nature portfolio

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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.

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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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.
x	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. <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>
x	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 <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
,	Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Data collection

Policy information about availability of computer code

LSM 700 confocal microscope (Carl Zeiss),

Real-time PCR analysis (Quantstudio5, Applied biosystems), Dish-type wheeled luminometer (AB-2550 Kronos-Dio, ATTO),

Comprehensive Lab Animal Monitoring System (CLAMS, Columbus Instruments),

Luminometer (PerkinElmer, Monza)

Data analysis Image analysis:

ZEN microscope software (version 2.1 blue edition, Carl Zeiss),

Image J (Version 1.52p)

Data analysis:

SPSS version 24 (IBM analytics),

JTK-CYCLE algorithm 'MetaCycle' package of R software (version 4.1.1),

Cosinor package of R software (version 4.1.3),

Graphpad Prism (version 7)

Microsoft Excel 2016,

The background-subtracted bioluminescence profiles were analyzed using the Cosinor analysis software (http://www.circadian.org).

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

Source	data fo	r figures	are prov	ided w	ith the	naner
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Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender

14 healthy Koreans (10 males, 4 females)

Population characteristics

The human participants who underwent testing were with no medical history of chronic illness or malignancy. The average age of total 14 subject was 23.1 + or - 1.8 years. Seven subjects (5 males, 2 females) were BMI < 23 kg/m2 and 7 subjects (5 males, 2 females) were BMI > 27 kg/m2, according to the definition of obesity from the International Diabetes Federation-Western Pacific Region. The characteristics of the study population are detailed in Supplementary Table 4.

Recruitment

Participants were recruited through local website advertising.

Ethics oversight

Institutional Review Board of Asan Medical Center (IRB approval number: 2008-0314, approved data: August 11th, 2008)

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

Field-specific reporting

Ρ	lease select the c	one below	that is the	e best fit for	your research. I	f you are not sure,	read the app	ropriate sections	before ma	king your selection

X	Life	sciences

Behavioural	l &	social	sciences

Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see $\underline{\text{nature.com/documents/nr-reporting-summary-flat.pdf}}$

Life sciences study design

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

Sample size

No statistical method was used to predetermine sample size in animal experiments. Cell numbers of relative experiments in this study were determined based on our experience and previous studies in this field.

Data exclusions

The animal data with failed virus and siRNA injection were excluded for data analysis.

Undetermined RT-qPCR data were excluded for data analysis.

Replication

All experiments were repeated at least two times and data were presented when replicates were successful.

Randomization

For i.p. or i.c.v. iARC injection experiments, mice were selected according to their body weight to match the average body weights between groups. Control and experimental samples were always processed in parallel to control covariates.

Blinding

Investigators were not blinded in conducting animal experiments or collecting samples for analysis. Where possible, researchers were blinded during data analysis.

