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PRMT7 Regulates Adipogenic Differentiation of hBMSCs by Modulating IGF−1 Signaling*

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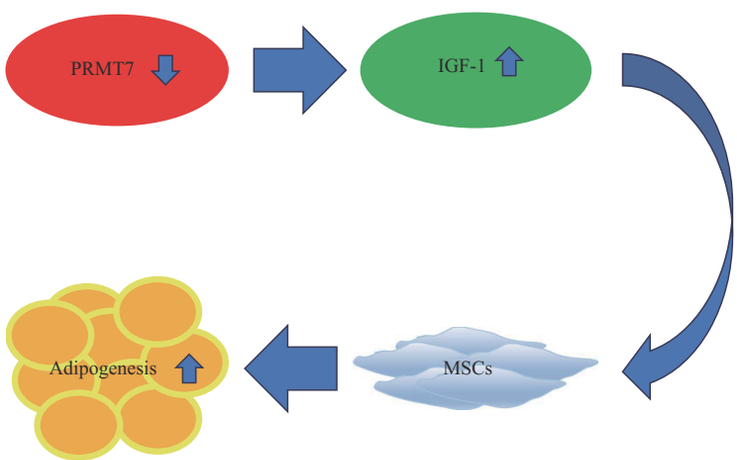
Graphical abstract



Abstract **Objective** Protein arginine methyltransferases (PRMTs) play pivotal roles in numerous cellular biological processes. However, the precise regulatory effects of PRMTs on the fate determination of mesenchymal stromal/stem cells (MSCs) remain elusive. Our previous studies have shed light on the regulatory role and molecular mechanism of PRMT5 in MSC osteogenic differentiation. This study aims to clarify the role and corresponding regulatory mechanism of PRMT7 during the adipogenic differentiation of bone marrow-derived mesenchymal stem cells (BMSCs). **Methods** (1) Human bone marrow-derived mesenchymal stem cells (hBMSCs) were cultured in a medium that induces adipogenesis. We used qRT-PCR and Western blot to monitor changes in PRMT7 expression during adipogenic differentiation. (2) We created a cell line with PRMT7 knocked down and assessed changes in PRMT7 expression and adipogenic capacity using Oil Red O staining, qRT-PCR and Western blot. (3) We implanted hBMSCs cell lines mixed with a collagen membrane subcutaneously into nude mice and performed Oil Red O staining to observe ectopic lipogenesis *in vivo*. (4) A cell line overexpressing PRMT7 was generated, and we examined changes in PRMT7 expression using qRT-PCR and Western blot. We also performed Oil Red O staining and quantitative analysis after inducing the cells in lipogenic medium. Additionally, we assessed changes in PPARγ expression. (5) We investigated changes in insulin-like growth factor 1 (IGF-1) expression in both PRMT7 knockdown and overexpressing cell lines using qRT-PCR and Western blot, to understand

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PRMT7’s regulatory effect on IGF-1 expression. siIGF-1 was transfected into the PRMT7 knockdown cell line to inhibit IGF-1 expression, and knockdown efficiency was confirmed. Then, we induced cells from the control and knockdown groups transfected with siIGF-1 in lipogenic medium and performed Oil Red O staining and quantitative analysis. Finally, we assessed PPARγ expression to explore IGF-1’s involvement in PRMT7’s regulation of adipogenic differentiation in hBMSCs. **Results** (1) During the adipogenesis process of hBMSCs, the expression level of PRMT7 was significantly reduced (P<0.01). (2) The adipogenic differentiation ability of PRMT7 knockdown group was significantly stronger than that of control group (P<0.001). (3) The ectopic adipogenic differentiation ability of PRMT7 knockdown group was significantly stronger than that of control group. (4) The adipogenic differentiation ability of the PRMT7 overexpression group was significantly weaker than that of the control group (P< 0.01). (5) The expression level of IGF-1 increased after PRMT7 knockdown (P<0.000 1). The expression level of IGF-1 decreased after PRMT7 overexpression (P<0.000 1), indicating that PRMT7 regulates the expression of IGF-1. After siIGF-1 transfection, the expression level of IGF-1 in all cell lines decreased significantly (P<0.001). The ability of adipogenic differentiation of knockdown group transfected with siIGF-1 was significantly reduced (P<0.01), indicating that IGF-1 affects the regulation of PRMT7 on adipogenic differentiation of hBMSCs. **Conclusion** In this investigation, our findings elucidate the inhibitory role of PRMT7 in the adipogenic differentiation of hBMSCs, as demonstrated through both *in vitro* cell-level experiments and *in vivo* subcutaneous transplantation experiments conducted in nude mice. Mechanistic exploration revealed that PRMT7’s regulatory effect on the adipogenic differentiation of hBMSCs operates *via* modulation of IGF-1 signaling pathway. These collective findings underscore PRMT7 as a potential therapeutic target for fatty metabolic disorders, thereby offering a novel avenue for leveraging PRMT7 and hBMSCs in the therapeutic landscape of relevant diseases.

Key words PRMT7, adipogenic differentiation, bone marrow mesenchymal stem cell, IGF-1 signal pathway
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The posttranslational modification of amino acid residues plays an important role in determining the protein structure and function[1]. One of the most important post-translational modification is arginine methylation, which is catalyzed by the protein arginine methyltransferase (PRMT) family[2]. Currently, nine members of the PRMT family have been identified and categorized into 3 groups based on their methylation products: Type I (PRMT1, 2, 3, 4, 6, and 8), Type II (PRMT5 and 9), and Type III (PRMT7). Both Type I and Type II generate monomethyl arginine (MMA) before catalyzing the formation of asymmetric dimethylarginine (aDMA) and symmetric dimethylarginine (sDMA), respectively, while PRMT7 mediates the formation of MMA on substrates[3]. The arginine methylation of histone and non-histone plays a major role in the regulation of various cellular activities, including adipogenesis, cancer, cellular stress, male reproduction and cellular senescence[4-6].

