

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

- | | | |
|-------------------------------------|-------------------------------------|--|
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | The statistical test(s) used AND whether they are one- or two-sided
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | A description of all covariates tested |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons |
| <input type="checkbox"/> | <input checked="" type="checkbox"/> | 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) |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
<i>Give P values as exact values whenever suitable.</i> |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | 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	Confocal images were taken on a Leica TCS SP5 II microscope equipped with HCX PL APO 63x/1.40-0.60 Oil CS and HCX PL FLUOTAR 100X/1.30 Oil immersion objective lens. The parameters of DXR Raman microscope were as follows: a 532 nm laser beam, high-resolution grating, 8 mW laser power, a 50-micron slit aperture, and 30 seconds of photobleaching.
Data analysis	Super-resolution images were calculated from the raw data using Leica Application Suite X software. All data were plotted using either OriginPro 2024b or Prism software (GraphPad Prism, versions 7 or 9) and analyzed for statistical significance using Prism software (GraphPad Prism, versions 7 or 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](#)

All data are included in the manuscript and its supplementary information files. The gel source images for the western blot can be found in Fig. 1d and Supplementary Fig. 4, which are provided with the manuscript and its supplementary information files.

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 authors declare that this study has no gender-related issues.
Reporting on race, ethnicity, or other socially relevant groupings	The authors declare that this study does not involve any issues related to race or ethnicity.
Population characteristics	This study does not address population characteristics.
Recruitment	This study does not involve recruitment.
Ethics oversight	This study has not used any animal or human samples so far, and therefore does not require ethics oversight.

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](https://www.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	We did not use any statistical methods to predetermine sample size for experimentation, except for fixed cell passages. For three repeated experiments of each sample, the same batch and passage of cells were used.
Data exclusions	No replicate data were excluded.
Replication	All our data were reliably reproducible. The number of individual biological repeats were stated in the figure legends.
Randomization	This study does not require randomization.
Blinding	No blinding was applied because the cell phenotypes were very straightforward.

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This study does not involve such research.
Research sample	This study does not involve such research.
Sampling strategy	This study does not involve such research.
Data collection	This study does not involve such research.

Timing	<input type="text" value="This study does not involve such research."/>
Data exclusions	<input type="text" value="This study does not involve such research."/>
Non-participation	<input type="text" value="This study does not involve such research."/>
Randomization	<input type="text" value="This study does not involve such research."/>

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	<input type="text" value="This study does not involve such research."/>
Research sample	<input type="text" value="This study does not involve such research."/>
Sampling strategy	<input type="text" value="This study does not involve such research."/>
Data collection	<input type="text" value="This study does not involve such research."/>
Timing and spatial scale	<input type="text" value="This study does not involve such research."/>
Data exclusions	<input type="text" value="This study does not involve such research."/>
Reproducibility	<input type="text" value="This study does not involve such research."/>
Randomization	<input type="text" value="This study does not involve such research."/>
Blinding	<input type="text" value="This study does not involve such research."/>

Did the study involve field work? ☐ Yes ☒ No

Field work, collection and transport

Field conditions	<input type="text" value="This study does not involve such research."/>
Location	<input type="text" value="This study does not involve such research."/>
Access & import/export	<input type="text" value="This study does not involve such research."/>
Disturbance	<input type="text" value="This study does not involve such research."/>

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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input type="checkbox"/> Clinical data
<input type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involved in the study
<input type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	Primary antibodies used: anti-RNF213 (1:200, ATLAS, HPA003347), anti-Ub (1:200, Novus Biologicals. NBP3-06879), anti-A β (1:2000, Biolegend, 6E10), anti-GAPDH (1:10000, Genetex, GTX110118). Secondary antibodies used: Thermo Fisher Scientific (1:200, Alexa-conjugated anti-rabbit, and anti-mouse), Jackson ImmunoResearch (1:3000, HRP-conjugated anti-mouse) and Abcam (1:10000, HRP-conjugated anti-rabbit).
Validation	All antibodies were used according to manufactures' instructions.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	SHSY5Y and BV2 were shared from professor Jyh-Lyh Juang (Institute of Molecular and Genomic Medicine, National Health Research Institutes, Taiwan) and professor Yi-Juang Chern (Institute of Biomedical Sciences, Academia Sinica, Taiwan), respectively. Commercial cell lines: cortical neurons (Applied StemCell, ASE-9741-C)
Authentication	The authors declare that none of the cell lines have authentication issues.
Mycoplasma contamination	The provider initially confirmed that the cell lines were tested and confirmed negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No Commonly misidentified cell lines were used in the study.

