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Western Blot quantification

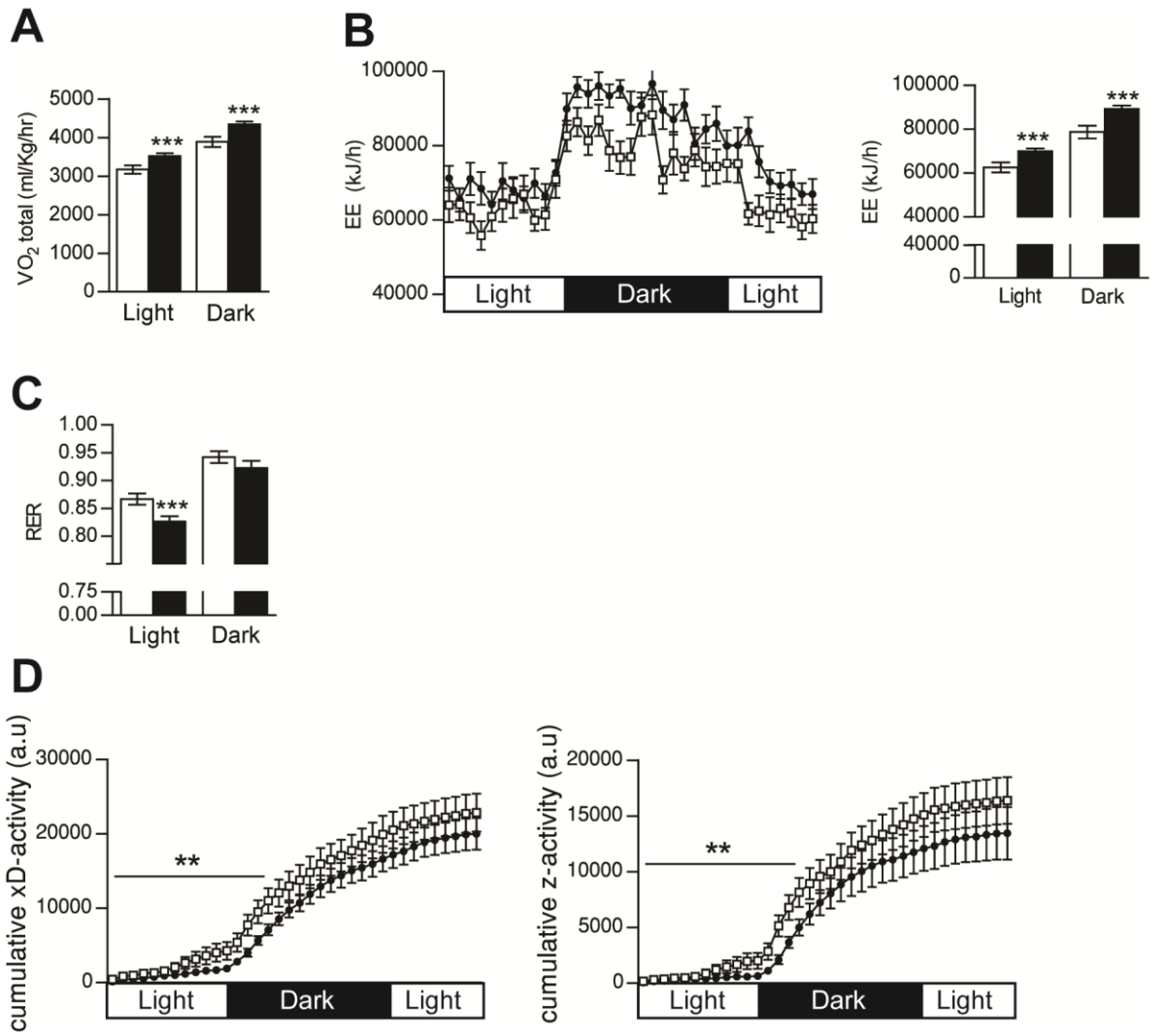


Figure S1. Impact of SIRT1 transgenesis on energy homeostasis.

