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Reporting Summary

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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	ELISA data was collected using the software Omega.LNK. Flow cytometry data was collected using FACSDiva version 8.0.2 EPU automated data acquisition software (Thermo Fisher). Bio-layer Inferometry data was collected by Data aquisition 10.0 (FORTEBIO)
Data analysis	MacVector 15.5.3 was used for sequence analysis and graphs were created using R language. Flow cytometry data was processed using FlowJo 10.5.0. GraphPad Prism 7 was used for data analysis. Ig gene sequence AB1 files were converted to FASTQ format using biopython package. FASTQ files were trimmed by quality using cutadapt v1.18 software. Igblast v1.9.0 was used for VDJ assignment and clone analysis was performed using Change-O software v0.3.7. For macaques, a custom VDJ database was created using previously reported Ig gene sequences. Bio-layer inferometry data was analysed using Data analysis HT 10.0 (FOREBIO). SPR from Biacore T200 software v3.0. Phenix v1.14, Coot v0.8.9, RELION v3.0, cryoSPARC v2.2, PyMOL v2.1, Chimera v1.13, , Molprobity v4.4, Resmap v1.1.4, and Privateer v1 were used for structural analysis.

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

Cryo-EM reconstructions of the RC1-10-1074, RC1-Ab275mur, RC1-Ab874nhp, and RC1-897nhp complexes have been deposited in the Electron Microscopy Data Bank under the accession numbers AAAA, BBBB, CCCC, and DDDD, respectively. Coordinates for atomic models of the RC1-10-1074, RC1-Ab275mur, RC1-Ab874nhp, and RC1-897nhp complexes have been deposited in the Protein Data Bank under the accession numbers WWWW, XXXX, YYYY, and ZZZZ, respectively. (Accession

numbers will be provided before publication).
Other data sets generated or analysed during the current study are available from the corresponding author upon request.

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	Groups of 3-5 mice were used for immunizations considering assay variability . 4 rabbits and 8 Rhesus macaques. No statistical analysis was performed to predetermine sample size but these are standard numbers for the field.
Data exclusions	No data were excluded
Replication	Immunization experiments in wild type mice were performed more than 3 times. Antibody binding to Env was confirmed using different methods: ELISA, OCTET, SPR and/or Cryo-EM. All attempts at replication were successful.
Randomization	C57BL/6J wild type mice were purchased from The Jackson laboratory and divided in groups of same age and sex.
Blinding	Mice were homogenous in sex and age prior to grouping. Blinding is not relevant in this study. Animal samples were analysed using objective, standardized assays that include appropriate controls. There is no subjective assessment of the animals.

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

Anti-mouse IgG (Jackson ImmunoResearch #115-035-071), anti-human IgG heavy chain (Jackson ImmunoResearch #109-035-098) or anti-human Ig heavy and light chain (Jackson ImmunoResearch #109-036-088) conjugated to horseradish peroxidase (HRP) were used in ELISAS.
Mouse (BD Biosciences #553142) and human (BD Biosciences #564219) Fc Block.
anti-CD4 APC-eFluor780 (Invitrogen, #47-0042-82, cloneRM4-5, Lot # 1994174), anti-CD8 APC-eFluor780 (Invitrogen, #47-0081-82, clone 53-6.7, Lot# 1989142), anti-F4/80 APC-eFluor780 (Invitrogen, #47-4801-82, clone BM8, Lot# 4338513), anti-NK1.1 APC-eFluor780 (Invitrogen, #47-5941-82, clone PK136, Lot#1983611), anti-CD11b APC-eFluor780 (eBioscience #47-0112-82, clone M1/70, Lot#4341634), anti-CD11c APC-eFluor780 (eBioscience #47-0114-82, clone N418, Lot#E10192-1633),anti-Gr-1 APC-eFluor780 (Invitrogen, #47-5931-82, clone RB6-BC5, Lot#1994248), anti-B220 APC (eBioscience, #17-0452-82, clone RA3-6B2, Lot#E07151-1635), anti-GL7 FITC (BD Biosciences #553666, clone GL7, Lot#6021860) and anti-CD95 BV421 (BD Biosciences #562633, clone Jo2, Lot#4234912) were used for cytometric analysis of mouse B cells.
anti-CD16 APC-eFluor780 (Invitrogen, #47-0168-41, clone eBioCB16 (CB16), Lot#1942879), anti-CD8a APC-eFluor780 (Invitrogen, #47-0086-42, clone OKT8 (OKT-8), Lot#1946503), anti-CD3 APC-eFluor780 (Invitrogen, #47-0037-41, clone OKT3, Lot#1915545), anti-CD14 APC-eFluor780 (eBiosciences, #47-0149-41, clone 61D3, Lot#4319282), anti-CD20 PeCy7 (BD, #335793, clone , Lot#8204544), anti-CD38 FITC (Stem Cell technologies, #60131FI, clone AT-1, Lot#18A86904), anti-IgG BV421 (BD Biosciences, #562581, clone G18-145, Lot#7355875), anti-IgM PerCP-Cy5.5 (BD Biosciences, #561285, clone G20,-127, Lot#7278582) were used for cytometric analysis of macaque B cells.

