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-disk confocal microscope (Dragonfly, Oxford Instruments) equipped with an ultrasensitive 1024×1024 EMCCD camera (iXon Life 888, Andor) and four laser lines (405, 488, 561, and 637nm) Spinning disk Olympus SR microscope equipped with a sCMOS Fusion BT camera (Hamamatsu), four laser lines, and 40X 1.4 and 60X 1.42 oil objectives nanoAcquity UltraPerformance Liquid Chromatography device (Waters Corporation) coupled to a quadrupole-Orbitrap mass spectrometer (Q-Exactive HF-X, Thermo Fisher Scientific) NovoCyte Flow cytometer (Agilent Technologies) PELCO easislicer (Ted Pella) Minux FS800 cryostat (RWD Life Science) ChemiDoc imaging system (Bio-Rad) Absorbance microplate reader Infinite M Plex (TECAN) CFX Opus 384 Real-Time PCR system (Bio-Rad) Trans-Blot Turbo Transfer System (Bio-Rad) MEA2100-Mini headstage (MultiChannel System)
Data analysis	Bitplane Imaris x64 (Oxford Instruments) version 9.7 GSEA (https://www.gsea-msigdb.org/gsea/index.jsp) FiJi 2.18 (ImageJ) CFX Maestro software (BioRad) FlowJo v10.2 FireLearn software (https://github.com/membrane-dynamics-and-viruses) in version 1.0.13-beta

geNorm software
R Studio 4.6
scikit-learn python library version 1.3.1
Multi Channel Experimenter software (Multichannel system)
GraphPad Prism version 10 and above
PhenoExam
clusterProfiler
Proline software version 2.6.2
ProStaR software
Microsoft Excel 2019
SaveRUNNER R package (https://github.com/giuliafiscon/SAveRUNNER.git)
ImageLab 6.1 software (Bio-Rad)

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

The proteomic data generated in this study have been deposited in the ProteomeXchange database under accession code PXD058349. Supplementary data and Source data are provided with this paper.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The data using brain explants originate from 1 female and 3 males. Statistics based on gender could not be performed due to the low number of samples.
Reporting on race, ethnicity, or other socially relevant groupings	NA
Population characteristics	All the data presented for organotypic culture of brain explant originate from 4 patients aged from 31 and 58 years old. They were all negative for SARS-CoV-2. All known clinical metadata are shown in Supplementary data S7.
Recruitment	Cadavers were chosen based on the absence of cerebral injury or trauma and the post-mortem interval (PMI) was not exceeding 8 h.
Ethics oversight	Institutional review board (IRB) of the CHU of Montpellier and French Biomedicine Agency. Family consent was obtained, and absence of opposition from the patient was checked at the French Biomedicine Agency for each patient.

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	Sample size was chosen based on available material, but no statistical test was perform to evaluate it.
Data exclusions	Data were not excluded
Replication	Number of replicates for each experiments are indicated in the figure legends.
Randomization	Our study was not randomized as patient samples were selected based on the cause of death and post-mortem delay

Blinding	Blinding was not applicable to our study because patient samples were chosen and studied one at a time.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

