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Corresponding author(s): Pinpin Wang, Jianchao Gui, Changshun Ruan

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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	Bibliometric data were collected from the citexs website (https:// www.citexs.com/). Gross images were collected from a bright-field microscope (OLYMPUS, IX73). Flow cytometry data were collected from a flow cytometer(Beckman, CytoFLEX S). Absorbance data were collected from microplate reader (Thermo Fisher Scientific, Multiskan GO). Data of characterization of exosomes were collected from TEM (FEI, Tecnai G2 12) and NTA (NanoFCM, N30E). Fluorescence image data of cells were collected from confocal laser scanning microscope (CLSM, Leica, SP8) and (Nikon, C2). qPCR data were collected from a qTOWER instrument (Analytik Jena GmbH). The rheological data were collected using a rotational rheometer (Anton Paar, MCR302). The fluorescence image data in vivo were collected using the IVIS (Caliper, IVIS Spectrum). Histological image data were collected from a digital pathology scanner (Leica, Aperio CS2). Public transcriptome datasets were collected from the GEO database (https://www.ncbi.nlm.nih.gov/geo/).
Data analysis	Microscopic images were analyzed by using ImageJ. Statistical data analyses were performed using GraphPadPrism 8. μCT data were analyses by SCANCO MEDICAL, Mimics and 3-Matic software. Sequence data were analyses using R.

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

Provide your data availability statement here.

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	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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	n =3 independent samples for Figure 1b, 2b-f, 3c-g, 4e, 6b, 6f, 6g. n =4 independent samples for Figure 1e, 1f, 4f, 4g, 4i-k, 5g. In Figure 6h, for GSE114007, n = 18 for normal samples, and n = 20 for OA samples; for GSE117999, n = 100 for normal and OA samples.
Data exclusions	No data was excluded from the analyses.
Replication	We performed each experiment for a minimum of three times.
Randomization	For in vivo and in vitro studies, samples were randomly allocated to different experimental groups.
Blinding	The OARSI and synovitis score were conducted in a blinded manner.

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

FITC-conjugated CD29 (102205, BioLegend), BV421-conjugated CD90 (202529, BioLegend), PE-conjugated CD45 (202207, BioLegend), APC-conjugated CD11b (562102, BD Pharmingen), FITC-conjugated CD68 (MA528262, Thermo Fisher Scientific), FITC-conjugated IgG Isotype Ctrl (400905, BioLegend), BV421-conjugated IgG1, κ Isotype Ctrl (400158, BioLegend), PE-conjugated IgG1, κ Isotype Ctrl (981804, BioLegend), APC-conjugated IgA, κ Isotype Ctrl (562140, BD Pharmingen), FITC-conjugated IgG1 Isotype Ctrl (MA518096, Thermo Fisher Scientific), CD63 (PA5-92370, Thermo Fisher Scientific), TSG101 (AV38773, Merck), CALNEXIN (NB100-1965, Novus Biologicals), iNOS (18985-1-AP, Proteintech), ARG-1 (66129-1-Ig, Proteintech), SOX-9 (ET1611-56, HuaBio), BCL-2 (ET1702-53, HuaBio), CD86 (13395-1-AP, Proteintech), CD206 (18704-1-AP, Proteintech), NOTCH-3 (TA7548S, Abmart), NRP-1 (ET1609-69, HuaBio), BRCA-1 (22362-1-AP, Proteintech), β-actin (66009-1-Ig, Proteintech), HRP-conjugated Goat Anti-Mouse IgG (SA00001-1, Proteintech), HRP-conjugated Goat Anti-Rabbit IgG (SA00001-2, Proteintech), Cleaved Caspase-3 (9661S, Cell Signaling Technology), CD86 (942-MSM2-P1ABX, Thermo Fisher Scientific), CD206 (ab64693, Abcam), Goat Anti-Mouse IgG (Alexa Fluor 488) (ab150117, Abcam), Goat Anti-Rabbit IgG (Alexa Fluor 555) (ab150086, Abcam), Collagen II (ab34712, Abcam), Goat Anti-Rabbit IgG (HRP) (ab97080, Abcam).

Validation

FITC-conjugated CD29 (102205, BioLegend, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

BV421-conjugated CD90 (202529, BioLegend, 5 μl per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

PE-conjugated CD45 (202207, BioLegend, 0.25 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

APC-conjugated CD11b (562102, BD Pharmingen, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

FITC-conjugated CD68 (MA528262, Thermo Fisher Scientific, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

FITC-conjugated IgG Isotype Ctrl (400905, BioLegend, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

BV421-conjugated IgG1, κ Isotype Ctrl (400158, BioLegend, 5 μl per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

PE-conjugated IgG1, κ Isotype Ctrl (981804, BioLegend, 0.25 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

APC-conjugated IgA, κ Isotype Ctrl (562140, BD Pharmingen, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

FITC-conjugated IgG1 Isotype Ctrl (MA518096, Thermo Fisher Scientific, 1 μg per 10^6 cells for FC), was validated for rat samples, validation information can be found on the manufacturer's website.

CD63 (PA5-92370, Thermo Fisher Scientific, 1/200 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

TSG101 (AV38773, Merck, 1/500 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

CALNEXIN (NB100-1965, Novus Biologicals, 1/500 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

iNOS (18985-1-AP, Proteintech, 1/1000 for WB and 1/200 for IF), was validated for rat samples, validation information can be found on the manufacturer's website.

