

Small extracellular vesicles produced by homeostatic phenotype BMSC promote bone regeneration by transferring anti-senescent factor JMJD6

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Supplementary Experimental Section

1 Cell proliferation assay

The proliferation capacity cells were evaluated using the CCK-8 Kit (Beyotime, China) following the manufacturer's instructions. Each well of a 96-well plate was seeded with 100 μ l containing 2000 cells, followed by the addition of 10 μ l CCK-8 detection solution per well. After continued incubation in a cell culture incubator for 1 h, absorbance was measured at 450 nm using a microplate reader (BioTek, USA).

2 SA- β -gal and γ -H2AX staining

For NM-cultured BMSC processing, cells were lysed using GelMA hydrogel lysis buffer (Engineering for Life, China) at 37°C for 4 h. The lysed NM-cultured BMSCs were seeded onto 10 cm culture dishes using conventional monolayer culture protocols and subjected to analysis once cell confluency reached 80%. For normal BMSC processing, cells were detached using trypsin digestion and reseeded onto 10 cm culture dishes upon reaching 80% confluency, followed by analysis after complete cell adhesion.

For SA- β -gal staining assay, each well received 1 ml of SA- β -gal staining solution (Solarbio, China), followed by overnight incubation at 37°C. After removing the staining solution, stained cells were visualized under a light microscope, and the proportion of positively stained cells was recorded.

For γ -H2AX staining assay, each well was blocked with immunoblotting buffer at room temperature for 20 min. Following removal of the blocking solution, cells were incubated with anti- γ -H2AX primary antibody (Beyotime, China) at 4°C overnight, then washed three times (5 min each) with washing buffer. Cells were subsequently incubated with Alexa Fluor 488-conjugated secondary antibody (Beyotime, China) at room temperature for 1 h, followed by two washing steps. Nuclear counterstaining was performed using DAPI solution (Beyotime, China) for 5 min at room temperature, followed by three washing cycles. Stained samples were examined and documented using an inverted fluorescence microscope.

3 The sEV identification

Transmission electron microscopy detection (TEM): 20 μ l of freshly prepared sEV solution were applied to a carbon-coated copper grid and incubated at room temperature for 15 min. Excess liquid was carefully removed with filter paper. The grid was then negatively stained with 2% uranyl acetate for 2 min, followed by removal of excess staining solution. After air-drying, the grid was placed in a TEM specimen holder. The sEV morphology and ultrastructural features were examined using TEM (Zeiss, Germany).

Nanoparticle tracking analysis (NTA): An appropriate volume of the sEV suspension was diluted, and 1 ml of the sample was loaded into a sample syringe. NTA was performed using a NanoSight NS300 system (Malvern Panalytical, UK) to automatically analyze and record sEV size distribution and concentration parameters.

In addition, western blot was used to detect the presence of classical sEV markers (HSP70, TSG101, CD63, and CD81) and the absence of negative markers (Calnexin), with cells as controls.

4 Osteogenic induction in vitro

Upon reaching 80% confluency, cells were switched from standard complete medium to osteogenic medium consisting of MEM- α supplemented with 10% sEV-depleted FBS, 50 μ g/ml ascorbic acid (Sigma, USA), 10 mM β -glycerophosphate disodium (BBI, China), and 0.1 μ M dexamethasone (Sigma, USA). The osteogenic medium was refreshed every 3 days. The osteogenic effect was detected after 7, 14, and 21 days, respectively.

5 Adipogenic induction in vitro

Adipogenic differentiation of BMSC was induced using the Adipogenic Differentiation Induction Kit for BMSC (OriCell, China). Cells to be induced were seeded in 24-well plates at a density of 2×10^4 cells/cm². When cell confluence reached 100%, the culture medium was replaced with adipogenic induction medium containing Solution A and Solution B. Medium replacement followed a cyclic regimen of three days with Solution A followed by one day with Solution B, maintaining this induction-maintenance cycle. The total induction period for this experiment was 14 days.

6 ALP and ARS assays

For ALP staining, aspirate culture medium and wash cells three times with PBS. Fix cells with 4% paraformaldehyde (Solarbio, China) for 15 min, followed by three PBS washes. After the final wash, remove residual liquid and add sufficient BCIP/NBT staining working solution (Beyotime, China) to fully cover the sample. Incubate at room temperature in the dark for 30 min. Remove the staining solution, wash with distilled water two times to terminate the reaction, and visualize staining under a microscope. Quantitative analysis was performed using Image J software.

For ALP activity assay, prepare chromogenic substrate solution and generate a standard curve according to the manufacturer's instructions. Aspirate culture medium and wash cells three times with PBS. Lyse samples using IP lysis buffer (without inhibitors) (Beyotime, China), homogenize appropriately, and centrifuge at 12,000g for 10 min. Collect the supernatant and measure ALP activity at 405 nm using an ALP activity detection kit (Beyotime, China) with a microplate reader (BioTek, USA).

For ARS staining, aspirate culture medium and wash cells three times with PBS. After the final wash, remove residual liquid and add sufficient Alizarin Red S staining solution (Beyotime, China) to uniformly cover cells. Incubate at room temperature for 30 min. Remove the staining solution, wash with distilled water two times to terminate the reaction, and visualize staining under a microscope. Quantitative analysis was performed using Image J software.

