/10.15283/ijsc20188
5. Zhou S, Zhang G, Wang K, et al. METTL3 potentiates osteogenic differentiation of bone marrow mesenchymal stem cells via IGF2BP1/m6A/RUNX2. Oral Dis. 2024;30(3):1313–21. http://doi.org/10.1111/odi.14526
6. Gerasymchuk M, Cherkasova V, Kovalchuk O, Kovalchuk I. The Role of microRNAs in Organismal and Skin Aging. Int J Mol Sci. 2020;21(15). http://doi.org/10.3390/ijms21155281
7. Chen X, Xie W, Zhang M, et al. The Emerging Role of Non-Coding RNAs in Osteogenic Differentiation of Human Bone Marrow Mesenchymal Stem Cells. Front Cell Dev Biol. 2022;10:903278. http://doi.org/10.3389/fcell.2022.903278
8. Sun X, Jia B, Qiu XL, et al. Potential functions of long non-coding RNAs in the osteogenic differentiation of human bone marrow mesenchymal stem cells. Mol Med Rep. 2019;19(1):103–14. http://doi.org/10.3892/mmr.2018.9674
9. Wang X, Liu Y, Lei P. LncRNA HOTAIRM1 promotes osteogenic differentiation of human bone marrow-derived mesenchymal stem cells by targeting miR-152-3p/ETS1 axis. Mol Biol Rep. 2023;50(7):5597–608. http://doi.org/10.1007/s11033-023-08466-6
10. Liu Y, Li Y, Zang J, et al. CircOGDH Is a Penumbra Biomarker and Therapeutic Target in Acute Ischemic Stroke. Circulation research. 2022;130(6):907–24. http://doi.org/10.1161/circresaha.121.319412
11. Chen W. SNHG7 promotes the osteo/dentinogenic differentiation ability of human dental pulp stem cells by interacting with hsa-miR-6512-3p in an inflammatory microenvironment. Biochem Biophys Res Commun. 2021;581:46–52. http://doi.org/10.1016/j.bbrc.2021.09.081
12. Liu B, Li J, Chen B, et al. Dental pulp stem cells induce anti-inflammatory phenotypic transformation of macrophages to enhance osteogenic potential via IL-6/GP130/STAT3 signaling. Ann Transl Med. 2023;11(2):90. http://doi.org/10.21037/atm-22-6390
13. Du Z, Zhao Y, Zhang K, et al. Undercarboxylated OCN Inhibits Chondrocyte Hypertrophy and Osteoarthritis Development through GPRC6A/HIF-1alpha Cascade. Int J Biol Sci. 2025;21(10):4353–73. http://doi.org/10.7150/ijbs.105560
14. Li Z, Jin C, Chen S, et al. Long non-coding RNA MEG3 inhibits adipogenesis and promotes osteogenesis of human adipose-derived mesenchymal stem cells via miR-140-5p. Mol Cell Biochem. 2017;433(1–2):51–60. http://doi.org/10.1007/s11010-017-3015-z
15. Li L, Fang J, Liu Y, Xiao L. LncRNA LOC100506178 promotes osteogenic differentiation via regulating miR-214-5p-BMP2 axis in human bone marrow mesenchymal stem cells. Peer J. 2020;8:e8909. http://doi.org/10.7717/peerj.8909
16. Salazar VS, Gamer LW, Rosen V. BMP signalling in skeletal development, disease and repair. Nat Rev Endocrinol. 2016;12(4):203–21. http://doi.org/10.1038/nrendo.2016.12
17. Chen Q, Shou P, Zheng C, et al. Fate decision of mesenchymal stem cells: adipocytes or osteoblasts? Cell Death Differ. 2016;23(7):1128–39. http://doi.org/10.1038/cdd.2015.168
18. Komori T. Regulation of Skeletal Development and Maintenance by Runx2 and Sp7. Int J Mol Sci. 2024;25(18). http://doi.org/10.3390/ijms251810102
19. Chen J, Liu D, Chen B, et al. The histone acetyltransferase Mof regulates Runx2 and Osterix for osteoblast differentiation. Cell Tissue Res. 2023;393(2):265–79. http://doi.org/10.1007/s00441-023-03791-5
20. Lombardi G, Delvin E. Micro-RNA: A Future Approach to Personalized Diagnosis of Bone Diseases. Calcif Tissue Int. 2023;112(2):271–87. http://doi.org/10.1007/s00223-022-00959-z
21. Li H, Xie H, Liu W, et al. A novel microRNA targeting HDAC5 regulates osteoblast differentiation in mice and contributes to primary

osteoporosis in humans. J Clin Invest. 2009;119(12):3666–77. http://doi.org/10.1172/JCI39832
22. Vimalraj S, Partridge NC, Selvamurugan N. A positive role of microRNA-15b on regulation of osteoblast differentiation. J Cell Physiol. 2014;229(9):1236–44. http://doi.org/10.1002/jcp.24557
23. Qiu J, Huang G, Na N, Chen L. MicroRNA-214-5p/TGF-beta/Smad2 signaling alters adipogenic differentiation of bone marrow stem cells in postmenopausal osteoporosis. Mol Med Rep. 2018;17(5):6301–10. http://doi.org/10.3892/mmr.2018.8713
24. Liu J, Chen M, Ma L, Dang X, Du G. piRNA-36741 regulates BMP2-mediated osteoblast differentiation via METTL3 controlled m6A modification. Aging (Albany NY). 2021;13(19):23361–75. http://doi.org/10.18632/aging.203630
25. Zhang N, Hu X, He S, et al. LncRNA MSC-AS1 promotes osteogenic differentiation and alleviates osteoporosis through sponging microRNA-140-5p to upregulate BMP2. Biochem Biophys Res Commun. 2019;519(4):790–6. http://doi.org/10.1016/j.bbrc.2019.09.058