(This supplemental figure is related to Figure 1 in the main text)

(A) Quantification of O_2 consumption during dark and light phase for wild-type (WT) and $SIRT1^{Tg/Tg}$ (Tg) mice. The results illustrate a higher O_2 consumption in Tg mice.

(B) Energy expenditure (EE) during dark and light phase for WT and Tg mice. The results illustrate a higher energy expenditure in Tg mice.

(C) Quantification of the respiratory exchange ratio (RER) during the dark and light phase for WT and Tg mice. The results illustrate a lower RER in Tg mice during the light phase.

(D) Cumulative xD and z-activity during light and dark phase. The results illustrate a lower activity of the Tg mice.

Through the figure, white bars and squares represent WT mice, while black bars and squares represent Tg mice. All values are shown as mean +/- SEM. * Indicates statistical significant difference vs. WT.

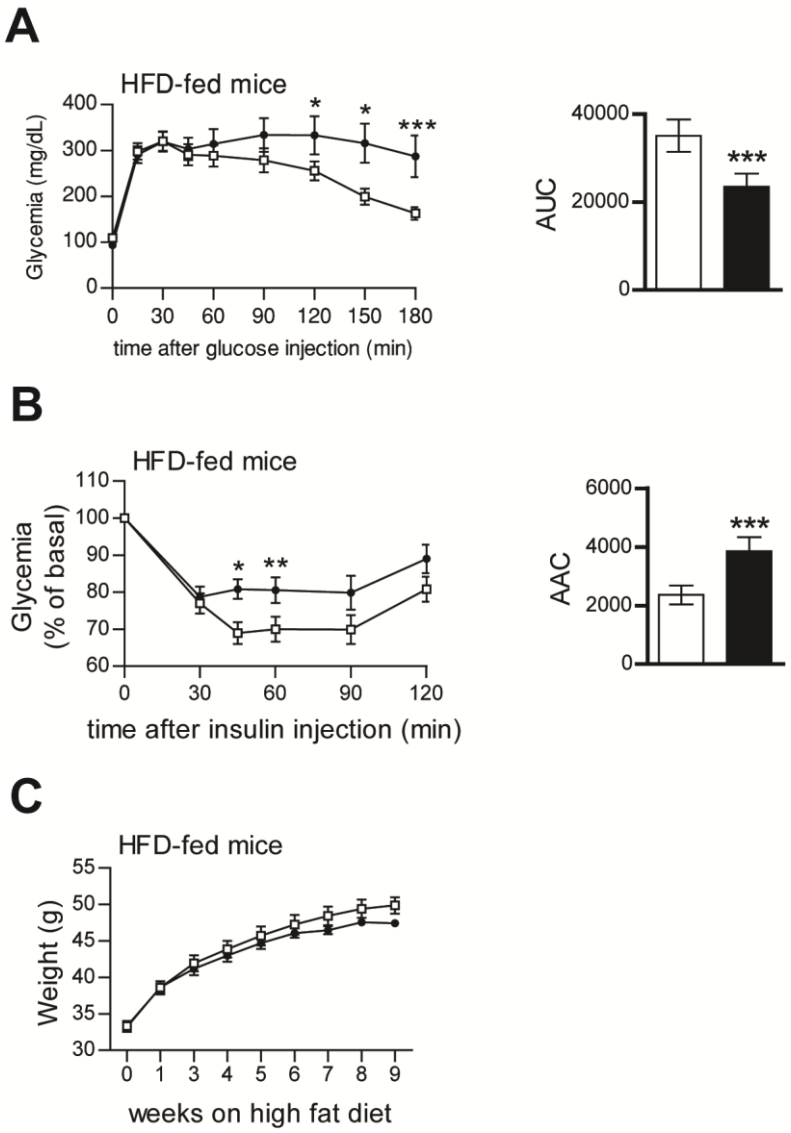


Figure S2. Impact of SIRT1 transgenesis on the effects of high-fat diet on body weight and glucose metabolism.

(This supplemental figure is related to Figure 2 in the main text)

(A) A glucose tolerance test (2 mg/kg) after an overnight fast reveals that Tg mice are protected against high-fat diet-induced glucose intolerance.

