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	Flow cytometry samples were acquired in a BD LSRFortessa™ and data were collected using BD FACSDiva™ V.8.0.2; For flow-cytometry-based neutralization assay, data were collected on BD FACSCanto™ II flow cytometer using BD FACSDiva Software Version 8.0.1, as well as FACSCelesta™ multicolor flow cytometer using BD FACSDiva Software Version 9.2; Western blot images were taken by Bio-Rad ChemiDoc system using Bio-Rad Image Lab Version 6.1.0 build 7; Viral RNA was quantified by a CFX96 Touch real-time PCR detection system (Bio-Rad, CFX Manager 3.1); Images of immunofluorescence data were taken by a Keyence BZ-X810 fluorescence microscope with Keyence BZ Series Application 01.02.02.04; Absorbance values were measured using a SpectraMax M2 microplate reader (Molecular Devices) with SoftMax Pro 7 Version 7.1.0 build 246936; AlphaFold 2 implementation in ColabFold (https://www.nature.com/articles/s41592-022-01488-1);
Data analysis	Flow cytometry analysis of cellular populations were performed with FlowJo (TreeStar) v10.10; Data visualization and statistical analysis were performed using GraphPad Prism 9.1.1 and GraphPad Prism 10.4.2 software; Western blot was analyzed by Bio-Rad Image Lab Version 6.1.0 build 7; ChimeraX 1.9 was used for visualization and calculation.

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

Minimum datasets generated during this study that are necessary to interpret, verify and extend the research are available as supporting information. Further information and requests for resources and reagents should be directed to and will be fulfilled by the corresponding authors.

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	Our study does not include human participants, this information has not been collected.
Reporting on race, ethnicity, or other socially relevant groupings	Our study does not include human participants, this information has not been collected.
Population characteristics	Our study does not include human participants, this information has not been collected.
Recruitment	Our study does not include human participants, this information has not been collected.
Ethics oversight	Our study does not include human participants, this information has not been collected.

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	Each experiment included between 2 to 8 mice per group, and each graph represented pooled data from at least two independent experiments (9 to 18 mice). The sex ratio for all experiments was approximately 1:1, and all experiments were started when mice were 4 to 8 weeks of age.
Data exclusions	All samples were included in the analyses unless identified as outliers. Outliers were detected for each group of mice prior to statistical testing using the outlier calculator in GraphPad Prism.
Replication	All replication attempts were successful, with replicate numbers provided for each experiment performed.
Randomization	Not relevant to this study design. Age-matched male and female mice were used in the study.
Blinding	The experiments were not blinded, as each immunized group was clearly labeled. However, all experiments and analyses were conducted in the same manner across groups, regardless of treatment or immunization, to minimize bias.

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

All antibodies were purchased from BioLegend/Tonbo Biosciences/eBioscience/Mabtech/BioXCell/Jackson Immunoresearch/BD Biosciences/MyBiosource/GeneTex/Thermo Fisher Scientific unless otherwise indicated. Antibodies (name, catalog number and clone) are 4G2 mAb (clone#D1-4G2-4-15), HRP-goat-anti-mouse IgG, HRP-anti-mouse (IgG (H+L), CD209 (561765, clone DNC246), CD8-depleting mAb (BE0061, clone 2.43), rat IgG2b,k control (BE0090, clone LTF-2), anti-mouse IFN-γ mAb (BE0054, R4-6A2) or rat IgG1k isotype control mAb (BE0088, HRPN), anti-ZIKV E domain III (MyBiosource, #MBS2564004), anti-ZIKV M pAb, HRP-anti-rabbit secondary Ab, AF-488-goat-anti-mouse IgG, CD107a (Biolegend, 12-1071-83, clone 1D4B), CD3ε (Biolegend, 100320, clone 145-2C11), CD4 (563790, clone GK1.5), CD8α (Biolegend, 100752, clone 53-6.7), CD44 (Biolegend, 103059, clone IM7), CD62L (Biolegend, 47-0621-82, MEL-14), purified rat anti-mouse CD16/CD32 (BD Biosciences, mouse Fc Block 553142, clone 2.4G2), IFNγ (Biolegend, 505806, clone XMG1.2), TNFα (eBiosciences, 17-7321-82, clone MP6-XT22), IL-2 (Biolegend, 503837, clone JES6-5H4). All flow cytometry antibodies were used at 1/200 dilution, the amount of antibodies vary whether the final volume was 100 or 200 uL.

