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.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

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

Roscovitine loading and its release from nanoparticles were determined using the Agilent 1260 Infinity II HPLC (Agilent).
Flow cytometry was conducted using the FACSCanto II system (BD Biosciences).
Immunofluorescent images were acquired using the Stellaris 8 confocal microscope (LEICA).
Nanoparticle hydrodynamic diameter, PDI, and zeta potential were determined using the Zetasizer Nano ZS (Malvern).
SEM images were obtained using the JSM-7800F Prime(JEOL) FE-SEM.
TEM images were obtained using the JEM-F200 (JEOL) FE-TEM.
Real-time PCR data were obtained using the StepOnePlus Real-Time PCR System (Applied Biosystems).
In vivo fluorescence of major organs was obtained using the IVIS Spectrum In Vivo Imaging System (PerkinElmer).
Blood biochemistries were measured using the DR-CHEM 350SS 19 (Fujifilm) and Hemavet 950 (Drew Scientific)
Echocardiography was recorded using a transthoracic echocardiography system equipped with a 15MHz L15-7io linear transducer (Affniti 50G, Philips).
Left ventricular pressure-volume parameters were recorded using a PV conductance system (MPVS Ultra, EMKA Technologies) coupled to a digital converter (PowerLab 16/35, ADInstruments).

Data analysis

Flow cytometry data were analyzed using FlowJo_V10 software (Tree Star).
Confocal microscopy images were processed using LAS X software (LEICA) and quantified using Caseviewer, Image J software v1.51. Fluorescence of major organs were analyzed using Living Image software v1.51.
Histological images were also analyzed using CaseViewer, Image J v1.51.
Global circumferential strain data was analyzed using EchoPAV v204 software (GE).
All statistical analyses and figure preparation were conducted with Graphpad PRISM version 10.2.1.
Data analyses was assisted with Microsoft Excel (Microsoft Office 2019).

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

All data supporting the findings of this study are available in the Article, Supplementary Information, and Source Data file. Additional requests for information can also be made available from the corresponding author upon reasonable request. 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	This study did not involve human participants, their data, or their biological material.
Reporting on race, ethnicity, or other socially relevant groupings	This study did not involve human participants, their data, or their biological material.
Population characteristics	This study did not involve human participants, their data, or their biological material.
Recruitment	This study did not involve human participants, their data, or their biological material.
Ethics oversight	This study did not involve human participants, their data, or their biological material.

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 sizes were determined by 'Mead's resource equation', which is widely used to estimate the sample size of laboratory animals for sufficient statistical power. Sample sizes are stated in the figure caption for each experiment. Reference : Hubrecht, Robert C., and James Kirkwood, eds. The UFAW handbook on the care and management of laboratory and other research animals. John Wiley & Sons, 2010. At least three samples per group were used for all experiments.
Data exclusions	No data were excluded from analyses.
Replication	In almost all cases, experiments were repeated to validate results and conclusions. In some cases, a single replicate is reported for simplicity (such as FACS dot plots). Results were found to be similar and repeatable across two to three independent studies.
Randomization	Alternating group randomization was conducted during the operational window for all in vivo experiments. No randomization was conducted during in vitro cell culture experiments to facilitate proper data completion and because locations of wells in well plates are unlikely to affect results.
Blinding	Operators were blinded to groups during acquisition and quantification of all image-based assays.

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This study did not involve behavioural or social sciences.
Research sample	This study did not involve behavioural or social sciences.
Sampling strategy	This study did not involve behavioural or social sciences.
Data collection	This study did not involve behavioural or social sciences.
Timing	This study did not involve behavioural or social sciences.
Data exclusions	This study did not involve behavioural or social sciences.
Non-participation	This study did not involve behavioural or social sciences.
Randomization	This study did not involve behavioural or social sciences.