(B) An insulin tolerance test (0.75 U/Kg) after a 6 hr fast reveals that Tg mice are protected against high-fat diet-induced insulin resistance

(C) Body weight curves of WT and Tg mice upon high-fat feeding.

Through the figure, white squares represent WT mice, while black squares represent Tg mice. All values are shown as mean +/- SEM. * Indicates statistical significant difference vs. WT.

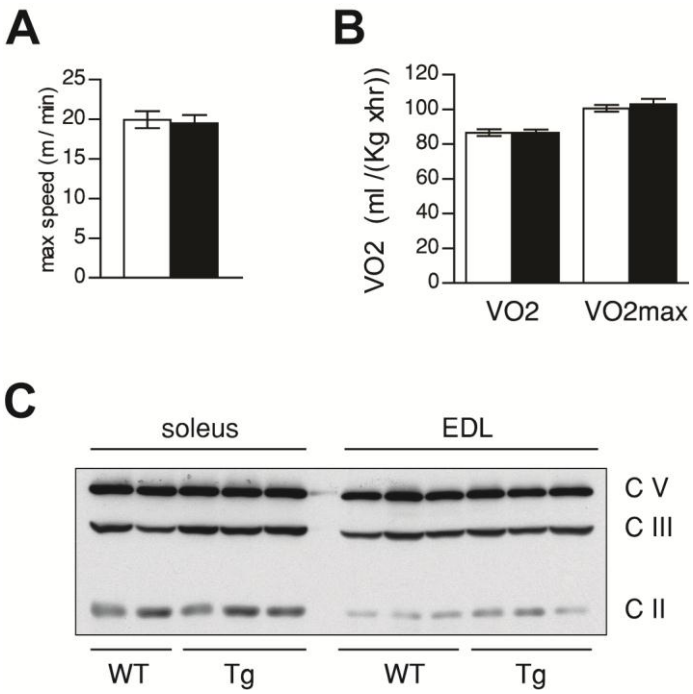


Figure S3. Impact of SIRT1 transgenesis on running speed, VO2 capacity and mitochondrial complexes in skeletal muscles.

(This supplemental figure is related to Figure 3 in the main text)

(A) Mice were place on a calorimetric treadmill in order to evaluate maximal running speed using a 10° degree inclination. No differences were observed between genotypes.

(B) As in (A), but VO2 was recorded at the beginning of the experiment, when mice are not running, and at the end, upon obvious signs of exhaustion. No differences were observed between genotypes.

(C) Protein levels of different mitochondrial complexes in an oxidative (soleus) and a glycolytic (EDL) skeletal muscle from WT and Tg mice.

