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 <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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 exa	ct sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement		
☐ X A stater	nent on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly		
The stat	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 descri	ption of all covariates tested		
A descri	ption 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 lues 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 <u>statistics for biologists</u> contains articles on many of the points above.		
Software a	nd code		
Policy informatio	n about <u>availability of computer code</u>		
Data collection	None of code for data collection was used in this study		
Data analysis	Prism 9, Excel		
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 <u>availability of data</u>

All manuscripts must include a <u>data availability statement</u>. 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 that support the findings of this study are available from the corresponding author upon reasonable request.

Reporting on sex and gender not applicable Population characteristics not applicable Recruitment not applicable Ethics oversight not applicable Note that full information on the approval of the study protocol must also be provided in the manuscript. 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.		
Population characteristics not applicable Recruitment not applicable Ethics oversight not applicable Note that full information on the approval of the study protocol must also be provided in the manuscript. Field-specific reporting		
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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.		
6 /		
X 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 for transgenic mice experiments (n = 6) were sufficient to show a significant difference among groups.		
Data exclusions No data were excluded		
Replication Experiments were done at least twice as triplicates		
Randomization We did not use randomization in our experiments		
Blinding We did not use blinding in our experiments		
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 Methods		
n/a Involved in the study n/a Involved in the study		
Antibodies ChIP-seq		
☐ Eukaryotic cell lines ☐ Flow cytometry		
Palaeontology and archaeology MRI-based neuroimaging		
Animals and other organisms Clinical data		
Dual use research of concern		

Eukaryotic cell lines

Policy information about <u>cell lines and Sex and Gender in Research</u>

Cell line source(s) Lenti-X 293T cells (Takara-bio)

HOS-ACE2/TMPRSS2 cells: prepared as previously described (Saito et al., Nature 2021 etc)

Authentication	None of the cells used in this study were authenticated
Mycoplasma contamination	All cell lines were confirmed mycoplasma negative by commercially available PCR method
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study

Animals and other research organisms

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research, and <u>Sex and Gender in Research</u>

Laboratory animals	huACE2 transgenic mice
Wild animals	No wild animals were used in this study
Reporting on sex	not applicable
Field-collected samples	No filed collected samples were used in this study
Ethics oversight	All experiments using huACE2 transgenic mice were performed in accordance with the Science Council of Japan's Guideline for Proper Conduct of Animal Experiments. The protocol in this study was approved by the Institutional Animal Care and Use Commettee of Tsukuba Primate Research Center, National Institutes of Biomedical Innovation, Health and Nutrition.

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