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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	N/A
Data analysis	GraphPad Prism 9.0, ImageJ software.

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

Data supporting the findings of this study are available from the corresponding authors 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	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	The sample sizes for this study were selected based on established standards from previous publications and are consistent with those commonly used in the field to achieve statistical significance in key comparisons. All sample sizes are reported in the manuscript.
Data exclusions	No data or samples were excluded from the analyses, except for instances of technical errors or assay failure, which were pre-defined as exclusion criteria. All collected data that met the inclusion criteria were included in the final statistical evaluation.
Replication	In vivo animal studies were conducted with six biological replicates (n=6). In vitro cellular experiments were independently repeated at least three times.
Randomization	To minimize allocation bias, animal subjects were randomly assigned to experimental groups following a randomization schedule. Similarly, treatment conditions for in vitro cell-based assays were randomly assigned to culture wells across multiple plates.
Blinding	Histopathological and immunohistochemical analyses were conducted by blinded observers. Specifically, OARSI scores were assessed by three independent researchers, and the rate of positive cells was quantified by three pathologists, all blinded to the experimental groups.

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 following primary antibodies were used for the respective assays. For immunofluorescence (IF) staining: type II collagen (Col2, 1:100, Proteintech) and matrix metalloproteinase 13 (MMP13, 1:100, Proteintech). For immunohistochemistry (IHC): IRAK4 (1:100, Abclonal), Col2 (1:100, Proteintech), MMP13 (1:100, Proteintech), p21 (1:50, Signalway Antibody), and iNOS (1:50, Proteintech). For western blotting, a comprehensive list of antibodies was employed, including IRAK4 (1:2000, Abclonal), Col2 (1:2000, abcam), MMP13 (1:2500, Abclonal), iNOS (1:5000, Proteintech), COX-2 (1:1000, Servicebio), TNF-α (1:2000, Proteintech), p16 (1:2000, BOSTER), p21 (1:2000, Signalway Antibody), OPA1 (1:2000, Affinity), Mfn2 (1:5000, Proteintech), p-Drp1 (1:1000, abcam), Drp1 (1:1000, abcam), Fis1 (1:2000, Proteintech), TRAF6 (1:1000, Abclonal), TAK1 (1:2000, Abclonal), p-IKKα (1:1000, Cell Signaling Technology), IKKα (1:2000, Proteintech), p-IκBα (1:1000, abcam), IκBα (1:2000, Abclonal), p-p65 (1:2000, Abclonal), p65 (1:5000, Proteintech), METTL3 (1:2000, Abclonal), p-ERK (1:2000, Servicebio), ERK (1:2000, Proteintech), p-JNK (1:2000, Affinity), JNK (1:10000, Proteintech), p-p38 (1:1000, Abclonal), p38 (1:2000, Abclonal), NOX2 (1:2000, Zen-Bio), and GAPDH (1:10000, Proteintech).
Validation	All antibodies used in this study were commercially obtained and well-validated. Detailed data can be found on the manufacturers' websites.

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	Primary chondrocytes were isolated from 5-day-old Sprague-Dawley (SD) rat pups. For the in vivo osteoarthritis (OA) model, eight-week-old male SD rats were used.
Wild animals	This study did not involve wild animals.
Reporting on sex	For the isolation of primary chondrocytes, neonatal rat pups were used without sex distinction. For the osteoarthritis (OA) model, exclusively male rats were utilized.
Field-collected samples	This study did not involve field-collected animal samples.
Ethics oversight	All animal procedures were approved by the Animal Ethics Committee of Renmin Hospital of Wuhan University (Approval No. 20220603A) and were conducted in accordance with the Guide for the Care and Use of Laboratory Animals issued by the National Research Council.

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	The apoptosis of chondrocytes was assessed by flow cytometry using an Annexin V-FITC Apoptosis Detection Kit (Solarbio, Beijing, China) according to the manufacturer's protocol. Chondrocytes were seeded in 6-well plates and exposed to different designated interventions.

	Post-treatment, cells were trypsinized, washed twice with PBS, and resuspended in PBS to generate a single-cell suspension. For apoptosis assessment, 500 µL of the suspension was aliquoted into a flow cytometry tube, stained with 5 µL Annexin V-FITC (gentle mixing), followed by addition of 10 µL propidium iodide (PI) solution. After 15-min incubation at room temperature in the dark, samples immediately underwent flow cytometric analysis.
Instrument	Beckman CytoFLEX flow cytometer
Software	FlowJo (v10) software was used to analyze the flow cytometry data.
Cell population abundance	The cell population abundance was within the normal range. The sample size was sufficient to ensure the statistical significance of the test results.
Gating strategy	The entire cell population was displayed and analyzed using forward scatter (FSC) and side scatter (SSC) parameters. A gate was set on the FSC vs. SSC plot to select the main population of intact cells while excluding debris and doublets, as determined from the scatter profiles of uncoated controls.

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