

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	no software used
Data analysis	GraphPad Prism 7.0.

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](#)

Data sources are provided for all main figures. Data supporting supplementary figures of this study are available from the corresponding authors on 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	sex ratio was reported
Reporting on race, ethnicity, or other socially relevant groupings	not described
Population characteristics	age, synovial fluids characteristics
Recruitment	rheumatology department of Lariboisière hospital, out patients and/or hospitalization
Ethics oversight	French national ethical committee Comité de protection des personnes participant à la recherche (DC 2020-3976)

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](https://www.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	in vivo, air pouch model : at least 7 mice per group
Data exclusions	only outliers when Grubbs confirmed
Replication	in vitro : at least 3 independent experiments
Randomization	mice were randomly assigned to receive tested drug or placebo
Blinding	no

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	anti-F4/80-APC (clone REA126; Miltenyi Biotechnology) and anti-Ly6G-PE (clone REA526; Miltenyi Biotechnology) Anti-LRRC8A antibody (Sigma SAB2108060) IL-1 β (Santa Cruz Biotechnology, sc-7884); LRRC8A (Sigma, HPA016811); Apoptosis-associated Speck-like protein containing a caspase activation and recruitment domain (CARD) (ASC; Santa Cruz Biotechnology, sc-22514-R); NLRP3 (Adipogen, AG-20B-0014); tubulin (DSHB clone 12G10); and GAPDH (Cell Signaling, 3683)
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Validation

Renaudin F, 2020, Ann Rheum Dis
Compan V, 2012, immunity

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	THP-1-Lucia NF-κB Cells, Invivogen
Authentication	antibiotic selection
Mycoplasma contamination	no
Commonly misidentified lines (See ICLAC register)	no

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	8-week-old wild-type (WT) C57Bl/6J mice, Janvier Lab 8-week-old Cx3cr1CreERT2/Lrrc8Aflox/flox C57Bl/6J mice
Wild animals	Mice were killed after experiments
Reporting on sex	male
Field-collected samples	air pouch liquid, air pouch membranes
Ethics oversight	French national ethical committee Le comité d'éthique en expérimentation animale Lariboisière/Villemin n°9 (APAFIS#28637)

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

Plants

Seed stocks	<i>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.</i>
Novel plant genotypes	<i>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.</i>
Authentication	<i>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, mosaicism, off-target gene editing) were examined.</i>

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	0.1 million cells in PBS
Instrument	BD FACS Canto II cytometer
Software	BD FACS

Cell population abundance

0.1 million

Gating strategy

For neutrophils (Ly6G) : non specific signal IgG-PE vs Ly6G-PE
For macrophages (F4/80) : non specific signal IgG-APC vs F4/80-APC
For expression of LRRC8-FITC : non specific signal IgG-FITC vs LRRC8-FITC

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