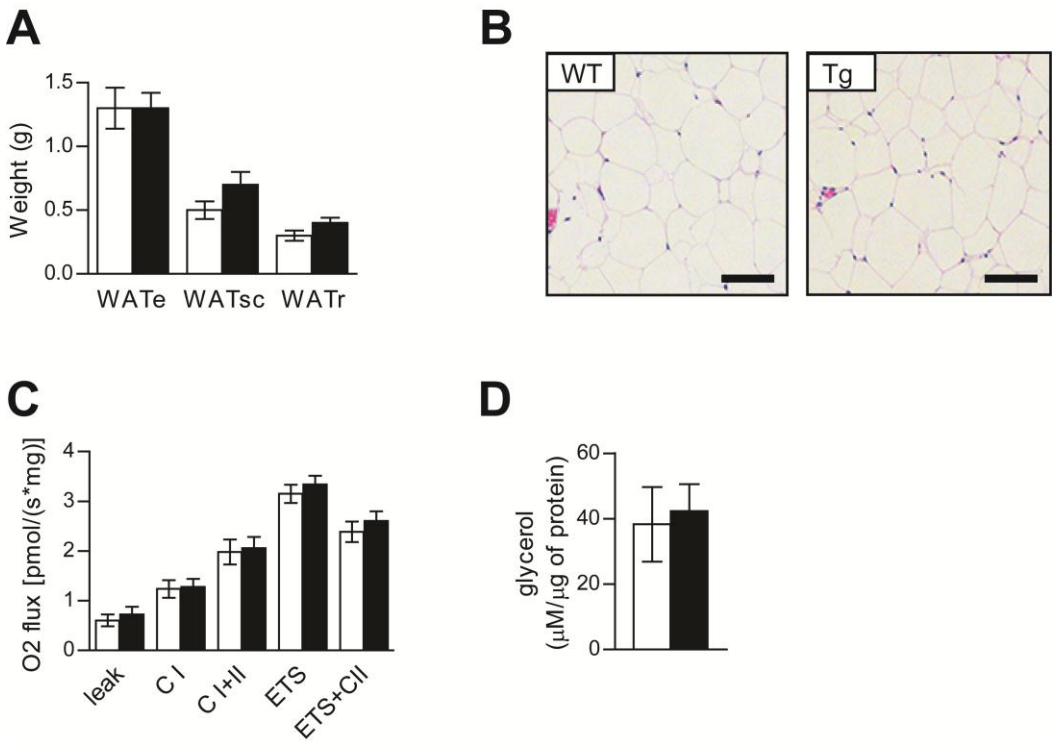


Figure S4. White adipose tissue biology is not affected by SIRT1 transgenesis under low fat diet.

(This supplemental figure is related to Figure 5 in the main text)

(A) Weight of epididymal (WATe), inguinal subcutaneous (WATsc) and retroperitoneal (WATr) white adipose depots in wild-type (WT) and SIRT1$^{Tg/Tg}$ (Tg) mice.

(B) Histological images of WATe from WT and Tg mice (bar = 600 μm).

(C) Respirometry analyses of WATe from WT and Tg mice reveal no difference between genotypes

(D) The lipolytic capacity of WAT, as monitored by glycerol release, is not affected by SIRT1 transgenesis

Through the figure, white bars represent WT mice, while black bars represent Tg mice. All values are shown as mean +/- SEM. * Indicates statistical significant difference vs. WT.

