nature portfolio

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Last updated by author(s): 2024-August 25

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	No original code was used for scientific results and conclusions. Data was collected using Microsoft Office programs
Data analysis	Data was analyzed using GraphPad Prism (Version 10), Microsoft Excel (Microsoft 365 products), Rosalind, and FlowJo (Version 10) 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

The main data supporting the results in this study are available within the paper and its Supplementary Information and provided as supplementary Source Data. Raw data for sequencing results can be found at https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE255666.

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 subjects
Reporting on race, ethnicity, or other socially relevant groupings	This study did not involve human subjects
Population characteristics	This study did not involve human subjects
Recruitment	This study did not involve human subjects
Ethics oversight	This study did not involve human subjects

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	Effect sizes were not predetermined. Details regarding sample size, technical/biological replicates are included in figure legends.
Data exclusions	Data exclusions are mentioned in manuscript and pertain to animals requiring pre-established euthanasia prior to termination of the experimental studies.
Replication	Observations were repeated across experiments and experimental repeats
Randomization	When possible, animals were randomized before treatment
Blinding	When possible, investigators were blinded during treatment administrations and data collection

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	Antibodies for in vivo use: Anti-PD-1 monoclonal antibody (mAb) (clone: RMP1–14), Bioxcell Anti-PD-L1 mAb (clone: 10F.9G2TM), Bioxcell

	IFNAR1 blocking mAb (clone: MAR1−5A3), Bioxcell CD4 mAb (Clone: GK1.5), Bioxcell CD8α mAb (Clone: 2.43), Bioxcell
Validation	Depleting and blocking antibodies have been validated in efficacy studies in tumor bearing mice; Flow antibodies have been validated by manufacturer

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Sources of cell lines disclosed in methods. B16F10-OVA were received as a kind gift from Richard Vile (Mayo Clinic). K2 glioma cells were received as a kind gift from Oren Becher (Northwestern University). GL261 cells were received as a kind gift from John Sampson (Duke University) and from the DCTD Tumor Repository at the NCI. 143B, KHOS, K7M2 and B16F0 were purchased from ATCC.
Authentication	Cell lines are authenticated by commercial vendor (e.g. ATCC), gross pathology and/or H&E staining from in vivo studies
Mycoplasma contamination	Our cell lines are routinely tested for contaminants
Commonly misidentified lines (See ICLAC register)	Misidentified cells were not used in the 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	C57Bl/6, Balb/c, and SCID (Strain: 001913), PMEL (Strain: 005023), IFNAR1 KO (Strain: 032045-JAX), IFN-γ (Strain: 002287) mice of 5-7 weeks of age were acquired from Jackson Laboratories. Fox Chase mice were utilized for inoculation of human cell lines
Wild animals	This study did not use wild animals but involved pet dogs enrolled onto a IACUC approved trial following owner's consent
Reporting on sex	Reported in Methods
Field-collected samples	Samples were not collected in the field
Ethics oversight	Research complies with ethical guidelines and was approved by the University of Florida institutional Animal Care and Use Committee

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

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

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	White blood cells were isolated via mechanical disruption and passed through a 70 µm filter (BD Biosciences, cat. 352350). Following centrifugation, the cell pellet was lysed using BD Pharm Lyse™ Lysing Buffer (BD, cat. 555899) and neutralized in complete T cell medium
Instrument	BD Symphony A3
Software	FlowJo 10
Cell population abundance	No FACsorting of rare populations performed
Gating strategy	Gating strategies provided in supplemental data

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