

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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 Aria III (BD Biosciences) CytoFLEX S (Beckman) Thermo Scientific Variokan LUX (Thermo Scientific) Octet RED96e System (Sartorius) ImmunoSpot 5.0.37 macroanalyzer (Cellular Technologies) Operetta CLSTM high-throughput system (PerkinElmer) Celigo Image Cytometer (Revvity, Lawrence, MA) CFX connected real-time PCR detection system (Bio-Rad)
Data analysis	GraphPad Prism (version 9) was used for all statistical analysis. FlowJo (version 10) was used for analyzing flow cytometry data. Octet Data Analysis software (version 12.2.0.20) was used to analyze BLI data. Coot (version 0.9.4), PyMOL (version 2.3.2), PHENIX1.15.2-3472 were used for structural related data analysis. Clustal Omega (https://www.ebi.ac.uk/Tools/msa/clustalo/) was used for sequence alignment.

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 the data supporting the findings of this study are available within the article, and its supplementary information files and source data are provided in this paper. The atomic coordinates have been deposited to the Protein Data Bank (PDB) with accession codes 8XK5, 8XK6, and 8XK8. The structures are available in the PDB under the following accession codes and links:

PDB: 8XK5 <https://doi.org/10.2210/pdb8XK5/pdb>

PDB: 8XK6 <https://doi.org/10.2210/pdb8XK6/pdb>

PDB: 8XK8 <https://doi.org/10.2210/pdb8XK8/pdb>

PDB: 8I4T <https://www.rcsb.org/structure/8I4T>

PDB: 5Y10 <https://www.rcsb.org/structure/5Y10>

PDB: 5Y11 <https://www.rcsb.org/structure/5Y11>

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

Reporting on race, ethnicity, or other socially relevant groupings

Population characteristics

Recruitment

Ethics oversight

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

Data exclusions

Replication

Randomization

Blinding

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	1. Ms CD19-PE-Cy7 (BD Biosciences, Cat#552854), 1:100 dilution. 2. Ms CD3e-BV510 (BD Biosciences, Cat#563024), 1:100 dilution. 3. Ms CD4-BV510 (BD Biosciences, Cat#563106), 1:100 dilution. 4. Ms CD8a-BV510 (BD Biosciences, Cat#563068), 1:100 dilution. 5. Ms CD95-PE-A (BD Biosciences, Cat#554258), 1:100 dilution. 6. Ms IgD-PerCp-Cy5.5 (BD Biosciences, Cat#564273), 1:100 dilution. 7. Pacific Blue™ anti-mouse CD38 (BioLegend, Cat#102720), 1:100 dilution. 8. APC-Streptavidin (BD Biosciences, Cat#554067), 1:1000 dilution. 9. Alexa Fluor™ 488 goat anti-human IgG (H+L) (Invitrogen, Cat#A-11013), 1:1000 dilution. 10. HRP goat anti-human IgG (H+L) (ABclonal, Cat#AS002), 1:20000 dilution. 11. BD Horizon™ Fixable Viability Stain 780 (BD Biosciences, Cat#565388), 1:1000 dilution. 12. I1, MAb4-5, SFTSV-N antibodies were prepared by our laboratories.
Validation	Commercial antibodies in this study were used according to the manufacturer's instructions, and validation of all antibodies was performed by the respective companies. 1. Ms CD19-PE-Cy7 (BD Biosciences, Cat#552854) was validated by two-color analysis of the expression of CD19 on mouse spleen B cells (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruope-cy-7-rat-anti-mouse-cd19.552854). 2. Ms CD3e-BV510 (BD Biosciences, Cat#563024) was validated by two-color flow cytometric analysis of CD3e expressed on mouse splenocytes (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv510-hamster-anti-mouse-cd3e.563024). 3. Ms CD4-BV510 (BD Biosciences, Cat#563106) was validated by two-color flow cytometric analysis of CD4 expression on mouse splenocytes (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv510-rat-anti-mouse-cd4.563106). 4. Ms CD8a-BV510 (BD Biosciences, Cat#563068) was validated by two-color flow cytometric analysis of CD8a expression on C57BL/6 mouse splenocytes (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv510-rat-anti-mouse-cd8a.563068). 5. Ms CD95-PE-A (BD Biosciences, Cat#554258) validated by flow cytometric analysis on mouse thymocytes. (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe.hamster-anti-mouse-cd95.554258). 6. Ms IgD-PerCp-Cy5.5 (BD Biosciences, Cat#564273) was validated by two-color flow cytometric analysis of IgD expression on mouse splenocytes (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/percp-cy-5-5-rat-anti-mouse-igd.564273). 7. Pacific Blue™ anti-mouse CD38 (BioLegend, CAT#102720) validated by flow cytometric analysis on C57BL/6 mouse splenocytes (https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-cd38-antibody-6652). 8. APC-Streptavidin (BD Biosciences, Cat#554067) was validated by flow cytometric analysis. (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-streptavidin.554067). 9. Alexa Fluor™ 488 goat anti-human IgG (H+L) (Invitrogen, Cat#A-11013) was validated by flow cytometric analysis, immunocytochemistry and immunohistochemistry. (https://www.thermofisher.cn/cn/zh/antibody/product/Goat-anti-Human-IgG-H-L-Cross-Adsorbed.Secondary-Antibody-Polyclonal/A-11013). 10. HRP goat anti-human IgG (H+L) (ABclonal, Cat#AS002) was validated by western blot analysis of extracts of human IgG (https://abclonal.com.cn/catalog/As002). 11. BD Horizon™ Fixable Viability Stain 780 (BD Biosciences, Cat#565388) was validated by fluorescent staining of jurkat cells. (https://www.bdbiosciences.com/zh-cn/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/fixable.viability-stain-780.565388). 12. I1, MAb4-5, SFTSV-N antibodies were validated by our laboratories.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	HEK293T (CRL-3216), Vero E6 (CRL-1586), s9f (CRL-1711) cells were purchased from ATCC. Expi293F (A14527) and Hi5 (B85502) cells were purchased from Thermo Fisher.
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Authentication	No further authentication was performed by the authors.
Mycoplasma contamination	Cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were 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	Female BALB/c mice (6-8 weeks old) were purchased from Vital River Laboratories (Beijing, China). The IFN- α/β receptor knockout mice (B6.129S2-Ifnar1tm1Agt/Mmjax, RRID: MMRRRC_032045-JAX), which were generated by Müller et al., were provided by Dr. Leike Zhang.
Wild animals	No wild animals were used in this study.
Reporting on sex	The Mice we used for this study are all female, and we did not set up different sex groups for comparative studies.
Field-collected samples	No field-collected sample was used in this study.
Ethics oversight	Animal experiments were approved by the Animal Care and Use Committee of Wuhan University (Approval: WDSKY0202201 and SKLV-AE2023 025), the Biosafety Committee and the Animal Ethical Committee of Wuhan Institute of Virology, Chinese Academy of Sciences (Approval: WIVA23202302).