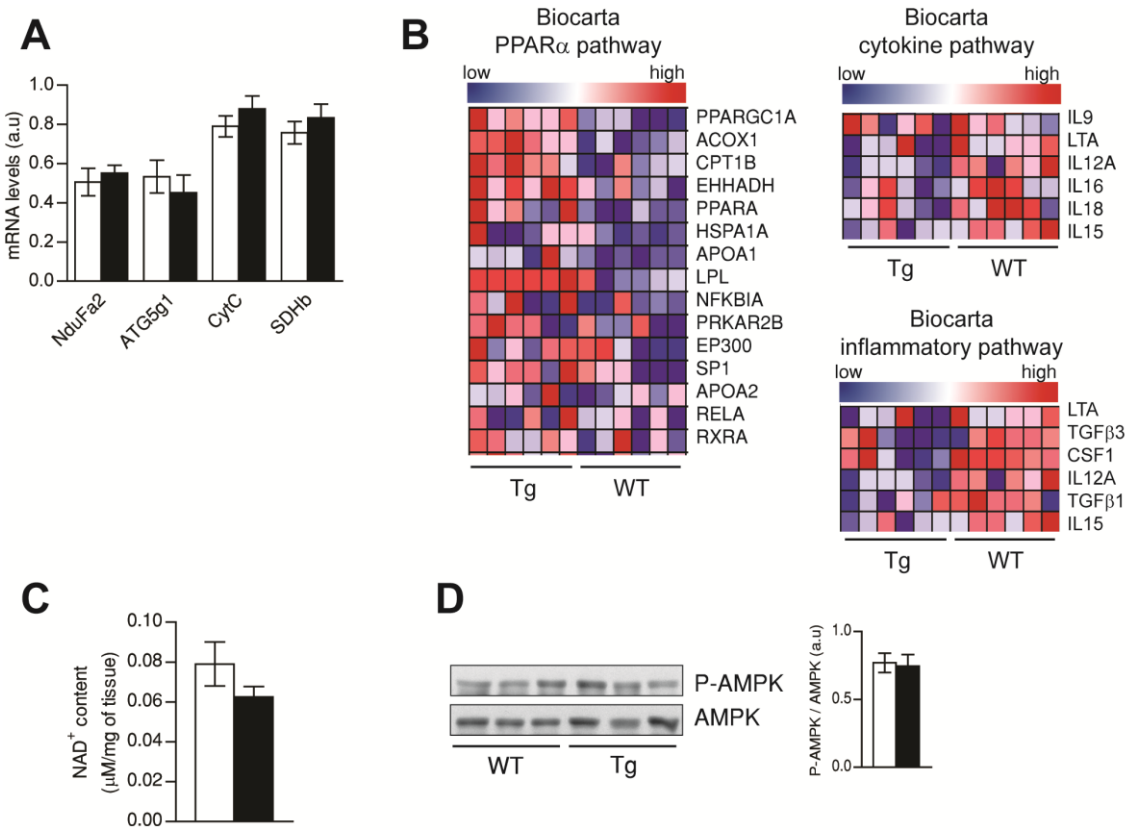


Figure S5. The influence of SIRT1 transgenesis on BAT metabolism.

(This supplemental figure is related to Figure 5 in the main text)

(A) mRNA levels of mitochondrial respiratory components in BAT from WT and Tg mice.

(B) Gene set enrichment analysis of the Biocarta PPARα, cytokine and inflammatory pathways in BAT from WT and Tg mice (respective nominal *p* value : 0.033 ; 0.018; 0.008).

(C) NAD^+ content is not modulated in BAT from WT and Tg mice.

(D) Protein analysis and quantification of the protein levels of P-AMPKα (Thr172) and total AMPKα in BAT from WT and Tg mice. The ratio P-AMPK/AMPK reveals no difference between genotypes.

Through the figure, white bars represent WT mice, while black bars represent Tg mice. All values are shown as mean +/- SEM. * Indicates statistical significant difference vs. WT.

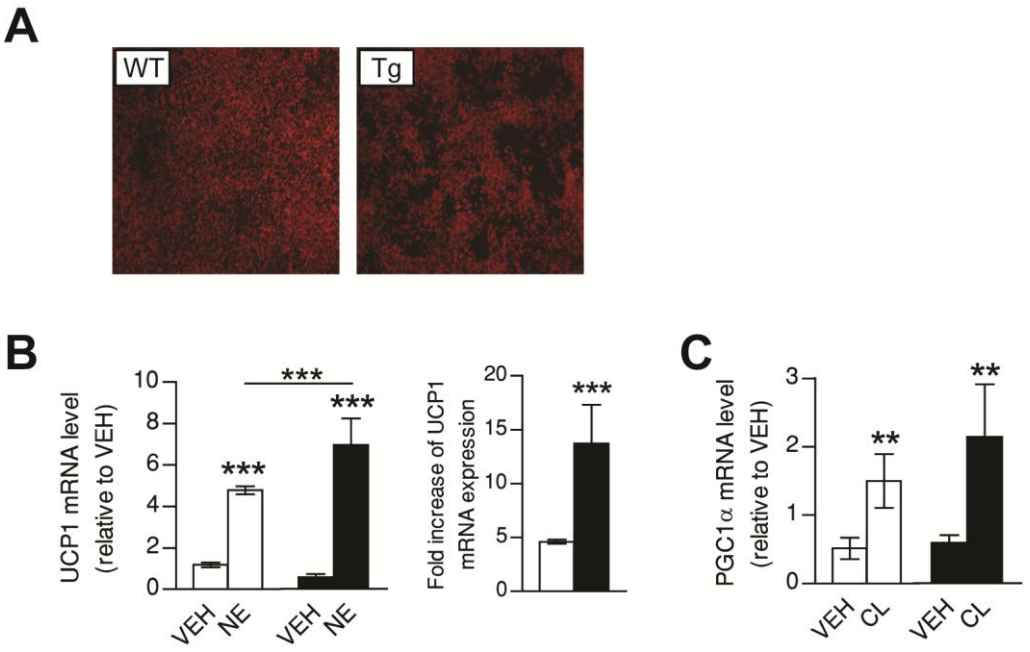


Figure S6. The influence of SIRT1 transgenesis on BAT differentiation and function.

(This supplemental figure is related to Figure 6 in the main text)

(A) Oil Red-O staining for differentiated wild-type (WT) and SIRT1 transgenic (Tg) primary brown adipocytes.

