nature portfolio

Corresponding author(s): Xiaodong Wang, Sanduo Zheng

Last updated by author(s): June 11, 2025

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	Nikon A1+SIM, TECNAI spirit G2 (FEI; Eindhoven, Netherlands) transmission electron microscope,Titan Krios G4 microscope (Thermal Fisher Scientific),PerkinElmer (EnSpire), ÄKTA pure system (Cytiva), Infinite M200 Pro microplate reader (Tecan), OPTIMAX 2010 X-Ray film processor, 1H NMR spectroscopy (Varian Inova-400 MHz spectrometer). HPLC purification using a Waters HPLC system equipped with an Atlantis T3 column (5 µm, 19 × 150 mm; Waters). Mobile phases consisted of 0.1% NH4HCO3/H2O (solvent A) and acetonitrile (solvent B). Elution was monitored with a 2998 PDA detector and 3100 MS detector using electrospray ionization (ESI). CryoEM data were collected on Titan Krios G3 or G4 with the detector Gatan or Falcon 4.
Data analysis	GraphPad Prism 8, ImageJ (version 1.50d), CellSens(version 4.1.1), NIS-Elements AR analysis (version 5.0), CryoSPARC4.3, COOT (version 0.9.8.91), Phenix1.20, PyMOL3.1.1, UCSF Chimera1.18, ChimeraX1.9

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

Atomic coordinate for SIR3-ADPR-bound SARM1 has been deposited in the PDB under accession number 9UGJ (https://doi.org/10.2210/pdb9ugj/pdb). The corresponding cryo-EM map has been deposited in the Electron Microscopy Data Bank under the accession number EMDB-64139 (https://www.ebi.ac.uk/emdb/EMD-64139).

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 methods were used to predetermine sample size. Experiments were performed with three or more replicates based on experience. For cell line experiments, three or more independent experiments were performed. For in vitro experiments, at least three biological replicates were used for statistical analysis. For primary cells experiments , at east three distinct samples were used.
Data exclusions	No data was excluded from studies.
Replication	All attempts at replication were successful. Number of replicates are noted at figures by individual dots, and/or specified at figure legends. Experiments were independently repeated at least three times with similar results. Cryo-EM structure determination was not replicated due to intensive nature of experiments.
Randomization	Throughout the whole experiment, samples were randomized into groups.
Blinding	No blinding was used throughout experiments. All data collected was quantifiable and blinding would not change any bias in data collected.

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

Rabbit polyclonal anti-SARM1 antibody (abcam, ab226930), anti-Flag M2 antibody (Sigma-Aldrich F1804), anti-DYKDDDDK (Invitrogen MA1-91878), LAMP1 antibody (Santa Cruze sc-20011), anti-NfM (Proteintech 25805-1-AP), anti-Tom20 (Santa Cruze sc-17764), anti-β-Actin-HRP (MBL, PM053-7), Anti-GAPDH mAb-HRP(MBL, M171-7), anti-DDDDK-HRP (MBL, M185-7), Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa FluorT 488(Invitrogen A-11001), Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Cyanine3 (Invitrogen A10520)

mouse anti-SARM1 antibody was generated and purified by the antibody facility of National Institute of Biological Sciences, Beijing.

Validation

All antibodies(expect mouse anti-SARM1 antibody) used in this study are commercially available and have been widely used in publications. They have been validated for the western blot or studies and immunofluorescence specificity for cells. The complete information and validation details are provided in the respective manufacturer's website data-sheets.

Rabbit polyclonal anti-SARM1 antibody (abcam, ab226930): Supplier has been validated in western blot of human HEK-293T whole cell lysate and immunofluorescence analysis of human HEK-293T cells. (PMID: 36055989)
anti-Flag M2 antibody (Sigma-Aldrich F1804): Supplier has been validated in immunofluorescence analysis of MDCK canine kidney epithelial cells transfected with FLAG tagged myr-PKCz. (PMID: 28053121)
anti-DYKDDDDK (Invitrogen MA1-91878): Supplier has been validated in immunofluorescence analysis of Chlamydia trachomatis FLAG®-tagged IncA (blue) in HeLa cells and Western blot analysis of HEK293 cells transfected with DYKDDDDK-tagged protein vector. (PMID: 33655280)
LAMP1 antibody (Santa Cruze sc-20011): Supplier has been validated in Western blot analysis of LAMP-1 expression in MDA-MB-231 and Immunoperoxidase staining of formalin fixed, paraffin-embedded human esophagus tissue. (PMID: 33655280)
anti-NfM (Proteintech 25805-1-AP): Supplier has been validated in Western blot analysis of NfM expression in mouse brain lysate, immunohistochemical analysis of paraffin-embedded mouse cerebellum tissue slide, and immunofluorescent analysis of (4% PFA) fixed mouse brain. (PMID: 33391504)
anti-Tom20 (Santa Cruze sc-17764): Supplier has been validated in Western blot analysis of Tom20 expression in Jurkat (A), Caki-1 (B), A549 (C), HeLa (D) and Raji (E) whole cell lysates and Direct immunoperoxidase staining of formalin fixed, paraffin-embedded human fallopian tube tissue showing cytoplasmic staining of glandular cells. (PMID: 38848361)
anti-β-Actin-HRP (MBL, PM053-7): Supplier has been validated in Western blot analysis of HEK293T lysate. (PMID:24647621)
Anti-GAPDH mAb-HRP(MBL, M171-7): Supplier has been validated in Western blot analysis of PC2 cell lysate. (PMID:23680462)
anti-DDDDK-HRP (MBL, M185-7): Supplier has been validated in Western blot analysis of N-terminal DDDDK-tag protein A. (PMID:23680462)
Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa FluorT 488 (Invitrogen A-11001): Supplier has been validated in Immunoflorescence of 4% PFA-fixed Hela cells NF-kappa-B (P65). (PMID:38030597)
Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Cyanine3 (Invitrogen A10520): Supplier has been validated in western blot of rabbit IgG Heavy Chain and Light Chain. (PMID:38291037)

The anti-SARM1 was validated and optimized for western blot and immunoflorescence experiment by our lab, and have published before. (https://newetds.lib.tsinghua.edu.cn/qh/paper/summary?dbCode=ETDQH&sysId=278848)

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	HEK 293T and Hela cell lines. All cell lines were initially purchased from the American Type Culture Collection (ATCC).
Authentication	Cell cultures purchased from ATCC were authenticated by Short Tandom Repeat (STR).
Mycoplasma contamination	Cell lines were not tested for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	NONE

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	Embryonic day 15-17 mouse (C57BL/6J) were obtained from Vital River Laboratory Animal Technology Co. and Embryonic day 15-17 SARM1 knockout mouse (C57BL/6J) were generated by the animal facility of the National Institute of Biological Sciences,Beijing. All mouse were housed under a 12:12 light-dark cycle at room temperature and 40% humidity.
Wild animals	NONE
Reporting on sex	NONE
Field-collected samples	NONE
Ethics oversight	This study was performed in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Biological Sciences, Beijing (Approval ID: NIBSLuoM15C).

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

Plants

Seed stocks	NONE
Novel plant genotypes	NONE
Authentication	NONE