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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☒	☐ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	GraphPad Prism Version 8
Data analysis	GraphPad Prism Version 8. Specimens were designed by CAD software (AutoCAD 2019, Product Version P.45.M.377) and saved as a Stereo Lithography (STL) file for 3D printing. Micro-CT images were analyzed by IMALYTICS Preclinical 2.1. software of the micro-CT. Raw sequencing date were deposited to the Genome Sequence Archive (GSA) database. Single-cell RNA Seq data were analyzed using R package: Seurat 4.3.0; SingleR 1.6.1; monocle 2.20.0; clusterProfiler 4.0.5; babelgene 22.9 and Python package: scvelo 0.1.25; scanpy 1.9.1; sklearn 1.0.2.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The single cell RNA-sequencing data generated in this study have been deposited in the Genome Sequence Archive (GSA) database with accession number CRA018756, which is now publicly available can be accessed from the following link [https://bigd.big.ac.cn/gsa/browse/CRA018756]. All other relevant data supporting the key findings of this study are available within the article and its Supplementary Information files or from the corresponding author upon reasonable request.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The findings in this study were not applied to only one sex or gender, and sex and gender were not considered in the study design.
Reporting on race, ethnicity, or other socially relevant groupings	BMSCs from Human BM aspirates were obtained in The Second Affiliated Hospital of Zhejiang University with written informed consent from orthopedic individuals with femoral fracture (Male, 2 donors, an average age of 37). Human child phalangeal bone tissues were obtained in Children's Hospital of Zhejiang University School of Medicine (Zhejiang University, China) with written informed consent from individuals after polydactyly resection surgery.
Population characteristics	See above
Recruitment	See above
Ethics oversight	Human BM aspirates were obtained in The Second Affiliated Hospital of Zhejiang University School of Medicine (Zhejiang University, China) with written informed consent from orthopedic individuals with femoral fracture (v 1.3, 2016.8.3). All samples were obtained and used according to standard guidelines approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University School of Medicine (Ethics number: 2016-033). Human child phalangeal bone tissues were obtained in Children's Hospital of Zhejiang University School of Medicine (Zhejiang University, China) with written informed consent from individuals after polydactyly resection surgery. Samples were obtained and used according to standard guidelines approved by the ethics committee of Children's Hospital of Zhejiang University (Ethics number: 2020-IRB-007).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We use the minimum number of animals (n≥3), depending on each experiment, necessary to achieve statistical significance. The detailed sample size for each experiment is shown in all the figure legends.
Data exclusions	We exclude animals that unexpectedly become morbid during the course of the experiment.
Replication	All of our findings were replicated and reproduced multiple times (at least three times of experiments were repeated independently). The only exceptions were incidents where animals died prematurely or unexpectedly before the requisite time point for analysis.
Randomization	Animals were allocated randomly into the different experimental group.
Blinding	Different, separate teams of investigators were used to perform procedures while others performed the analysis. Investigators performing analysis were blinded from on the procedure done to each animal to eliminate bias.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

The samples were treated with primary antibodies at 4 °C overnight, including Ki67 (1:250 dilution, ab16667, Abcam, USA), γh2AX (1:250 dilution, ab22551, Abcam, USA), RUNX2 (1:200 dilution, ab76956, Abcam, UK), Collagen I (1:100 dilution, ab260043, Abcam, UK), OCN (1:50 dilution, MAB1419, R&D Systems, USA), NGFR (1:50 dilution, NBP2-67296, NOVUS, USA), CGRP (1:100 dilution, ab81887, Abcam, UK), beta III Tubulin (1:500 dilution, ab18207, Abcam, UK), Collagen X (1:100 dilution, 14-9771-82, Invitrogen, USA), CD31 (1:100 dilution, ab222783, Abcam, UK), CD200 (1:100 dilution, AF2724, R&D Systems, USA), Thy1 (1:200 dilution, ab181469, Abcam, UK), PDGFR alpha (1:250 dilution, ab203491, Abcam, UK), KRT8 (1:100 dilution, ab53280, Abcam, UK), HAS1 (1:250 dilution, PA5-95599, Invitrogen, USA), MSX1 (1:100 dilution, ab93287, Abcam, UK). After incubation with primary antibody, samples were then incubated with Alexa Fluor® secondary antibodies (G-Rabbit Alexa Fluor® 488, A11008; Goat anti mouse Alexa Fluor® 488, A11001; G-Rabbit Alexa Fluor® 546, A21430-f; Donkey-Mouse Alexa Fluor® 405, ab175658) (diluted 1:500) for 1 h at room temperature.

Validation

Antibodies were validated according to manufacture's description.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals

SD rats (~ 250 g, 8~10 weeks old, Male) were used in this study. All surgical procedures were performed under 4% isoflurane anesthesia. Surgical sites were sterilized using iodine solution after hair removal using a clipper.

Wild animals

This study did not involve wild animals.

Reporting on sex

The findings in this study were not applied to only one sex or gender, and sex and gender were not considered in the study design.

Field-collected samples

This study did not involve samples collected from the field.

Ethics oversight

The rats used in this study were fed in separated cages in a temperature, humidity-controlled (~25°C, 50–80%) and 12 h light/dark cycle room. All animals were treated according to standard guidelines approved by the Zhejiang University Ethics Committee (Ethical NO. ZJU20210114).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks

Not applicable.

Novel plant genotypes

Not applicable.

Authentication

Not applicable.