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	Serial EM (3.8.6) was used for cryo-EM data collection.
Data analysis	MotionCor2, CTFFind4, cryoSPARC v3.1, deepEMhancer, ResMap (1.1.4), CHIMERAX (1.4), COOT (0.8.1), PHENIX (1.19.2), MolProbity (4.3.1), PyMOL (2.0), GraphPad Prism(9.0.0), Data Analysis 9.0.

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 atomic coordinates data generated in this study have been deposited in the Protein Data Bank (PDB) database under accession code 8Z4E. The corresponding electron microscopy maps have been deposited in the Electron Microscopy Data Bank (EMDB) with the accession codes EMD-39762. Other structures for analysis, including 2CML, 4QN6, 6Q23, 6PZY, 8EZ3, 8EZ7, 8E6J, 8GAV, 4QNP, 6PZW, 6U02, were obtained from the PDB. Source data are provided in this paper.

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	Female
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	Written informed consent was obtained from the donor following the approval from the Research Ethics Committee of Shenzhen Third People's Hospital, China.

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	3,437 micrographs were used for determining N6_DQ/18_14D/1G01 complex. No statistical methods were used to predetermine sample size. Sample size for the cryo-EM studies was determined by availability of microscope time and to ensure unambiguous modeling of most of residues that allowed us to obtain a high-resolution reconstruction
Data exclusions	No data was excluded from the analyse.
Replication	All biochemical experiments were performed at least three times. All replicas of data produced similar results.
Randomization	For in vivo experiment, the mice were randomly grouped.
Blinding	Investigators were not blinded to group allocation.

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	The heavy chain and light chain of antibodies (18_14D, 1G01, MEDI8852, 13C6, HENV-32 and mutant antibody) were cloned into pCAGGS plasmids, and plasmids were transfected into HEK293T or HEK293F cells at a ratio of 1:2 to express antibody proteins. After

5 days, the supernatants were collected, and soluble protein were purified using a Protein A column(Cytiva). The proteins were further purified via gel filtration chromatography with a Superdex 200 column (Cytiva). HRP-conjugated goat anti-human or mouse IgG antibody solution (Sangon Biotech) were used in ELISA. Antibodies used for screening of human antibodies are purchased from BD Biosciences and Jackson ImmunoResearch.
FITC Mouse IgG2a, κ Isotype Control (555573) Clone G155-178 from BD Pharmingen™
PE-Cy™7 Mouse Anti-Human CD19 (560728) Clone HIB19 from BD Pharmingen™
Allophycocyanin-conjugated AffiniPure Goat Anti-Human Serum IgA, α Chain Specific (Jackson ImmunoResearch, 109-135-011)
R-Phycoerythrin-conjugated AffiniPure F(ab)2 Fragment Donkey Anti-Human IgM, Fc5μ Fragment Specific (Jackson ImmunoResearch,709-116-073)

Validation

Commercial antibodies has been validated by the manufacture. The validation materials can be found on the companies' website. We tested the avidity of other antibodies in the ELISA or BLI assay.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Insect cell lines (High Five), purchased from the Invitrogen company, were used for protein expression. HEK293T cell and HEK293F,purchased from Thermofisher scientific and stored in our lab, are used for protein expression. MDCK, purchased from ATCC , is used for virus amplification, virus inhibition assay and ADCC reporter bioassay; ADCC bioeffector cell FcγRIIIa cells, purchased from Promega , is used for ADCC reporter bioassay;
Authentication	These cells are routinely maintained in our lab. No other authentication at the lab level was performed.
Mycoplasma contamination	All cells were tested negative for Mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cells 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	6–8-week-old BALB/c mice were purchased from Vital River and were housed in a specific pathogen free (SPF) animal facility on a 12-hour light/dark cycle under ambient conditions with free access to food and water.
Wild animals	The study did not involve wild animals.
Reporting on sex	Female
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All the procedures in the murine study were reviewed and approved by the Laboratory Animal Welfare and Ethics Committee in Shenzhen Third People's Hospital, China.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

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	Convalescent PBMC of H5N6 infected patients (collected on day 18 after illness onset), and cells were washed twice with 2% FBS in PBS.
Instrument	BD Aria III
Software	FlowJo 10
Cell population abundance	Cell population abundance was shown in Extended Data Fig. 1.
Gating strategy	CD19+IgM–IgA–IgD–

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