Mineralization quantification assay, following ARS staining, aspirate all liquid from wells and add 1 ml of 10% cetylpyridinium chloride solution (Aladdin, China) per well. Incubate at room

temperature for 15 min, then transfer 150 µl of solution from each well to a 96-well plate. Measure absorbance at 562 nm using a multimode microplate reader (BioTek, USA).

7 Oil red O staining

Following 14 days of adipogenic induction, BMSCs with sufficient lipid droplets observed under microscopy were subjected to Oil Red O staining. Cells were washed three times with PBS and fixed with 4% paraformaldehyde solution at room temperature for 30 min. The Oil Red O working solution (Beyotime, China) was prepared and filtered through a 0.22 µm filter to remove particulate impurities. Fixed cells were washed three times with PBS before incubation with the filtered Oil Red O stain at room temperature for 30 min. After staining, cells were washed three times with PBS to remove excess dye, and adipogenic differentiation was visualized under microscopy. Following imaging documentation, isopropanol was added to the stained wells and incubated at room temperature for 10 min in the dark to elute lipid droplets from the cellular matrix. The supernatant was then transferred to a new 96-well plate, and absorbance was measured at 510 nm using a microplate reader. The adipogenic differentiation capacity of BMSCs was evaluated based on the OD₅₁₀ values.

8 RNA extraction, reverse transcription, and RT-qPCR

Total RNA was extracted from samples using TRIzol reagent (ThermoFisher, USA). Reverse transcription was performed using BlazeTaq RTase Mix (GeneCopoeia, China). RT-qPCR was conducted using BlazeTaq SYBR Green qPCR Mix (GeneCopoeia, China) on a CFX Connect Real-Time System (Bio-Rad, USA). GAPDH served as the internal reference gene for mRNA normalization. Relative expression levels were calculated using the $2^{-\Delta\Delta Ct}$ method. The primers are listed in [Table S1](#).

9 Western blot

Total protein was extracted from **sEVs** and cells using RIPA lysis buffer (Beyotime, China) containing protease inhibitors. Lysates were centrifuged at 12,000g for 15 min, and supernatants were collected. Proteins were separated via SDS-PAGE (Epizyme Biotech, China) and transferred to polyvinylidene difluoride (PVDF) membranes (Merck, USA). Membranes were blocked with protein-free rapid blocking buffer (Epizyme Biotech, China) for 15 min at room temperature, followed by overnight incubation with primary antibodies at 4°C. After three washing steps, membranes were incubated with HRP-conjugated secondary antibodies for 1 h. Following three additional washes, chemiluminescent signals were detected using an ECL detection kit (Proteintech, China). Target bands were visualized using the Bio-Rad VersaDoc Imaging System (Bio-Rad, USA). β -actin, GAPDH, or Vinculin served as controls depending on experimental design. **The relative protein expression value of the target gene is calculated as the ratio of the band intensity of the target gene to that of its internal reference gene.** Antibody information is provided in [Table S2](#).

10 Cell survival assay

NM-cultured BMSC were transferred to 15 ml centrifuge tubes and washed three times with PBS. Constructs were then submerged in 250 μ l of Calcein AM/PI staining solution (Beyotime, China) and incubated at 37°C in the dark for 30 min. Following incubation, constructs were visualized under a fluorescence microscope using appropriate filter sets: Calcein AM (green fluorescence, Ex/Em = 494/517 nm) and PI (red fluorescence, Ex/Em = 535/617 nm).

11 Cell cycle assay

Carefully aspirate the supernatant and resuspend cells in 1 ml of ice-cold PBS. Transfer the cell suspension to a 1.5 ml microcentrifuge tube. Centrifuge at 1000 g for 5 min to pellet cells, then carefully remove the supernatant. Gently tap the tube bottom to disperse cell clumps without creating foam. Fix cells by resuspending in 1 ml of ice-cold 70% (v/v) ethanol and mixing gently. Incubate at 4°C for 2 h, followed by centrifugation at 1000 g for 5 min. Stain cells using a cell cycle and apoptosis detection kit (Beyotime, China) according to the manufacturer's instructions, incubating at 37°C in the dark for 30 min. Analyze NM-cultured BMSC using a flow cytometer.

12 D-gal induces cellular senescence

A 20 mg/ml working solution of D-gal powder (Beyotime, China) was prepared using complete culture medium. When target cells reached 80% confluency, the complete medium was replaced with the D-gal working solution, and cells were returned to the incubator for continued culture. After 48 h of D-gal treatment, cells were washed three times with PBS, and the medium was replaced with fresh complete culture medium prior to proceeding with subsequent experimental steps.

13 Bulk RNA sequencing and transcriptome assay

Total RNA was used as input material for the RNA sample preparations. Fragmentation was carried out using divalent cations under elevated temperature in 5 $\times$ First Strand Synthesis Reaction Buffer. First strand cDNA was synthesized using random hexamer primer and M-MuLV Reverse Transcriptase (RNase H free). Second strand cDNA synthesis was subsequently performed using DNA Polymerase I and RNase H. Remaining overhangs were converted into blunt ends via exonuclease/polymerase activities. After adenylation of 3' ends of DNA fragments, Adaptor with hairpin loop structure were ligated to prepare for hybridization. In order to select cDNA fragments of preferentially 370~420 bp in length, the library fragments were purified with AMPure XP system. Then PCR was performed with Phusion High-Fidelity DNA polymerase, Universal PCR primers and Index Primer. At last, PCR products were purified (AMPure XP system) and library quality was assessed on the Agilent Bioanalyzer 2100 system.