The substrates of PRMT7 include both histones and non-histones. In terms of epigenetic regulation, while H4R3 is the primary substrate for *Trypanosoma brucei* protein arginine methyltransferase 7 (*Tb*PRMT7)[7-8]. H4R17 and H4R19 are the preferred substrates for PRMT7 in mammals[9]. Interestingly, PRMT5 can catalyze H4R3 methylation, and this process is greatly facilitated by the PRMT7-catalyzed methylation of H4R17[10] . In addition, two cytoplasmic proteins, heat shock protein70 (HSP70)[11] and eukaryotic translation initiator factor 2α (eIF2α)[12], are characterized as PRMT7 substrates. In addition, PRMT7 regulates the methylation levels of Sm proteins, the latter being highly susceptible to methylation by PRMT5[13-16]. PRMT7 has been shown to be involved in the functioning of stem cells, including muscle stem cells and embryonic stem cells, although its association with MSCs has not been widely investigated.

Multiple signaling pathways modulate the function and lineage commitment of stem cells. insulin like growth factor 1 (IGF-1) signaling plays an important role in several developmental and physiological processes[17]. IGF-1 is a crucial factor involved in adipogenic differentiation[18-20]. The disruption of adenosine 5'-monophosphate-activated protein kinase (AMPK)-TBC1D1 linkage causes an increase in adipose gene expression and induces obesity through the promotion of IGF-1 secretion[21]. IGF-1 can effectively promote the adipogenesis of adipose stem cells. *In vivo* use of IGF-1 leads to the recruitment of endogenous cells and induction of

adipogenesis[22]. In the context of myocardial injury, insulin like growth factor 1 receptor (IGF-1R) signaling is a critical pathway for controlling the formation of adipose tissue by retargeting cell commitment in the Wilms tumor 1 (Wt1) +lineage cells[23]. In conclusion, IGF-1 plays an important role in the formation of adipose tissue.

In this study, we demonstrated that PRMT7 plays an important role in the adipogenic differentiation of MSCs, and found a previously undescribed role of PRMT7 in MSC adipogenic commitment through the modulation of IGF-1 signaling. Collectively, PRMT7 might be a molecular target for the treatment of metabolic diseases.

1 Materials and methods

1.1 Ethics approval

Animals were supplied by the Vital River Corporation (Beijing, China). All animal studies were approved by the Institutional Animal Care and Use Committee of the Peking University Health Science Center (LA2014233). All procedures of *in vivo* study on the animals were carried in accordance with the National Institutes of Health guide for the care and use of laboratory animals and ARRIVE guidelines and conformed to the provisions of the Declaration of Helsinki (as revised in Edinburgh 2000).

1.2 Culture and adipogenic induction of human bone marrow mesenchymal stromal/stem cells（hBMSCs）

All cell-based experiments utilized hBMSCs from 3 different donors. Primary hBMSCs were procured from ScienCell Research Laboratories (7500, San Diego, CA, USA). Cells were cultured at 37℃ in a humidified atmosphere of 95% air and 5% CO_2. The proliferation medium (PM) consisted of 1% penicillin/streptomycin (Invitrogen, Carlsbad, CA, USA), 10% fetal bovine serum (FBS; PAA Laboratories GmbH, Linz, Austria), and α-MEM (Invitrogen). The proliferation medium was supplemented with 200 μmol/L indomecin (Sigma-Aldrich), 10 μmol/L insulin (Sigma-Aldrich), 500 μmol/L 3-isobutyl-1-methylxanthine (Sigma-Aldrich), and 100 nmol/L dexamethasone (Sigma-Aldrich) to form a lipogenic induction medium. The medium was changed every two days.

1.3 Lentivirus infection

Lentiviruses were purchased from GenePharma (Shanghai, China) and included lentiviruses targeting PRMT7 (PRMT7sh-1, PRMT7sh-2) and negative control (NC); PRMT7-overexpressing lentivirus (PRMT7) and vector. The viral supernatant with multiplicity of infection (MOI) of 100 and polybrene (5 mg/L) were added to hBMSCs, and the medium was changed after 24 h of transfection. Puromycin (1 mg/L; Sigma-Aldrich, USA) was added at 72 h to screen for stably transfected cells. Non-targeting control shRNA (NC): TTCTCCGAACGTGTCACGT; PRMT7sh-1: GGATGTGGTCGTGGAACAAGC; PRMT7sh-2: GCTGCCCATGTTCAGCATAGA.

1.4 Oil Red O staining

hBMSCs were cultured in proliferation medium or lipogenic medium for 14 d, respectively, and subsequently stained with Oil Red O. The cells were washed 3 times with PBS and fixed in 10% formalin for 30 min. Thereafter, the cells were rinsed with 60% isopropanol and stained with 0.3% Oil Red O buffer. After successful staining was confirmed by microscopic observation, the cells were washed 3 times with distilled water and photographed. For quantitative assessment, the stained cells were eluted with 100% isopropanol and their spectrophotometric absorption was quantified at 520 nm against a blank (100% isopropanol).

