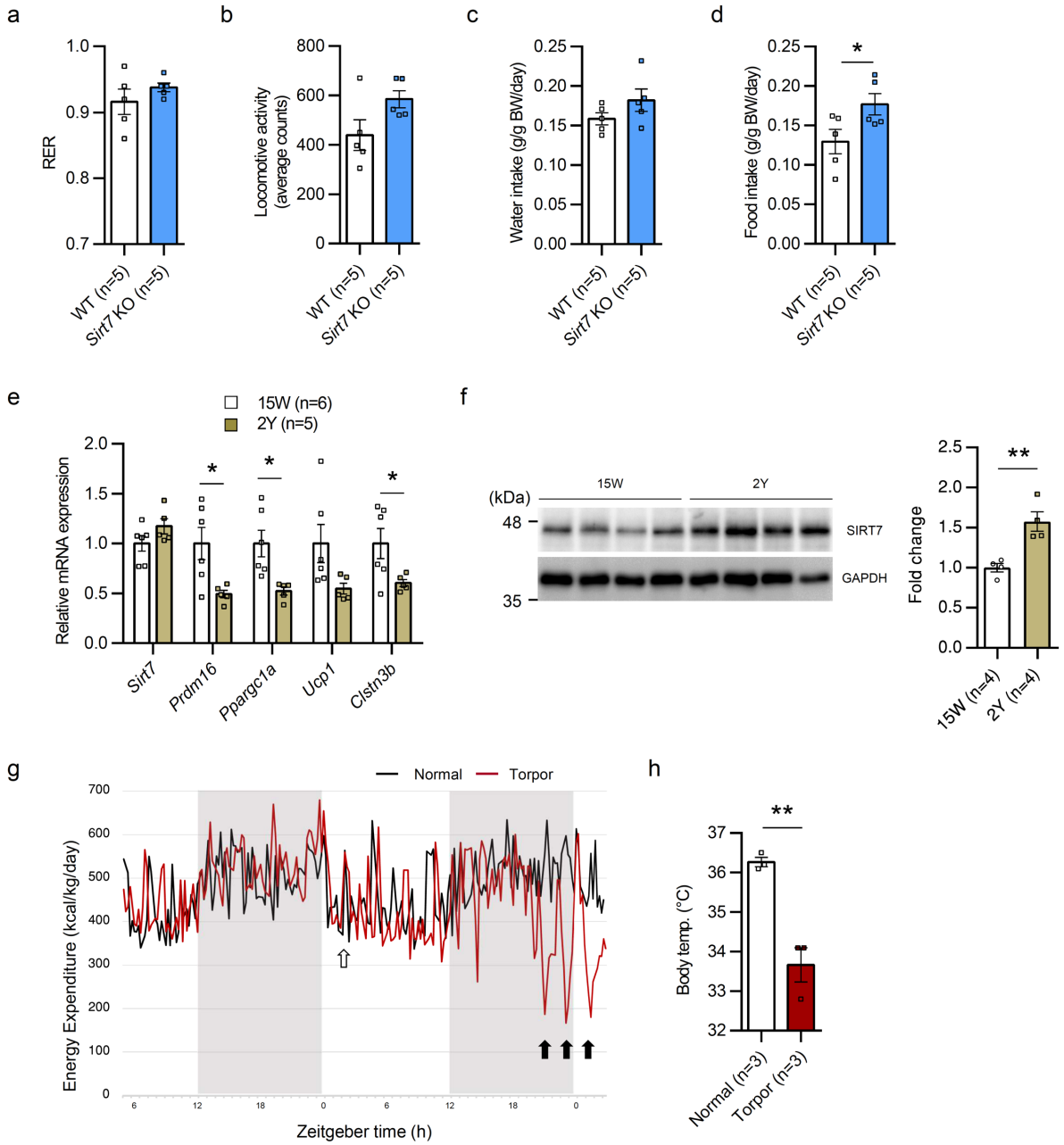


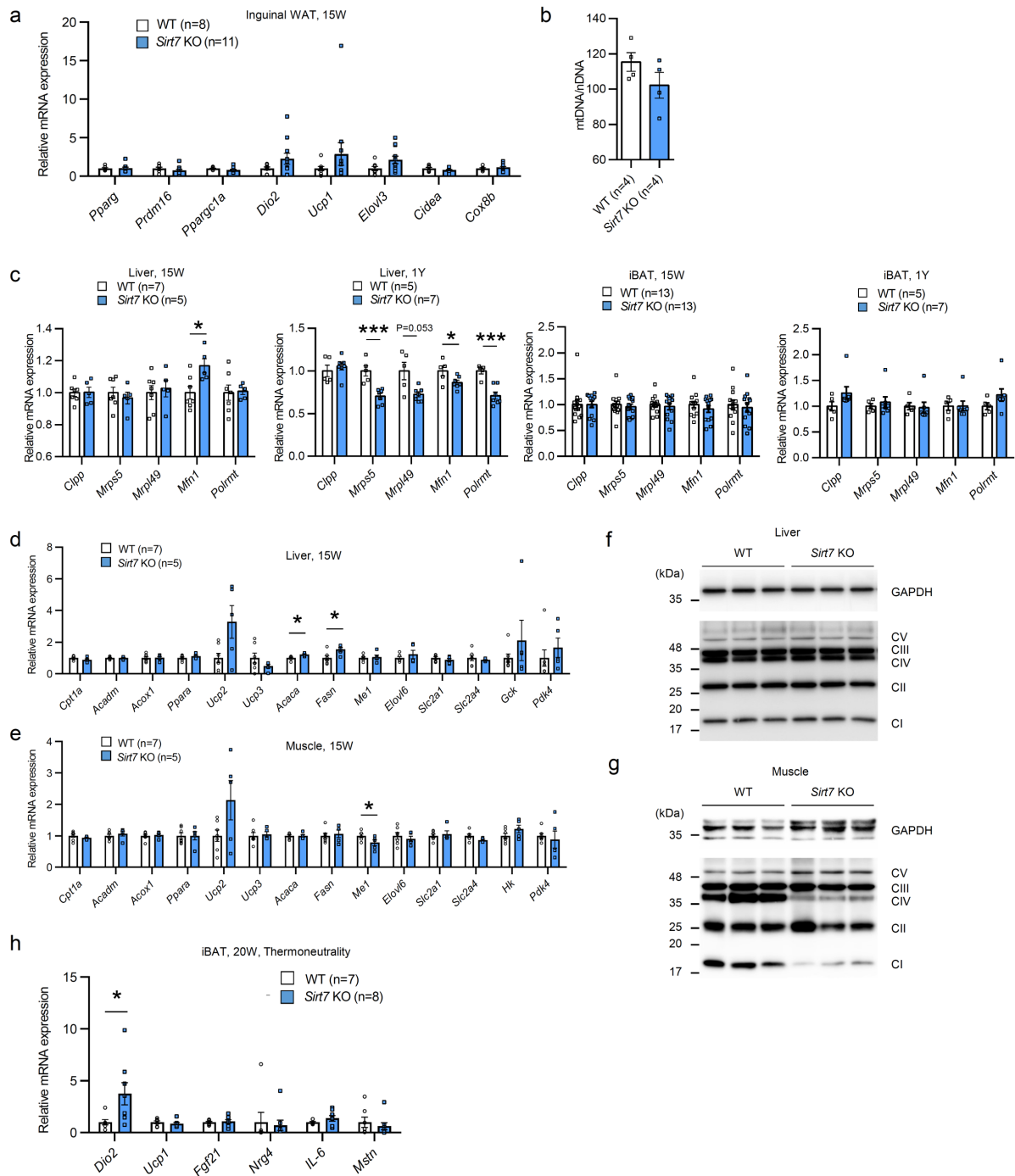
Supplementary Fig. 1 *Sirt7* KO mice display increased energy expenditure and body temperature under normal conditions.

a Body temperature in 11-week-old male WT and *Sirt7* KO mice upon cold exposure at 4°C. $p = 0.0328$ (0 h), $p = 0.0485$ (3 h), $p = 0.0018$ (5 h). **b–d** Data of indirect calorimetry experiments and body temperature from 16-week-old female WT and *Sirt7* KO mice. VO_2 rates (**b**), energy expenditure (**c**), and body temperature at ZT10 (**d**). $p = 0.0483$ in (**b**); $p = 0.0466$ (Dark) in (**c**); $p = 0.0135$ in (**d**). **e–g** Data of indirect calorimetry experiments and body temperature from 2-month-old male WT and another independent line of *Sirt7* KO mice³⁵. VO_2 rates (**e**), energy expenditure (**f**), and body temperature at ZT10 (**g**). $p = 0.0323$ in (**e**); $p = 0.0503$ (Dark), $p = 0.0288$ (Light), $p = 0.0350$ (Total) in (**f**); $p = 0.0242$ in (**g**). Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. Two-way ANOVA with Bonferroni's multiple comparisons test (**b**, **e**); two-tailed Student's *t*-test (**a**, **c**, **d**, **f**, **g**). * $p < 0.05$, ** $p < 0.01$. Source data are provided in Source data file.