The clustering of the index-coded samples was performed on a cBot Cluster Generation System using TruSeq PE Cluster Kit v3-cBot-HS (Illumina, USA) according to the manufacturer's

instructions. After cluster generation, the library preparations were sequenced on an Illumina Novaseq platform and 150 bp paired-end reads were generated.

14 Proteome assay

Each protein sample was taken and the volume was made up to 100 μ l with DB lysis buffer (8M Urea, 100 mM TEAB, pH 8.5), trypsin and 100 mM TEAB buffer were added, sample was mixed and digested at 37°C for 4 h. Then trypsin and CaCl_2 were added digested overnight. Formic acid was mixed with digested sample, adjusted pH under 3, and centrifuged at 12000 g for 5 min at room temperature. The supernatant was slowly loaded to the C18 desalting column, washed with washing buffer (0.1% formic acid, 3% acetonitrile) 3 times, then added elution buffer (0.1% formic acid, 70% acetonitrile). The eluents of each sample were collected and lyophilized.

Prepare mobile phase A (100% water, 0.1% formic acid) and B (80% acetonitrile, 0.1% formic acid). The lyophilized powder was dissolved using 10 μ l A solution, centrifuged at 14,000g for 20 min at 4°C, and 200 ng of the supernatant sample was injected into the sample for liquid-quality detection. A Vanquish Neo upgraded UHPLC system was used with a C18 pre-column of 174500 (5 mm $\times$ 300 μ m, 5 μ m, ThermoFisher, USA) heated at 50°C in a column oven, and a C18 analytical column of ES906 (PepMap TM Neo UHPLC 150 μ m $\times$ 15 cm, 2 μ m, ThermoFisher, USA). A ThermoFisher orbitrap astral mass spectrometer and an Easy-spray ion source were used, the ion spray voltage was set to 1.9 kV, the ion transfer tube temperature was set to 290°C, and the mass spectrum was in a data-dependent acquisition mode, with a full first-stage mass spectrometry scanning range of 380-980 m/z. The primary MS resolution was set to 240,000 (200 m/z), AGC was set to 500%, the parent ion window size was set to 2-Th, the number of DIA windows was 300, the NCE was set to 25%, the secondary m/z acquisition range was from 150 to 2000, the sub-ion resolution Astral was set to 80,000, and the maximal injection time was 3 ms.

15 The sEVs in vitro and in vivo internalization

The sEVs were stained by 10 mg/ml DiI (Beyotime, China) at room temperature for 10 min in the dark. Centrifuge at 100,000 g for 70 min to remove residual fluorescent dye.

BMSCs passaged to the 3rd generation were seeded at a density of 2×10^4 cells/ml in 20 mm glass bottom cell culture dishes. When the cells had adhered and reached 60% confluence, they were incubated with CCK-F (Beyotime, China) for 30 min. Then, the medium was replaced, and 20 μ g of DiI-labeled sEV^{Ho-BMSC} or sEV^{BMSC} was added to fresh medium and incubated overnight. The medium was then removed, and the cells were rinsed three times with PBS. The cells were fixed with 4% paraformaldehyde for 15 min, followed by incubation with DAPI (Beyotime, China) for 15 min. After three rinses with PBS, the cells were observed under a laser confocal microscope (Zeiss, Germany).

The sEVs were fluorescently labeled with DiI dye and intra-lesional injected. Seventy-two hours later, bone tissue was harvested, and all cells were flushed out from the bone marrow cavity. BMSCs were then labeled with a fluorescent antibody against the stem cell-specific surface marker CD90,

followed by flow cytometry analysis. Cells that were double-positive for DiI and CD90 were identified as BMSCs that had taken up sEVs in vivo.

16 Transwell assay

The migration of BMSCs was evaluated using the transwell (Corning, USA) with 8 μ m pores. The cells were seeded at a density of 2×10^4 cells/well in the upper chamber, supplemented with 1% FBS, while the complete medium supplemented with 10% FBS was added to the lower chamber. The cells were incubated for 12 hours, then non-migrating cells were erased with a cotton swab. The migrated cells were fixed with 4% paraformaldehyde, washed with PBS, stained with 0.1% crystal violet staining solution, dried, and observed by invert microscopy. The number of migrated cells was analyzed using ImageJ software.

17 Micro-CT

To evaluate bone regeneration, the rat tibia was scanned using a high-resolution micro-CT scanning system (PerkinElmer, USA). Images were acquired at the following settings: 6.5 μ m voxels, medium resolution, 85 kV, 200 μ A, 1 mm Al filter, and 384 ms for integration. The 3D image reconstruction was reconstructed from a series of 2D images (CTvox, version 3.3.0). The bone volume fraction (BV/TV), trabecular thickness (Tb. Th), and trabecular number (Tb. N) parameters were analyzed using Inveon Research Workplace.

