nature portfolio

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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	Raw sequence alignment and annotation was performed in DRAGEN RNA (version 4.4.4) from Illumina BaseSpace
Data analysis	Counts matrix construction, quality control, and normalization was performed in R (version 4.4.0) using the dplyr (v1.1.4) and edgeR (v4.4.0) packages. Model training and testing was performed using the R packages stats (v3.6.2), e1071 (v1.7-16), randomForest (v4.7-1.2), and pROC (v1.19.0.1). Data visualization and presentation used ggplot2 (v4.0.1) and statistical analysis and data presentation used GraphPad Prism 10.6.0.

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

Flow cytometry data was deposited to Flow Repository and is available under Repository ID FR-FCM-Z7CJ [http://flowrepository.org/id/FR-FCM-Z7CJ]. RNAseq data has been deposited to GEO and is available under accession codes GSE267142 [www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE267142], GSE267143

[www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE267143] GSE267144 [www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE267144], and GSE316836 [www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE316836]. The previously published sequencing data [13] used in this work is available via accession number GSE126060 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE126060]. Source Data are provided with this paper.

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	Sex was self-reported (11 male and 11 female patients/donors). Age range was 20-94 and average age was 68. Sex-based analyses were not performed due to the limited sample size.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity or other subgroup based analyses were not performed due to the limited sample size.
Population characteristics	Inclusion Criteria o Ability to read and speak English to allow for written informed consent, phenotyping, and patient reported outcomes measures or the ability to read and speak English to allow for verbal informed consent and patient reported outcome measures; o Willingness to participate in longitudinal follow-up (questionnaires and outcomes measures) for 6-months after their treatment o Primary hip arthroplasty for individuals with both clinical and radiographic findings of OA of the hip; o Burn patients o Kellgren/Lawrence III or IV osteoarthritis confirmed by routine radiographs. Exclusion Criteria o Other non-osteoarthritis diagnoses for total hip arthroplasty (e.g., dysplasia); o Previous hip arthroplasty on the same side; o Planned contralateral hip arthroplasty during the 6-month follow up, as this would influence postoperative pain and functional assessments; o Inability to provide written informed consent or provide verbal informed consent for participating in the patient reported outcome measures only; o Severe physical impairment (e.g., blindness, deafness, paraplegia); o Co-morbid medical conditions that may significantly impair physical functional status (e.g., history of non-skin malignancy, or autoimmune disorder) o Illicit drug or unreported opioid use (unreported opioid use would be considered opioid misuse or abuse and thereby exclusionary); o Medical or psychiatric conditions that in the judgment of study personnel would preclude participation in this study o Pregnant; o Liver failure; o Self-reported liver cirrhosis; o Self-reported hepatitis; o Uncontrolled diabetes' o Severe Cardiovascular disease (examples: history of myocardial infarction, unstable angina, severe coronary artery disease, congestive heart failure, or severe valvular abnormalities) that is self-reported by patient or by medical record.
Recruitment	The University of Texas Southwestern Medical Center, Outpatient Clinic was the primary site for this study. Men and women who are scheduled to undergo primary, unilateral total hip arthroplasty (THA) were recruited from surgical clinics and orthopedic patient workshops at UTSW. Comprehensive written informed consent was obtained by a dedicated study coordinator who was available to the subjects throughout their involvement in this study. The informed consent process was conducted by the study staff and included a verbal and written explanation of the study, including the purpose, testing procedures, time commitment, inclusion/exclusion criteria, risks and benefits, alternative treatments, confidentiality, study personnel contacts, and required regulatory information. All individuals were given the opportunity to ask questions. Once all questions and concerns were addressed to the participant's satisfaction, the participant signed the consent form. Only the subjects signed the consent form. A copy of the signed consent form was provided to the participant for his/her records. Following informed consent, the study participant was assigned an anonymous study identification number.
Ethics oversight	Approval was obtained from The University of Texas Southwestern Medical Center IRB (STU-2020-0552).

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	No sample size calculation was performed.
Data exclusions	No data were excluded from analysis.
Replication	Sequencing was replicated at least using 2 mice each group and independent sequencing runs when available. All attempts at replication gave similar results.
Randomization	Age and sex matched mice were used for different experimental groups.
Blinding	Not relevant for objective measures

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
[ ]	[x] Antibodies
[x]	[ ] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used	chicken anti-GFP (1-200, Aves Labs, GFP-1020), goat anti-dsRed (1-200, LifeSpan Biosciences, LS-C340696), rabbit anti-Aggrecan (1-35, EMD Millipore, AB1031). Secondary antibodies included donkey anti-chicken Alexa Fluor 488 (1-250, Jackson Immunoresearch), donkey anti-rabbit Alexa Fluor 647 (1-250, Jackson Immunoresearch), and donkey anti-goat CF-555 (1-500, Biotium), PDGFRa-SB600 (APA5, Invitrogen), CD90-eFluor450 (Thy-1.1, Invitrogen), CD45-BUV395 (30-F11, BD), Ter119-BUV395 (Ter-119, BD)
Validation	All antibodies used are commercially available and validated by the manufacturers.

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	Gli1creERT mice (JAX:007913), Adiponectin-cre mice (JAX:028020), Rosa-LSL-tdTomato mice (JAX:007909), Col1a1(2.3kB)-GFP mice (JAX:013134), C57B6 mice, 8–12-week-old
Wild animals	The study did not involve wild animals.
Reporting on sex	8–12-week-old, randomized male and female mice were used in all experiments. Sex was not considered in the study design.
Field-collected samples	The study did not involve field-collected samples.
Ethics oversight	All mice studies were reviewed and approved by the University of Texas Southwestern Medical School Institutional Animal Care and Use Committee (Protocol 2020-102949).

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

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

Flow Cytometry

Plots

Confirm that:

☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	The sample preparation and biological source of the cells is described in the manuscript.
Instrument	SORP 5 Laser BD FACSAria Fusion Cell Sorter, BSL2+ Bio-hood (BD Biosciences)
Software	Flow cytometry data was analyzed using FCS Express 7 software.
Cell population abundance	Cell sorting via Flow Cytometry was not performed.
Gating strategy	The gating strategies are described in the manuscript Supplementary Figure 1 and Methods. Unstained control cells and compensation beads were used for performing compensation. We used PDGFRa+CD90+ MPCs isolated from bone tissue using previously established protocols56, 57 and PBMCs for determining the gating strategy. For transgenic mouse experiments, we also used Gli1CreERT2-tdTomato+ control cells isolated from periosteum as compensation controls and for determining gates.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.