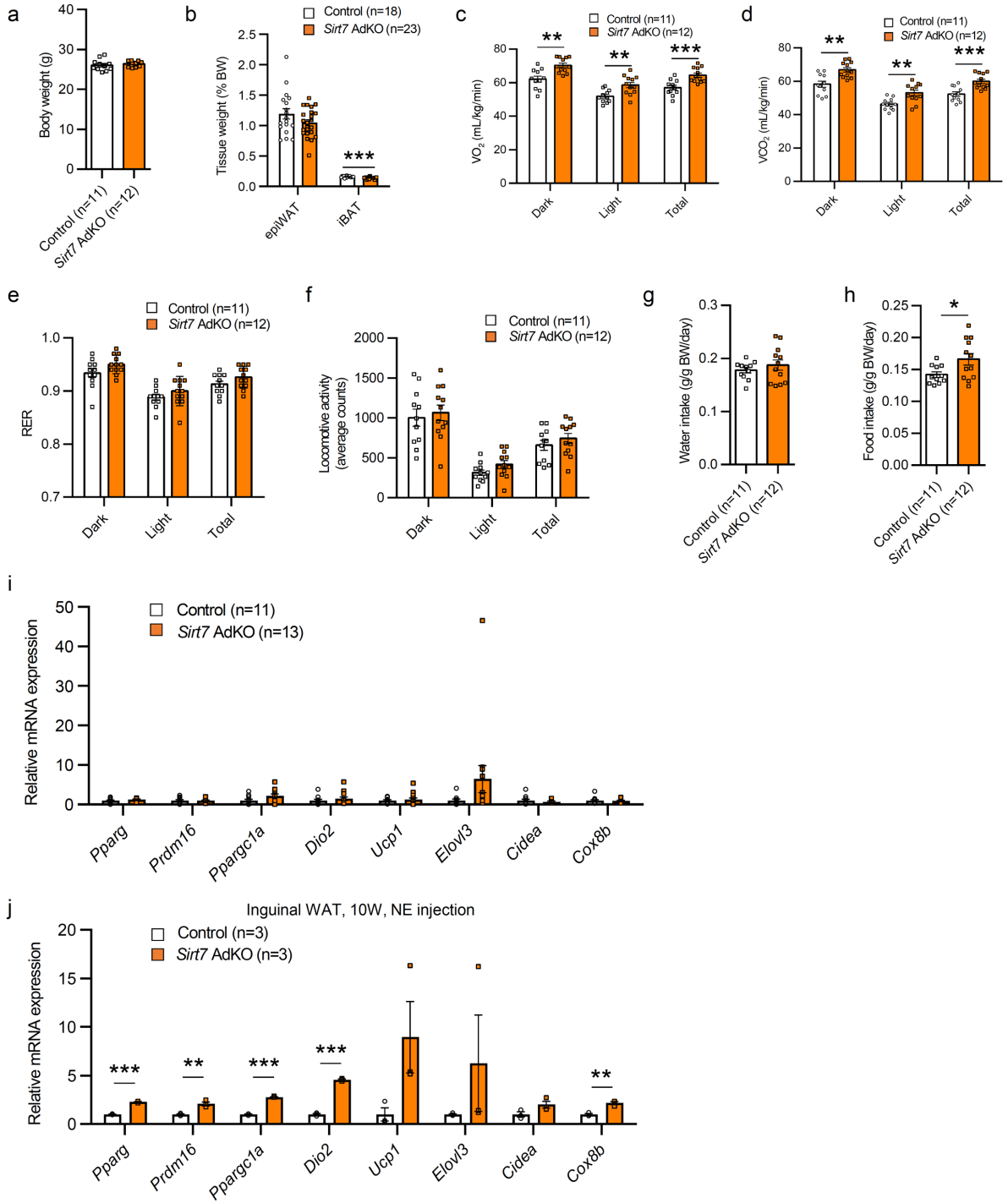
Supplementary Fig. 2 *Sirt7* KO mice exhibit excessive energy expenditure and thermogenesis in the hypometabolic state.

a–d Data of indirect calorimetry experiments from 2-year-old male WT and *Sirt7* KO mice. RER (**a**), locomotor activity (**b**), water intake (**c**), and food intake (**d**). $p = 0.0488$ in (**d**). **e** Real-time qPCR analysis of BAT-related genes in iBAT of 15-week-old and 2-year-old male WT mice. $p = 0.0250$ (*Prdm16*), $p = 0.0153$ (*Ppargc1a*), $p = 0.0664$ (*Ucp1*), $p = 0.0464$ (*Clstn3b*). **f** Western blot analysis of SIRT7 in iBAT of 15-week-old and 2-year-old male WT mice. $p = 0.0050$. **g, h** Data of indirect calorimetry experiments and body temperature during artificially-induced daily torpor in 18-week-old male WT mice. Representative pattern of energy expenditure (**g**). The mouse was placed in the chamber at 20°C for 3 days; food was removed on the second day (open arrow) in the Torpor groups. A typical daily torpor pattern started after 20 h of fasting (filled arrow). Body temperature after 24 h fasting (**h**). $p = 0.0044$. Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. $*p < 0.05$, $**p < 0.01$ by two-tailed Student's t-test. Source data are provided in Source data file.