18 Histology examination

Rat tibiae were fixed in 4% paraformaldehyde, decalcified, paraffin-embedded, and sectioned. Sections underwent hematoxylin and eosin (H&E) staining and Masson's trichrome staining. Histological slides were independently evaluated in a double-blind manner by two senior pathologists (aware only of sample numbers without knowledge of group allocations), and a third expert was consulted for arbitration in cases of discrepancy. For immunohistochemistry, deparaffinized sections were rehydrated and subjected to antigen retrieval using 10 mM citrate buffer (pH 6.0) via microwave irradiation (15 min). The bone tissue slices were permeabilized with 0.5% Triton X-100 for 20 min, followed by blocking with 10% FBS/PBS for 1 h. Primary antibodies were applied for overnight incubation at 4°C. After washing, slices were incubated with secondary antibodies for 1 h at room temperature. Nuclear counterstaining was performed with DAPI (Beyotime, China). Images were captured using a fluorescence microscope (Olympus, Japan) and analyzed as previously described. Quantification involved calculating the percentage of positive-stained areas using the formula: (positive pixel density/selected region area) $\times$ 100%, with all measurements performed using ImageJ software. Antibody information is provided in [Table S2](#).

19 Transfection of overexpression plasmids

When BMSCs reached 80% confluency, the culture medium was replaced with Opti-MEM (Gibco, USA). Cells were transfected with a JMJD6 overexpression plasmid (Gencefe Biotech,

China) using Lipofectamine 2000 (Invitrogen, USA) according to the manufacturer's instructions. After 4 h of incubation, the transfection medium was replaced with complete medium to resume standard culture conditions.

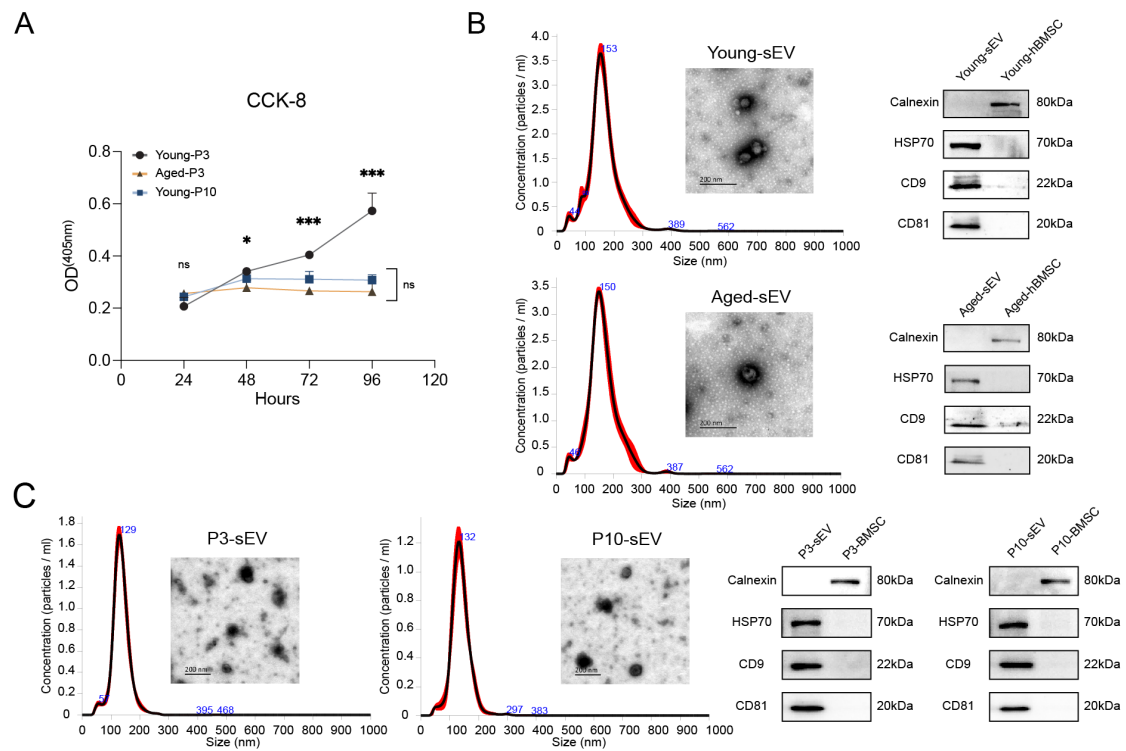


Figure S1. The proliferation capacity of hBMSCs and characterization of BMSC-derived sEVs.

(A) CCK-8 assay results of BMSCs from young donors at passage 3 (Young-P3) and passage 10 (Young-P10), and from elderly donors at passage 3 (Aged-P3) during in vitro culture.

(B) NTA results, representative TEM images, and surface marker expression profiles of BMSC-derived sEVs from young donors (Young-sEV) and elderly donors (Aged-sEV). Scale bar represents 200 μ m.

(C) NTA results, representative TEM images, and surface marker expression profiles of P3 rBMSCs (P3-sEV) and P10 rBMSCs (P10-sEV). Scale bar represents 200 μ m.

ns $p \geq 0.05$, * $p < 0.05$, *** $p < 0.001$.

