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	Spinning disc confocal microscope images were collected using slidebook. LSM 880 confocal images were collected using Zeiss Black. Leica images were collected on Leica LASX software.
Data analysis	3D Single particle imaging analysis was performed using matlab and labview. Codes are available on github: Matlab- (https://github.com/VolkerKirchheim/TrackBrowser_Matlab.git), labview- (https://github.com/VolkerKirchheim/TrackBrowser_LabView.git)

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

Source data will be uploaded prior to publication of the manuscript.
Requests for further data and reagents should be made through the lead contact, Bimal Desai.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	*Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.*
Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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.

☒ 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	Experiment sample sizes are indicated in the figure legends and/or listed within the figure panel. Statistical analyses are described in the figure legend. No power analysis was used for sample sizes and replicates, but were determined based on the literature and experimental experience.
Data exclusions	No data was excluded from the analyses
Replication	Replication is indicated in figure legend or figures where applicable. All infection assays were run in triplicate with a minimum of five planes of view for each n. Single particle imaging was performed on a minimum of 9 separate cells per time point and treatment.
Randomization	While formal randomization did not occur as this work consists of treatment of cell culture lines, coverslips of siRNA treated, genetically edited cells, and genetically identical mice were randomly selected for treatment with various viruses on day of experimentation. Coverslips for pharmacological testing were randomly selected for assignment to drug groups.
Blinding	Initial infection assays (VSV-G, VSV-Rabies, VSV-Ebola, VSV-Lassa, VSV-LCMV) ins SVG-A and HeLa cells were performed blinded to virus and siRNA treatment/ genotype. Initial influenza infection in vero cells was performed blinded to siRNA treatment. Quantification of mouse histology was performed 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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[x]	[ ] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used: Rabbit anti-mouse TRPM7 antibody was generated by LifeProtein. All other antibodies were obtained commercially: Rabbit anti-human TRPM7: ab245408; Rabbit anti-rab5: CST C8B1; Rabbit anti-GFP: abcam ab6556; Rabbit anti-EGFR: CST D38B1; Rabbit anti-β-actin: CST D6A8, Mouse-anti-influenza A virus Nucleoprotein Antibody (ab20343).

Validation: Rabbit anti-mouse TRPM7 antibody was validated by lifeProein by ELISA and in the manuscript with overexpression of mouse TRPM7 constructs in human SVG-A cells. Human TRPM7 is not detected by this antibody but mouse TRPM7 constructs overexpressed are detected at 210 kDa (fig. 4a). A non-specific band is seens at ~45 kDa. All other antibodies were validated by the producer and literature.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): HeLa cells were obtained from ATCC (CCL-2)
HEK293T cells were obtained from ATCC (CRL-3216)
MDCK cells were obtained from ATCC (CCL-34)
Parental SVG-A cells were originally obtained from Dr. Walter J. Atwood, Brown University
VeroE6 and Vero-TMPRSS2 cells were obtained from Dr. Siyuan Ding, Washington University St. Louis

Authentication: All cells were monitored for changes in proliferation and cell morphology. Cells were passaged up until 20 passages when a new aliquot of cells would be thawed for passaging to avoid.

Mycoplasma contamination: Cells were routinely tested for mycoplasma using venor one step PCR mycoplasma test.

Commonly misidentified lines (See ICLAC register): *Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Animals and other research organisms

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

Laboratory animals: Trpm7fl/fl(LysM cre) C57BL/6J were used at 12 weeks. C57BL/6J female mice from Jackson were used at 8 weeks.

Wild animals: *Provide details on animals observed in or captured in the field; report species and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.*

Reporting on sex: Sex was not a variable of these ex vivo experiments, however we have seen no differences in gender in previous use of this strain (Trpm7fl/fl(LysM cre) of mice.

Field-collected samples: *For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.*

Ethics oversight: University of Virginia IACUC

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