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Last updated by author(s): Jul 26, 2021

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 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	cellSens Imaging Software (Olympus), EC800 flow cytometry analyzer (Sony), Seahorse XFe24 Analyzer (Agilent)
Data analysis	MetaMorph ver. 7.8 (Molecular devices), Photoshop CC (Adobe), Image J (https://imagej.nih.gov/ij/), JMP 14.2.0 (SAS), Genetyx ver. 10 (Genetyx Corporation), LipidSearch 4.2 software (Mitsui knowledge industry), OrthoDB v10 (https://www.orthodb.org), VL3-BA (http://www.pondr.com/), DisMeta (http://www-nmr.cabm.rutgers.edu/bioinformatics/disorder/), COILS (https://embnet.vital-it.ch/software/COILS_form.html), ProtScale (https://web.expasy.org/protscale/), CIDER (http://pappulab.wustl.edu/CIDER/), TargetP-2.0 (http://www.cbs.dtu.dk/services/TargetP/), iPSORT (http://ipsort.hgc.jp/how.html)

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 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 lipidomic data are available in Metabolights repository under the accession number MTBLS3155 and Supplementary Table S1. All the data supporting the findings of this study are available within the paper and its supplementary information files.

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 not predetermined, but available or obtained samples were proceeded to analysis.
Data exclusions	No data were excluded from the analysis.
Replication	n = 2 for mass spectrometric analyses of CL. n = 9 for Real-time ATP rate assay.
Randomization	Mice of the equivalent age and the same sex in different genotype groups were randomly proceeded to transmission electron microscopy analysis. Mice body weights were analyzed cross-sectionally.
Blinding	Blinding was not performed because genotyping was necessary for the experiments.

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Rabbit polyclonal anti-Mieap (Miyamoto et al., 2011), Mouse monoclonal anti-GFP (Santa Cruz, Cat# sc-9996), Mouse monoclonal anti-FLAG (Sigma Aldrich, Cat# F1804), Goat anti-rabbit IgG secondary antibody, Alexa Fluor 546 (Thermo Fisher Scientific, Cat# A-11010), Goat anti-mouse IgG secondary antibody, Alexa Fluor 546 (Thermo Fisher Scientific, Cat# A-11003), Goat anti rabbit IgG 10nm gold (BBI Solutions, Cat# EM.GAR10), Rabbit polyclonal anti-GST (Santa Cruz, Cat# sc-459), Goat anti-rabbit IgG-HRP (Santa Cruz, Cat# sc-2004)
Validation	Rabbit polyclonal anti-Mieap antibody was generated and validated, previously (Miyamoto et al., 2011). The other antibodies were experimentally validated in a number of publications.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	The following cell lines were purchased from the American Type Culture Collection: A549 (tissue, lung cancer; gender, male), U373MG (tissue, glioblastoma; gender, male), LS174T (tissue, colon cancer; gender, female), and 293 (tissue, embryonic kidney).
Authentication	The cell lines have not been authenticated.
Mycoplasma contamination	The cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other organisms

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

Laboratory animals	C57BL/6J WT mice were obtained from CLEA Japan (Tokyo, Japan). The Mieap-knockout (Mieap−/−) mice were generated by using the Cre/loxP recombination system as previously reported (Tsuneki et al., 2015).Briefly, the floxed and trapped alleles were generated using a single construct bearing a genetrap cassette doubly flanked by LoxP and FRT located between exons 5 and 8 of the mouse Mieap gene, which is located on chromosome 5. The Mieap homozygous (Mieap−/−) deficient mice were generated by mating between bleeding pairs of the Mieap heterozygous (Mieap+/−) mice.
Wild animals	N/A
Field-collected samples	N/A
Ethics oversight	The animal experiment protocols were approved by the Committee for Ethics in Animal Experimentation (approved protocol No. T17-043), and the experiments were conducted in accordance with the Guideline for Animal Experiments of the National Cancer Center.

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

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	The LS174T-cont and Mieap-KD cells cultured under a normal condition were harvested by trypsin-EDTA treatment. After adding complete growth media to inactivate trypsin, cells were centrifugated, washed with PBS, and incubated with 5 µM 2',7'-dichlorofluorescin-diacetate (Sigma) for 20 min at 37°C. After washed with PBS, the cells were immediately analyzed with a flow cytometry analyzer, using the 488 nm line.
Instrument	EC800 flow cytometer (Sony)
Software	EC800 analysis software (Sony)
Cell population abundance	Cell sorting was not performed.
Gating strategy	Cell debris were excluded using the FSC-A and SSC-A. Doublets were excluded using the FSC-H and FSC-A.

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