(B) Ucp1 mRNA levels in differentiated WT and Tg primary brown adipocytes treated with NE. Fold-increase over the vehicle-treated group is shown on the right.

(C) PGC1α mRNA levels in differentiated WT and Tg primary brown adipocytes treated with CL. Fold-increase over the vehicle-treated group is shown on the right.

White bars represent WT mice, while black bars represent Tg mice. All values are mean +/- SEM of three samples per tissue and genotype. * Indicates statistical significant difference vs. respective WT group.

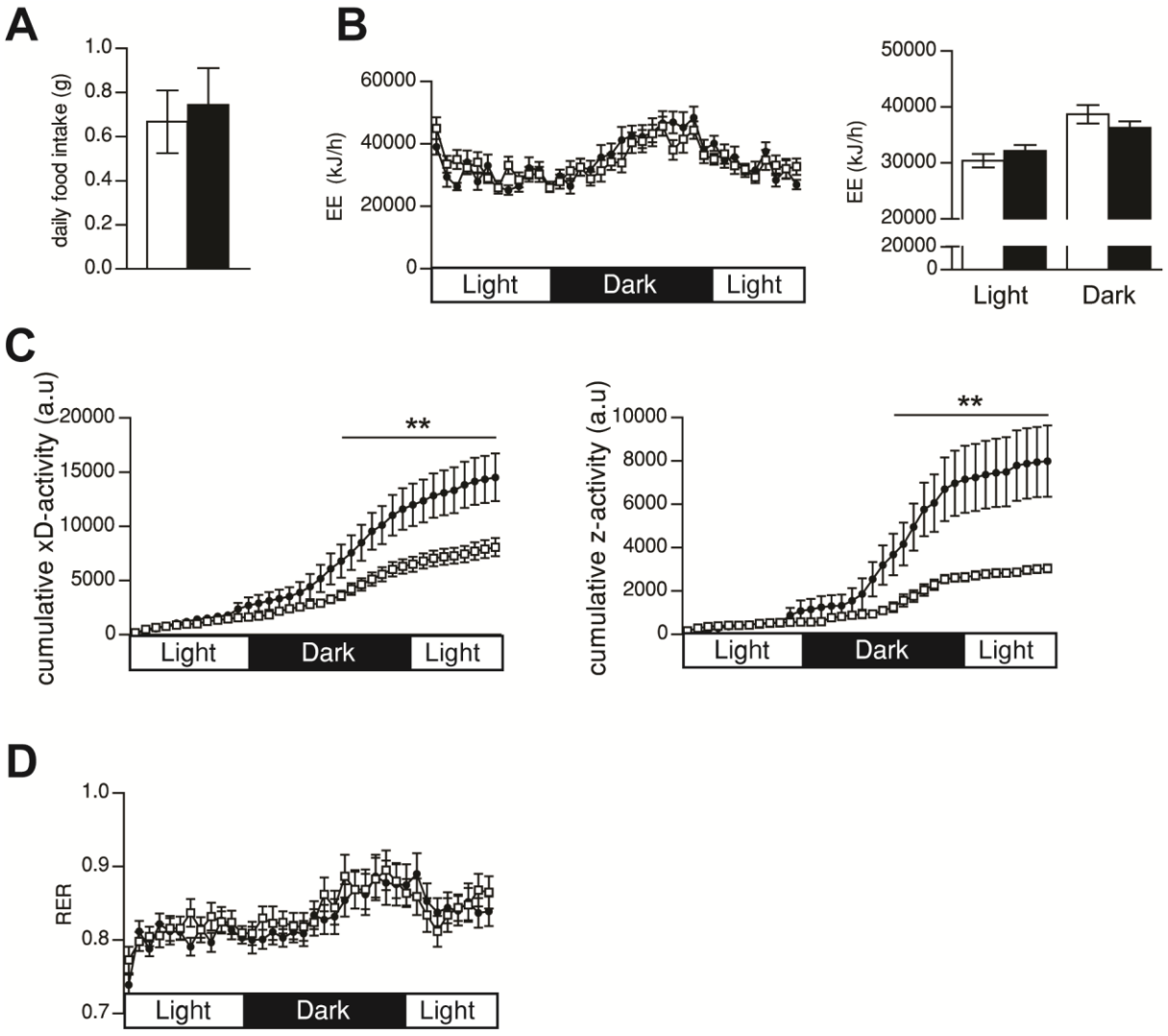


Figure S7. The influence of SIRT1 transgenesis on energy expenditure in thermoneutrality.

