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.

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	FACS DIVA, Microsoft Excel, Alpha view SA v3.4.0, Gens v3.12, AID software
Data analysis	Graphpad Prism v9, Flowjo, Microsoft Excel, ImageJ, Kallisto, Sleuth, WebGestalt

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 RNA-Seq data sets are made available via public repositories (GEO accession number: GSE237445, and https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE237445t)

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	Blood from women and men eligible were recruited in the study. We did not discriminate based on sex/gender, race or ethnicity. Efforts were made to maintain similar gender and race distribution between the groups. Also there was no gender based analysis done in the B cell analysis study, as number of volunteer was only eight.
Reporting on race, ethnicity, or other socially relevant groupings	Efforts were made to maintain similar race and ethnicity distribution representing the demographics of Pittsburgh.
Population characteristics	Only Healthy volunteers involved in the study. Age 40.25 ± 8.3
Recruitment	The blood samples were obtained from volunteers after providing written informed consent as part of a study entitled "Banking of Biological Samples and Collection of Clinical Data for Connective Tissue Disease" at the Division of Rheumatology and Clinical Immunology, U. Pitt
Ethics oversight	All human subjects' studies were approved by the University of Pittsburgh Institutional Review Board.

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 size was calculated based on previous work and preliminary data. Studies were powered to detect 20-25% differences at p< 0.05 (details of sample size mentioned in each figure legend). In case of high variability, increased number of animals were used and the studies were re-powered accordingly.
Data exclusions	Some data excluded based on the predefined exclusion criteria, only if there a measurement errors, processing errors, poor sampling or outside of 3-sigma limits
Replication	For all the studies, data from at least 2-3 independent experiments was pooled to ensure that effects seen are consistent and reproducible.
Randomization	Age and sex matched animals were randomly allocated in different groups for in-vivo studies.
Blinding	All experiments done unblinded

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-B220 (BD Biosciences, Clone: RA3-6B2), anti-GL7 (BD Biosciences, Clone: GL-7), anti-CD95 (Invitrogen, Clone: 15A7), NP (Bioresearch Technologies), anti-lgGl (BD Biosciences, Clone: ASS-1), anti-CD138 (BD Biosciences, Clone: 281-2), anti-CD4 (Biolegend, Clone: GKl.5), anti-CD44 (Invitrogen, Clone: IM7), anti-CD62L (BD Biosciences, Clone: MEL-14), anti-CXCRS (Biolegend, Clone: Ll38D7), anti-PD-1 (Biolegend, Clone: RMPl-30), anti-CD25 (BD Biosciences, Clone: 7D4), anti-CXCR4 (Invitrogen, Clone: 2Bll), anti-CD86 (Biolegend, Clone: GL-1), anti-CDS (Biolegend, Clone: 53-6.7), Ki67 (Invitrogen, Clone: SolA15) and Influenza specific Tetramer (Influenza A NP 366-374: NIH Tetramer Core Facility). Surface staining of human B cells was performed with human anti-GPR109A antibody (Invitrogen, Clone: 4NZBRGO),
Validation	The antibodies to be used in these studies was obtained from reputable commercial entities (e.g., R&D Systems, eBiosciences, Cell Signaling Technology). We have validated each batch by appropriate assay. Signaling antibodies will be validated by molecular size of reactive species on western blots and combined with western blotting of HEK293T cell lysates transfected with respective cDNA-containing vectors. Confirmation in primary cell lines will be performed by comparing staining in cells treated with siRNA against the relevant antigen. Flow cytometry Abs was validated by staining control tissues to confirm known staining patterns (e.g., spleen, kidney), using KO cells as negative controls where available. Such validation steps have long been a standard practice in my group.

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	Mice, C57BL6, Niacrl -/-, muMT
Wild animals	Not applicable
Reporting on sex	Both male and female mice were used, analyzed together or separately.
Field-collected samples	Not applicable
Ethics oversight	All animal experiments were conducted following the National Institute of Health guidelines under protocols approved by the University of Pittsburgh Institutional Animal Care and Use Committee.

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	*Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.*
Study protocol	*Note where the full trial protocol can be accessed OR if not available, explain why.*
Data collection	*Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.*
Outcomes	*Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.*

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, mosiacism, 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	Mice spleens are subjected to mechanical dissociation to prepare single cell suspensions, followed by RBC lysis by ACK lysing buffer (Gibco)
Instrument	BD Fortessa, BD ARIA
Software	Acquisition: FACS DIVA; Analysis Flowjo
Cell population abundance	94% of sorted population of Antigen specific Germinal Center B cells. Purity was determined flow cytometry by staining relevant marker after doublets and dead cell discrimination.
Gating strategy	FSC-A vs SSC-A (lymphocyte gate), FSC-A Vs FSC-H (single cells), B220 Vs Live dead Ghost 510 (Live B cells), CD95 Vs GL7 (Germinal center B cells, GCBC), gated to find NP-specific GCBC

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