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	No software was used for open source data collection
Data analysis	Zen Blue (Zeiss Zenn 3.1 Blue edition) from Carl Zeiss was used for image analysis for images obtained with the Zeiss LSM780 confocal microscope. GraphpadPrism 8 software was used for plotting graphs and statistical analysis. Densitometry was carried out with GE Amersham Imager 600 software. Flow cytometry data was analyzed with FACSDIVA 8.1 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 authors declare that all data reported in this study are available within the paper and its supplementary information files.

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	All experiments were performed minimum 3 times for statistical significance. Total number of animals included in each experiment is mentioned in corresponding figure legends.
Data exclusions	No data was excluded
Replication	All experiments were replicated at least 3 independent times.
Randomization	Animals were chosen from a certain age-group that has been established as models for infection in lab. The infection model is unbiased for sex of animals used.
Blinding	Experiments and data analysis were independently performed by authors and cross- checked for conclusive interpretation.

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
N/A	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
N/A	☐ Human research participants
N/A	☐ Clinical data
N/A	Dual use research of concern

Methods

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

Antibodies

Antibodies used

Antibody Catalogue Number Company
Syndecan-1 ab34164 Abcam (MA, USA)
EDIM NSP5
EDIM VP6 Gift from John Patton's lab
(Indiana University Bloomington, USA)
MNV-1 VP1
MNV-1 NS4, Propol
Human norovirus NS-7
Human norovirus VLP-1 Gift from Kim Green's lab
(NIAID, NIH, Bethesda, USA)
NKCC1 Gift from Matt Hoffman's lab
(NIDCR, NIH, Bethesda, USA)
Epcam-APC 17-5791-82 ThermoFisher
CD45 12-0451-82 ThermoFisher Scientific
B220 557390 Pharmingen

Validation

1. Syndecan-1: Mouse monoclonal [B-A38] to Syndecan-1. Validated Applications: Flow Cyt, IHC-P. PMID: 31226359
2. EDIM-NSP5: Guinea Pig. PMID: 17182692
3. EDIM-VP6: Guinea Pig. PMID: 30092198
4. MNV-1 VP-1: Guinea Pig. PMID: 30092198

5. MNV-1 Propol: Rabbit. PMID: 16873239
6. Human Norovirus NS-7, NS-6, VLP-1: Rabbit. PMID: 32488028
7. NKCC1: Goat. PMID: 30159893
8. Human Norovirus VP-1: Guniea Pig. PMID: 31551337
9. Epcam-APC: Rat. The G8.8 monoclonal antibody reacts with the 40 kDa mouse EpCAM (epithelial cellular adhesion molecule). Validated Applications: Flow, IHC-P,F, ChIP, Functional Assay. PMID: 31672973
10. CD-45: Rat. The 30-F11 monoclonal antibody reacts with all isoforms of mouse CD45, also known as Leukocyte Common Antigen (LCA). CD45 is expressed by all hematopoietic cells excluding mature erythrocytes and platelets. The cytoplasmic portion of CD45 has tyrosine phosphatase enzymatic activity and plays an important role in activation of lymphocytes. PMID: 30365542
11. B220: Rat. The RA3-6B2 monoclonal antibody specifically binds to an epitope on the extracellular domain of the transmembrane CD45 glycoprotein which is dependent upon the expression of exon A and specific carbohydrate residues. It is expressed on B lymphocytes at all stages from pro-B through mature and activated B cell, but it is decreased on plasma cells and a subset of memory B cells. The levels of CD45R expression on the B-cell lineage appear to be developmentally regulated.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	RAW264.7 : ATCC TIB-71 RRID# CVCL_0493 HeLa: ATCC, CCL-2 NS-SV-TT-DC nd NS-SV-AC: Gift from J.A. Chiorini Lab, AAV Biology Section, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD, USA. PMID: 7687310
Authentication	NS-SV-TT-DC authentication was STR fingerprinting. NS-SV-AC authentication not carried out by us.
Mycoplasma contamination	Cell lines were negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	*No commonly misidentified cell lines were used in this study.*

Palaeontology and Archaeology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.*
Specimen deposition	*Indicate where the specimens have been deposited to permit free access by other researchers.*
Dating methods	*If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