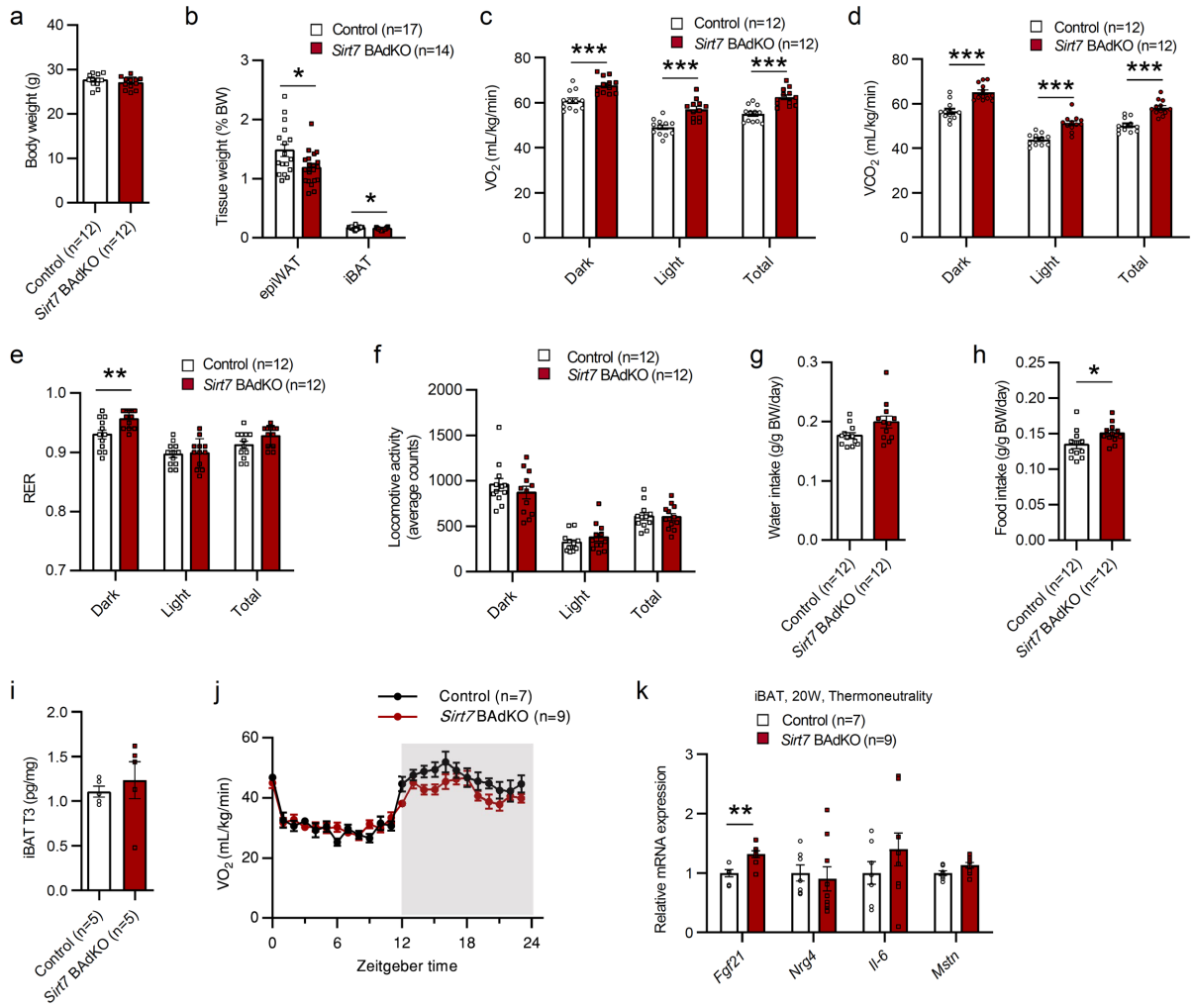
Supplementary Fig. 3 SIRT7 suppresses energy expenditure and thermogenesis via multiple pathways.

a Real-time qPCR analysis of BAT-related genes in inguinal WAT of 15-week-old male WT and *Sirt7* KO mice. **b** Evaluation of the mtDNA copy number in iBAT of 15-week-old male WT and *Sirt7* KO mice by determining the ratio of mtDNA to nuclear DNA (nDNA). **c** Real-time qPCR analysis of nuclear-encoded mitochondrial transcripts in liver and iBAT of 15-week-old and 1-year-old male WT and *Sirt7* KO mice. The expression of the mitochondrial unfolded protein response gene *Clpp* is increased in hematopoietic stem cells isolated from *Sirt7* KO mice⁴⁵, and the expression of genes related to mitochondrial biogenesis, namely, *Mrps5*, *Mrpl49*, *Mfn1*, and *Polrmt*, is reduced in the liver of aged *Sirt7* KO mice³⁵. $p = 0.0174$ (*Mfn1*) in liver, 15 weeks. $p = 0.0009$ (*Mrps5*), $p = 0.0525$ (*Mrpl49*), $p = 0.0424$ (*Mfn1*), $p = 0.0005$ (*Polrmt*) in liver, 1 year. **d, e** Real-time qPCR analysis of energy metabolism-related genes in liver (**d**) and skeletal muscle (**e**) of 15-week-old male WT and *Sirt7* KO mice. $p = 0.0101$ (*Acaca*), $p = 0.0269$ (*Fasn*) in (**d**); $p = 0.0499$ (*Me1*) in (**e**). **f, g** Western blot analysis of OXPHOS complexes I–IV in liver (**f**) and skeletal muscle (**g**) of 15-week-old male WT and *Sirt7* KO mice. **h** Real-time qPCR analysis of batokine genes in iBAT of 20-week-old male WT and *Sirt7* KO mice at thermoneutrality. $p = 0.0375$ (*Dio2*). Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ by two-tailed Student's *t*-test. Source data are provided in Source data file.



