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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	Data were collected by using standard features of NIS Elements Viewer (version 4.11.0) and FIJI (Version 1.0).
Data analysis	Data were primarily collected and organized in Microsoft Excel (Version 16.14.1) and Graphpad Prism (Version 7.0a). Select analysis were performed in MATLAB (Version R2018a, 9.4.0.813654), as described in Methods.

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 main data supporting the results of this study are available within the Article and its Supplementary Information. Source data for the figures in this study are available from the corresponding author upon reasonable request. RNA-seq data is available at NCBI GEO under accession number GSE128313.

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 the throughput of technique used. Sample sizes were sufficient to show the same trends between the three or more replicates performed for each experiment, and by statistical testing.
Data exclusions	Data were not excluded from analysis.
Replication	Each experiment was repeated 3 or more times, with similar results observed each time.
Randomization	Mice were assigned randomly to experimental groups.
Blinding	Blinding was not performed for this study.

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	For immunostaining: Primary antibodies were administered at manufacturer recommended concentration: anti-CD45 (clone HI30, Becton Dickinson, 555482, 1:100), anti-CD45 (clone 30-F11, Becton Dickinson, 553080), anti-human mitochondria (clone 113-1, MilliporeSigma, MAB1273, 1:100, lot#2722860), anti-Ki67 (clone 8D5, Cell Signaling Technology, 9449, 1:800, lot#4), and anti-phospho-histone H2A.X (Ser139, clone 20E3, Cell Signaling Technology, 9718, 1:400, lot#13). The secondary antibodies used were Alexa Fluor 488 goat anti-mouse IgG (H+L) (Invitrogen, A28175, 1:100) and Alexa Fluor 568 goat anti-rabbit IgG (H+L) (Invitrogen, A11011, 1:100). For western blotting: Primary antibodies were administered at the manufacturer recommended concentration: anti-actin (clone Ab-5, Becton Dickinson, 612656, 1:10000), anti-Akt (clone C67E7, Cell Signaling Technologies, 4691, 1:1000, lot#20), anti-p-Akt (Ser473) (clone D9E, Cell Signaling Technologies, 4060, 1:2000), anti-Erk (clone L34F12, Cell Signaling Technologies, 4696, 1:2000, lot#22), anti-p-Erk (clone D13.14.4E, Cell Signaling Technologies, 4370, 1:2000, lot#12). Secondary antibodies: anti-mouse IgG HRP-linked antibody (Cell Signaling Technologies, 7076, 1:1000), anti-rabbit IgG HRP-linked antibody (Cell Signaling Technologies, 7074, 1:1000).
Validation	Antibodies were validated by the manufacturer prior to purchasing. Additionally, antibodies were verified for western blotting based on the correct molecular weight identified and for immunofluorescence by comparison of their cellular distribution to that obtained by the manufacturer.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Parental cell lines were purchased from American Type Culture Collection (ATCC). Select cell lines were modified from the parental line, as described in Methods.

Authentication	Cell lines were originally authenticated by ATCC, and were not further authenticated as part of this study.
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination, as assessed by PCR.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	For mammary fat pad injection, Eight-to-twelve-week-old female NOD SCID mice weighing 19-25g were obtained from Charles River (Fredrick, MD). For tail vein injection, Eight-to-twelve-week-old female athymic nude-Foxn1nu mice weighing 19-25g were obtained Charles River (Fredrick, MD).
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve samples collected from the field.
Ethics oversight	All animal studies were performed following Institutional Animal Care and Use Committee procedures and guidelines at the University of Maryland, Baltimore, under an approved protocol.

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