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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	Pseudovirus neutralization data collected on BertholdTech ICE software version 1.0.9.5 Viral RNA Ct collected on Roche LightCycler 480 Software release 1.5.1.62 Cytopathic effects were observed using a bright-field Olympus IX83 microscope Anti-Spike ELISA data collected on Euroimmun Analyzer I software version 1.9.5.3 Anti-spike ELISA data collected on Liason XL software version 4.2.2.4 Anti-nucleocapsid ELISA data collected on Abbot's Alinity i software version 3.2.1 Anti-nucleocapsid ELISA data collected on Roche's Elecsys on a Cobas 8000 CO software version 73470001-06-06
Data analysis	Pseudovirus neutralization data anaylzed with Graph Pad Prism 7 Figures were generated using Graph Pad Prism 9 Sequence analysis done using Geneious R10v10.0.9 Final figures compiled on Adobe Illustrator CC2018 Statistical analysis performed using R libraries: R-base: 3.6.3; lmtest: 0.9.38; bnlearn: 4.5; nlme: 3.1.149; ggeffects: 0.16.0 Microsoft Excel for Mac, Version 16.16.21

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

All data including virus spike sequences are available in the manuscript main figures or supplementary material.

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	The sample size could not be initially estimated because of the dynamic nature of SARS-CoV-2 pandemic. Based on previous experiences with with antibody responses to viral pathogens (Simek et al., 2009 Journal of Virology, Schommers et al., 2020 Cell, Rusert et al., 2016 Nature medicine), a sample size of about 1000 individuals was estimated to be sufficient to account for variability in antibody responses.
Data exclusions	No data was excluded.
Replication	Neutralization data presented is mean of two-independent technical replicates.
Randomization	Not applicable
Blinding	All antibody measurements were obtained using the sample study IDs. The clinical characteristics were combined with antibody data for final analysis.

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

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HEK-293T-ACE2 cells available from ATCC Vero E6 cells from ATCC Catalog # CRL-1586 293T-ACE2 cells avialable from BEI resources Catalog # 52511
Authentication	Cell lines were not authenticated
Mycoplasma contamination	Cell lines were not checked for Mycoplasma

Commonly misidentified lines (See ICLAC register)	No misidentified cell lines used

Human research participants

Policy information about studies involving human research participants

Population characteristics	Study inclusion criteria was i.) ≥18 years old and ii.) history of SARS-CoV-2 positive polymerase chain reaction (PCR) from nasopharyngeal swab or collected sputum, and/or iii.) an onset of COVID-19 specific symptoms longer than 3 weeks ago.
Recruitment	Participants were invited to participate in the study and all individuals fulfilling the inclusion criteria were enrolled with written informed consent without any bias based on age, gender, COVID-19 disease severity or past medical history.
Ethics oversight	Protocols 20-1187 and 16-054, approved by the Institutional Review Board (IRB) of the University Hospital Cologne

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	DRKS00010169 and DRKS00021468
Study protocol	The study protocol is available from the corresponding author upon request.
Data collection	Outpatient unit at the University Hospital Cologne (from April/2020 to December/2020)
Outcomes	Samples and clinical data were collected under the stated protocols aiming to determine the immune response to infectious pathogens in general and SARS-CoV-2 in particular. Measures of immunity were assessed using the methods described in this manuscript; clinical data were obtained through use of questionnaires. There are no traditional primary and secondary outcomes in these trials.