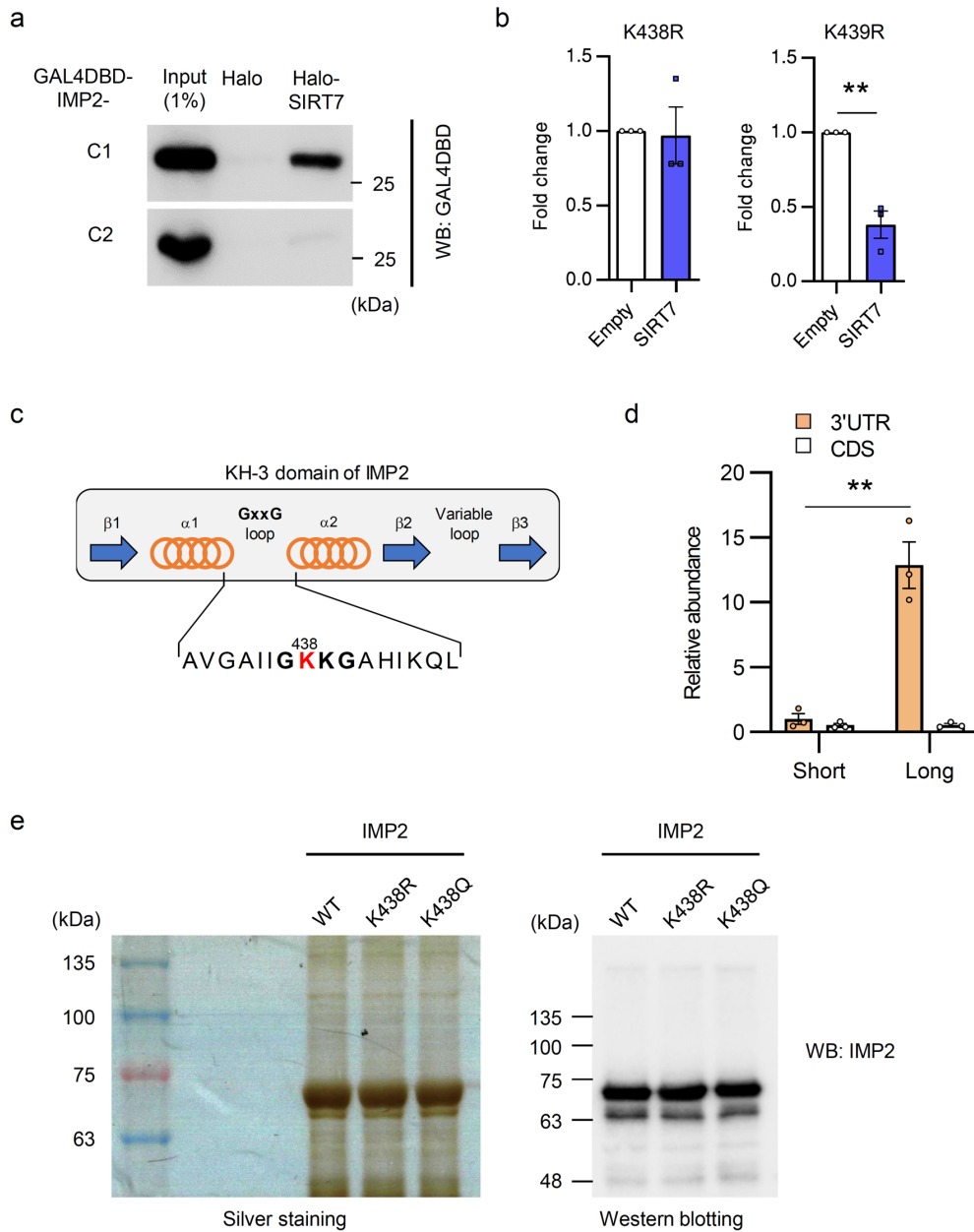
Supplementary Fig. 4 SIRT7 deficiency in adipose tissue elevates the whole-body energy expenditure and body temperature.

a–h Data of indirect calorimetry experiments from 12-week-old male *Adipoq-Cre* control and *Sirt7* AdKO mice. Body weight (**a**), percent tissue weight calculated relative to body weight (**b**), average VO_2 (**c**), average VCO_2 (**d**), RER (**e**), locomotor activity (**f**), water intake (**g**), and food intake (**h**). $p = 0.0007$ (iBAT) in (**b**); $p = 0.0012$ (Dark), $p = 0.0033$ (Light), $p = 0.0007$ (Total) in (**c**); $p = 0.0010$ (Dark), $p = 0.0025$ (Light), $p = 0.0004$ (Total) in (**d**); $p = 0.0279$ in (**h**). **i** Real-time qPCR analysis of BAT-related genes in inguinal WAT of 12-week-old male *Adipoq-Cre* control and *Sirt7* AdKO mice. **j** Real-time qPCR analysis of BAT-related genes in inguinal WAT of 10-week-old male *Adipoq-Cre* control and *Sirt7* AdKO mice administered 1 mg/kg/day norepinephrine (NE) for 5 days. $p = 2.7\text{E}-05$ (*Pparg*), $p = 0.0077$ (*Prdm16*), $p = 2.8\text{E}-05$ (*Ppargc1a*), $p = 9.7\text{E}-06$ (*Dio2*), $p = 0.0039$ (*Cox8b*). Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ by two-tailed Student's *t*-test. Source data are provided in Source data file.