The following antibodies were used for immunofluorescence in this study:
rabbit polyclonal anti-MAP2 (GeneTex, GTX133109, 1:100), 20 references from manufacturer's website.
rabbit monoclonal anti-Homer1 (Synaptic Systems, 160 003, 1:100), > 80 references from manufacturer's website.
mouse monoclonal anti-Bassoon (Abcam, ab82958, clone [SAP7F407], 1:100), Antibody validated in IHC on an automated Leica Biosystems BOND RX™ stainer by manufacturer.
guinea pig anti-synaptophysin (Synaptic System, 101 308, 1:100), KO validated by manufacturer.
rabbit anti-synaptopodin (Synaptic Systems, 163 002, 1:100), KO validated by manufacturer.
rabbit anti-PSD95 (Synaptic System, 124 008, 1:100), KO validated by manufacturer.
goat anti-GFAP (Novus Biologicals, NB100-53809, 1:100), 22 references from manufacturer's website.
rat anti-CTIP2 (Bcl11b) at 1:200 (BioLegend, #650602, clone 25B6), 6 references from manufacturer's website.
mouse anti-S100β at 1:200 (Sigma-Aldrich, S2657, clone clone SH-B4), validated in IHC and WB on manufacturer's website.
rabbit anti-LACV cross-reactive hyperimmune plasma (cross-reactivity with TAHV) at 1:50 (gift from Dr. Karin Peterson)
donkey anti-rabbit IgG Alexa Fluor Plus 488 (Thermo Fisher Scientific, A21206, 1:1000),
donkey anti-guinea pig IgG Alexa Fluor 647 (JacksonImmuno, RRID: AB_2340476, 1:1000),
donkey anti-mouse IgG Alexa Fluor Plus 647 at 1:1000 (Thermo Fisher Scientific, A32787, 1:1000).

The following antibodies were used for immunoblotting in this study:
rabbit polyclonal anti-MAP2 (GeneTex, GTX133109, 1:200), 20 references from manufacturer's website.
goat anti-GFAP (Novus Biologicals, NB100-53809, 1:200), 22 references from manufacturer's website.
mouse anti-CD56/NCAM1 (BioLegend, 304601, , clone MEM-188, 1:200), 10 references from manufacturer's website.
rabbit anti N-cadherin, (GeneTex, GTX127345, 1:200), KO/KD orthogonal validation by manufacturer, and 97 references from manufacturer's website.
mouse anti-VAP-A, (Santa Cruz Biotechnology, SC-293278, 1:200, clone 4C12), 10 references from manufacturer's website.
rabbit anti-Calreticulin, (Thermo Fisher Scientific, PA3-900, 1:200), 260 references from manufacturer's website.
mouse anti-PSD95 (GeneTex, GTX634291, 1:200, clone GT1234), 2 references from manufacturer's website.
mouse anti-synaptophysin (BioLegend, 837103, 1:200, clone SP17), 5 references from manufacturer's website.
rabbit anti-synaptopodin (Synaptic Systems, 163 002, 1:200), KO validated by manufacturer.
rabbit anti-homer1 (Synaptic Systems, 160 003, 1:200), > 80 references from manufacturer's website.

The following antibodies were used for flow cytometry in this study:
APC-conjugated anti-human NCAM1/CD56 antibody (BioLegend, 362503, clone 5.1H11, 1:200), 31 references from manufacturer's website.
FITC-conjugated anti-human CD15 antibody (BioLegend, 301903, clone HI98, 1:200), 28 references from manufacturer's website.

Validation

Except for TAHV antibody provided and validated in Dr. Karin Peterson lab, all other antibodies are commercially available, and validated by the manufacturer and/or scientific publications.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

Vero E6 cells (ATCC CRL-1586)
H9 cells (WiCell)
hiPSCs (HPSI0214i-wibj_2; HipSci, Culture Collections).
LUHMES cells (from the Leist's lab https://doi.org/10.1111/j.1471-4159.2011.07255.x)

Authentication

The cell lines used were not authenticated

Mycoplasma contamination	All cells were tested negative.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cells were used.

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	Swiss Albino wildtype male mice
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	*Indicate if findings apply to only one sex; describe whether sex was considered in study design, methods used for assigning sex. Provide data disaggregated for sex where this information has been collected in the source data as appropriate; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex-based analyses where performed, justify reasons for lack of sex-based analysis.*
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	All the mouse experiments were approved and performed in accordance with Institutional Animal Ethics Committee (IAEC) approved by the Committee for Control and Supervision of Experiments on Animals (CCSEA), Ministry of Fisheries, Animal Husbandry and Dairying, Department of Animal Husbandry and Dairying Government of India, New Delhi. The experimental protocol was approved by the IAEC of Devi Ahilya Vishwavidyalaya, Indore (registration no. 779; Protocol approval number:779/PO/Re/S/2003/CCSEA/IAEC/2025/002).

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

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*