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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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	no software was used
Data analysis	GraphPad 7 (Prism) for Mac OS Kaluza 1.3 (Beckman coulter) Adobe Photoshop CC 2015 Clustal Omega(EMBL-EBI) TMHMM Server v. 2.0 (Expasy) MassHunter(Agilent)

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 upon request. 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 microarray data used in this study has been deposited into the NCBI GEO database (GEO accession numbers GSE49784 and GSE118365). The data set will be released to the public before publication of this paper. All data generated or analyzed during this study are included in the article and its Supplementary Information.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	No statistical calculation was performed to predetermine sample size because it is difficult to estimate the extent of biological variation in each case. Nonetheless, for cell culture experiments, we usually have duplicates or triplicates per experiment and repeat the experiment three to four times, which usually provides statistically significant differences. For animal experiments, we usually require 15-20 mice for each sex of experimental and control mice to distinguish a difference of 10-15% in metabolic parameters with power >= 0.80 and p <= 0.05 in the two-tailed t test. In this study, the differences were larger so that the numbers of mice we used were less than this estimation.
Data exclusions	If experimental procedures or measurements fail so that accurate data cannot be obtained for certain samples, these particular data sets would be excluded from the final data analyses. Reasons for which included suboptimal lentivirus knockdown efficiency and poor resolution of HPLC' s chromatogram.
Replication	For primary cell cultures, replicates of cells from the same animal are considered to be technical replicates. Therefore, we usually use three to four animals (biological replicates) and make at least two-three technical replicates per animal. For established cell lines, independent experimental procedures or treatments are considered to be biological/technical replicates. We usually have duplicates or triplicates per experiment and repeat the experiment three to four times, which provides 6-12 independent data points. For animal experiments, we use at least two to three different cohorts (different litters). Each cohort include at least 3-4 mice each for sex and genotype. Replicate experiments were successful.
Randomization	For cell culture experiments, no randomization is usually performed. For animal experiments, each cohort is usually chosen randomly, and experimental procedures are applied to animals in a random order.
Blinding	Investigators were not blinded to group allocation during data collection and analysis. Data reported for mouse experiments and cell cultures experiment are not subjective but rather based on quantitative High Performance Liquid Chromatography (HPLC) and Mass Spectrometry, flow cytometry, and scintillation counter detection.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique materials are readily available from the authors for distribution to academic scientists. For for-profit companies and institutes, the Material Transfer Agreement will need to be processed between Washington University and these companies/ institutes.

Antibodies

Antibodies used	We used: The polyclonal rabbit anti-mouse Slc12a8 (catalog #ARP44039, Aviva, CA), polyclonal rabbit anti-mouse Caveolin-1 (catalog #3238, Cell Signaling, MA), monoclonal anti-GAPDH (catalog # MAB374, Millipore, CA,), anti-FLAG MS (1:500, #F3165, Sigma, MO). Polyclonal rabbit antiserum was produced against a synthetized N-terminal peptide (AQRSPQELFHEAAQQGC) of mouse Slc12a8 by Covance. Polyclonal goat anti-rabbit IgG (H+L) conjugated with Alexa Flour 488 (catalog#A-11034, Invitrogen) and Zombie Dye (catalog #423101 , Biolegend).
Validation	The polyclonal rabbit anti-mouse Slc12a8 (catalog #ARP44039, Aviva, CA), polyclonal rabbit anti-mouse Caveolin-1 (catalog #3238, Cell Signaling, MA), monoclonal anti-GAPDH (catalog # MAB374, Millipore, CA,), anti-FLAG MS (1:500, #F3165, Sigma, MO) were validated by manufacturer for Western blot analysis on murine cell lines. Polyclonal rabbit antiserum was produced against a synthetized N-terminal peptide (AQRSPQELFHEAAQQGC) of mouse Slc12a8 by Covance. We have validated Covance's Slc12a8 antisera by performing Western blot analysis on mouse tissues from Slc12a8KO mice and their wild-type littermates. Polyclonal goat anti-rabbit IgG (H+L) conjugated with Alexa Flour 488 (catalog#A-11034, Invitrogen) and Zombie Dye (catalog #423101 , Biolegend) were validated by manufacture for Flow Cytometry analysis.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	NIH3T3 cell line was originally purchased from the American Type Culture Collection (ATCC).
Authentication	None of the cell lines used have been authenticated
Mycoplasma contamination	The NIH3T3 cell line we used in this study was tested and found negative for micoplasma contamination.
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	We used : Female C57BL/6J mice (Provider:Jackson Laboratories) at 2-24 months of age, Male C57BL/6J mice (Provider:Jackson Laboratories) at 3-4 months of age, Female C57BL/6J mice (From NIA housed in Charles River facility) at 3-26 months of age and whole-body Slc12a8KO mice and their wild-type littermates (strain:C57BL/6J) at 2-10 months of age, generated and housed in our laboratory.
Wild animals	This study did not involve wild animals
Field-collected samples	This study did not involve samples collected from the field.

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	NIH3T3 cells were incubated with DMSO 0.1%, FK866 100 nM or FK866 100 nM and NMN 100 uM for 48h at 37C. Cells were

Sample preparation	then washed once with cold PBS, treated with 0.02%EDTA in PBS and stained for flow cytometry using a polyclonal rabbit anti-mouse Slc12a8 antibody(ARP44039) at 1:200, a secondary goat anti-rabbit IgG conjugated with Alexa Fluor 488 at 1:2000 and the survival market Zombie Dye at 1:400 for 25 min at 4C. For the intracellular staining, cells were fixed in 2% PFA for 10 min at RT and then permeabilized in saponin-conteining buffer for 10 min at RT. Slc12a8 staining was performed in permeabilization buffer for 25 min at 4C. 1x 106 cells for each condition were used for flow cytometry analysis.
Instrument	Gallios Flow cytometer 10 color/3 laser from Beckman Coulter (serial number AU25604)
Software	Kaluza 1.3
Cell population abundance	We used NIH3T3 cell line so only one type of cell. The purity of the samples was not determined
Gating strategy	NIH3T3 cells were a unique and homogeneous population on FSC/SSC gates. NIH3T3 cells stained with only secondary antibody conjugated with Alexa Flour 488 were used as negative control. Positive cells for Slc12a8/Alexa Flour 488 staining were selected, based on Zombie Dye/SSC negative cells.

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