Supplementary Fig. 5 Brown adipocytic SIRT7 suppresses energy expenditure and thermogenesis *in vivo*.

a–h Data of indirect calorimetry experiments from 12-week-old male *Ucp1-Cre* control and *Sirt7* BAdKO mice. Body weight (**a**), percent tissue weight calculated relative to body weight (**b**), average VO_2 (**c**), average VCO_2 (**d**), RER (**e**), locomotor activity (**f**), water intake (**g**), and food intake (**h**). $p = 0.0428$ (epiWAT), $p = 0.0474$ (iBAT) in (**b**); $p = 0.0004$ (Dark), $p = 0.0001$ (Light), $p = 0.0001$ (Total) in (**c**); $p = 2.7E-05$ (Dark), $p = 8.3E-06$ (Light), $p = 5.0E-06$ (Total) in (**d**); $p = 0.0087$ (Dark) in (**e**); $p = 0.0335$ in (**h**). **i** T3 level in iBAT of 12-week-old male *Ucp1-Cre* control and *Sirt7* BAdKO mice. **j, k** VO_2 rates of indirect calorimetry experiments (**j**) and real-time qPCR analysis of batokine genes in iBAT (**k**) from 20-week-old male *Ucp1-Cre* control and *Sirt7* BAdKO mice at thermoneutrality. $p = 0.0016$ (*Fgf21*). Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. Two-way ANOVA with Bonferroni's multiple comparisons test (**j**); two-tailed Student's *t*-test (**a–i, k**). $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. Source data are provided in Source data file.



f

Proteins containing KH domain

AKAP1; **ANKHD1**; **ANKRD17**; ASCC1; BICC1; DDX43; DDX53; DPPA5; **FMR1**; FUBP1; **FUBP3**; **FXR1**; FXR2; GLD1; **HDLBP**; HNRPK; IGF2BP1; **IGF2BP2**; **IGF2BP3**; KHDRBS1; KHDRBS2; KHDRBS3; **KHSRP**; **KRR1**; MEX3A; MEX3B; MEX3C; MEX3D; NOVA1; NOVA2; PCBP1; PCBP2; PCBP3; PCBP4; PNO1; PNPT1; QKI; SF1; TDRKH

Supplementary Fig. 6 Deacetylation of IMP2 by SIRT7 attenuates the translation of *Ucp1* mRNA.

a Mapping of the region of the interaction between IMP2 and SIRT7. Halo-SIRT7 pull-down assay with lysates of HEK293T cells expressing the indicated IMP2 deletion mutants fused with GAL4DBD. See also Fig. 8c. **b** Quantification of the acetylated IMP2 relative to IMP2 (n = 3) in the experiment of Fig. 8d. $p = 0.0025$. **c** Topology of the KH-3 domain and amino acid sequence around K438 of mouse IMP2. **d** Binding of IMP2 to *in vitro*-transcribed short and long *Ucp1* 3'-UTR (n = 3 independent samples per group). The *Ucp1* coding sequence (CDS) was used as a negative control. $p = 0.0030$. **e** Generation of recombinant protein in *E. coli* for IMP2^{WT}, IMP2^{K438R}, and IMP2^{K438Q}. To confirm that equal amounts of these recombinant proteins were used in the insect cell-free translation system, silver staining and WB were performed. This confirmation was performed once. **f** Candidate SIRT7-interacting proteins in KH domain family. The 10 proteins marked in red have been reported to be candidate SIRT7-interacting proteins⁴⁹. See Discussion for details. WB, western blotting. Data are presented as means \pm SEM. All numbers (n) are biologically independent samples. * $p < 0.05$, ** $p < 0.01$ by two-tailed Student's *t*-test. Source data are provided in Source data file.

