

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

Data analysis

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](#)

There are no restrictions on data associated with this study. Source data are provided with the manuscript as a source data file. Larger data files (TLCs) are deposited at mendeley data and are openly accessible (DOI: 10.17632/6447jjvd9r.1).

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	The sample sizes used for every experiment were determined based on the availability of samples, experimental technical logistics, and statistical criteria.
Data exclusions	No data was excluded from the analysis performed for this study.
Replication	In this study, biological replicates were used for cellular assays and experiments were reproduced at least twice to confirm the reproducibility of the experimental findings. To ensure reproducibility and robustness of in-vitro data, different analytical techniques (i.e. TLC and MS) were used in independent experiments.
Randomization	Randomization was not applicable for this study.
Blinding	Blinding was used when applicable, i.e. cell culture experiments were done by experimenter A who seeded cells and randomized the labelling and experimenter B performing the experiment and data processing. The labelling was revealed after the data were processed. In-vitro and in-vivo experiments 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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

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

Antibodies

Antibodies used	Anti-6X His tag [®] antibody (1:3000, Cat#ab18184; RRID:AB_444306), Goat Anti-Rabbit IgG Antibody (H+L) (1:10000, Cat#PI-1000-1; RRID:AB_2916034), Sheep Anti-Mouse IgG ECL Antibody, HRP Conjugated (1:10000, Cat#NA9310-1ml; RRID:AB_772193), ANTI-FLAG [®] M2-Peroxidase (HRP) (1:1000, Cat#A8592; RRID:AB_439702), LIPH antibody (1:500, Cat#16602-1-AP, RRID:AB_2135352), Rabbit Anti-Endothelial Lipase Polyclonal, Antibody, Unconjugated (1:500, Cat#bs-2397R, RRID:AB_10856235); Anti-CLN5 (1:1000, ABCAM, #ab170899).
Validation	All the antibodies used for immunoblotting and immunofluorescence have been previously used in publications and /or validated by manufacturer (refer to website)

Eukaryotic cell lines

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

Cell line source(s)	American Type Culture Collection (ATCC), Thermo Fisher Scientific
Authentication	HEK293 (Cat#PTA-4488, RRID:CVCL_0045) , COS-7 (Cat#CRL-1651; RRID:CVCL_0224), HepG2 (Cat#HB-8065;RRID:CVCL_0027), Expi293F (Cat#A14527; RRID:CVCL_D615)
Mycoplasma contamination	All cell lines used in this study tested negative for mycoplasma contamination
Commonly misidentified lines (See ICLAC register)	No commonly misidentified lines were used in this study.

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	B6.129S-Lipgtm1Tq/J (Lipg-ko) mice were obtained from the Jackson Laboratory. Mice were maintained on a regular light-dark cycle (14h light, 10h dark) at a room temperature (RT) of 23 ± 1°C and kept ad libitum on a standard laboratory chow diet (4.5% w/w fat, Ssniff Spezialdiaeten, R/M-H Extrudate, V1126-027).
Wild animals	No wild animals were used in this study.
Reporting on sex	Male mice aged 15–21 weeks were used for the experiments.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All studies involving animals are reported in accordance with the ARRIVE guidelines for reporting experiments involving animals. Experimental procedures were approved by the Ethics committee of the University of Graz, and the Austrian Federal Ministry of Education, Science and Research (protocol number 2022-0.466.992) and were conducted in accordance with the council of Europe Convention (ETS 123). All animal procedures were performed as humanely as possible to minimize suffering.

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