1.5 RNA isolation and quantitative RT−PCR（qRT−PCR）

Total RNA was extracted from cells inoculated in 6-well plates using Trizol reagent (Invitrogen, Carlsbad, CA, USA). The synthesis of cDNA (complementary DNA) was performed using the PrimeScript RT Reagent Kit (Takara, Tokyo, Japan), according to the manufacturer's instructions. qRT-PCR reactions were performed using SYBR Green Master Mix (Roche Applied Science, Mannheim, Germany). The primers used for amplifying PRMT7, peroxisome proliferator-activated receptor γ (PPARγ), enhancer binding protein α（C/EBPα）, lipoprotein lipase（LPL）, IGF-1 and glyceraldehyde-3-phosphate dehydrogenase (GAPDH; internal control for mRNAs) are listed in Table 1.

Table 1　Sequences of RNA oligonucleotides

Name	Forward primer (5'→3')	Reverse primer (5'→3')
GAPDH	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG
PRMT7	CCGTGGCACAACCTCTACTT	CACAGGTCCCTGAACTCCAC
PPARγ	GAGGAGCCTAAGGTAAGGAG	GTCATTTCGTTAAAGGCTGA
C/EBPα	GGGCCAGGTCACATTTGTAAA	AGTAAGTCACCCCCTTAGGGTAAGA
LPL	CGGATTAACATTGGAGAAGCTATCCG	AGCTGGTCCACATCTCCAAGTC
IGF-1	AATCAGCAGTCTTCCAACCCAA	TGGTGTGCATCTTCACCTTCAA

1.6　Western blot analysis

Cells were collected in 1.5 ml EP tubes and rinsed with PBS. The lysis buffer (radioimmunoprecipitation assay (RIPA) buffer containing 2% protease inhibitor cocktail) was subsequently added into the tube, and the cells were lysed on ice for 30 min. The total protein concentration of the harvested supernatant was detected using a Pierce BCA protein assay kit (Thermo Scientific). Each sample contained an equal amount of protein. Protein samples were separated on sodium dodecyl sulfate-polyacrylamide gel and transferred to polyvinylidene difluoride (PVDF) membranes. The protein bands were detected using an ECL Western blot Kit (CWBIO, Beijing, China) and quantified with the ImageJ software (National Institutes of Health, USA). GAPDH was used as an endogenous control for normalization. The following antibodies were used for the detection of proteins: PRMT7 (1∶1 000, 78 ku, Abcam, Cambridge, UK); PPARγ (1∶1 000, 57 ku, Cell Signaling Technology); GAPDH (1∶2 500, 40 ku, Abcam, Cambridge, UK); and IGF-1 (1∶1 000, 22 ku, Abcam, Cambridge, UK).

1.7　*In vivo* adipose tissue formation assay

All mice were purchased from Vital River Corporation (Beijing, China) and housed in a specific pathogen-free environment. The cells were cultured in adipogenic induction medium for 1 week before transplantation. Next, we incubated these cells with Collagen Sponge (Wuxi Biot Bioengineering Institute, Wuxi, China) (8 mm×8 mm×2 mm) for 2 h at 37℃, before implanting the complexes into the subcutaneous space on the back of nude mice. Eight weeks later, the transplants were harvested and histological assessments were performed.

1.8　Histological staining

Samples were fixed in 4% paraformaldehyde and thereafter embedded in a Tissue-Tek OCT freezing medium (Sakura Finetek Inc., Torrance, CA, USA) before being cut into sections for Oil Red O staining.

1.9　RNA interference

Cells were inoculated in well plates. After the cell fusion reached 70%, small interfering RNA (siRNA) was transfected into them using a Lipo3000 kit (Invitrogen, Shanghai, China). The cells were collected for assay after 48 h of incubation. NC sense: UUC UCC GAA CGU GUC ACG UTT; NC antisense: ACG UGA CAC GUU CGG AGA ATT; SiIGF-1 sense: GAGUGCAGGAAACAAGAACUA-TT; SiIGF-1 antisense: UAGUUCUUGUUUCCUG-CACUCTT.

1.10　Statistical analysis

All data are expressed as mean±standard deviation (SD). Data were analyzed using the GraphPad software (GraphPad Software, San Diego, CA, USA). Shapiro-Wilk test was used to test the normality of the distribution of all data. Independent two-tailed Student's *t* test, one-way ANOVA, two-way ANOVA and Tukey's post hoc test were performed to examine the level of significance. $P<0.05$ was considered statistically significant.

2　Results

2.1　PRMT7 expression levels decrease significantly during adipogenic differentiation

To explore the role of PRMT7 in the adipogenic differentiation of hBMSCs, we detected the expression of PRMT7 in hBMSCs during adipogenic differentiation. Results from qRT-PCR and Western blot revealed that PRMT7 decreased during the adipogenic differentiation of hBMSCs (Figure 1a−f). All data were normally distributed and statistically significant ($P<0.05$).