All antibodies were used at 1:200 dilution.

Validation	All the used antibodies are commercially available and have been validated by the following manufacturers BD Biosciences, eBiosciences, Invitrogen, Jackson ImmunoResearch, Biolegend and Stem Cell technologies. Validation reports can be found on their websites using the catalogue number indicated above. In addition , the cytometry analysis performed in this manuscript validates the use of these antibodies.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK293-6E cells (National Research Council of Canada) Expi293F cells (Thermo Fisher) E. coli C41(DE3) cells (Novagen)
Authentication	Cell lines were obtained from and authenticated by vendors or scientific collaborators.
Mycoplasma contamination	The cell lines were not contaminated by mycoplasma as determined by using the Lonza Mycoplasma Detection Kit.
Commonly misidentified lines (See ICLAC register)	None

Animals and other organisms

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

Laboratory animals	Mice carrying the Ig V(D)J genes encoding the iGL IgH and IgL corresponding to the human PGT121 and 10-1074 broadly neutralizing antibodies (GLHL121 knock-in mice) were used for immunizations. C57BL/6J male mice from The Jackson laboratory were used for immunizations. Male and female mice of 6-8 weeks of age were used for experiments. Six-month-old New Zealand White rabbits (Covance) were used for immunizations. Sixteen male and female rhesus macaques (Macaca mulatta) of Indian genetic origin of 2 to 4 years of age were used for immunizations.
Wild animals	This study does not involve wild animals.
Field-collected samples	*For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.*
Ethics oversight	All procedures in mice were performed in accordance to protocols approved by the Rockefeller University IACUC. All procedures performed in rabbits were done by Covance and approved by Denver PA IACUC Committee, #0003-18. Rhesus macaques were housed and cared for in accordance with Guide for Care and Use of Laboratory Animals Report no. NIH 82-53 (Department of Health and Human Services, Bethesda, Maryland, 1985) in a biosafety level 2 NIH facility. All animal procedures and experiments were performed according to protocols approved by the Institutional Animal Care and Use Committee of NIAID, NIH.

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	Single cell suspensions were obtained from the draining lymph nodes and spleens of immunized mice, and mature B-cells were isolated by negative selection using anti-CD43 magnetic beads (MACS) following the manufacturer's instructions. Frozen PBMCs or cells from lymph node biopsies obtained from the naïve and immunized macaques were thawed and washed in RPMI medium 1640 (1x) (Gibco #11875-093).
Instrument	BD FACSAria II
Software	FACSDiva version 8.0.2.

Cell population abundance	Germinal center B cells that bound to RC1 but not to RC1-glycanKO were found in mice and macaques at frequencies between 0.2 and 5%.
Gating strategy	Single RC1 positive RC1-glycanKO negative mouse B cells were isolated by gating on single cells, Live/dead marker (Zombi NIR) negative, CD4 negative, CD8 negative, F4/80 negative, NK1.1 negative, CD11b negative, CD11c negative, Gr-1 negative, B220 positive, CD95 positive, GL7 positive, RC1 positive and RC1-glycan KO negative. Single macaque cells binding to RC1 but not to RC1-glycanKO were isolated by gating on single cells, Live/dead marker (Zombi NIR) negative, CD16 negative, CD8a negative, CD3 negative, CD14 negative, CD20 positive, CD38 positive, IgG positive and negative, IgM positive and negative, RC1 positive and RC1-glycanKO negative.

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