nature portfolio

Corresponding author(s): C. Ronald Kahn

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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.

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	No custom code or software was used.
Data analysis	For bioinformatic analysis of smRNA-seq, the raw data was de-multiplexed and mapped to the mm10 genome using the STAR pipeline and miRbase v22.1 annotations. Low expressing miRNAs (defined as miRNAs with fewer than 10 reads) were filtered out, and counts were normalized by weighted trimmed mean of M-values (TMM). Values were then transformed for linear modeling (Voom transformation), and counts were transformed to counts per million (CMP) and log2CPM. Heatmaps, unsupervised clustering, and dimension reduction for principal component analyses were performed in R Software (v4.3.1) using the edgeR, limmaR, tidyR, and ggplot2 packages. miRNA target prediction was performed using the microT-CDS, miR-Tarbase, and TargetScan V8.0 algorithms. Pathway analyses were performed using the miRPath V4.0 software, and targeted genes were visualized using the KEGG Pathway database pathway diagrams. All other statistical analyses were performed using GraphPad Prism Software. Nonparametric analyses were performed where assumptions of equal variance or normality of distribution were not met.

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

All data are present in the manuscript and/or supplementary materials. Source data are available through the Gene Expression Omnibus under accession number GSEXXXXXX (will be made available prior to publication). All materials, methods, and data are available upon request to either M.L. or C.R.K.

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	No sample size calculations were performed. Appropriate sample size was selected based on standard practice in the field.
Data exclusions	No data were excluded.
Replication	All experiments were replicated at least two separate times and by a separate person when possible.
Randomization	UPRT mice, DicerKO mice, and wild-type litter-mate controls were randomly allocated into groups, controlling for age and body weight.
Blinding	Investigators were blinded during data collection.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used: HA-Tag (C29F4) Rabbit mAb, Cell Signaling #3724; Streptavidin (HRP), Abcam ab7403; Alix Antibody (1A12), Santa Cruz sc-53540; Caveolin-1, Cell Signaling #3238; CD9 Antibody (C-4), Santa Cruz sc-13118; Argonaute 2 (C34C6), Cell Signaling #2897; Anti-Apolipoprotein B antibody, Abcam ab20737; Anti-Apolipoprotein A1 antibody [HL1713], Abcam ab308187; FoxO1 (C29H4), Cell Signaling #2880; PGC1a Antibody (4A8), Santa Cruz sc-517380; Total OXPHOS Rodent WB Antibody Cocktail, Abcam ab110413; Phospho-AMPKα (Thr172) (40H9), Cell Signaling #2535; AMPKα (D5A2), Cell Signaling #5831; β-Actin (13E5), Cell Signaling #4970; GAPDH (14C10), Cell Signaling #2118. All antibodies were used at a 1:1,000 dilution.

Validation: All antibodies used are validated by the manufacturer and routinely by our laboratory.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): C2C12 mouse myoblast cell line (CRL-1772, ATCC), human brown adipocyte cell line (hTERT A41hBAT-SVF, CRL-3385, ATCC), human white adipocyte cell line (hWAT, hTERT A41hWAT-SVF, CRL-3386, ATCC).

Authentication: Cells are routinely maintained and authenticated using known markers and genotyping.

Mycoplasma contamination: All cell lines used were routinely tested for mycoplasma and were free of contamination.

Commonly misidentified lines (See ICLAC register): N/A

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: The UPRT mice (Tg(CAG-GFP,-Uprt)985Cdoe/J, strain #021469) were a generous gift from Dr. Oliver Rando (UMass Medical School). Dicer-floxed mice (B6.Cg-Dicer1tm1Bdh/J, strain #006366) and Ucp1-Cre mice (Tg(Ucp1-cre)1Evdr/J, strain #024670) were purchased from Jackson Laboarories (Maine, US). All experiments were performed on male mice 8-12 weeks of age, using wild-type (floxed) littermate mice as controls.

Wild animals: N/A

Reporting on sex: There are no known sex-specific differences in miRNA expression in brown fat and thus we did not anticipate differences in miRNA secretion.

Field-collected samples: N/A

Ethics oversight: All experiments were performed in accordance with the Institutional Animal Care and Use Committee (IACUC) at the Joslin Diabetes Center, under protocol number IACUC: 2020-02.

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

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A