qPCR primer pairs for mouse mRNA			
Symbol	Name	Sequence	
		Forward	Reverse
<i>Rpl19</i>	ribosomal protein L19	AAGCCTGTGACTGTCCATTTC	CTTCTTGGATTCCCAGGTATC
<i>Pparg</i>	peroxisome proliferator-activated receptor gamma	GGAAGACCACTCGCATTCTT	TGCGACTTTGGTATTCTTGGAG
<i>Prdm16</i>	PR domain containing 16	GGCGAGGAAGCTAGCCAAA	GGTCTCTCTCGGCACTCT
<i>Ppargc1a</i>	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	GAAATCCGAGCGGAGCTGAA	GAATAGGGCTGCGTGCCATC
<i>Cebpb</i>	CCAAT/enhancer binding protein (C/EBP), beta	CAACCTGGAGACGCAGCACAAAG	CTAGCAGTGGCCCCGCCGAGG
<i>Ebf2</i>	early B cell factor 2	GCTGCGGGAACCGGAACGAGA	ACACGACCTGGAACCGCCTCA
<i>Dio2</i>	deiodinase, iodothyronine, type II	AGTCAAGAAGGTGGCATTTCG	ACAGCTTCCTCTAGATGCCT
<i>Ucp1</i>	uncoupling protein 1	GGCAACAAGAGCTGACAGTAAAT	GGCCCTTGTAACAACAATAATAC
<i>Elovl3</i>	elongation of very long chain fatty acids-like 3	TTGGGGATAGGGGGTGTGTG	TCTCCCTCCCTCCAAGTC
<i>Cidea</i>	cell death-inducing DFFA-like effector a	CTTGGGGTGGTACCCAGTG	ATCCACGCAGTCCACACACA
<i>Cox3</i>	mitochondrially encoded cytochrome c oxidase III	GCAGGATTCTTCTGAGCGTTCT	GTCAGCAGCCTCCTAGATCATGT
<i>Cox8b</i>	cytochrome c oxidase subunit 8B	GAACCATGAAGCCAACGACT	GCGAAGTTCACAGTGGTTCC
<i>Clstn3b</i>	calsyntenin 3	CTCCGCAGGAACAGCAGCCC	AGGATAACCATAAGCACCAG
<i>S100b</i>	S100 protein, beta polypeptide, neural	TGGTTGCCCTCATTGATGTCT	CCCATCCCCATCTTCGTCC
<i>Bmp8b</i>	bone morphogenetic protein 8b	CAACCACGCCACTATGCAG	CACTCAGCTCAGTAGGCACA
<i>Fgf21</i>	fibroblast growth factor 21	GCCATTCACTTTGCTGAGC	ATCCATTCCATCAGGGCTGC
<i>Nrg4</i>	neuregulin 4	ATGCCAACAGATCACGAGC	TCTTCAGTGTCTCTGTGGCTG
<i>Il-6</i>	interleukin 6	CCACGGCCTTCCTACTTCA	TTCCACGATTTCCAGAGAACA
<i>Mstn</i>	myostatin	AGTGGATCTAAATGAGGGCAGT	GTTTCAGGGCGCAGCTTAC
<i>Sirt7</i>	sirtuin 7	TGCCAGGCACTTGGTTGTCT	TAGGCTCCGCTTCGCTTAGG
<i>Clpp</i>	caseinolytic mitochondrial matrix peptidase proteolytic subunit	TGTTGCGGGAACGCATCGTGT	TAGATGGCCAGGCCCGCAGTT
<i>Mrps5</i>	mitochondrial ribosomal protein S5	TCCCTGCATTGTGTAGCTTG	GAGCTGTCTTCACTGCCAAA
<i>Mrpl49</i>	mitochondrial ribosomal protein L49	GAGCGACGAACAAAGTAGGG	TACCAAAATCCCAGAGCCAC
<i>Mfn1</i>	mitofusin 1	AGGGGACCGATGGAGATAAG	AAGAGGGCACATTTGCTTTG
<i>Polrmt</i>	polymerase (RNA) mitochondrial (DNA directed)	GCAACATGTCTGAGGGAGT	GCACCTTCTTACCCTCATC
<i>Cpt1a</i>	carnitine palmitoyltransferase 1a, liver	CCATGATGGACCCCAACA	TGGACAACCTCCATGGCTCA
<i>Acadm</i>	acyl-Coenzyme A dehydrogenase, medium chain	GCAGCTGGCGCTGTGGGGCT	CGGCGTCAGTGGCTAGCTGATTG
<i>Acox1</i>	acyl-Coenzyme A oxidase 1, palmitoyl	GGGAGTGTACGGGTACATG	CCGATATCCCCAACAGTGATG
<i>Ppara</i>	peroxisome proliferator activated receptor alpha	TTGAAGGAGCTTTGGGAAGA	AGGAAGCCGTTCTGTGACAT
<i>Ucp2</i>	uncoupling protein 2 (mitochondrial, proton carrier)	GAGGGTCCACGCAGCCTCTA	GCATGCTCTGAGCCCTTGGT
<i>Ucp3</i>	uncoupling protein 3 (mitochondrial, proton carrier)	GTGGCCCTGCACTACCCAAC	CGGTGTCCAGGGGAAAAGTG
<i>Acaca</i>	acetyl-Coenzyme A carboxylase alpha	CCAGCTGATCCTGCGAACCT	GAACATTCCCAGCAAGCCATC
<i>Fasn</i>	fatty acid synthase	TCTGGCCAACCTCATTGGT	GAAGCTGGGGTCCATTGTG
<i>Me1</i>	malic enzyme 1, NADP(+)-dependent, cytosolic	CTGGCCAGGGCAACAATTCC	TAGAGCCGGCCTTCTTGCAG
<i>Elovl6</i>	ELOVL family member 6, elongation of long chain fatty acids	GGAGCAGAGGGCGAGAGAAC	GAGCGCTTCCGAAGTTCAA
<i>Slc2a1</i>	solute carrier family 2 (facilitated glucose transporter), member 1	GCTTATGGGCTTCTCCAACT	GGTGACACCTCTCCACATAC
<i>Slc2a4</i>	solute carrier family 2 (facilitated glucose transporter), member 4	ACCCCTCATTCCCCTGTGT	ACCCCTCTGCAGACCCCTTC
<i>Gck</i>	glucokinase	CCCACAAATGCTCCAGTCC	GTGGGAGGCCAGAAGCTGAA
<i>Pdk4</i>	pyruvate dehydrogenase kinase, isoenzyme 4	CGCGCTCTGACCCGCAGCC	GCCAGGCGGACGGGCAGCTC
<i>Hk1</i>	hexokinase 1	TGCCTCTGGGCTTACCTTC	CCACACAGTCGGTGGCTTTG
<i>Ucp1 3'-UTR</i>	uncoupling protein 1, 3'-UTR	GCAACTTGAGGAAGAGATA	GATTCTTTGGTTGGTTTATTTC
<i>Ucp1 CDS</i>	uncoupling protein 1, coding sequence	GGCCCTTGTAACAACAACA	GTCGGTCTTCTTGGTGTA