Palaeontology and Archaeology

Specimen provenance	This study does not involve such research.
Specimen deposition	This study does not involve such research.
Dating methods	This study does not involve such research.
<input type="checkbox"/> Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight	This study does not involve such research.

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

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	Animal experiments require a proposal, but this study has not yet involved such experiments.
Wild animals	Animal experiments require a proposal, but this study has not yet involved such experiments.
Reporting on sex	Animal experiments require a proposal, but this study has not yet involved such experiments.
Field-collected samples	Animal experiments require a proposal, but this study has not yet involved such experiments.
Ethics oversight	Animal experiments require a proposal, but this study has not yet involved such experiments.

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	No clinical samples, trials, or cohort-related associations were involved in this study.
Study protocol	No clinical samples, trials, or cohort-related associations were involved in this study.

Data collection

No clinical samples, trials, or cohort-related associations were involved in this study.

Outcomes

No clinical samples, trials, or cohort-related associations were involved in this study.

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No Yes

- | | | |
|-------------------------------------|--------------------------|----------------------------|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Public health |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | National security |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Crops and/or livestock |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Ecosystems |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other significant area |

Experiments of concern

Does the work involve any of these experiments of concern:

No Yes

- | | | |
|-------------------------------------|--------------------------|---|
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Demonstrate how to render a vaccine ineffective |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Confer resistance to therapeutically useful antibiotics or antiviral agents |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enhance the virulence of a pathogen or render a nonpathogen virulent |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Increase transmissibility of a pathogen |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Alter the host range of a pathogen |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable evasion of diagnostic/detection modalities |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Enable the weaponization of a biological agent or toxin |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> | Any other potentially harmful combination of experiments and agents |

Plants

Seed stocks

This item is not included in our study.

Novel plant genotypes

This item is not included in our study.

Authentication

This item is not included in our study.

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

May remain private before publication.

This item is not included in our study.

Files in database submission

This item is not included in our study.

Genome browser session

(e.g. [UCSC](#))

This item is not included in our study.

Methodology

Replicates	This item is not included in our study.
Sequencing depth	This item is not included in our study.
Antibodies	This item is not included in our study.
Peak calling parameters	This item is not included in our study.
Data quality	This item is not included in our study.
Software	This item is not included in our 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	This item is not included in our study.
Instrument	This item is not included in our study.
Software	This item is not included in our study.
Cell population abundance	This item is not included in our study.
Gating strategy	This item is not included in our study.
<input type="checkbox"/> Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.	

Magnetic resonance imaging

Experimental design

Design type	This item is not included in our study.
Design specifications	This item is not included in our study.
Behavioral performance measures	This item is not included in our study.

Acquisition

Imaging type(s)	This item is not included in our study.
Field strength	This item is not included in our study.
Sequence & imaging parameters	This item is not included in our study.
Area of acquisition	This item is not included in our study.
Diffusion MRI	<input type="checkbox"/> Used <input type="checkbox"/> Not used

Preprocessing

Preprocessing software	This item is not included in our study.
------------------------	---

Normalization	<input type="text" value="This item is not included in our study."/>
Normalization template	<input type="text" value="This item is not included in our study."/>
Noise and artifact removal	<input type="text" value="This item is not included in our study."/>
Volume censoring	<input type="text" value="This item is not included in our study."/>

Statistical modeling & inference

Model type and settings	<input type="text" value="This item is not included in our study."/>
Effect(s) tested	<input type="text" value="This item is not included in our study."/>
Specify type of analysis: <input type="checkbox"/> Whole brain <input type="checkbox"/> ROI-based <input type="checkbox"/> Both	
Statistic type for inference	<input type="text" value="This item is not included in our study."/>
(See Eklund et al. 2016)	
Correction	<input type="text" value="This item is not included in our study."/>

Models & analysis

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Functional and/or effective connectivity
<input checked="" type="checkbox"/>	<input type="checkbox"/> Graph analysis
<input checked="" type="checkbox"/>	<input type="checkbox"/> Multivariate modeling or predictive analysis
Functional and/or effective connectivity	<input type="text" value="This item is not included in our study."/>
Graph analysis	<input type="text" value="This item is not included in our study."/>
Multivariate modeling and predictive analysis	<input type="text" value="This item is not included in our study."/>