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This study did not involve ecological, evolutionary or environmental sciences.
Research sample	This study did not involve ecological, evolutionary or environmental sciences.
Sampling strategy	This study did not involve ecological, evolutionary or environmental sciences.
Data collection	This study did not involve ecological, evolutionary or environmental sciences.
Timing and spatial scale	This study did not involve ecological, evolutionary or environmental sciences.
Data exclusions	This study did not involve ecological, evolutionary or environmental sciences.
Reproducibility	This study did not involve ecological, evolutionary or environmental sciences.
Randomization	This study did not involve ecological, evolutionary or environmental sciences.
Blinding	This study did not involve ecological, evolutionary or environmental sciences.

Did the study involve field work? ☐ Yes ☒ No

Field work, collection and transport

Field conditions	This study did not involve any field work.
Location	This study did not involve any field work.
Access & import/export	This study did not involve any field work.
Disturbance	This study did not involve any field work.

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

We report the use of the following antibodies in this study:
anti-mouse/human CD11b antibody (Clone: M1/70, Biolegend, 1:200, FITC and PE/Cy7)
anti-mouse Ly6G antibody (Clone: 1A8, Biolegend, 1:200, APC/Cy7)
anti-mouse F4/80 antibody (Clone: BM8, Biolegend, 1:200, APC)
anti-mouse CD80 antibody (Clone: 16-10A1, Biolegend, 1:200, PE)
anti-mouse CD86 antibody (Clone: GL-1, Biolegend, 1:200, PE-Cy7)
anti-mouse CD45 antibody (Clone: 30-F11, Biolegend, 1:200, Alexa Fluor 647)
anti-mouse Ly6C antibody (Clone: HK1.4, Biolegend, 1:200, PE)
anti-rat CD45 antibody (Clone: OX-1, Biolegend, 1:100, Pacific Blue)
anti-rat CD43 antibody (Clone: W3/13, Biolegend, 1:100, PE)
anti-rat CD161 antibody (Clone: 3.2.3, Biolegend, 1:100, PE-Cy7)
anti-rat CD3 antibody (Clone: 1F4, Biolegend, 1:100, PE)
anti-rat His48 antibody (Clone: HIS48, Invitrogen, 1:100, FITC)
anti-rat CD43 antibody (Clone: W3/13HLK, Invitrogen, 1:100, PE)
anti-rat B220 antibody (Clone: HIS24, Invitrogen, 1:100, PE-Cy7)
anti-rat CD68 antibody (Clone: QA20A71, Biolegend, 1:100, PE)
anti-rat CD86 antibody (Clone: 24F Biolegend, 1:100, APC)
anti-rat CD80 antibody (Clone: 3H5, BD Biosciences, 1:100, BV421)
anti-cTnT antibody(Host: mouse, Abcam, 1:200)
anti-CD31 antibody (Host: goat, Novus Biologicals, 1:200)
anti-MPO antibody (Host: rabbit, Boster Bio,1:200)
anti-CD68 antibody (Host: mouse, Abcam, 1:200)
anti-iNOS antibody (Host: rabbit, Abcam, 1:200)
anti-CD206 antibody (Host: rabbit, Abcam, 1:200)
anti-Arg1 antibody (Host: rabbit, Novus Biologicals, 1:300)
anti-mouse Alexa Fluor 594 secondary antibody (Invitrogen, 1:500)
anti-mouse Alexa Fluor 647 secondary antibody (Invitrogen, 1:500)
anti-goat Alexa Fluor 488 secondary antibody (Invitrogen, 1:500)
anti-goat Alexa Fluor 594 secondary antibody (Invitrogen, 1:500)
anti-rabbit Alexa Fluor 488 secondary antibody (Invitrogen, 1:500)

Validation

We only used antibodies that had undergone prior validation performed by established manufacturers whose products are extensively used by the scientific community (Biolegend, Invitrogen, BD Biosciences, Abcam, Novus Biologicals, Boster Bio). Relevant data are readily available on the manufacturers' official websites.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	This study did not use any cell lines.
Authentication	This study did not use any cell lines.
Mycoplasma contamination	This study did not use any cell lines.
Commonly misidentified lines (See ICLAC register)	This study did not use any cell lines.

