

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
<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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P 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 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	Immunohistochemistry (IHC), immunofluorescence (IF), and hematoxylin and eosin (H&E) micrographs were captured using Zeiss Zen Blue edition software, version 2.3. Flow cytometry datasets were amassed via a CytoFLEX instrument from Beckman Coulter. Electron microscopy images were captured using a JEM-1400 transmission electron microscope from Japan Electron Optics Laboratory Co., Ltd. Western Blot analyses were conducted and data collected employing a Tanon 5200 Intelligent Imaging System.
Data analysis	ImageJ Versions 1.52a, GraphPad Prism Versions 8.0.2, CellRanger Versions 4.0.0, R Versions 4.0.0, Seurat Versions 4.0.0, Cellchat Versions 1.1.3, CytExpert Versions 2.5.0.77, DoubletFinder Versions 2.0.3, SCENIC version 1.2.1, CellPhoneDB Versions 2.1.7, CopyKat Versions 1.1.0.

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](#)

The scRNA-seq data generated in this study have been deposited in the Genome Sequence Archive in the National Genomics Data Center under the accession

number code CRA018502 [<https://ngdc.cncb.ac.cn/gsa/browse/CRA018502>]. The remaining data are available within the Article, Supplementary Information or Source Data File. For additional details or requests for resources and reagents, please contact the corresponding author, Demeng Chen, at chendm29@mail.sysu.edu.cn. 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

Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design; whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data, where this information has been collected, and if consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.

Reporting on race, ethnicity, or other socially relevant groupings

Please specify the socially constructed or socially relevant categorization variable(s) used in your manuscript and explain why they were used. Please note that such variables should not be used as proxies for other socially constructed/relevant variables (for example, race or ethnicity should not be used as a proxy for socioeconomic status). Provide clear definitions of the relevant terms used, how they were provided (by the participants/respondents, the researchers, or third parties), and the method(s) used to classify people into the different categories (e.g. self-report, census or administrative data, social media data, etc.) Please provide details about how you controlled for confounding variables in your analyses.

Population characteristics

Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."

Recruitment

Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.

Ethics oversight

Identify the organization(s) that approved the study protocol.

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

The experimental cohort, composed of C57BL/6N mice, included at least six biologically independent samples per group. Sample sizes were determined based on established methodologies and statistical guidelines detailed in related literature (PMID: 28285905, 33945793). Statistical analysis followed established protocols to ensure robust experimental design. For flow cytometry, immune cell samples used n = 3 biological replicates per group. Sample sizes were determined by field-standard protocols to balance statistical power and ethical compliance. Mice were randomized into age/sex-matched cohorts from homogeneous populations, minimizing bias through standardized allocation procedures. Experimental rigour and reproducibility were maintained per literature guidekines.

Data exclusions

No data was excluded in this study.

Replication

The replicability of findings was validated through multiple biologically independent trials. Figure legends specify sample sizes and emphasize the consistency of results across these independent experiments.

Randomization

The mice were randomly assigned to separate/groups cages for experiments.

Blinding

Although the study design did not allow for blinding procedures, all experimental measures were conducted under standardized conditions. Data from both control and experimental groups were collected under identical parameters, minimizing the potential for observer bias and subjective interpretation in the study's conclusions.

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-Ki67 Novus Cat#NB500-170
 Anti-Caspase3 Cell Signaling Technology Cat#9661S
 Anti-Sox9 Merck millipore Cat#AB5535
 Anti-Annexin I Santa Cruz Cat#sc-12740
 Anti-Fpr1 Immunoway Cat#YT1768
 Anti-Fpr1 Novus Cat#NLS1878
 Anti-BNIP3 Cell Signaling Technology Cat#44060
 Anti-BNIP3 Santa Cruz Cat#sc-56167
 Anti-Ly6g Abcam Cat#ab25377
 Anti-Sell Santa Cruz Cat#sc-390756
 Anti-Tcr g/d Invitrogen Cat#13-5711-82
 Anti-Granzyme A ABclonal Cat#A6231
 Anti-Cd8a Abcam Cat#ab316778
 Anti-Cytochrome C Cell Signaling Technology Cat#11940
 Anti-α-Tublin Proteintech Cat#66031-1-Ig
 HRP-conjugated Affinipure Goat Anti-Mouse IgG(H+L) Proteintech Cat#SA00001-1
 HRP-conjugated Affinipure Goat Anti-Rabbit IgG(H+L) Proteintech Cat#SA00001-2
 Anti-GZMB Santa Cruz Cat#sc-8022
 Anti-Perforin Cell Signaling Technology Cat#44865
 Anti-CTLA-4 Proteintech Cat#98147-1-RR
 PE Anti-Mouse TIM-3 BioLegend Cat#165403
 Ghost Dye™ Red 780 Tonbo Biosciences Cat#13-0865
 PE-Cyanine7 Anti-Mouse CD45 Tonbo Biosciences Cat#60-0451
 APC Anti-Mouse CD3 (17A2) Tonbo Biosciences Cat#20-0032
 PE Anti-Mouse Ly-6G (1A8) Tonbo Biosciences Cat#50-1276-U025
 Brilliant Violet 421™ Anti-Mouse TCR g/d BioLegend Cat#118119
 FITC Anti-Mouse CD8a Tonbo Biosciences Cat#35-0081
 PE Donkey anti-rabbit BioLegend Cat#406421
 PE Goat anti-mouse BioLegend Cat#405307
 Brilliant Violet 510™ Donkey anti-rabbit BioLegend Cat#406419
 Brilliant Violet 510™ Goat anti-mouse BioLegend Cat#405331
 Control IgG BioXcell Cat#BE0088, BE0089, BE0090, BE0091
 anti-PD-1 BioXcell Cat#BE0146
 anti-LAG-3 BioXcell Cat#BE0174
 anti-Tcr g/d BioXcell Cat#BE0070
 anti-Cd8a BioXcell Cat#BE0061
 anti-LAG-3 BioXcell Cat#BE0174