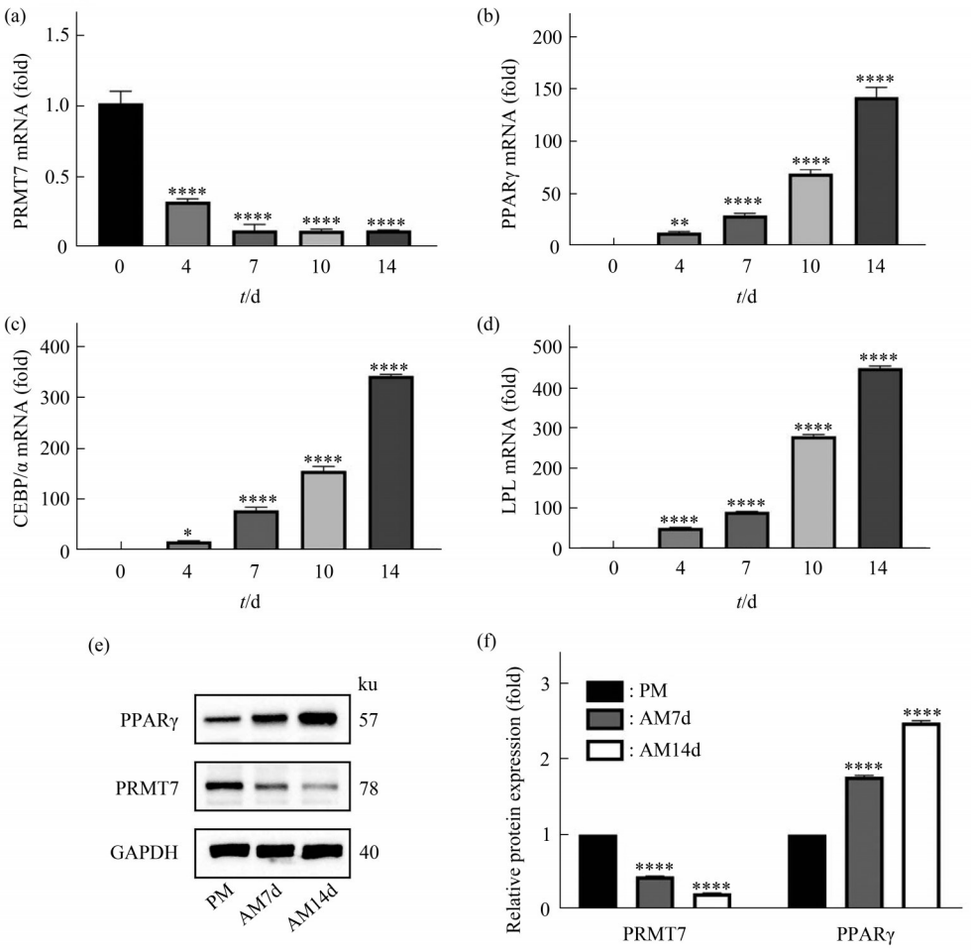

Fig. 1 PRMT7 is downregulated during the adipogenic differentiation of hBMSCs

Expression of PRMT7 decreased gradually during adipogenesis detected by qRT-PCR and Western blot analysis. (a−d) The expression of PRMT7, PPARγ, CEBP/α and LPL were determined by qRT-PCR. (e, f) The expression of PRMT7 and PPARγ were determined by Western blot. All data are presented as mean±SD (n=3, *P<0.05, **P<0.01, ****P<0.000 1). Shapiro-Wilk test and one-way ANOVA. PM: proliferation medium; AM: adipogenic medium.

2.2 Knockdown of PRMT7 promotes adipogenic differentiation of hBMSCs *in vitro*

PRMT7 stable knockdown hBMSCs were established to further investigate the effect of PRMT7 on the adipogenic differentiation. We transfected shRNAs (PRMT7sh-1, PRMT7sh-2) into hBMSCs. The analysis of immuno-fluorescence, qRT-PCR and Western blot confirmed the successful lentiviral transduction and the knockdown efficiency (Figure 2a−c). The PRMT7-deficient cells significantly promoted adipogenesis (Figure 2d, e). Additionally, qRT-PCR and Western blot analysis demonstrated that knockdown of PRMT7 also resulted in an increase in PPARγ expression during adipogenic differentiation (Figure 2f−h). All data were normally distributed and statistically significant (P<0.05).

