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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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 software was used.
Data analysis	Data were analyzed using Graphpad Prism V8.3.0, FlowJo V10, and CTL ImmunoSpot® 7.0.11.0 Professional Analyzer DC

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

Data have been deposited in Figshare: 10.6084/m9.figshare.12290696

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	NHP - Since this is a model with no prior data, it was not possible to perform a power analysis. The sample size was based on experience with other nonhuman primate models of respiratory disease where the numbers used were sufficient for statistical analyses. Mice - Sample size was determined based on previous experience measuring the immunogenicity of vaccines in inbred and outbred mice where the numbers used were sufficient for statistical analyses.
Data exclusions	No data were excluded.
Replication	Lung histology: for each animal (n=12 (vaccinated) or 6 (control)), 3 sections were evaluated from all 6 lung lobes. Cytokine analysis: serum samples were analyzed in duplicate from each animal for each timepoint; n=12 (vaccinated) or 6 (control) Serological analysis: Serum samples were analyzed in duplicate from each animal for each timepoint; n=12 (vaccinated) or 6 (control). Mouse experiments were repeated twice All repeats were successful. qRT-PCR assays were performed with in-house validated standards. Flow cytometry and ELISpot assays were performed with positive controls (PMA/IONO stimulation).
Randomization	Animals were randomly assigned to groups
Blinding	Blinding was done for the following personnel: - Person scoring animals daily - Veterinary pathologists reviewing histology - Clinical veterinarians performing exams

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
☐	☒	Animals and other organisms
☒	☐	Human research participants
☒	☐	Clinical data

Methods

n/a	Involved in the study	
☒	☐	ChIP-seq
☐	☒	Flow cytometry
☒	☐	MRI-based neuroimaging

Antibodies

Antibodies used	in-house SARS-2 rabbit sera, GenScript CD4-BUV496, BD, cat#557984, clone 500A2, dilution 1 in 100 CD8-PerCPCy5.5, BD, cat# 564667, clone GK1.5, dilution 1 in 100 CD62L-BV711, eBioscience/Thermofisher, cat# 45-0081-82, clone 53-6.7, dilution 1 in 200 CD127-BV650, BioLegend, cat# 103028, clone IM7, dilution 1 in 100 TNF-a-A488, BioLegend, cat# 104445, clone MEL-14, dilution 1 in 100 IL-2-PECy7, BioLegend, cat# 121610, clone 1D4B, dilution 1 in 1000 IL-4-BV605, BioLegend, cat# 135043, clone A7R34, dilution 1 in 100 IL-10-PE, eBioscience/Thermofisher, cat# 48-7311-82, clone XMG1.2, dilution 1 in 100 IFN-g-e450, eBioscience/Thermofisher, cat# 25-7021-82, clone JES6-5H4, dilution 1 in 100 anti-monkey IgG (gamma) antibody, peroxidase-labeled, Seracare, cat# 5220-0333/074-11-021, Lot# 10329492, dilution 1:2500 anti-monkey IgM antibody, peroxidase-labeled, Rockland, cat# 617-105-007, Lot# 27986, dilution 1:5000 anti-mouse IgM antibody, peroxidase-labeled, Abcam, cat# ab98672, Lot# GR325319-6, dilution 1:5000 Alkaline Phosphatase-conjugated goat anti-mouse IgG, Sigma, cat# A3562, Lot# SLBK6489v, dilution 1:5000
Validation	Validation of cross-reactivity of SARS-CoV to SARS-CoV-2 in IHC was done in-house by embedding SARS-CoV-2 infected Vero cells in histogel and producing and staining histology slides. All other antibodies validated by supplier: Monkey IgM: Assay by immunoelectrophoresis resulted in a single precipitin arc against anti-Alkaline Phosphatase (calf intestine), anti-Goat Serum, Monkey IgM and Monkey Serum. No reaction was observed against other Monkey heavy or light chain proteins. Mouse IgM: Minimal cross-reactivity Human, Rat Mouse IgG: Anti-Mouse IgG (whole molecule)-Alkaline Phosphatase antibody is specific for normal mouse serum and mouse IgG. In Ouchterlony double diffusion assays, the antibody reacts with mouse IgG1, IgG2a, IgG2b, IgG3, IgA, and IgM.

All other antibodies were validated for use with mouse samples by the supplier.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	VeroE6: Ralph Baric, University of North Carolina, Chapel Hill, USA (not commercial) GripTite 293 MSR cell line: ThermoFisher, Cat# R79507 T-Rex-293 cell line: ThermoFisher, Cat# R71007
Authentication	Not authenticated in-house.
Mycoplasma contamination	Mycoplasma testing confirmed negative at regular intervals.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Rhesus macaques, Chinese origin, adult (2-6 years), 17 males, 1 female Mice – Female BALB/cOlaHsd (BALB/c) (Envigo) and outbred Crl:CD1(ICR) (CD1) (Charles River) mice of at least 6 weeks of age
Wild animals	No wild animals were used.
Field-collected samples	No samples were collected in the field.
Ethics oversight	Mice - Mice were used in accordance with the UK Animals (Scientific Procedures) Act under project license number P9804B4F1 granted by the UK Home Office. NHP - All animal experiments were approved by the Institutional Animal Care and Use Committee of Rocky Mountain Laboratories, NIH and carried out by certified staff in an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International accredited facility, according to the institution's guidelines for animal use, following the guidelines and basic principles in the NIH Guide for the Care and Use of Laboratory Animals, the Animal Welfare Act, United States Department of Agriculture and the United States Public Health Service Policy on Humane Care and Use of Laboratory Animals.

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

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	Sample preparation: Single cell suspension of murine splenocytes were prepared by passing cells through 70µM cell strainers and ACK lysis prior to resuspension in complete medium. Cells were stimulated at 37oC for 6 hours with 2µg/ml S1 or S2 pools of peptide, media or cell stimulation cocktail (containing PMA-Ionomycin, Biolegend), together with 1µg/ml Golgi-plug (BD) with the addition of 2µl/ml CD107a-Alexa
Instrument	BD Fortessa X2
Software	BD FACSDiva Software Version 8.0.2, FlowJo version 10 for analysis
Cell population abundance	An acquisition threshold was set at a minimum of 5000 events in the live CD3+ gate
Gating strategy	Antigen specific T cells were identified by gating on LIVE/DEAD negative, doublet negative (FSC-H vs FSC-A), size (FSC-H vs SSC), CD3+, CD4+ or CD8+ cells and cytokine positive. Cytokine positive responses are presented after subtraction of the background response detected in the corresponding unstimulated sample (media containing CD107a and Golgi-plug) of each individual spleen sample.

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