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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	Data were collected using a Fortessa (BD biosciences) for flow cytometry experiments, a BD™FACSAria III cell sorter for cell sorting experiments,, a Zeiss LSM 800 with Airyscan for confocal microscopy images, an Agilent AriaMx Real-Time PCR system for qPCR, an Illumina Nextseq 500 for RNA sequencing, and HPLC-MS was performed using an Agilent 6546 Accurate-Mass Q-ToF/1260 series HPLC instrument.
Data analysis	Statistical testing for flow cytometry and functional assays was performed using GraphPad Prism version 9. RNA sequencing data was analyzed in R version 4.1.1 using Seurat version 4.0. HPLC-MS data was analyzed in Agilent Mass Hunter Workstation Software (version B.07.00) and using automated peak-picking algorithms by R (version 3.4.2) package XCMS.

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.

April 2023

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

Source data are provided with this paper. Raw lipidomic data is available on Zenodo at: https://zenodo.org/records/13284701. The FASTQ files for all synovial single-cell and bulk RNA sequencing data generated in this study have been deposited in the dbGAP database under accession number phs003304.v1.p1. FASTQ data is available under restricted access due to NIH guidelines on human genomic data. Access can be obtained by a permanent senior scientific scientist at an institution by submitting a data access request to dbGAP through the eRA commons. The raw FASTQ data is protected and is not available due to data privacy laws. dbGAP will determine how long access will be granted. This data falls under the health/medical/biomedical data use limitation. The raw, sanitized FASTQ files for adipose tissue single-cell RNA sequencing generated in this study have been deposited in the GEO database under accession number GSE233500. The processed count data for synovial and adipose single-cell and bulk RNA sequencing count matrices generated in this study have been deposited in the GEO database under super series number GSE233504. Within this super series, Adipose single cell RNA sequencing is available under accession number GSE233500, fibroblast bulk RNA sequencing is available at GSE233501, and synovium single cell RNA sequencing is available at GSE233502. The flow, qPCR, mouse measurements, and all other data generated in this study are provided in the Supplementary Information/Source Data file. The results published here are in whole or in part based on data obtained from the ARK Portal (arkportal.synapse.org).
Code to reproduce analyses is available on Zenodo available at: Adipocyte associated glucocorticoid signaling regulates normal fibroblast function which is lost in inflammatory arthritis (zenodo.org)

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 not involved in the study design. We did not perform analyses comparing sex since the study was not designed or powered to assess sex differences. The sex of each donor is supplied in the supplementary data. Eight males and eight female synovial tissues were sequenced, and three females and two male adipose tissues were sequenced. Sex was based on self-reporting. Consent has been given for sharing individual level data for all data except for donors in table 1, cohort 2. These specimens were collected at BWH autopsy department and have had identifiers removed.
Reporting on race, ethnicity, or other socially relevant groupings	Race was reported in aggregate for the samples and was not considered in study design. Information on ethnicity was not collected. The detailed population characteristics of the healthy synovial cohort and adipose patient are described in full in supplementary tables 1 and 2. Race and ethnicity of RA and OA synovial tissues were not collected (see referenced publication in the text for detailed information of n these datasets).
Population characteristics	The healthy human synovial cohort population characteristics are listed in table 1, and the adipose tissue cohort population characteristics are listed in table 2. Healthy synovial patients all had no history of arthritis, autoimmune disease, or recorded traumatic injury to the knee. The adipose tissue cohort were all obese but did not have any (or only one) health event considered to be metabolically unhealthy (as defined in supplementary Table 2). The patient characteristics for the AMP phase 2 RA and OA data, and the remission synovium, are listed in the referenced publications. Briefly, the RA and OA patients were similar to each other in age, sex, disease activity, and other clinical parameters. Detailed population characteristics are in supplementary table 1 of the cited manuscript, "Deconstruction of rheumatoid arthritis synovium defines inflammatory subtypes," Nature 2023, Zhang et al. For remission samples, all three samples were female and ranged from age 42 to 66. All had similar disease activity. Detailed population characteristics are in supplementary table 4 of the cited manuscript, “Distinct synovial tissue macrophage subsets regulate inflammation and remission in rheumatoid arthritis” in Nature Medicine 2020, Alivernini et al.
Recruitment	Patients were recruited post-mortem and selected based on biological parameters described in the methods.
Ethics oversight	The institutional review board (IRB) committee at Brigham and Women's Hospital approved the sample collection.

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	Sample size was chosen based on preliminary studies which informed us of the effect size and enabled us to either increase or maintain the tested sample size in subsequent experiments.
Data exclusions	No data was excluded.
Replication	In vitro experiments were typically performed multiple times with consistent findings. Human studies which could not be repeated were supported by mouse experiments when possible.
Randomization	All mice were given the same treatment. Littermate controls were used. No mice were excluded from the study.
Blinding	Investigators were single blinded while performing injections and while measuring joints in in vivo mouse experiments.