Palaeontology and Archaeology

Specimen provenance	This study did not involve palaeontology or archaeology.
Specimen deposition	This study did not involve palaeontology or archaeology.
Dating methods	This study did not involve palaeontology or archaeology.

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight: This study did not involve palaeontology or archaeology.

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

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	BALB/c mice (female,6-10 weeks old) and Fischer 344 (male, 8-11 weeks old) rats purchased from JA bio (Gyeonggi, Republic of Korea) and KOATECH (Gyeonggi, Republic of Korea) were utilized in this study. Housing conditions for all animals are as follows: a 12 hour light/dark cycle, temperature between 20 and 24°C , and 45-55% humidity.
Wild animals	No wild animals were involved in this study.
Reporting on sex	MI studies involved rats of the same sex (male) as sex differences can affect cardiovascular outcomes.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	All animal procedures were performed in accordance with the Institutional Animal Care and Use Committee Guidelines (IACUC) of The Catholic University of Korea (Approval number: CUMC-2022-0081-02). All animal procedures also conformed to the guidelines from Directive 2010/63/EU of the European Parliament on the protection of animals used for scientific purposes or the NIH guidelines.

Ethics oversight

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	This study did not involve clinical data.
Study protocol	This study did not involve clinical data.
Data collection	This study did not involve clinical data.
Outcomes	This study did not involve clinical data.

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☒	☐	Public health
☒	☐	National security
☒	☐	Crops and/or livestock
☒	☐	Ecosystems
☒	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☒	☐	Demonstrate how to render a vaccine ineffective
☒	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐	Increase transmissibility of a pathogen
☒	☐	Alter the host range of a pathogen
☒	☐	Enable evasion of diagnostic/detection modalities
☒	☐	Enable the weaponization of a biological agent or toxin
☒	☐	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	This study did not involve plants.
Novel plant genotypes	This study did not involve plants.
Authentication	This study did not involve plants.

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	This study did not involve ChIP-seq.
Files in database submission	This study did not involve ChIP-seq.
Genome browser session (e.g. UCSC)	This study did not involve ChIP-seq.

Methodology

Replicates	This study did not involve ChIP-seq.
Sequencing depth	This study did not involve ChIP-seq.
Antibodies	This study did not involve ChIP-seq.
Peak calling parameters	This study did not involve ChIP-seq.
Data quality	This study did not involve ChIP-seq.
Software	This study did not involve ChIP-seq.