(F) Hierarchical clustering heatmap of differentially expressed genes between con-BMSC and NM-BMSC.

(G) GO enrichment results of differentially expressed genes between con-BMSC and NM-BMSC.

(H) KEGG enrichment results of differentially expressed genes between con-BMSC and NM-BMSC.

(I) Venn diagram comparing downregulated genes in NM-BMSC with publicly available datasets (GSE93218, GSE247989, GSE174619, GSE52896).

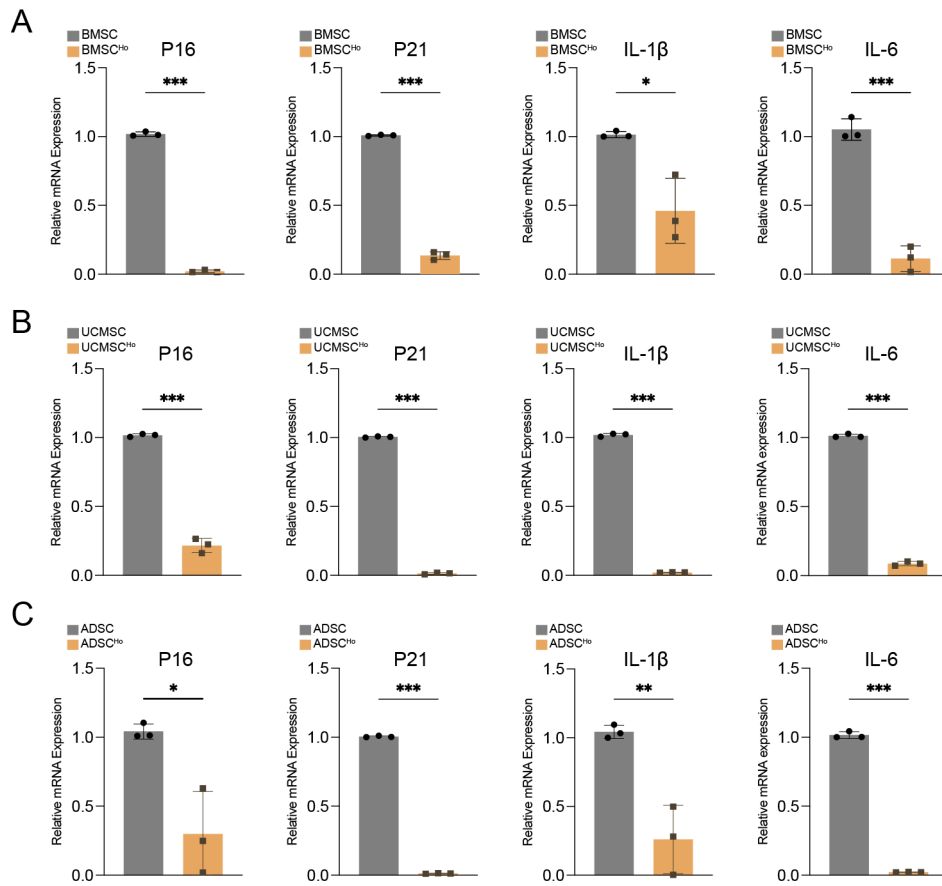


Figure S3. NM-culture reduces the expression levels of senescence-associated genes and SASP genes.

(A) Relative mRNA expression levels of P16, P21, IL-1β and IL-6 gene in conventional/NM-cultured BMSC after D-gal-induced senescence.

(B) Relative mRNA expression levels of P16, P21, IL-1β and IL-6 gene in conventional/NM-cultured UCMSC after D-gal-induced senescence.

(C) Relative mRNA expression levels of P16, P21, IL-1β and IL-6 gene in conventional/NM-cultured ADSC after D-gal-induced senescence.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

