

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 Immunofluorescence images were captured using Zeiss Zen 2.3 imaging software; Flow cytometry data were obtained by BD Accuri C6 or BD FACS Aria ii.

Data analysis All the statistical analysis were performed on Graphpad Prism 9. All the flow cytometry data were processed using Flowjo v10. RNA-seq analyses were performed using the OmicStudio tools at <http://www.omicstudio.cn>.

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 main data supporting the results in this study are available within the paper and its Supplementary Information. The raw and analyzed datasets generated during the study are available for research purposes from the corresponding authors on reasonable request. The sequencing data of the transcriptomic analyses in this study have been deposited at Sequence Read Archive (SRA). SRA records are accessible with the following link: <https://www.ncbi.nlm.nih.gov/sra/>

PRJNA1175425. 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	The study did not involve human participants.
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](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 determination of sample sizes was based on the relevant literature and on previous experimental experiences.
Data exclusions	No data were excluded.
Replication	The experiments were repeated, and the experimental findings were reproducible.
Randomization	All samples and organisms were randomly allocated into each group.
Blinding	Blinding was applied to most of experiments. It was not used when the experiments involved multiple steps and when the scientists needed to keep careful tracking of the conditions.

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	Involves the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involves the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	Anti-PD-1 (BioCell, Cat. BE0273), anti-CD8 α (Biolegend, Cat. 100763), anti-Asialo GM1 (Biolegend, Cat. 146002), anti-CD45-Percp (Biolegend, Cat. 109825), anti-CD11c-FITC (Biolegend, Cat. 117305), anti-CD80-APC (Biolegend, Cat. 104713), anti-CD86-PE (Biolegend, Cat. 105007), anti-CD3-FITC (Biolegend, Cat. 100203), anti-CD4-APC (Biolegend, Cat. 100411), anti-CD8-PE (Biolegend,
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Cat. 100707), anti-CD45-FITC (Biolegend, Cat. 157608), anti-CD3-APC (Biolegend, Cat. 100235), anti-CD49b-Percp-cy5.5 (Biolegend, Cat. 103519), ANTI-Ki67-FITC (Biolegend, Cat. 652409), anti-CD69-FITC (Biolegend, Cat. 104506), anti-CD8-PERCP-CY5.5 (eBioscience Cat. 45-0081), anti-IFNR-PE (Biolegend, Cat. 164504), anti-PD-1-APC (Biolegend, Cat. 109112), anti-TCF7-Alexa flour 594 (R&D, cat. FAB8224T-100UG), anti-CXCR3-Pecy7 (Biolegend, Cat. 126515), anti-Grzb-pecy7 (Biolegend, Cat. 372213), anti-CD44-PE (eBioscience, Cat.12-0041), anti-CD62L-APC (eBioscience, Cat.17-0621), His-Tag (Peotein Tech, 10001-0-AP), HRP-conjugated anti-rabbit secondary antibody (Protein Tech, SA00001-2), anti-Flag-HRP (Sigma-Aldrich, A8592).

Validation All the antibodies used in this study are commercially available and have been validated by the commercial suppliers for research use. The validation report could be available on their website.

Eukaryotic cell lines

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

Cell line source(s)	H22, CT-26 cells were obtained from the Cell Bank, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences. Rat N1S1 cell was a gift from Lishui Hospital pf Zhejiang University.
Authentication	Identify of the cell lines were frequently checked by their morphological features but have not been authenticated by theshort tandem repeat (STR) profiling.
Mycoplasma contamination	All cell lines were tested for mycoplasma contamination, no mycoplasma contamination was found.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines used in this study.

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	Female BALB/c mice (6–8weeks) and Sprague-Dawley (SD) rats were procured from the Laboratory Animal Center of Soochow University and utilized by the approved protocols of the Laboratory Animal Center of Soochow University. Mice were housed in individually ventilated cages with five mice per cage and kept on in a regular 12-h: 12-h light: dark cycle (8:00 AM-8:00 PM light; 8:00 PM-8:00 AM dark), with controlled temperature and humidit. All the mice were supplied with food and water.
Wild animals	The study did not involve wild animals.
Reporting on sex	Sex was considered in safety assessments. Male and Female SD rats were equally used in this study.
Field-collected samples	The study did not involve samples collects from field.
Ethics oversight	The animals were utilized by the approved protocols of the Laboratory Animal Center of Soochow University with an approval number of SYXK(Su)2021-0073.

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

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

See section 'In vivo assessment of immune responses' in Methods.

Instrument

BD Accuri C6 plus and BC FACS Aris II.

Software

Flow Jo V10.

Cell population abundance

Flow cytometry was used for quantification only No-sort fractions were collected.

Gating strategy

Gating strategies are referred to those described in the website (<https://www.bio-rad-antibodies.com/blog/a-guide-to-gating-in-flow-cytometry.html>). Cells were first gated on FSC/SSC. Surface and intracellular antigen gating was performed. Different populations of immune cells based on their expression of distinct markers.

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