

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 No software was used for data collection.

Data analysis All analysis was performed in Geneious v11.1.5, R v3.5.0 or Harmony software (PerkinElmer). All code can be found at github.com/Flu1/Corona.

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

Raw sequences were deposited at www.ebi.ac.uk/ena, project number PRJEB40394.

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	Sample size was chosen for ferret experiments at the maximum available given the financial and logistical constraints involved in the experiment. All assays throughout were repeated on the day with at least 3 replicates, which has proven in the past to be sufficient to see a significant effect. Assays were further performed on at least 2 separate occasions (details provided in figure legends)
Data exclusions	2 post-mortem samples were excluded from the analysis as they had low number of reads similar to the negative control sample and therefore were likely contamination.
Replication	Ferret experiments were not replicated due to cost limitations. Other experimental data shown is representative of multiple experiments which replicated the findings. All assays throughout were repeated on the day with at least 3 replicates. Assays were further performed on at least 2 separate occasions (details provided in figure legends)
Randomization	Randomization was not relevant for this study as assays were read in an unbiased manner - ie there was little or no interpretation involved that could be influenced by unconscious bias.
Blinding	Blinding was not possible/relevant for this study as assays were read in an unbiased manner - ie there was little or no interpretation involved that could be influenced by unconscious bias.

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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input checked="" type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	mouse anti-FLAG (diluted 1/2000; F1804, Sigma), mouse anti-tubulin (diluted 1/5000; abcam; ab7291), mouse anti-p24 (diluted 1/2000; abcam; ab9071), rabbit anti-TMPRSS2 (diluted 1/2000; abcam; ab92323), rabbit anti-Fragilis/IFITM3 (diluted 1/2000; abcam; ab109429), rabbit anti-SARS spike protein (diluted 1/2000; NOVUS; NB100-56578) or rabbit anti-SARS-CoV-2 nucleocapsid (diluted 1/3000; SinoBiological; 40143-R019), IRDye [®] 680RD Goat anti-mouse (diluted 1/10,000; abcam; ab216776), IRDye [®] 680RD Goat anti-rabbit (diluted 1/10,000; abcam; ab216777), IRDye [®] 800CW Goat anti-mouse (diluted 1/10,000; abcam; ab216772), IRDye [®] 800CW Goat anti-rabbit (diluted 1/10,000; abcam; ab216773))
Validation	These are all commercially available antibodies with validation data available on the manufacturer's website. All antibodies used were specifically against the human version of antigens and used in this manuscript against the human version - therefore species validation is irrelevant. All antibodies were specifically chosen as they had been validated by Western Blot by the manufacturers.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Vero E6 - ATCC [®] CRL-1586; HEK 293T - ATCC [®] CRL-11268; Caco-2 - ATCC [®] HTB-37; Calu-3 - ATCC [®] HTB-55; VeroE6/TMPRSS2 - Centre for AIDS Reagents, NIBSC (100978).
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Authentication	We did not authenticate the cell lines.
Mycoplasma contamination	We did not test for mycoplasma.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in the study.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	Outbred female ferrets (16-20 weeks old), weighing 750-1000 g were used.
Wild animals	Study did not use wild animals.
Field-collected samples	Study did not use field-collected samples.
Ethics oversight	Animal research was carried out under a United Kingdom Home Office License, P48DAD9B4.

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

Human research participants

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

Population characteristics	Information is irrelevant to the study which used a small set of human post-mortem samples from the Imperial College Healthcare Tissue Bank (ICHTB).
Recruitment	Human samples used in this research project were obtained from the Imperial College Healthcare Tissue Bank (ICHTB).
Ethics oversight	ICHTB is approved by Wales REC3 to release human material for research (17/WA/0161), and the samples for this project (R20012) were issued from subcollection reference number MED_MO_20_011.

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