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	Flow cytometry: Human: CD45 in APC-Cyaine7 (2D1, Biolegend, cat. No. 368516), CD31 in AF700 (WM59, Biolegend, cat. No. 303133), CD90 in BV421 (5E10, BD Biosciences, cat. No. 562556), podoplanin in PE (NC-08, Biolegend, cat. No. 337003), CD146 in BV510 (P1H12, Biolegend, cat. No. 361021), CD14 in PE-Cyanine7 (63D3, Biolegend, cat. No. 367111), and CD3 in APC (Biolegend, cat. No. 317317), fixable viability dye (UV455, eBioscience, cat. No. 65-0868-14), Fc block (Biolegend, cat no 422301), HCS LipidTOX (ThermoFisher, H34475). Mouse: CD31 in BV785 (Biolegend, cat. No. 102435), CD146 in PerCP/Cyanine 5.5 (Biolegend, cat. No. 134709, CD55 in APC (Biolegend, 131811), Pdgfra in BV421 (Biolegend, cat. No. 135923), CD45 in AF700 (Clone I3/2.3, Biolegend,147715), CD3 in FITC (Clone 17A2, Biolegend,100204), F4/80 in APC-cy7 (Clone BM8, ThermoFisher, 47-4801-82), CD4 in BV605 (Clone RM4-5, Biolegend,100548), CD8 in BV711 (Clone SK1, Biolegend,100759), PDPN in PE-Cyanine7 (eBioscience, cat. No. 25-5381-82), Fc block (Biolegend, cat no 101319). Immunofluorescence: The following anti-human primary antibodies were applied: PDPN (eBioscience, 16-9381-81), PRG4 (Millipore Sigma, MABT401), PLIN2 (Thermo Fisher, 15294-1-AP), CD45 (Thermo Fisher, A304-376A-T), or COL1A1 (R&D Systems, AF6220). Anti-mouse antibodies: PDPN (eBioscience, clone eBio8.1.1, cat. No. 14-5381-82), PDGFRA (R&D Systems, polyclonal Goat IgG, cat. No. AF1062-SP), or Cadherin 11 (clone 23C6, mouse anti-mouse). Secondary antibodies: donkey anti–rat AF488, 712-545-153; donkey anti–rabbit AF647, 711-605-152; donkey anti-mouse Cy3, 715-165-150; donkey anti-goat AF647 cat. No. 705-605-003; goat anti-syrian hamster Cy3 cat. No. 107-165-142; donkey anti-mouse AF488 cat. No. 715-545-150; all from Jackson Immunoresearch,).
Validation	Flow cytometry and immunofluorescence antibodies were tested in tissues known to contain the cell populations targeted by each antibody, and cell proportions quantified by flow cytometry were validated by other methods (histology, single cell RNA sequencing) to validate their accuracy.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Human visceral pre-adipocytes were purchased from Lonza (PT-5005). The sex of cultured human fibroblast lines generated in-house were not recorded and are unknown.
Authentication	Pre-adipocytes were able to be differentiated to adipocytes as assessed visually by accumulation of lipid droplets and by qPCR for expression of Adiponectin, which is only expressed by mature adipocytes. These ensured that this was in fact a preadipocyte cell line.

Mycoplasma contamination	The cell lines were not tested for mycoplasma.
Commonly misidentified lines (See ICLAC register)	N/A

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	Mice were used between the ages of 9-12 weeks old. B6N.Cg-Tg(Pdgfra-cre/ERT)467Dbe/J, B6.Cg-Nr3c1tm1.1Jda/J mice, C57BL/6-Gt(ROSA)26Sortm1(HBEGF)Awai/J (iDTR) and B6;FVB-Tg(Adipoq-cre)1Evdr/J (ADIPOQ-cre) mice were utilized. Sex was considered in the study design. We used close to equal numbers of male and female mice across conditions to avoid sex-driven effects. Sex was not considered in the analysis as we were not sufficiently powered to study sex effects. For Nr3c1 knockout experiments, 9 male and 8 female genotype control mice were used, and 9 male and 9 female Pdgfra-CreER+ Nr3c1 fl/fl mice were used. For inducible adipocyte depletion experiments, 6 genotype control and 7 iDTR; Adipoq-Cre mice were utilized.
Wild animals	The study did not involve wild animals.
Reporting on sex	The findings apply to both male and female mice. Transgenic and control littermates were sex-matched during the study. Sample size was not large enough to perform sex-based analysis.
Field-collected samples	The study did nat involve samples collected from the field.
Ethics oversight	The institutional animal care and use committee (IACUC) at Brigham and Women's Hospital approved the animal work in this study under protocol number 2016N000519.

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	Human synovial tissue from healthy, OA, or RA patients was digested and cells strained through a 70 micron mesh before staining. Murine synovial tissue was digested and cells strained through a 70 micron mesh before staining.
Instrument	BD LSR fortessa cell analyzer, model number 647800L6
Software	FlowJo v10.8.1 was used to analyze the data.
Cell population abundance	Post-sort purity was above 90% as determined by flow cytometry.

Gating strategy

Events were gated to exclude debris falling in the lower left corner of the FSC vs SSC plot, and fibroblsts were defined as live, CD31- CD146- CD45- cells. Positive and negative gates were determined by visual inspection of the flow plots.

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