qPCR primer pairs for mouse genome			
Symbol	Name	Sequence	
		Forward	Reverse
<i>mt-Nd1</i>	NADH dehydrogenase 1, mitochondrial	CCTATCACCCCTGCCATCAT	GAGGCTGTTGCTTGTGTGAC
<i>Pecam1</i>	platelet/endothelial cell adhesion molecule 1	ATGGAAAGCCTGCCATCATG	TCCTTGTTGTTCAGCATCAC
Cloning primer pairs for cDNA			
Symbol	Forward	Reverse	
<i>Imp2</i>	agaattcATGATGAACAAGCTGTACATTGGG	actcgagTCACTTGCTGCGCTGTGGGCGACTCCC	
Guide oligonucleotides for sgRNAs			
Symbol	Forward	Reverse	
<i>Imp2</i>	caccgGGGAACAAGGCCACGGCCCC	aaacgGGGCCGTGGCCTTGTCCCC	

Supplementary Table 1 Information of primers.

Name	Host & Clonality / Source & Identifier	Dilution
anti-UCP1	Rabbit Polyclonal / Abcam, ab10983	1:1000 dilution in TBST 5% BSA
anti-GAPDH	Rabbit Monoclonal (14C10) / Cell Signaling Technology, #2118	1:1000 dilution in TBST 5% BSA
Total OXPHOS Rodent WB Antibody Cocktail	Mouse Monoclonal (20E9DH10C12, 21A11AE7, 13G12AF12BB11, 1D6E1A8, 15H4C4) / Abcam, ab110413	1:250 dilution in TBST 1% skim milk
anti-Tyrosine Hydroxylase	Sheep Polyclonal / Sigma-Aldrich, AB1542	1:1000 dilution in TBST 5% BSA
anti-RNA Pol II	Mouse Monoclonal (4H8) / Active Motif, #39097	1:2000 dilution in TBST 3% skim milk
anti-SIRT7	Rabbit Monoclonal (D3K5A) / Cell Signaling Technology, #5360	1:3000 dilution in TBST 5% BSA
anti-IGFBP2(IMP2)	Rabbit Polyclonal / MBL, #RN008P	1:1000 dilution in TBST 5% BSA
anti-DYKDDDDK (FLAG) tag	Mouse Monoclonal (1E6) / Fujifilm Wako Pure Chemical Corporation, #018-22381	1:2000 dilution in TBST 3% skim milk
anti-HA tag	Rat Monoclonal (3F10) / Roche Applied Science, #11867423001	1:1000 dilution in TBST 5% BSA
anti-acetylated-lysine	Rabbit Polyclonal / Cell Signaling Technology, #9441	1:1000 dilution in TBST 5% BSA
HRP-conjugated Affinipure Goat anti-Rabbit IgG(H+L)	Goat Polyclonal / Proteintech, #SA00001-2	1:10000 dilution in TBST 5% skim milk
HRP-conjugated Affinipure Goat anti-Mouse IgG(H+L)	Goat Polyclonal / Proteintech, #SA00001-1	1:10000 dilution in TBST 5% skim milk
HRP-conjugated Affinipure Goat anti-Rat IgG(H+L)	Goat Polyclonal / Proteintech, #SA00001-15	1:10000 dilution in TBST 5% skim milk
HRP-conjugated Affinipure Rabbit anti-Sheep IgG(H+L)	Rabbit Polyclonal / Proteintech, #SA00001-16	1:10000 dilution in TBST 5% skim milk

Supplementary Table 2 Information of antibodies.

All antibodies used in this study are commercially available and have been validated by companies. The details of manufactures' validation can be found on the web site of each manufacture. See also the Reporting Summary.