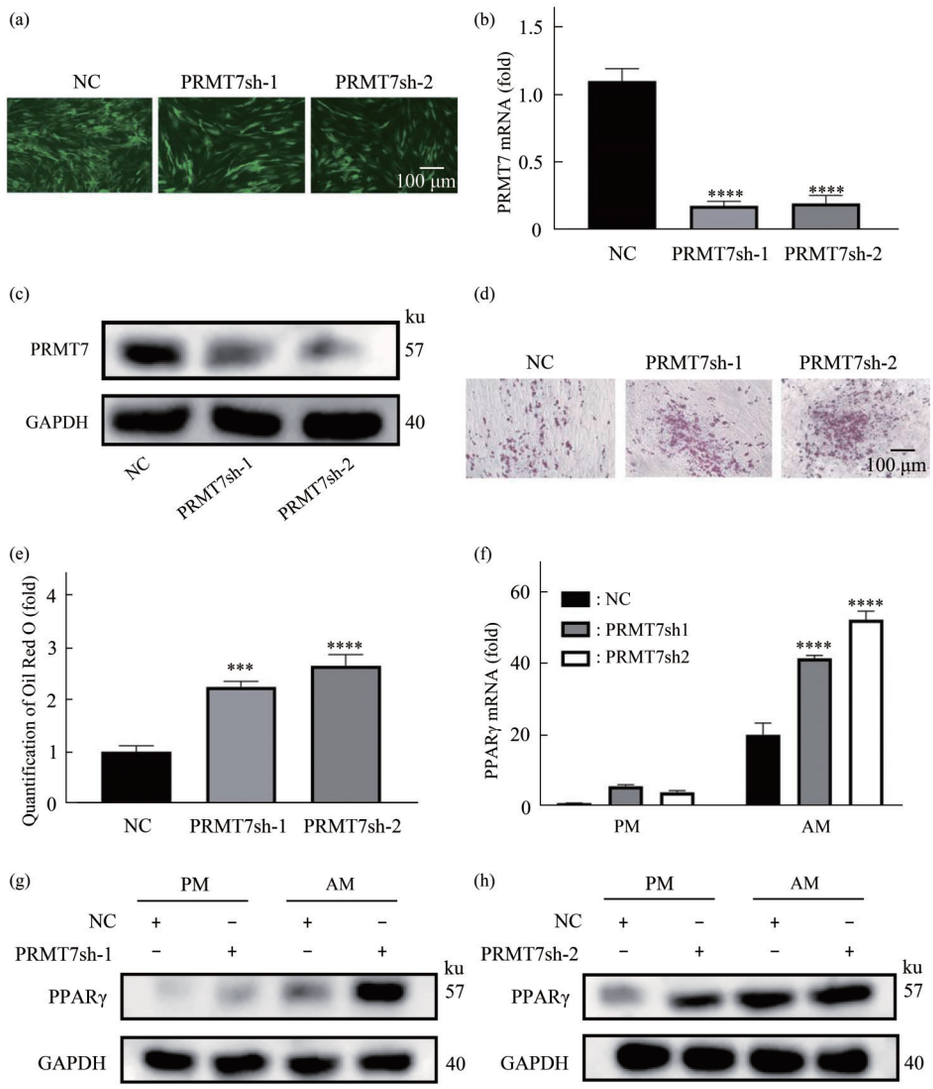

Fig. 2　Knockdown of PRMT7 promotes adipogenic differentiation of hBMSCs *in vitro*

(a−c) The knockdown efficiency of PRMT7 was determined by immuno-fluorescence, qRT-PCR and Western blot; (d, e) PRMT7 knocking down increased the adipose formation capability of hBMSCs; (f−h) PPARγ expression was determined by qRT-PCR and Western blot. n=3. All data are presented as mean±SD (***P<0.001, ****P<0.000 1). Shapiro-Wilk test, one-way ANOVA and two-way ANOVA. PM: proliferation medium; AM: adipogenic medium.

2.3　Knockdown of PRMT7 promotes the formation of new adipose tissue

To further study the role of PRMT7 in adipogenesis *in vivo*, we incubated hBMSCs (PRMT7sh-1, PRMT7sh-2 or NC) with collagen sponges and implanted them into the dorsal side of nude mice (Figure 3a). The complexes were recovered after 8 weeks. The PRMT7 knockdown group was found to have an increased amount of adipose tissue-like structures, as shown by Oil Red O staining (Figure 3b).

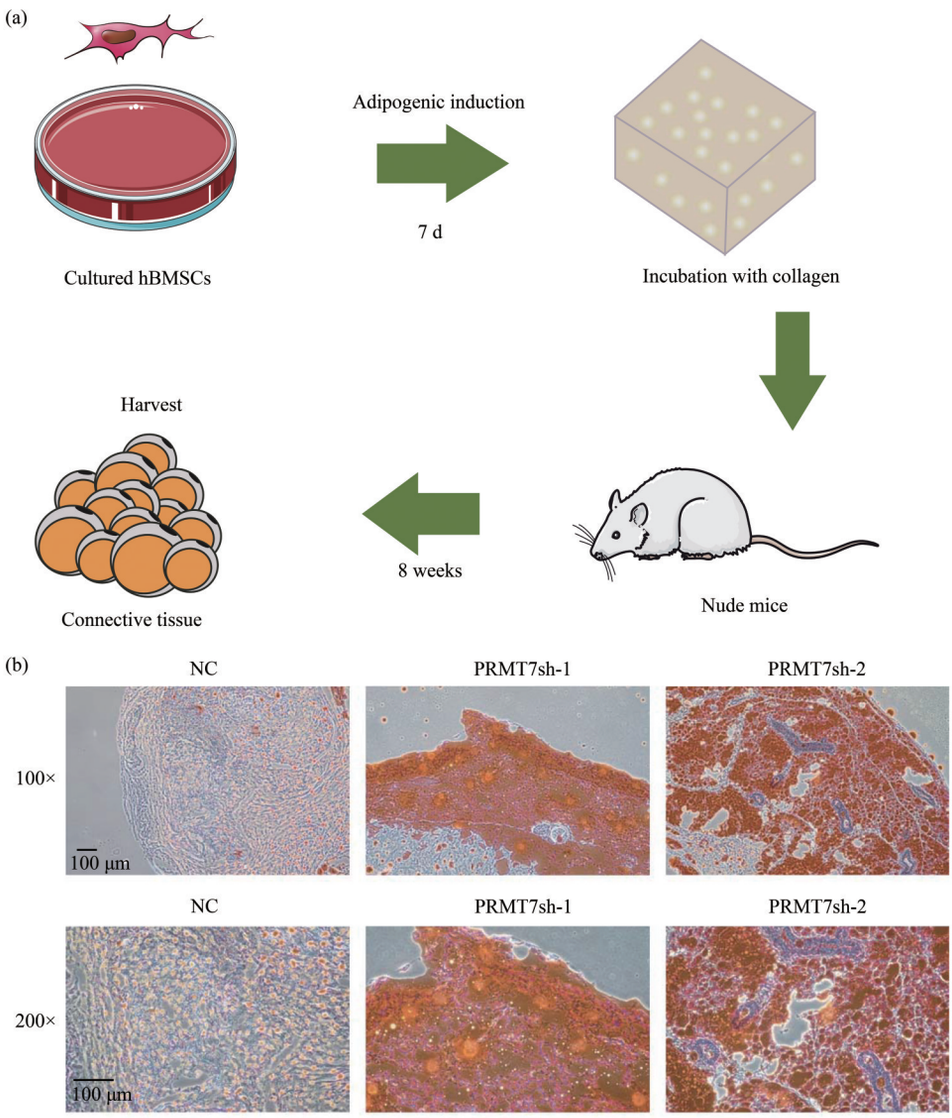

Fig. 3　Knockdown of PRMT7 promotes the formation of new adipose tissue

(a) Schematic diagram of the experimental procedure; (b) Oil Red O staining in the NC, PRMT7sh-1 and PRMT7sh-2 groups. n=3.

