

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 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	Sequences were obtained from GISAID using the search parameters defined in the methods section. Monoclonal antibody binding data were collected with Octet RED96 system (FortéBio). Monoclonal antibody neutralization data (luminescence) were collected with Synergy H1 microplate reader (BioTek). Sera neutralising antibody data were read on a Glomax luminometer (Promega).
Data analysis	Graphad Prism v9 for statistical analyses and to produce figures. Monoclonal antibody binding data were analyzed by Pall FortéBio/Sartorius analysis software (version 12.0). Stata V13 for correlation analyses. PyMol v1.4 (Schodinger) to produce figures. Software versions and parameters used for all software are reported in full in the methods section.

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 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

The data analysed during the current study are available freely online in the GISAID database (<https://gisaid.org>) though specific files may be requested from the corresponding author on reasonable request. Pymol structures were all obtained from PDB and are available using the accession numbers described in the methods.

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](https://www.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	n=37. No sample size calculation was performed. The sample size of this study is sufficient to obtain a relevant analysis.
Data exclusions	No exclusions.
Replication	We performed 2 independent experiments and presented representative data with technical replicates. All data were reproducible.
Randomization	This is not relevant to the study as it is not an interventional study.
Blinding	No blinding undertaken as this is not an interventional study.

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
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	The source of monoclonal antibodies used in this study is described in Extended Data Table 1 and in the Method session.
Validation	The monoclonal antibodies were validated by binding and neutralization assays as described in the references of Extended Data Table 1.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	HEK 293T and ExpiCHO cells were used for transfection work to produce pseudoviruses and mAbs, respectively.
Authentication	No cell lines used were authenticated. No new cell lines were generated.
Mycoplasma contamination	All cell lines used were tested (by PCR) and were mycoplasma free.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used in this study.

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics	Individuals receiving the Pfizer BNT162b2 mRNA vaccine were consented for the study. Median age was 62 years (IQR 47-84) and 35% were female.
Recruitment	Participants were consented into the COVID-19 cohort of the NIHR Bioresource. Consecutive individuals were enrolled without exclusion.
Ethics oversight	The study was approved by the East of England – Cambridge Central Research Ethics Committee (17/EE/0025).

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