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	For in vitro experiments, cells were cultured in a humidified, 5% CO2 incubator at 37°C prior to analysis. Cells were detached from the wells (using 5-10 mM EDTA in the case of bone-marrow derived macrophages), transferred to Eppendorf tubes, centrifuged at 500xg for 5 minutes at 4°C, and washed with 1 mL of cell staining buffer (Biolegend, Cat No: 420201) or 1 mL PBS if cells were to be stained with Zombie dyes (Biolegend) immediately thereafter. If zombie dye staining was conducted, it was conducted at room temperature, for 15 minutes, at a titration of 1:250. To reduce nonspecific antibody binding, cells were incubated with 100 µg/ml of IgG (from a species different from that of the host animal) (Invitrogen) for 15 minutes at 4°C prior to staining with fluorescence-conjugated antibodies. After incubation, cells were washed with 1 mL of cell staining buffer to remove free antibodies. Fluorescence-conjugated antibodies were then titrated in cell staining buffer and incubated with cells at 4°C for 30 minutes. After incubation, cells were washed with 1 mL of cell staining buffer, resuspended in 1% paraformaldehyde and kept in the dark at 4°C until use. For all in vitro experiments, cells were analyzed on the same day of staining (within 3 hours). For in vivo experiments, single cell suspensions were obtained by either (1) lysing red blood cells with Gibco ACK Lysing Buffer (Thermo Fisher) for blood samples (followed by washing in ice cold PBS) or (2) homogenizing tissues using a gentleMACS Dissociator (Miltenyl Biotec) and subsequently filtering through a 100 µm cell strainer. Single cell suspensions were centrifuged at 500xg for 5 minutes at 4°C and washed with 1 mL of cell staining buffer or 1 mL PBS if cells were to be stained with Zombie dyes immediately thereafter. For the experiments in Supplementary Fig. 11, zombie dye staining was conducted at room temperature for 15 minutes at a titration of 1:250, after which cells were moved to 96-well U bottom plates (Corning). To reduce nonspecific binding, cells were incubated with 100 µg/ml of IgG for 15 minutes at 4°C prior to staining with fluorescence-conjugated antibodies. Cells were washed again with cell staining buffer to remove free antibodies. Fluorescence-conjugated antibodies were titrated in cell staining buffer and incubated with cells at 4°C for 30 minutes. For experiments requiring permeabilization, Tru-Nuclear Transcription Factor Buffer Set (Biolegend) was used according to the manufacturer's protocol optimized for cells in a 96 well plate. After incubation, cells were resuspended in cell staining buffer and kept in the dark at 4°C until use. For all in vivo experiments except the experiment pertaining to results in Supplementary Fig. 11c and e, cells were analyzed on the same day of staining (within 3 hours). For Supplementary Fig. 11c and e, cells were analyzed the next day (within 12 hours).
Instrument	FACSCantoTM II system (BD Biosciences)
Software	FlowJo_V10 software (Tree Star)
Cell population abundance	Over 50,000 cells in vivo and 10,000 cells of interest in vitro were analyzed for each sample.
Gating strategy	FSC-A/SSC-A or FSC-H/SSC-H was used to distinguish between cells and debris, FSC-A/FSC-H or SSC-A/SSC-H was used to gate for singlets. Mouse neutrophils were defined as (CD45+)Ly6g+CD11b+ cells, mouse macrophages were defined as F4/80+ cells, and mouse monocytes were defined as CD45+Ly6g-CD11b+Ly6C+ cells. Rat neutrophils were defined as as CD45+His48+SSChigh cells, rat monocytes were defined as CD45 +CD43highHis48low (nonclassical) and CD45+CD43lowHis48high (classical) cells, rat B cells were defined as CD45+B220+ cells, rat T cells were defined as CD45+CD3+ cells, rat NK cells were defined as CD45 +CD161+ cells, and rat macrophages were defined as CD68+ cells. Fluorescent minus one (FMO) samples were used to facilitate discrimination between negative and positive fluorescent signals. Samples involving analysis of neutrophils were not permeabilized to ensure preservation of cell morphology and granularity. Stepwise gating strategies for each experiment is detailed in the Supplementary Information section.

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

Magnetic resonance imaging

Experimental design

Design type	This study did not involve magnetic resonance imaging.
Design specifications	This study did not involve magnetic resonance imaging.
Behavioral performance measures	This study did not involve magnetic resonance imaging.
Imaging type(s)	This study did not involve magnetic resonance imaging.
Field strength	This study did not involve magnetic resonance imaging.
Sequence & imaging parameters	This study did not involve magnetic resonance imaging.
Area of acquisition	This study did not involve magnetic resonance imaging.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	This study did not involve magnetic resonance imaging.
Normalization	This study did not involve magnetic resonance imaging.
Normalization template	This study did not involve magnetic resonance imaging.
Noise and artifact removal	This study did not involve magnetic resonance imaging.
Volume censoring	This study did not involve magnetic resonance imaging.

Statistical modeling & inference

Model type and settings	This study did not involve magnetic resonance imaging.
Effect(s) tested	This study did not involve magnetic resonance imaging.

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)	This study did not involve magnetic resonance imaging.
Correction	This study did not involve magnetic resonance imaging.

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity	This study did not involve magnetic resonance imaging.
Graph analysis	This study did not involve magnetic resonance imaging.
Multivariate modeling and predictive analysis	This study did not involve magnetic resonance imaging.