ARG-1 (66129-1-Ig, Proteintech, 1/10000 for WB and 1/800 for IF), was validated for rat samples, validation information can be found on the manufacturer's website.

SOX-9 (ET1611-56, HuaBio, 1/10000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

BCL-2 (ET1702-53, HuaBio, 1/10000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

CD86 (13395-1-AP, Proteintech, 1/2000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

CD206 (18704-1-AP, Proteintech, 1/1000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

NOTCH-3 (TA7548S, Abmart, 1/1000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

NRP-1 (ET1609-69, HuaBio, 1/2000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.

BRCA-1 (22362-1-AP, Proteintech, 1/2000 for WB), was validated for rat samples, validation information can be found on the

manufacturer's website.
β-actin (66009-1-Ig, Proteintech, 1/50000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.
HRP-conjugated Goat Anti-Mouse IgG (SA00001-1, Proteintech, 1/5000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.
HRP-conjugated Goat Anti-Rabbit IgG (SA00001-2, Proteintech, 1/5000 for WB), was validated for rat samples, validation information can be found on the manufacturer's website.
Cleaved Caspase-3 (9661S, Cell Signaling Technology, 1/400 for IF), was validated for rat samples, validation information can be found on the manufacturer's website.
CD86 (942-MSM2-P1ABX, Thermo Fisher Scientific, 2-4 μg/mL for IF), was validated for rat samples, validation information can be found on the manufacturer's website.
CD206 (ab64693, Abcam, 1 μg/mL for IF), was validated for rat samples, validation information can be found on the manufacturer's website.
Goat Anti-Mouse IgG (Alexa Fluor 488) (ab150117, Abcam, 1/500 for IF), was validated for rat samples, validation information can be found on the manufacturer's website.
Goat Anti-Rabbit IgG (Alexa Fluor 555) (ab150086, Abcam, 1/500 for IF), was validated for rat samples, validation information can be found on the manufacturer's website.
Collagen II (ab34712, Abcam, 1/200 for IHC-P), was validated for rat samples, validation information can be found on the manufacturer's website.
Goat Anti-Rabbit IgG (HRP) (ab97080, Abcam, 1/1000 for IHC-P), was validated for rat samples, validation information can be found on the manufacturer's website.

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 (1-week old, 8-week old) were purchased from Guangzhou Vital River Laboratory Animal Technology Co., Ltd. For CPCs and BMSCs extraction, the 1-week old rats were sacrificed once received; For OA test, the 8-week rats were housed under a 12/12h light/dark cycle, 24-26 °C, and 60% humidity. Anesthesia was performed with 5% isoflurane and 02. Animals were placed on a 37 °C warm heating pad, isoflurane was lowered to 2 to 2.5% to maintain anesthesia during the entire surgery, After wound closure, animals were injected with 8 U/ml penicillin and transferred back into their cage. Animals were euthanized by CO2 asphyxiation at the end of the experiment.
Wild animals	The study didn't involve wild animals.
Reporting on sex	For the in vivo OA experiment, male SD rats were used according to previous reports: ① A small molecule promotes cartilage extracellular matrix generation and inhibits osteoarthritis development. Nat Commun 10, 1914 (2019).② Cholesterol-induced LRP3 downregulation promotes cartilage degeneration in osteoarthritis by targeting Syndecan-4. Nat Commun 13, 7139 (2022). For primary cell extraction male and female rats were randomly used.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	The animal experiments were approved by the Institutional Animal Care and Use Committee of Shenzhen Institute of Advanced Technology, Chinese Academy of Science.

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

Plants

Seed stocks	n/a
Novel plant genotypes	n/a
Authentication	n/a

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	After centrifugation at 500 × g for 5 min, the cells were resuspended with PBS (100 μg per 10^6 cells). For live-dead gating, Fixable Viability Stain 780 was applied to cell suspension (1:1000) and incubated for 15 minutes at room temperature in dark. After PBS washes twice, cell surface staining was performed in PBS with antibodies mixture and incubated for 30 min in dark at 4°C. Next, wash cells twice with PBS. Finally, the cells were suspended with 200ul PBS for detection. The antibodies in this study were: FITC-conjugated CD29 (102205, BioLegend), BV421-conjugated CD90 (202529, BioLegend), PE-conjugated CD45 (202207, BioLegend), APC-conjugated CD11b (562102, BD Pharmingen), FITC-conjugated CD68 (MA528262, Thermo Fisher Scientific), FITC-conjugated IgG Isotype Ctrl (400905, BioLegend), BV421-conjugated IgG1, κ Isotype Ctrl (400158, BioLegend), PE-conjugated IgG1, κ Isotype Ctrl (981804, BioLegend), APC-conjugated IgA, κ Isotype Ctrl (562140, BD Pharmingen), FITC-conjugated IgG1 Isotype Ctrl (MA518096, Thermo Fisher Scientific).
Instrument	Flow cytometer(Beckman, CytoFLEX S).
Software	CytExpert 2.4.
Cell population abundance	Frequencies of each cell population are displayed in all flow cytometry dot plots in main and supplementary Figures.
Gating strategy	Facs gating strategy based on doublet cells and dead cells exclusion. Isotype controls were used as negative controls.

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