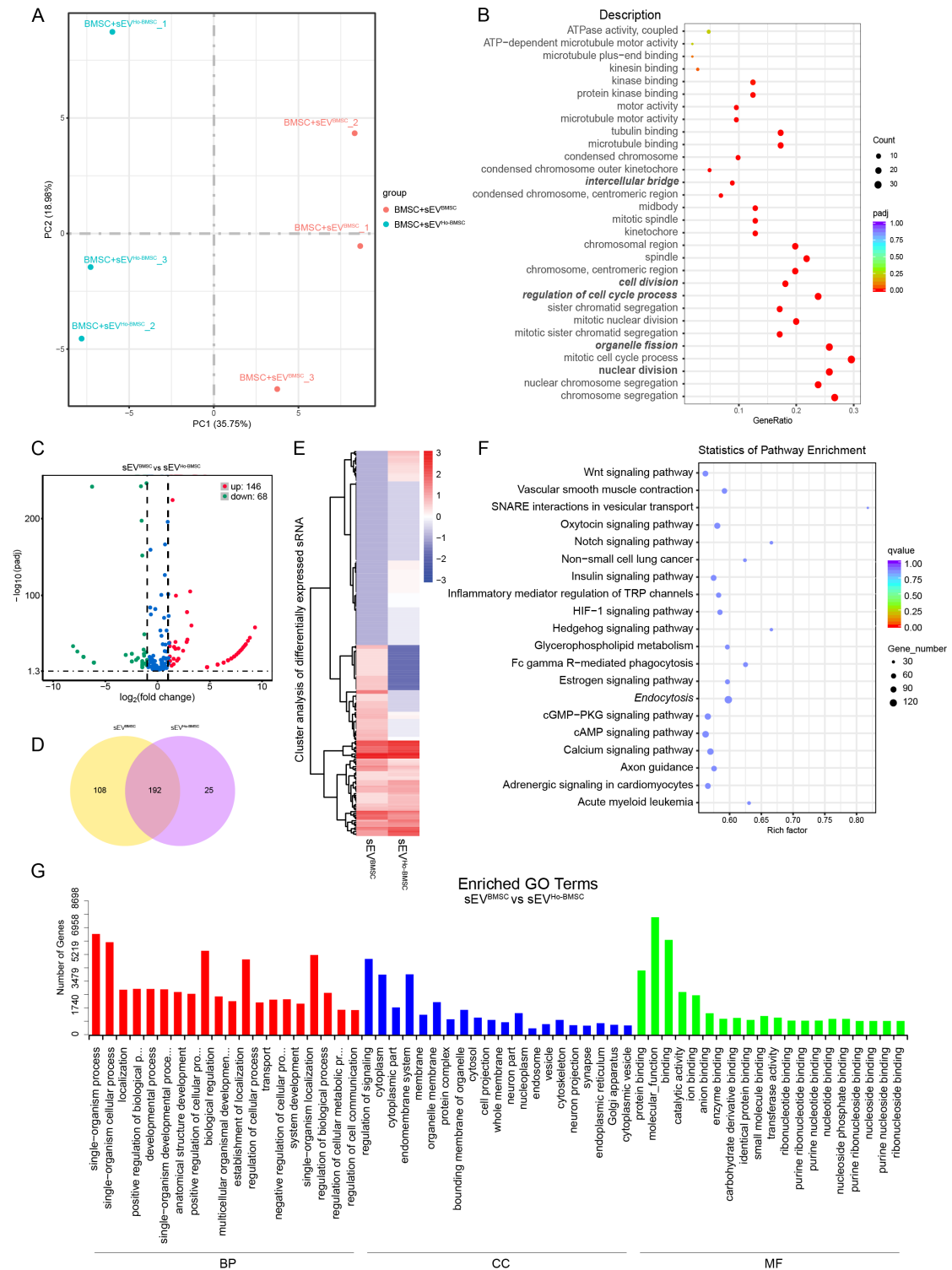


Figure S4. Comprehensive profiling of sEV^{BMSC} and $sEV^{Ho-BMSC}$ cargo miRNAs.

(A) PCA results of transcriptomic profiles comparing BMSC co-cultured with sEV^{BMSC} (BMSC+ sEV^{BMSC}) and $sEV^{Ho-BMSC}$ (BMSC+ $sEV^{Ho-BMSC}$).

(B) GO enrichment results of differentially expressed genes between BMSC+ sEV^{BMSC} and BMSC+ $sEV^{Ho-BMSC}$.

- (C) Volcano plot of differentially abundant miRNAs between sEV^{BMSC} and $sEV^{Ho-BMSC}$.
- (D) Venn diagram analysis showing overlapping and unique miRNA populations in sEV^{BMSC} and $sEV^{Ho-BMSC}$.
- (E) Hierarchical clustering heatmap of differentially abundant miRNAs between sEV^{BMSC} and $sEV^{Ho-BMSC}$.
- (F) KEGG enrichment results of differentially abundant miRNAs between sEV^{BMSC} and $sEV^{Ho-BMSC}$.
- (G) GO enrichment results of differentially abundant miRNAs between sEV^{BMSC} and $sEV^{Ho-BMSC}$.

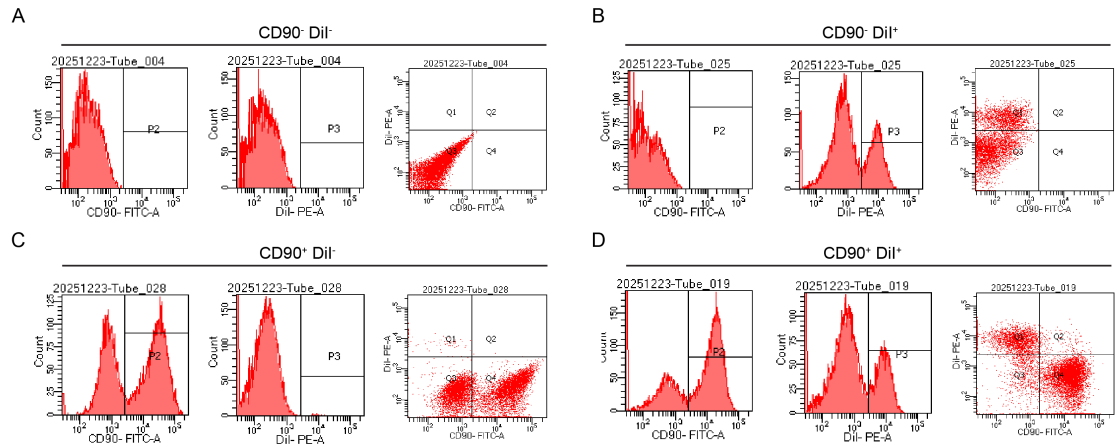


Figure S5. The sEV^{Ho}-BMSC taken up by BMSCs in vivo.