2.4　Overexpression of PRMT7 inhibits adipogenic differentiation

We constructed PRMT7 stably overexpressing hBMSCs to further elucidate the role of PRMT7 in adipogenic differentiation. Fluorescent staining, qRT-PCR and Western blot analysis confirmed that PRMT7 expression was significantly elevated after transfection (Figure 4a−c). The overexpression of PRMT7 lead to a significant inhibition of lipogenesis (Figure 4d, e). Consistently, the expression of PPARγ in PRMT7-overexpressing hBMSCs were found to be significantly downregulated during adipogenic differentiation (Figure 4f, g). All data were normally distributed and statistically significant (P<0.05).

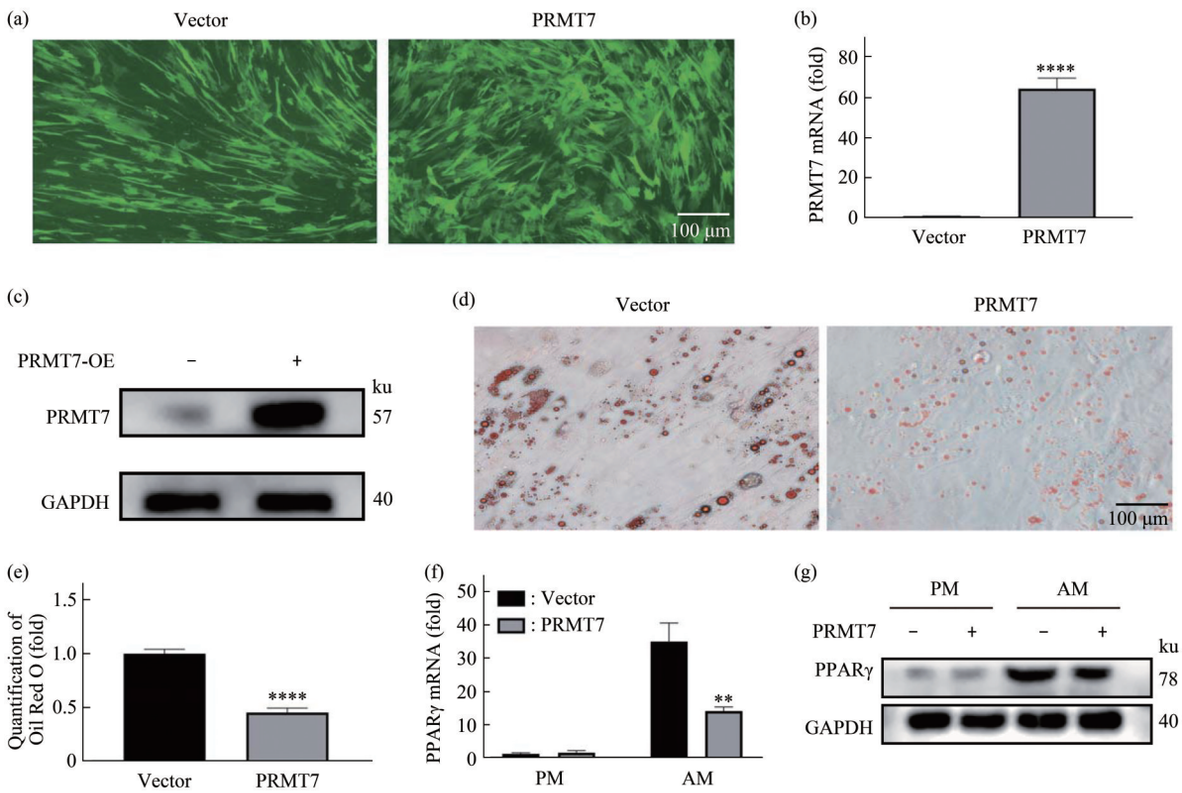

Fig. 4　Overexpression of PRMT7 inhibits adipogenic differentiation of hBMSCs

(a−c) The overexpression efficiency of PRMT7 was determined by immuno-fluorescence, qRT-PCR and Western blot; (d, e) PRMT7-overexpressing decreased adipose formation capability of hBMSCs; (f, g) PPARγ expression was determined by qRT-PCR and Western blot. n=3. All data are presented as mean±SD (**P<0.01, ****P<0.000 1). Shapiro-Wilk test, Student's t test and two-way ANOVA. PM: proliferation medium; AM: adipogenic medium; OE: overexpression.

2.5　Knockdown of PRMT7 promotes the expression of IGF−1

To investigate the underlying mechanism, we examined several key factors associated adipogenesis. We found that PRMT7 negatively regulates IGF-1 expression (Figure 5a−d). To ascertain if PRMT7 regulates adipogenesis through the IGF-1 signaling pathway, we inhibited the expression of IGF-1 in PRMT7 knockdown hBMSCs. Figure 5e shows the knockdown efficiency of IGF-1. IGF-1 knockdown significantly counteracted the enhanced adipogenesis resulting from PRMT7 knockdown (Figure 5f−h). All data were normally distributed and statistically significant (P<0.05).