Validation

Antibodies were initially validated by their respective manufacturers, and optimal dilutions were determined in-house using splenocytes and established panels.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

C6/36 Aedes albopictus mosquito cells (CRL-1660), BHK-21 cells (CCL-10), and U937-DC-SIGN cells (CRL-3253 -male) and 293T cells (CRL-11268 -female) are from ATCC. Vero-hfurin cells were provided by a collaborator at NIH VRC as specified in the manuscript (established according to DOI: 10.1016/j.virol.2016.06.022).

Authentication

The cell lines used were authenticated by their provider. In the lab, U937 DC-SIGN cells were authenticated using flow cytometry to check the expression of DC-SIGN after cell culture.

Mycoplasma contamination

All cell lines were routinely tested for Mycoplasma, and all negative by PCR.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified line was 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

C57BL/6 WT, Ifnar1−/− [IFNα/β receptor-deficient]) and HLA-B*0702 Ifnar1−/− mice aged 4–8 weeks were obtained from Jackson Laboratories (#000664), from Dr. Wayne Yokoyama (Washington University in St. Louis, USA) and from Dr. Alessandro Sette (LJI, USA), respectively.
For vaccination, mice were primed at 4-5 weeks. For transfer studies, mice were used at the age of 8 weeks.
Temperature: The temperature is set to 72°F +/- 3°F by heating or cooling to protect the animals from temperature extremes. Temperatures 4°F above the set point are monitored for a three-day trend and then documented by the technician on the room log with a follow-up email to DLAC Management. Facilities will adjust the temperature to bring the room back into range. Temperatures 4°F below the set point are monitored for a drop below 68°F, then adjusted to get the room back into range. Temperatures 5°F beyond the set point are immediately documented and followed up with an email/call to DLAC management. Alarm set points are 67°F and 77°F.
Humidity: The relative humidity is monitored but not controlled. The acceptable range is 30-70%. If the humidity falls below 30% or rises above 70% for longer than two days, technicians may take corrective measures under the direction of DLAC Management.
Light Cycle: The building monitoring system controls lighting to provide a regular 12-hour light/12-hour dark cycle. Report variation in the set light/dark cycle to DLAC.

Wild animals

The study did not involve wild animals.

Reporting on sex

The sex ratio for all experiments was approximately 1:1, and all experiments were started when mice were 4 to 8 weeks of age. Sex-based comparisons were not performed.

Field-collected samples	The study did not involve samples collected from the field
Ethics oversight	All experiments were performed in strict accordance with recommendations set forth in the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the Institutional Animal Care and Use Committee at the La Jolla Institute for Immunology (# AP00001029).

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

Plants

Seed stocks	Our study does not include plants.
Novel plant genotypes	Our study does not include plants.
Authentication	Our study does not include 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	For single-cell suspensions of splenocytes, spleens were gently mashed with a syringe plunger followed by filtering through a 70-µm cell strainer. Red blood cells were lysed with ACK lysing buffer (Gibco). For purified CD8+ T cells, the spleens were harvested and prepared single-cell suspensions of splenocytes and CD8+ T cells were purified using an EasySep CD8+ T cell isolation kit (Negative selection, Stemcell). U937-DCSIGN cells were infected, washed and stained.
Instrument	Flow cytometry samples were acquired in a BD LSRFortessa™ flow cytometer, BD FACSCanto™ II flow cytometer, and FACSCelesta™ multicolor flow cytometer.
Software	Samples were acquired using BD FACSDiva™ V.8.0.2 (LSRFortessa), BD FACSDiva Software Version 8.0.1 (FACSCanto), BD FACSDiva Software Version 9.2 (FACSCelesta), Prism software v.9.1.1 & V10.4.2 and analyzed using FlowJo version 10.10.
Cell population abundance	For purified CD8+ T cells, the spleens were harvested and CD8+ T cells were purified using an EasySep CD8+ T cell isolation kit (Stemcell). More than 90% of the cells were CD8 T cells.
Gating strategy	Cells were gated based on FSC/SSC, then singlets were selected based on SSC-W/SSC-H and FSC-W/FSC-H, then live CD3+ cells based on viability dye and CD3. CD4+ and CD8+ T cells were selected based on CD4 and CD8 markers, then activated cells from each group CD4+ or CD8+ T cells (based on CD44+ CD62L−). CD4+ or CD8+ T cells producing cytokines (IFNγ, TNF and IL-2) or the degranulation marker CD107a were selected. Cells producing IFNγ+/TNF+/IL-2 triple positive were identified from IFNγ+/TNF+ cells producing IL-2 using a Boolean algorithm.

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