(A) Flow cytometry analysis of DiI-negative, CD90-negative cells, indicating non-BMSCs that did not uptake sEV^{Ho}-BMSC.

(B) Flow cytometry analysis of DiI-positive, CD90-negative cells, indicating non-BMSCs that did uptake sEV^{Ho}-BMSC.

(C) Flow cytometry analysis of DiI-negative, CD90-positive cells, indicating BMSCs that did not uptake sEV^{Ho}-BMSC.

(D) Flow cytometry analysis of DiI-positive, CD90-positive cells, indicating BMSCs that did uptake sEV^{Ho}-BMSC.

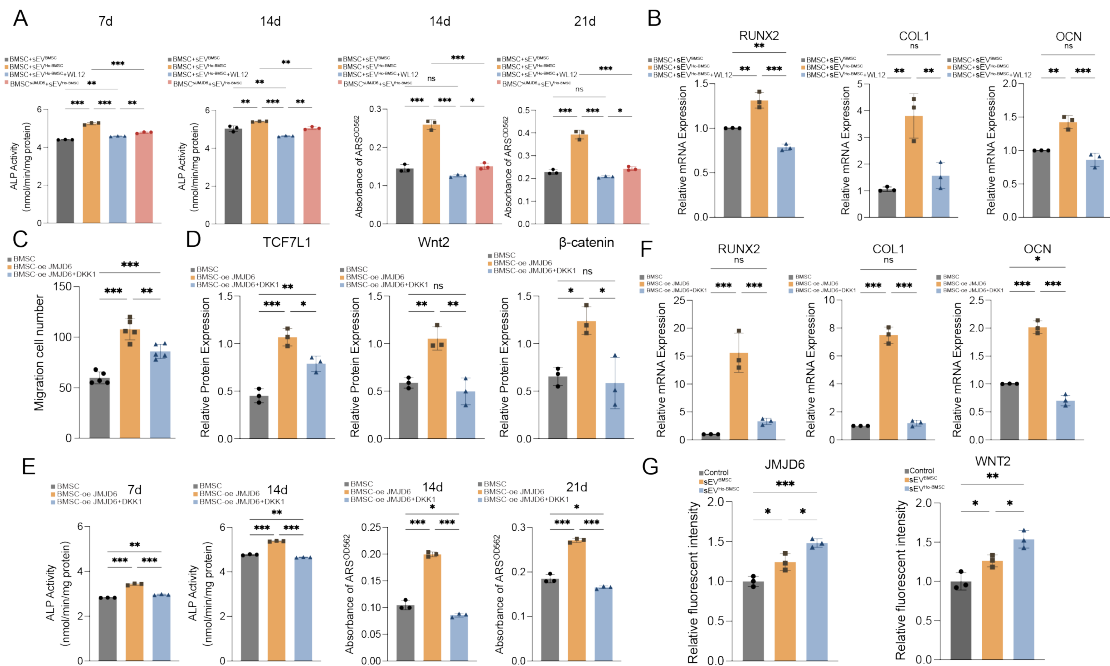


Figure S6. Relative expression of osteogenic markers.

(A) Detection results of ALP activity and mineralization levels in control BMSC, BMSC+seV^{BMSC}, BMSC, BMSC+seV^{BMSC}+WL12, and BMSC+seV^{BMSC}+siJMJD6 after osteogenic induction. Related to Fig 9E.

(B) Relative mRNA expression levels of Runx2, Collagen 1, Ocn gene in control BMSC, BMSC+seV^{BMSC}, and BMSC+seV^{BMSC}+WL12 after osteogenic induction.

(C) Transwell quantitative analysis of control BMSC, BMSC+oeJMJD6, and BMSC+oeJMJD6+DKK1. Related to Fig 9H.

(D) Relative protein expression quantification results of TCF7L1, Wnt2 and β -catenin protein in control BMSC, BMSC+oeJMJD6, and BMSC+oeJMJD6+DKK1. Related to Fig 9J.

(E) Detection results of ALP activity and mineralization levels in control BMSC, BMSC+oeJMJD6, and BMSC+oeJMJD6+DKK1 after osteogenic induction. Related to Fig 9K.

(F) Relative mRNA expression levels of Runx2, Collagen 1, Ocn gene in control BMSC, BMSC+oeJMJD6, and BMSC+oeJMJD6+DKK1 after osteogenic induction.