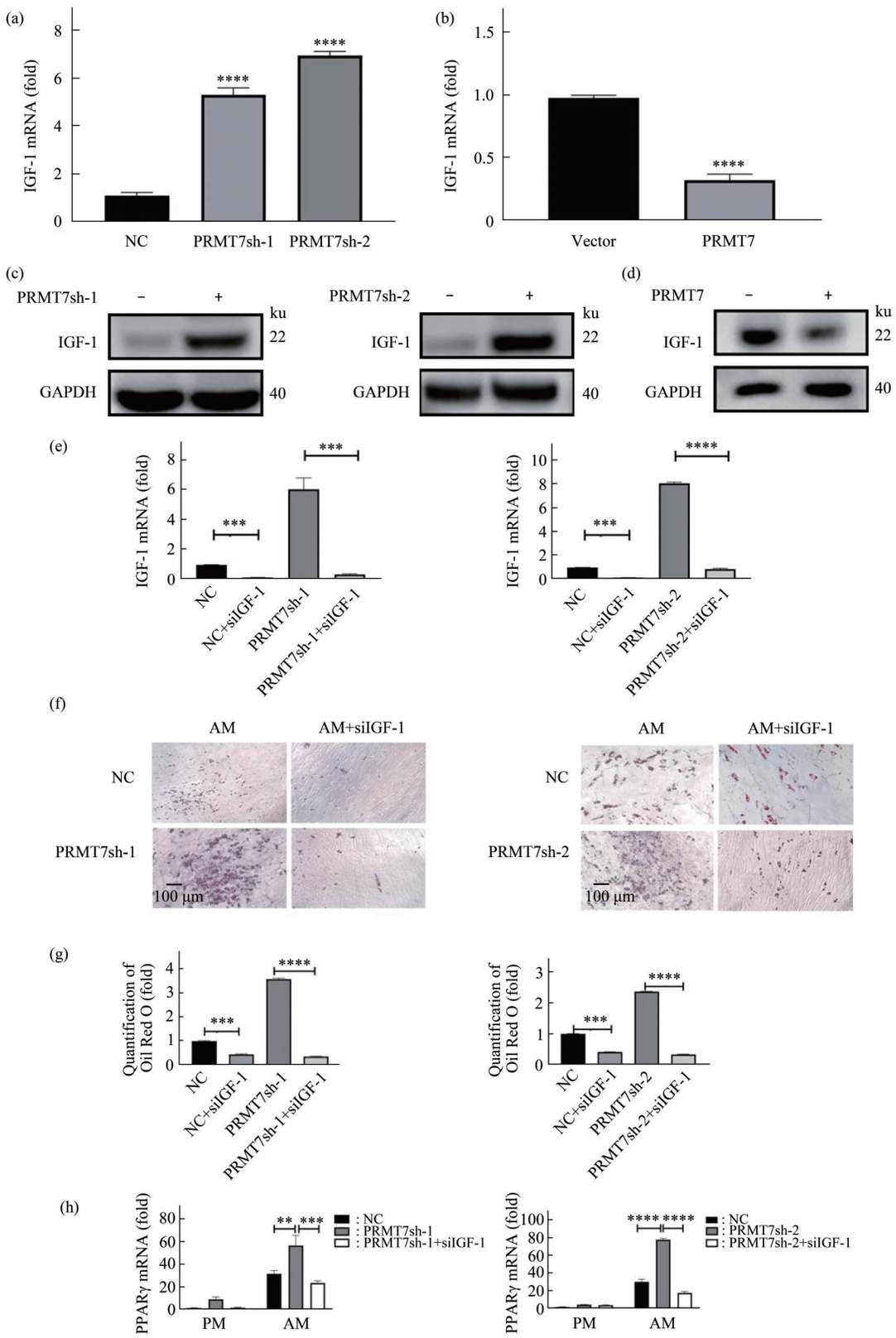

Fig. 5　Knockdown of PRMT7 promotes the expression of IGF−1

(a−d) The expression levels of IGF-1 and PRMT7 were correlated negatively in hBMSCs; (e) inhibition of IGF-1 expression level was confirmed by qRT-PCR; (f, g) IGF-1 slicing inhibited the adipose formation capability of PRMT7 knocked down cells; (h) PPARγ expression was determined by qRT-PCR. n=3. All data are presented as mean±SD (**P<0.01, ***P<0.001, ****P<0.000 1). Shapiro-Wilk test, Student's t test, one-way ANOVA and two-way ANOVA. PM: proliferation medium; AM: adipogenic medium.

3 Discussion

Bone marrow adipose tissue is an essential component of the bone marrow. It provides energy to endocrine organs and plays an important role in various physiological processes, including metabolism, bone homeostasis, haematopoiesis and cancer[24]. In addition, bone marrow adipose tissue has been shown to be associated with a wide range of skeletal disorders, including osteoporosis[25]. A growing body of evidence strongly supports the idea that the production of large amounts of bone marrow adipose tissue is an important cause of bone loss[26]. Bone marrow mesenchymal stem cells (BMSCs) have the potential to differentiate into multiple cell types. Enhanced adipogenic differentiation or decreased osteogenic differentiation of BMSCs may result in bone loss[27]. It has been shown that, with advancing age, BMSCs tend to differentiate into adipocytes, thereby leading to a decrease in osteoblasts and resulting in osteoporosis in the elderly[28]. The study of the mechanism of BMSC differentiation would enable us to regulate the differentiation of MSCs, thereby allowing for the use of MSCs in clinical therapy. In our study, we observed that hBMSCs with reduced levels of PRMT7 showed a propensity to differentiate into adipocytes, while the adipogenic differentiation of hBMSCs overexpressing PRMT7 was diminished. These findings strongly indicate that a decrease in PRMT7 levels could potentially contribute to the development of various diseases associated with increased adipose tissue. The dysregulation of PRMT7 appears to play a critical role in adipogenesis, highlighting its importance as a potential therapeutic target for conditions related to adipose tissue disorders. This study underscores the significance of further elucidating the intricate mechanisms underlying PRMT7's involvement in adipogenic processes, which may offer novel insights into the pathogenesis and treatment of adipose-related diseases.

