

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 Softmax 7.1; Cary WinUV; Agilent 7700x.

Data analysis Sigma plot (SPSS) in an Excel add-in ED50V10; Prism 8.0 (GraphPad Software Inc.);

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

Supplementary Information and Source data are provided with this Article. Additional data that support the findings of this study are available from the corresponding author upon reasonable request (Hongzhe SUN: hsun@hku.hk).

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	The sample size of n=5 each group was chosen for animal studies. For in vitro biochemical studies, three biological repeats, followed by repeating the experiments twice for confirmation were widely accepted and used in published papers.
Data exclusions	No data were excluded from the analysis.
Replication	All the experiments were subjected to at least three biological replicates unless specified.
Randomization	Hamsters were allocated randomly into experimental groups.
Blinding	The investigators were not blinded to allocation during experiments and outcome assessment.

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	Alexa Fluor secondary antibody (Invitrogen, Cat No. #A32731); rabbit-anti-SARS-CoV-2-NP serum was made in house.
Validation	The antibody is validated for the indicated use by the manufacturer.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Human colon epithelial (Caco2) cells, African green monkey kidney (VeroE6) cells and human lung epithelial cell (Calu-3) were purchased from American Type Culture Collection (ATCC). HEK293-hACE2 stable cells were kindly provided by Dr. Li Liu (AIDS Institute, The University of Hong Kong).
Authentication	The cell lines used in this study were not authenticated since they were purchased from commercial source and were extensively validated before shipping.
Mycoplasma contamination	The cell lines used in this study were confirmed to be free of mycoplasma contamination by Plasmotest (InvivoGen).
Commonly misidentified lines (See ICLAC register)	No cell lines used in this study were listed in ICLAC.

Animals and other organisms

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

Laboratory animals	Male and female Syrian hamsters, aged 6-10 weeks old, were obtained from the Laboratory Animal Unit of The University of Hong Kong. The animals were given access to standard pellet feed and water ad libitum until virus challenge in our Biosafety Level-3 animal facility.
Wild animals	This study did not involve any wild animals.
Field-collected samples	This study did not involve samples collected from the field.
Ethics oversight	All experimental protocols were approved by the Animal Ethics Committee in the University of Hong Kong (CULATR) and were performed according to the standard operating procedures of the biosafety level 3 animal facilities (Reference code: CULATR 5370-20)

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