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	Maxwell® 16 Instrument, CFX96 Touch Deep Well Real-Time PCR Detection System Biorad, Qiagen TissueLyser II, Agilent 2100 bioanalyzer, Illumina NextSeq 2000, NovaSeqX+ platform, Leica TCS SP8 Confocal System, dual camera sCMOS Hamamatsu ORCA FLASH, CytoFLEX Flow Cytometer.
Data analysis	Sequana 0.15.3, Snakemake 7.32.4, Fastp 0.22.0, Bowtie2, STAR, FeatureCounts 2.0.1, MultiQC 1.11, DESeq2 library 1.34.0, Cytoscape app ClueGO 2.5.3, Icy software version 3, ImageJ 2.14.0/1.54f, Clustal-Omega 1.2.4, IQ-TREE v2.0.6, GraphPad Prism (version 9.5.1), Floreada.io website (version SIMD), SWISS-MODEL Workspace server (https://swissmodel.expasy.org/, SMTL version 2023-04-05, PDB release 2023-03-31)

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

RNA-seq data have been deposited to the Gene Expression Omnibus (GEO) database under the accession number GSE295802 (https://urldefense.com/v3/__https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE295802__;!!JFdNOqOXpB6UZW0!sR4HNvjW7T4xwxbEqgJZGtFaMjiKrZTv5ak9KxavvdWnzi4ilMhOFBaWUu0vEL095w7RAiqp-l4Ge0U4ic8$; token for accession: cvovusmypdwtfaj). Data are publicly available. Source data are provided with this paper. Others requests for data may be directed to and will be fulfilled by the corresponding author, Nadia Benaroudj.

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	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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	No statistical analyses were performed to predetermine the sample sizes. 4 hamsters were used in each group in this study. This sample size was chosen according to institutional directives with the 3Rs rules (Replacement, Reduction and Refinement). For all experiments, n=3 is the minimum number of independent subjects necessary to perform statistical analyses.
Data exclusions	No data were excluded from the analyses
Replication	In all experiments, we performed at least two or three replicates, as indicated in the paper.
Randomization	Randomization was not relevant for this study, as we only compared the same kinds of cells under laboratory condition, and data and analyses are objective and not prone to influence by researcher bias.
Blinding	Blinding was not applied in this study because the experimental design did not involve treatment versus control group or subjective assessments that could introduce observer bias. The research does not include human participants, clinical interventions or conditions where knowledge of experimental groups could influence data collection or analysis. Objective measurements and standardized protocols were used to avoid potential bias. Therefore, blinding was not relevant to our study design.

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

For immunofluorescence assay : anti-ZO1 (13663; Cell Signaling) at 1 :100, anti-ZO2 (2847; Cell Signaling) at 1 :100, ActiStain555 phalloidin (PHDH1; Tebu) at 100 nM, anti-JAM1 (82196; Cell Signaling) at 1 :100, anti-connexin-43 (3512; Cell Signaling) at 1 :100, Alexa Fluor 555 (A-21428) or 488 (A-11008) antibody (ThermoFisher) at 1 :500, DAPI (62248; ThermoFisher) at 1µg/mL, anti-pan-cadherin (PA5-16766; ThermoFisher) at 1 :100.
For immunoblot assay : anti-ZO1 (13663; Cell Signaling) at 1 :1000, anti-ZO2 (2847; Cell Signaling) at 1 :1000, anti-Profilin-1 (3246; Cell Signaling) at 1 :1000, anti-WAVE-2 (3659; Cell Signaling) at 1 :1000, anti-pRac1 (2461; Cell Signaling) at 1 :1000, anti-pCofilin (3313; Cell Signaling) at 1 :1000, anti-Cofilin (5175; Cell Signaling) at 1 :1000, anti-GAPDH (5174; Cell Signaling) at 1 :1000, anti-MLC2 (8505; Cell Signaling) at 1 :1000, anti-pMLC2 (3671; Cell Signaling) at 1 :1000, anti-PERK (3192; Cell Signaling) at 1 :1000, anti-pPERK (PA5-40294; ThermoFisher) at 1 :1000, anti-IRE1 (3294; Cell Signaling) at 1 :1000, anti-pIRE1 (PA1-16927; ThermoFisher) at 1 :1000, anti-3xFLAG (87537; Cell Signaling) at 1 :1000, HRP-conjugated antibody (7074S; Cell Signaling) at 1 :1000, anti-pan-cadherin (PA5-16766; ThermoFisher) at 1 :1000.

Validation

Validations were performed by IF or Western Blot in samples known to express the protein of interest.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

The HEK293T cell line (ATCC, CRL-3216) was a gift from Mme Delphine BRUN (Institut Pasteur Paris). The HepG2 cell line (ATCC, HB-8065) was a gift from Dr Ludovic Tailleux (Institut Pasteur Paris).

Authentication

HEK293T and HepG2 were authenticated by the suppliers but they were not authenticated by the authors of the study.

Mycoplasma contamination

Cells were not assessed for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

Commonly misidentified cell lines were not used in this study.

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

Four-week-old male Golden Syrian hamsters (RjHan:AURA, Janvier Labs)

Wild animals

Wild animals were not used.

Reporting on sex

Only male hamsters were used to avoid physiological variations due to the sex cycle in female hamsters and to ensure consistency of responsiveness. The purpose of this study was not to examine sex differences, therefore, we used male hamsters exclusivel

Field-collected samples

Field-collected samples were not used.

Ethics oversight

Protocols for animal experiments are conformed to the guidelines of the Animal Care and Use Committees of the Institut Pasteur (Comité d'éthique d'expérimentation animale CETEA # 220016), agreed by the French Ministry of Agriculture. All animal procedures carried out in our study were performed in accordance with the European Union legislation for the protection of animals used for scientific purposes (Directive 2010/63/EU).

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

Plants

Seed stocks	Not applicable for this study
Novel plant genotypes	Not applicable for this study
Authentication	Not applicable for this study

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	For labelling apoptotic/necrotic cells, uninfected or infected cells were washed with cold phosphate-buffered saline and resuspended with 1X annexin-binding buffer containing 5 µL Alexa Fluor 488 Annexin V and 1 µL 100 µg/mL PI working solution (V13241; ThermoFisher). Cells were incubated at room temperature for 15 minutes. After the incubation period, 400 µL 1X annexin-binding buffer was added and cells were keeped on ice before the analysis by flow cytometry. or For Fluo-8 AM straining, uninfected or infected cells were incubated with Fluo-8 AM (Abcam) at a concentration of 4 µM for 1 hr, after which they were washed twice with complete FluoroBrite DMEM medium prior to the analysis time by flow cytometry.
Instrument	CytoFLEX Flow Cytometer (Beckman Coulter)
Software	Floreada.io website (version SIMD)
Cell population abundance	Pure cell culture was used.
Gating strategy	FSC/SSC to PE/FITC for Apoptotic/Necrotic assays. FSC/SSC to FITC for Fluo-8 AM assays.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.