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 in this study to collect data
Data analysis	Prism 8.0 was used to perform all data analysis. Structural figures were generated from publicly available data (Protein Data Base) using UCSF ChimeraX.

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 data supporting the findings of this study are available within the paper, in the Source Data, and from the corresponding author upon request. There are no restrictions in obtaining access to primary data. Models of mAb complexes were generated from their respective PDB files with the following accession codes: COV2-2196 (PDB: 7L7D); COV2-2130 (PDB: 7L7E); S309 (PDB: 6WPS); REGN-10987 (PDB: 6XDG); REGN-10933 (PDB: 6XDG)); LY-CoV555 (PDB: 7KMG) LY-CoV016 (PDB: 7C01); CT-P59 (PDB: 7CM4) and SARS2-38 (PDB: 7MKM).

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	No sample sizes were chosen a priori. All experiments were repeated at least three independent times, each with multiple technical replicates. Sample sizes were selected based on prior neutralization experiments with monoclonal antibodies and the ability to assess for loss of activuty
Data exclusions	No data was excluded.
Replication	All experiments had three biological and with each experiment two technical replicates were performed.
Randomization	No randomization was performed. This was not relevant to our in vitro study.
Blinding	No blinding was performed during the experimental set up phase (for convenience), although the data analysis was performed in a blinded manner

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	Human mAbs: COV2-2196, COV2-2130, S309, REGN10933, REGN10987, LY-CoV555, LY-CoV016, CT-P59, AZD7442, AZD8895, and AZD1061. Mouse mAbs: SARS2-2, SARS2-11, SARS2-16, SARS2-31, SARS2-38, SARS2-57, and SARS2-71 (mouse mAbs from the Diamond laboratiry); HRP-conjugated goat anti-mouse IgG (Sigma, A8924, 1:1000)
Validation	All primary mAbs were validated using purified SARS-CoV-2 RBD or S proteins using an ELISA. All secondary antibodies were validated by each respective manufacturer per their associated DataSheets.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Vero-TMPRSS2, Diamond laboratory; Vero-hACE2-TMPRSS2, Graham laboratory, VRC/NIH; Expi-CHO (ThermoFisher, A29127), Expi 293F (ThermoFisher, A14527)
Authentication	These cells grew as expected and propagated SARS-CoV-2 as expected. In addition, flow cytometry was used to confirm exoression of the transgenes.
Mycoplasma contamination	All cell lines are routinely tested each month and were negative for mycoplasma.
Commonly misidentified lines (See ICLAC register)	This study did not involve any commonly misidentified cell lines.