Validation

All primary antibodies were used following the manufacturer's recommended dilutions and buffers. The antibodies were verified by the supplying company as listed on the manufacturer's website.

Eukaryotic cell lines

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

Cell line source(s)

HL60; 293T; Moc1

Authentication

All the cells were identified by Short Tandem Repeat Sequence (STR) genotyping (CellCook Biotech Co., Ltd, Guangdong, China).

Mycoplasma contamination All the cells were tested negative for mycoplasma.

Commonly misidentified lines (See [ICLAC](#) register) No commonly misidentified cell lines were used.

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 K14CreER (Strain ID: 005107) and Sox9CreER (Strain ID: 018829) mouse was obtained from the Jackson Laboratory (Bar Harbor, ME, USA). K14DreER (Strain ID: NM-KI-190125) and R26-Ai66-DTR (Strain ID: NM-KI-190086) mice were purchased from Shanghai Model Organisms (Shanghai, China). R26-Ai66-tdTomato mice were generated as previously described (PMID: 30773487). WT C57BL/6, LyzCreER (Strain ID: T052789), Anxa1flox (Strain ID: T016067) and Fpr1flox (Strain ID: T052005) mice were obtained from GemPharmatech (Nanjing, China). All animal subjects were accommodated under specific pathogen-free conditions, maintained on a 12h light/dark circadian cycle, and granted ad libitum access to sustenance and hydration. All animal protocols received ethical clearance from the IACUC, SYSU.

Wild animals No wild animals were used in this study.

Reporting on sex Experimental procedures were designed to be gender-neutral, incorporating both male and female mice without distinction.

Field-collected samples The study did not involve samples collected from field.

Ethics oversight All animal experiments were approved by the Animal Ethics Committee of the First Affiliated Hospital of Sun Yet-sen University (approval number SYSU-IACUC-2020-000437, SYSU-IACUC-2021-000121 and SYSU-IACUC-2023-000861).

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, mosaicism, 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 A single-cell suspension of mouse oral tumor cells was prepared. Before staining, the cells were washed with staining buffer (2% bovine growth serum in PBS) and adjusted to a concentration of 1×10^7 cells/mL. The cells were then stained with antibodies and incubated in staining buffer for 2 hours at 4°C to complete the extracellular staining process. Samples were analyzed on a flow cytometer (CytoFLEX, Beckman Coulter, Brea, USA), and the resulting data were processed using CytExpert software (version 2.5.0.77). Sorting of live Fpr1+ neutrophils were performed on a flow cytometer (FACSAria Fusion, BD, Franklin Lakes, USA).

Instrument FC Cell Sorters: FACSAria Fusion, BD.
FC Analysers: CytoFLEX, Beckman Coulter

Software CytExpert Versions 2.5.0.77

Cell population abundance According to the estimated size and particle size of the forward and lateral scattering cells, as well as the accompanying

positive or negative signals, the cell population is established for flow analysis.

Gating strategy

NONE

☒ 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

All mice were scanned with a 3.0T MR scanner (MAGNETOM Vida, Siemens Healthcare, Erlangen, Germany) using a 16-channel mouse coil (CG-MUC48-H300-AS, Shanghai Chenguang Medical Technology Co., Ltd., Shanghai, China).

Design specifications

The imaging protocol comprised axial T2-weighted imaging (T2WI) with turbo spin echo (TSE), coronal T2WI with TSE, and axial T1-weighted imaging (T1WI) with StarVIBE.

Behavioral performance measures

State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)

Specify: functional, structural, diffusion, perfusion.

Field strength

Specify in Tesla

Sequence & imaging parameters

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.

Area of acquisition

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Diffusion MRI

☐

Used

☒

Not used

Preprocessing

Preprocessing software

Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

Normalization

If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.

Normalization template

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.

Noise and artifact removal

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

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

Statistic type for inference

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

(See [Eklund et al. 2016](#))

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

n/a	Involvement in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis
Functional and/or effective connectivity	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).
Multivariate modeling and predictive analysis	Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.