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 & experimenta	al systems - Methods				
n/a Involved in the study	n/a Involved in the study				
Antibodies	ChIP-seq				
Eukaryotic cell lines	Flow cytometry				
Palaeontology and archa	aeology MRI-based neuroimaging				
Animals and other organ	nisms				
X Clinical data					
Dual use research of cor	ncern				
Antibodies					
	ti-NAMPT, mouse monoclonal (Adipogen, Catalog #:AG-20A-0034, RRID:AB_2490117, 1:1500) ti-FOXO1, rabbit monoclonal (Cell signaling, Catalog #:2880s, RRID:AB_2106495, 1:1000)				
	ti-FOXO1, rabbit monocional (Cen signaling, Catalog #:2880s, KKID:AB_2106495, 1:1000) ti-SIRT1, mouse monocional (Santa Cruz, Catalog #:sc-74465, RRID:AB_1129462, 1:1000)				
	ti-SIRT2, rabbit monoclonal (Cell signaling, Catalog #:12650, RRID:AB_1129402, 1:1000)				
	ti-Flag, mouse monoclonal (Sigma, Catalog #:F3165, RRID:AB_259529, 1ug)				
	ti-Acetylated lysine, rabbit polyclonal (Cell signaling, Catalog #:9441, RRID:AB 331805, 1:1000)				
	ti-c-Fos, rabbit polyclonal (Synaptic systems, Catalog #:226 003, RRID:AB_2231974, 1:1000)				
	ti-β-actin, mouse monoclonal (Santa Cruz, Catalog #:sc-47778, RRID:AB_626632, 1:1000)				
	ti-β-endorphin, rabbit polyclonal (Phoenix, Catalog #:H02233, RRID:AB_2314007, 1:1000)				
	ti-GFP, goat polyclonal (Abcam, Catalog #: ab6673, RRID:AB_305643, 1:1000)				
	ti-rabbit secondary antibody, donkey polyclonal, Alexa-Flour 488-conjugated (Invitrogen, Cat#: A21206; RRID: AB_141708)				
	ti-rabbit secondary antibody, donkey polyclonal, Alexa-Flour 555-conjugated (Invitrogen, Cat#: A31572; RRID: AB_162543)				
Validation An	tibody validation information can be found on manufacturers' website.				
	ti-NAMPT (mouse), https://adipogen.com/ag-20a-0034-anti-nampt-visfatin-pbef-mab-omni379.html				
	DXO1 (rabbit), https://www.cellsignal.com/products/primary-antibodies/foxo1-c29h4-rabbit-mab/2880				
	ti-SIRT1 (mouse), https://www.scbt.com/p/sirt1-antibody-b-7				
	ti-SIRT2 (rabbit), https://www.cellsignal.com/products/primary-antibodies/sirt2-d4o5o-rabbit-mab/12650				
	ti-Flag (mouse), https://www.ceinigrian.com/KR/ko/product/sigma/f3165				
	ti-Acetylated lysine (rabbit), https://www.cellsignal.com/products/primary-antibodies/acetylated-lysine-antibody/9441				
	ti-c-Fos (rabbit), https://www.citeab.com/antibodies/509572-226-003-c-fos-rabbit-polyclonal-affinity-purifieda				
	ti-β-actin (mouse), https://www.scbt.com/p/beta-actin-antibody-c4				
	ti-β-ENDORPHIN (rabbit), https://www.phoenixpeptide.com/products/view/Antibodies/H-022-33				
	ti-GFP (goat), https://www.abcam.com/gfp-antibody-ab6673.html				
Eukaryotic cell lines					
Policy information about <u>cell lin</u>	nes and Sex and Gender in Research				
Cell line source(s)	SH-SY5Y human neuroblastoma cell line were obtained from the ATCC (Cat#:CRL-2266).				
(1)	N1 embryonic mouse hypothalamus cell line were obtained from the CEDARLANE (Cat#:CLU101).				
Authentication	SH-SY5Y cells and N1 cells were from commercial sources and thus not subsequently validated.				
Mycoplasma contamination	SH-SY5Y cells and N1 cells were not contaminated with mycoplasma.				
Commonly misidentified line	S None.				

Animals and other research organisms

(See <u>ICLAC</u> register)

Policy information about <u>studies involving animals</u>; <u>ARRIVE guidelines</u> recommended for reporting animal research, and <u>Sex and Gender in Research</u>

Laboratory animals	C57BL/6 male mice were purchased from Orient Bio (Seongnam, korea). Mice with tdTomato-labelled POMC neurons were generated by mating POMC-Cre mice (provided by Dr. Joel K. Elmquist, University of Texas Southwestern Medical Center) with mice carrying the reporter Rosa26-loxP-STOP-loxP-tdTomato allele (Jackson Laboratory, 007909). NPY-hrGFP mice (Jackson Laboratory, 006417) were used for the purpose of AgRP neuron labeling. PER2:LUC knock-in mice used for the SCN clock study were provided by Dr. Joshep S. Takahashi (University of Texas Southwestern Medical Center).
Wild animals	The study did not involve wild animals.
Reporting on sex	All studies were conducted in male mice.

Field-collected samples

The study did not include field-collected samples.

Ethics oversight

All animal procedures were approved by the Asan Institutional Animal Care and Use Committee of the Institute for Life Science under the project license 2012-11-024.

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