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Corresponding author(s): DBPR, NCOMMS-23-04548

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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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	EVOS FL Auto Software, Revision 2.0; Zetasizer software 7.11; BD FACSDiva v9.0; Synergy H1 plate reader Gen 5 v2.09; FEI Tecnai G2 Spirit BioTWIN; Nikon NIS-Elements; Odyssey® CLx Near-Infrared Imaging System, image Studio v5.2;
Data analysis	GraphPad Prism, Version 8.3.0; FlowJo X 10.0.7r2; ImageJ 1.51j8; Microsoft excel

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the plots within this paper and other finding of this study are available from the supplementary data and corresponding author upon reasonable request.

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	All the experiments were repeated at least three times independently and standard deviations were calculated from those data.
Data exclusions	On principle, data were only excluded for failed experiments, reasons for which included suboptimal activation and microbial contamination.
Replication	Replicate experiments were successful.
Randomization	NA
Blinding	Investigators were not 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
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used

Rab5 (C8B1) Rabbit mAb, Cell Signaling Technology 3547T
EEA1 (C45B10) Rabbit mAb ,Cell Signaling Technology 3288T
LAMP1 (D2D11) XP® Rabbit mAb, Cell Signaling Technology 9091T
Clathrin Heavy Chain (D3C6) XP® Rabbit mAb, Cell Signaling Technology 4796T
Flotillin-1 (D2V7J) XP® Rabbit mAb, Cell Signaling Technology 18634T
Tf (CD71 (D7G9X)) XP® Rabbit mAb, Cell Signaling Technology 13113T
GAPDH (D16H11) XP® Rabbit mAb, Cell Signaling Technology 5174T
4F2hc/CD98 (D3F9D) XP® Rabbit mAb, Cell Signaling Technology 47213S
Neuropilin-1 (D62C6) Rabbit mAb, Cell Signaling Technology 3725S
CDH1, E-Cadherin (24E10) Rabbit mAb, Cell Signaling Technology 3195
CDH1, E-Cadherin (24E10) Mouse mAb, Cell Signaling Technology 14472S
β-Actin (BA3R) Mouse mAb, Thermo Fisher MA5-15739
IRDye® 680RD Donkey anti-Rabbit IgG, Li-Cor 926-68073
IRDye® 800CW Donkey anti-Mouse IgG, Li-Cor 926-32212
IRDye® 800CW Streptavidin, Li-Cor 926-32230
Neutravidin, Oregon Green 488, Invitrogen A6374
Neutravidin, DyLight 550, Invitrogen 84606
Donkey anti-mouse IgG, AF488, Invitrogen A32766
Donkey anti rabbit IgG, AF488, Invitrogen A21206
Donkey anti rabbit IgG, AF647, Invitrogen A31573

Validation

Antibodies were used as specified by the manufactures protocol for immunofluorescence staining, WB and flow cytometry. Antibody specificity was evaluated using the proper negative controls.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	H1975, A549 and PC3, MCF10CA1a cells were purchased from American Type Culture Collection (Manassas, VA). MIA PaCa 2 cells were provided by Dr. Commisso (SBP Medical Discovery Institute, CA).
Authentication	NA
Mycoplasma contamination	We have tested all cell lines to rule out mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	A549 cells are newly are recently acquired from ATCC.

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	Sample preparation listed in Methods
Instrument	Fortessa X-20, LSR II H1010, and LSR II H4760 (BD Bioscience, San Jose, CA, USA)
Software	BD FACSDiva v9.0 for data collection and FlowJo X 10.0.7r2 for analysis
Cell population abundance	No sorting was performed with the flow cytometer
Gating strategy	For all experiments FSC-A/ SSC-A gates of the starting cell population were used to discriminate between viable cells and cell debris. Singlet and doublet cells were discriminated using FSC-A/ FSC-H gating. Singlet cells were then used for further quantification.

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