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Last updated by author(s): May 12, 2021

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	Source data for all figures are available at https://github.com/joshsbloom/swabseq All protocols and primers are available under an Open Covid License at https://www.notion.so/Octant-COVID-License-816b04b442674433a2a58bff2d8288df
Data analysis	All code can be accessed on https://github.com/joshsbloom/swabseq.

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 main data supporting the results in this study are available within the paper and its Supplementary Information. Source data for all figures are available on https://github.com/joshsbloom/swabseq. All protocols and primers are available under an Open Covid License at https://www.notion.so/Octant-COVID-License-816b04b442674433a2a58bff2d8288df. Videos of the workflow for SwabSeq assay are available at https://figshare.com/projects/Additional_SwabSeq_Data/113643.

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	We used 1,215 samples across three validation studies (Supplementary Figs. 5 (n = 380), 9 (n = 298) and 11 (n = 537). Sample sizes for each study were set so that at least 30 positive samples and 30 negative samples could be obtained in order to comply with FDA regulations for emergency-use authorization.
Data exclusions	Samples were excluded if their provenance could not be verified or if the patient withdrew consent.
Replication	We performed additional validations in the UCLA Student Health population, which was generally younger and asymptomatic compared to the population in the UCLA ED.
Randomization	There was no randomization into different clinical trials. Samples were all processed similarly, and then grouped upon results of the nasal swab run by gold-standard RT-qPCR.
Blinding	The Swabseq testing laboratory was blinded to the results from the RT-qPCR tests.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Remnant nasophargeal samples and saliva samples were obtained from UCLA Health patients and UCLA Student Health Center.
Recruitment	Recruitment and testing were performed by physicians at UCLA.
Ethics oversight	UCLA IRB

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