(G) Quantification results of immunofluorescence staining for JMJD6 and Wnt2 protein localization in rat bone defect models treated with seV^{BMSC} or seV^{BMSC}+BMSC. Related to Fig 9N.

ns $p \geq 0.05$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

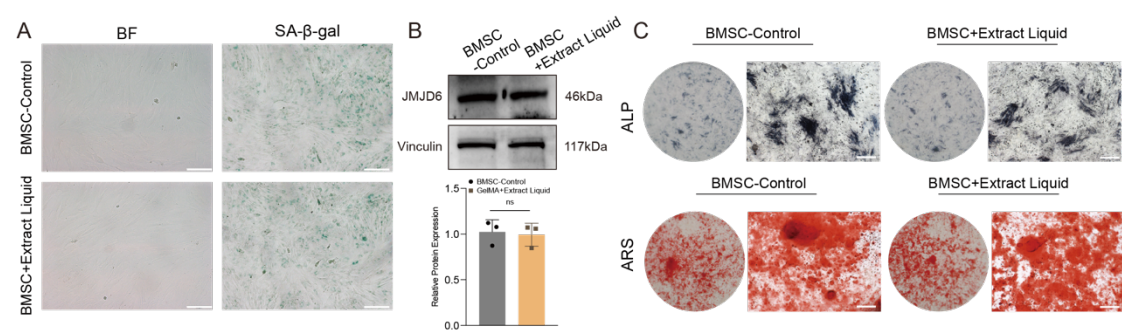


Figure S7. Effects of GelMA hydrogel on BMSCs.

(A) Representative light microscopy and SA-β-gal staining images of BMSCs co-cultured with GelMA hydrogel extracts (BMSC+Extract liquid) and control BMSC (BMSC-Control). Scale bar represents 100 μm.

(B) Relative protein expression levels and quantification results of JMJD6 protein in BMSC+Extract liquid and BMSC-Control.

(C) Representative images of ALP and ARS staining in BMSC+Extract liquid and BMSC-Control after osteogenic induction. Scale bar represents 200 μm.

ns $p \geq 0.05$.

Table S1. Primers used in this study

Gene symbol	Forward sequence (5'- 3')	Reverse sequence (5'- 3')
rGapdh	CAAGTTCAACGGCACAGTCAAGG	ACATACTCAGCACCAGCATCACC
rIL-1 β	TCTCACAGCAGCATCTCGACAAG	CCACGGGCAAGACATAGGTAGC
rIL-6	TGGAGTTCCGTTTCTACCTG	TTCATATTGCCAGTTCTTCG
rP21	ACTTCGGCATCAGTGGACA	AGACATCAGAGCGGACATCA
rP53	CTCCTCCCCCAGCAAAAGA	GTAGACTGGCCCTTCTTGGT
rJmjd6	AGGTGACCCGAGAAGAAGGA	AGGGGTTTGAATTCGGGTGG
rLama-1	GGCAGAAGCATTGGACAGAGACC	ATTCGCCGTCTTGTGAGCATCTG
rCyp19a1	ACCCGAGCCTGTGGAGAACG	GTCACCCAGCCTGTCCAAATGC
rLif	TGTAAATGCCACCTGCGCCATAC	TGCCGTTGAGTTGAGCCAGTTG
rPpar- γ	CTTGACAGGAAAGACAACGG	GCTTCTACGGATCGAAACTG
rC/EBP- α	GACATCAGCGCCTACATCGA	CCCGGGTAGTCAAAGTCACC
rFabp4	TCGTCATCCGGTCAGAGAGT	CACATGTACCAGGACCCAC
rRunx2	TTTCAGACCCCAGGCAGTTC	CGTGTGGTAGTGAGTGGTGG
rOcn	CCTGACTGCATTCTGCCTCT	CCACCTTACTGCCCTCCTG
rColla1	CTGGCAACCTCAAGAAGTCC	CAAGTTCCGGTGTGACTCG
rTcf7l1	CCTTGTGATAGCCCTGCGTC	TCTCCGGTTTGGTGGTGAGT
rWnt2	TGTGTGACAATGTGCCAGGT	TGGTCTCTGTCCAGGGTGTT
r β -catenin	CCGCATGGAGGAGATAGTTG	CAATGGGAGAATAAAGCAACTG
hJMJD6	TTGGACCCGGCACAATACTA	TCTGCCCTTTCCACGTTATCC
hGAPDH	CGGACCAATACGACCAAATCCG	AGCCACATCGCTCAGACACC

Table S2. Antibodies used in this study

Antibody	Host	Supplier	Catalog	Dilution
P21	Mouse	ProteinTech	28248-1-A	1:1000
P53	Rabbit	ProteinTech	10442-1-AP	1:1000
Calnexin	Rabbit	Abcam	ab133615	1:1000
HSP70	Mouse	Abcam	ab181606	1:1000
CD9	Rabbit	Abcam	ab263019	1:1000
CD81	Rabbit	Abcam	ab109201	1:1000
COL1	Mouse	ProteinTech	66761-1-Ig	1:1000
RUNX2	Rabbit	ProteinTech	20700-1-AP	1:1000
OPN	Rabbit	ProteinTech	30200-1-AP	1:1000
JMJD6	Rabbit	ProteinTech	16476-1-AP	1:1000 (WB); 1:50 (IF)
TSG101	Rabbit	Abcam	ab125011	1:1000
TCF7L1	Rabbit	ProteinTech	14519-1-AP	1:1000
WNT2	Rabbit	ProteinTech	27214-1-AP	1:1000 (WB); 1:50 (IF)
β -catenin	Rabbit	ProteinTech	51067-2-AP	1:2000
CD90	Mouse	ProteinTech	66766-1-Ig	1:50
Vinculin	Rabbit	ProteinTech	26520-1-AP	1:3000
GAPDH	Mouse	ProteinTech	60004-1-Ig	1:3000
β -Actin	Rabbit	ProteinTech	81115-1-RR	1:3000