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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 <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main

Statistical parameters

text	, or I	Methods section).
n/a	Coi	nfirmed
	\boxtimes	The $\underline{\text{exact sample size}}$ (n) for each experimental group/condition, given as a discrete number and unit of measurement
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	\boxtimes	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.
	\boxtimes	A description of all covariates tested
		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	\boxtimes	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
\boxtimes		For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings

Our web collection on <u>statistics for biologists</u> may be useful.

Software and code

Policy information about availability of computer code

State explicitly what error bars represent (e.g. SD, SE, CI)

Clearly defined error bars

Data collection Microscopy: EVOS FLc (Thermo Fisher Scientific), BZ-X700 (KEYENCE).

QPCR: StepOne (Applied Biosystems).

Illumina sequencing: Illumina Miseq. Sequences were aligned to the Silva reference database using QIIME.

Metabolites analysis: QTRAP 5500 (AB SCIEX), Xevo TQD (waters)

Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated

Data analysis Bioinformatic and statistical analysis were used with R package (version 3.4.3).

Image J (NIH) was used to measure adipocyte diameter using stained sections of adipose tissue.

For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes

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

Associated raw data is indicated in the appropriate figure legends and a data availability statement is provided in the materials and methods section. Fastq files of the Illumina short read sequences used in the commensal bacteria composition analysis will be made available on DNA Data Bank of Japan (DDBJ) under the following BioProject accession number: DRA008263 (Figure 1), and DRA008264 (Supplemental Figure 3).

The raw data of lipid metabolome have been deposited into the National Institutes of Health for Metabolomics Workbench under the DataTrack ID1695 (Figure 4) and DataTrack ID1702 (Supplemental Figure 4).

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Please select the b	est 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 scier	nces study design
All studies must dis	sclose on these points even when the disclosure is negative.
Sample size	In our experience, the sample sizes chosen are sufficient to obtain reliable results. These sample sizes are in lie with the standard practice for data published in this field. Samples are always pooled across multiple independent biological replicates. Statistical analysis was applied after data collection. Exact sample size number for each experiment is reported in the figure legends.
Data exclusions	None
Replication	For each experiment, the findings were reliably reproduced and reported in the figure legends and materials and methods.
Randomization	Data collection and analysis was carried out on randomly selected samples.
Blinding	Investigators were not formally blinded to group allocation during data collection or analysis. However, more than two independent investigators scored the results of an un-biased experiments that did not have an a priori hypothesis.

Reporting for specific materials, systems and methods

Materials & experimental systems			Methods		
n/a	Involved in the study	n/a	Involved in the study		
	☑ Unique biological materials	X	ChIP-seq		
	Antibodies	\times	Flow cytometry		
	Eukaryotic cell lines	\times	MRI-based neuroimaging		
\boxtimes	Palaeontology				
	Animals and other organisms				
\boxtimes	Human research participants				

Unique biological materials

Policy information about <u>availability of materials</u>

Obtaining unique materials All unique materials are readily available from authors or commercial sources as listed in the materials and methods.

Antibodies

Antibodies used F4/80 antibody (Abcam, ab6640, CI:A3-1)

Caveolin-1 antibody (BD, 610406, 2297)

F4/80 antibody (https://www.abcam.co.jp/f480-antibody-cia3-1-ab6640.html) Validation

Caveolin-1 antibody (http://www.bdbiosciences.com/eu/reagents/research/antibodies-buffers/cell-biology-reagents/cell-

biology-antibodies/purified-mouse-anti-cave olin-1-2297 cave olin-1/p/610406)

Eukaryotic cell lines

Policy information about cell lines

STC-1 cells (ATCC), GLUTag cells (gifted by Drucker DJ), and Flp-In™ 293 T-REx cells (Invitrogen) Cell line source(s)

Authentication This STC-1 cell lines have been authenticated by ATCC.

This Flp-In™ 293 T-REx cell lines have been authenticated by Invitrogen.

Mycoplasma contamination Cell line cultures were free of mycoplasma 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 C57BL/6 (wild-type, Gpr40-/-, and Gpr120-/-) male mice.

Wild animals Wild animals were not used.

Field-collected samples Field-collected samples were not used.