Through mechanism investigation, our findings demonstrate a clear negative correlation between the expression levels of PRMT7 and IGF-1. Moreover, we observed that reducing IGF-1 levels effectively mitigated the adipogenic differentiation induced by PRMT7 knockdown. This underscores the pivotal role of PRMT7 in modulating various cellular processes through modulating the activity of its substrate. Specifically, prior studies have shown that PRMT7 exerts its influence on diverse cellular processes by catalyzing the methylation of specific substrates. For instance, it has been elucidated that PRMT7 facilitates myogenic cell differentiation by catalyzing the methylation of arginine residue 70 of p38MAPK[29]. However, there remains a critical need to delve deeper into the intricate mechanisms underlying the regulatory interplay between PRMT7 and IGF-1. It is imperative to ascertain whether PRMT7 modulates the expression of IGF-1 through arginine methylation and elucidate the specific signaling pathways activated by IGF-1 that ultimately impact adipogenic differentiation in the future study.

Knockout mice can mimic human patients in research and have become an indispensable technology for basic life science research in modern times. Previous studies, using the conditional knockout mice model by the Cre/LoxP system and powered by *Prx1-Cre*, have shown that the conditional knockdown of the methyltransferase METTL3 in bone marrow mesenchymal stem cells may lead to insufficient osteogenic differentiation potential, damaged bone formation, and increased bone marrow obesity in mice[30]. One investigator used *Osx* (*Sp7-Cre*) to study the differentiation of mesenchymal stem cells and found that the conditional knockdown of Cdc20 inhibited osteogenic differentiation of BMSCs[31] and promoted the adipogenic differentiation of BMSCs[32]. In this study, we confirmed the negative regulatory effect of PRMT7 on the adipogenic differentiation ability of hBMSCs through *in vitro* adipogenic induction and subcutaneous transplantation experiments in nude mice. Given the complexity of organisms, the construction of animal knockout models can provide a more faithful representation of the effect of PRMT7 on adipogenic function *in vivo*.

4 Conclusion

Overall, our study showed that PRMT7 expression was impaired during the adipogenesis of mesenchymal stem cells. The knockdown of PRMT7 significantly enhanced the adipogenic differentiation, and PRMT7-overexpressing cells displayed decreased capability for adipogenic differentiation. Mechanically, we found that PRMT7 knockdown

could activate the expression of IGF-1, and determined that PRMT7 regulates adipogenic differentiation through IGF-1 signaling.

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精氨酸甲基转移酶（PRMT）7通过IGF-1信号通路调控人骨髓间充质干细胞成脂分化的研究*

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摘要　目的　本研究旨在明确精氨酸甲基转移酶（PRMT）7在人骨髓间充质干细胞（hBMSCs）成脂分化过程中的变化以及是否调控hBMSCs成脂分化，进而探索相应的调控机制。**方法**　通过定量反转录PCR（qRT-PCR）和蛋白质印迹（Western blot）检测hBMSCs成脂分化过程中PRMT7的变化；通过qRT-PCR和Western blot实验证明PRMT7稳定敲低细胞系构建成功。进行油红O染色和定量分析，以及qRT-PCR和Western blot实验检测PRMT7稳定敲低细胞系成脂分化水平的变化；通过裸鼠体内异位成脂实验，油红O染色检测PRMT7稳定敲低细胞系体内异位成脂的效果；通过qRT-PCR和Western blot证明PRMT7稳定过表达细胞系构建成功。进行油红O染色和定量分析以及qRT-PCR和Western blot实验检测PRMT7稳定过表达细胞系成脂分化水平的变化；通过qRT-PCR和Western blot实验检测敲低PRMT7和过表达PRMT7的细胞中IGF-1表达水平的变化。在PRMT7稳定敲低细胞系中转染siIGF-1并通过qRT-PCR和Western blot检测IGF-1的表达水平验证敲低效率。通过油红O染色和定量分析，qRT-PCR实验检测转染siIGF-1的敲低组hBMSCs成脂分化水平的变化。**结果**　本文发现：在hBMSCs成脂过程中，PRMT7表达水平明显降低（$P<0.01$）；敲低PRMT7后hBMSCs的成脂分化能力增强（$P<0.001$）；敲低PRMT7后hBMSCs的体内异位成脂分化能力增强；过表达PRMT7后hBMSCs的成脂分化能力减弱（$P<0.01$）；PRMT7敲低后IGF-1表达水平增加（$P<0.000\ 1$）；PRMT7过表达后IGF-1表达水平降低（$P<0.000\ 1$）；转染siIGF-1后，各细胞系IGF-1表达水平明显降低（$P<0.001$）；敲低组转染siIGF-1后成脂分化能力明显降低（$P<0.01$）。**结论**　本研究通过细胞水平和裸鼠皮下移植实验发现PRMT7显著抑制hBMSCs成脂分化，机制研究发现PRMT7对hBMSCs成脂分化的调控作用依赖IGF-1信号通路。上述研究表明，PRMT7可能是治疗相关疾病的潜在分子靶点，为PRMT7和hBMSCs应用于相关疾病治疗提供了新思路。

关键词　精氨酸甲基转移酶7，成脂分化，骨髓间充质干细胞，IGF-1信号通路
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