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

Plants

Seed stocks	<i>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.</i>
Novel plant genotypes	<i>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.</i>
Authentication	<i>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, mosaicism, off-target gene editing) were examined.</i>

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	Isolation of SFTSV Gn-specific B cells: After the final boost, mice were sacrificed, and splenocytes were harvested for antigen-specific B cell sorting. Briefly, the SFTSV Gn were randomly biotinylated with EZ-link™ NHS-PEG4-Biotin (Thermo Scientific), and the isolated cells were stained with 0.5 $\mu\text{g}/\text{mL}$ biotinylated SFTSV Gn for 30 min at 4°C. Then, the cells were stained with Fixable Viability Stain 780 (BD Biosciences, 565388), Ms CD3e-BV510 (BD Biosciences, 563024), Ms CD4-BV510 (BD Biosciences, 563106), Ms CD8a-BV510 (BD Biosciences, 5630681), Ms CD19-PE-Cy7 (BD Biosciences, 552854), Ms IgD-PerCp-Cy5.5 (BD Biosciences, 564273), Pacific Blue™ anti-mouse CD38 (BioLegend, 102720), CD95-PE-A (BD Biosciences, 554258) and APC-Streptavidin for 30 min at 4°C. After washing, the cells were loaded on FACS Aria III (BD Biosciences). The target cells (780-, CD3/4/8-, CD19+, IgD-, CD95+, and APC+) were sorted into 96-well PCR plates (Bio-Rad) and stored at -80°C. Antibody binding test: The coding region of SFTSV Gn head domain was cloned into the mammalian expression vector. The Gn mutant plasmids were generated by site-directed mutagenesis. 293T cells were transiently transfected with Gn, Gc, or Gn mutant plasmids. 48 h post-transfection, the cells were harvested and fixed with 4% PFA. Cells were then washed and permeabilized with PBS with
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0.1% saponin, followed by the staining with indicated SFTSV mAbs in permeabilization buffer at 4 µg/mL. After washing twice, the cells were incubated with Alexa Fluor™ 488 goat anti-human IgG (H+L) (Invitrogen, A-11013).

Instrument

FACS Aria III (BD Biosciences), CytoFLEX S (Beckman)

Software

FlowJo version 10

Cell population abundance

Cell debris and dead cells are excluded based on forward and side scatter density plots (FSC-A/SSC-A). For the isolation of SFTSV Gn-specific B cells, Fixable Viability Stain 780 antibody was used to excluded dead cells and Ms CD3e-BV510, Ms CD8a-BV510 and Ms cD4-BV510 were used to excluded T cells. Ms IgD-PerCp-Cy5.5 was used to exclude naive B cells. APC-Streptavidin was used to recognize biotinylated SFTSV Gn. Then, SFTSV Gn-specific B cells were selected (780-, CD3/4/8-, CD19+, IgD-, CD95+, and APC+).

In the antibody binding assay, wild-type Gn and Gc expression plasmids were included as positive and negative controls to guide gating strategies.

Gating strategy

For the isolation of SFTSV Gn-specific B cells, all targeted cells (780-, CD3/4/8-, CD19+, IgD-, CD95+, and APC+) were sorted into 96-well PCR plates. About 5000-10000 events from total cells were analyzed for antibody binding test, and residues were considered critical if the binding level decreased >70% compared to the wild-type Gn.

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