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

Animals and other organisms

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

Laboratory animals	All animals were maintained at NHLBI Animal Care Facility, Bethesda, USA. Mouse, BALB/c (Stock: 000651), C57BL/6J (stock 000664), B6.129S(Cg)-Stat1tm1Dlv/J (Stock No: 012606) originally procured from Jacksons Laboratories. Cd300lfem1Cbwi/J breeding pairs were a kind gift from Dr. Craig B. Wilen (Yale School of Medicine, New Haven, CT, USA). The Cd300lf-/- allele was created by Dr. Herbert W. Virgin (Washington University at Saint Louis) using CRISPR/cas9 endonuclease-mediated genome editing in C57BL/6J mouse zygotes. B6.IFNAR-/- mice breeding pair were a kind gift from Dr. Daniela Verthelyi, Food and Drug Administration, MD, USA.
Wild animals	N/A
Field-collected samples	N/A
Ethics oversight	All animal experiments were performed in an American Association for the Accreditation of Laboratory Animal Care (AAALAC) accredited animal facility. Housing and breeding (animals that aged more than 6 weeks) in accordance with the procedure outlined in the guide for the Care and Use of Laboratory Animals under an animal study proposal approved by the NHLBI Animal Care and Use Committee.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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.*

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☐	☐	Public health
☐	☐	National security
☐	☐	Crops and/or livestock
☐	☐	Ecosystems
☐	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☐	☐	Demonstrate how to render a vaccine ineffective
☐	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☐	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☐	☐	Increase transmissibility of a pathogen
☐	☐	Alter the host range of a pathogen
☐	☐	Enable evasion of diagnostic/detection modalities
☐	☐	Enable the weaponization of a biological agent or toxin
☐	☐	Any other potentially harmful combination of experiments and agents

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	*For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.*
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

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	SMGs were extracted from animals after euthanization and homogenized in ice-cold 1XPBS (supplemented with 10% FBS). Homogenate was centrifuged at X1000 rpm for 5 minutes at 4℃ to pellet down cells which was further incubated for 20 minutes at 37℃ in 3ml of Gentle Collagenase/Hyaluronidase solution (StemCell Technologies, Cambridge, MA, USA, Catalogue No. 07919) with shaking. Thereafter centrifuged the solution again at X1000 rpm for 5 minutes at 4℃ to collect the pellet and discard the sup. The pellet was further trypsin treated for 5 minutes at 37℃ and passed through 70mm filter to eliminate un-dissociated tissue. The filtrate was then treated with a 4:1 NH4Cl: PBS solution to eliminate blood cells and subjected to centrifugation at X1000 rpm for 5 minutes at 4℃. Leaving the red layer of cells at bottom the entire supernatant consists of single cell isolation from tissue. Cell number was counted and incubated with anti-EpCAM conjugated to APC (ThermoFisher Scientific, Catalogue No. 17-5791-82) and anti-CD45 conjugated to PE (ThermoFisher Scientific, Catalogue No. 12-0451-82) for 1 hour at 4°C. Cells were subsequently washed and stained with live/dead Aqua stain (ThermoFisher Scientific, Catalogue No. L34957). Resuspended cells were sorted on ARIAIIu (BD) cell sorter equipped with 355nM, 407nM, 488nM, 532nM and 640nM LASER lines using FACSDIVA 8.1 software at 70 psi pressure using 70-micron nozzle. Debris were removed based on scattering properties using FSC and SSC parameters. Live gated cells were purified for Leukocytes identified as CD45+ EpCAM- live cells where as CD45-EpCAM+ cells were identified as epithelial cells.
Instrument	Resuspended cells were sorted on ARIAIIu (BD) cell sorter equipped with 355nM, 407nM, 488nM, 532nM and 640nM LASER lines using FACSDIVA 8.1 software at 70 psi pressure using 70-micron nozzle.
Software	FACSDIVA 8.1 software
Cell population abundance	Cell population abundance: 105 cells were obtained in each group CD45 and Epcam positive from both adult and mouse pup submandibular glands.

Gating strategy

Debris were removed on the basis of scattering properties using FSC and SSC parameters. Live gated cells were purified for Leukocytes identified as CD45+ EpCAM- live cells where as CD45-EpCAM+ cells were identified as epithelial cells.

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

Magnetic resonance imaging

Experimental design

Design type

Indicate task or resting state; event-related or block design.

Design specifications

Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.

Behavioral performance measures

State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)

Specify: functional, structural, diffusion, perfusion.

Field strength

Specify in Tesla

Sequence & imaging parameters

Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.

Area of acquisition

State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software

Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).

Normalization

If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.

Normalization template

Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.

Noise and artifact removal

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference (See Eklund et al. 2016)

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity	*Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).*
Graph analysis	*Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).*
Multivariate modeling and predictive analysis	*Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.*