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	RPA primers were designed using ADAPT (https://adapt.guide).
Data analysis	Data panels were primarily generated with Prism 8 (GraphPad). RT-qPCR data were analysed using the Standard Curve (SC) module of the Applied Biosystems Analysis Software.

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 data (and code and detailed methods) used in the design of primers and crRNAs are available at adapt.sabetilab.org. Raw data for the clinical samples are available in the Supplementary Information. All raw and analysed datasets generated during the study are available for research purposes from the corresponding author on reasonable 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	Experiments with synthetic targets had 2–6 technical replicates. Experiments with patient samples had 1 replicate, owing to sample-volume constraints.
Data exclusions	No data were excluded from the analyses.
Replication	Data are representative of results for experiments that were performed more than once.
Randomization	Nasopharyngeal swab samples in each batch of tests were randomly placed on ice.
Blinding	The investigators were not blinded.

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)	All cell lines were purchased from American type Culture collection (ATCC).
Authentication	No authentication was done after purchasing the cells through ATCC.
Mycoplasma contamination	All cell lines tested negative for mycoplasma.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Human research participants

Policy information about studies involving human research participants

Population characteristics	De-identified nasopharyngeal swab patient samples were used in the study. Information regarding population characteristics was not provided.
Recruitment	No participant was specifically recruited for this study.
Ethics oversight	To conduct this research, de-identified nasopharyngeal swab patient samples were purchased from Boca Biolistics (USA) and processed under a non-human subjects research determination from the Broad Institute Office of Research Subject Protections (NHSR-4318). Additional de-identified patient samples were obtained from the Center for Disease Control and

Prevention (CDC). This was reviewed by the CDC and the study was conducted consistent with applicable federal law and CDC policy. Following the regulations for the protection of human subjects in research (Code of Federal Regulations 45 CFR 46.102(1)), the CDC determined that the collection of these samples was not considered to be human subject research. CDC samples were processed at the Broad Institute under an exempt determination issued by the Broad Institute Office of Research Subject Protections (EX-7209). SARS-CoV-2 clinical excess samples were obtained from the Rhode Island Department of Health under a waiver of consent and processed at the Broad Institute with approval from the MIT Institutional Review Board (Protocol #1612793224).

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