(This supplemental figure is related to Figure 7 in the main text)

(A) Daily food intake of WT and Tg mice housed at thermoneutrality.

(B) Energy expenditure (EE) during dark and light phase for WT and Tg mice.

(C) Total activity of WT and Tg mice housed at thermoneutrality.

(D) Respiratory Exhange Ratio of WT and Tg mice housed at thermoneutrality.

White square represent WT mice, while black squares represent Tg mice. All values are mean +/- SEM of three samples per tissue and genotype. * Indicates statistical significant difference vs. respective WT group.

Supplemental table 1. List of Antibodies

Antibodies	**Manufacturer**	**reference**
α-Tubulin	Sigma	T9026
SIRT1	Abcam	ab12193
complex I : NDUFA9	Mitosciences	ab14713
Complex II : SDHA	Abcam	ab14715
Complex III: UQCRC1	Abcam	ab14705
Complex V : ATP5A	Abcam	ab109865
GAPDH	cell signaling	2118
UCP1	Abcam	ab10983
phospho HSL	Cell signaling	4139S
HSL-Total	Cell signaling	4107S
NFkB p65 (acetilated)	Abcam	ab52175
NFkB p65	Santa Cruz	sc-8008
Prdm16	R&D system	AF6295
PPARγ	cell signaling	2443
Porin 31HL (VDCA1)	Mitosciences	ab14734
Phospho-(Ser/Thr) PKA Substrate	Cell Signaling	9621
Phospho-AMPK	Cell Signaling	2535
Total AMPK	Cell Signaling	2532
FoxO1	Cell Signaling	9454

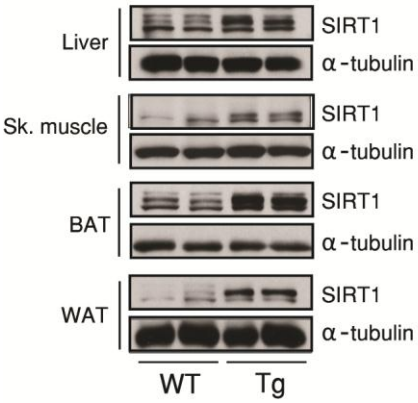
Supplemental table 2. List of oligonucleotides for mtDNA measurement and qRT-PCR

Gene	sequence	
b-2-microglobuline	F	ATGGGAAGCCGAACATACTG
	R	CAGTCTCAGTGGGGGTGAAT
cyclophilin	F	CAGGGGAGATGGCACAGGAG
	R	CGGCTGTCTGTCTTGGTGCTCTCC
sirt1	F	TGTGAAGTTACTGCAGGAGTGTAAA
	R	GCATAGATACCGTCTCTTGATCTGAA
NduFa2	F	GCACACATTTCCCCACACTG
	R	CCCAACCTGCCCATTCTGAT
ATG5g1	F	GCTGCTTGAGAGATGGGTTC
	R	AGTTGGTGTGGCTGGATCA
cytochrome c	F	TCCATCAGGGTATCCTCTCC
	R	GGAGGCAAGCATAAGACTGG
SDHb	F	GGACCTATGGTGTTGGATGC
	R	GTGTGCACGCCAGAGTATTG
ppara	F	AGGAAGCCGTTCTGTGACAT
	R	TTGAAGGAGCTTTGGGAAGA
lcad	F	GTAGCTTATGAATGTGTGCAACTC
	R	GTCTTGCGATCAGCTCTTTCATTA
mcad	F	GGCCATTAAGACCAAAGCAGA
	R	GTGTCGGCTTCCACAATGAAT
cpt2	F	AGCCAGTTCAGGAAGACAGA
	R	GACAGAGTCTCGAGCAGTTA
cpt1	F	CCCATGTGCTCCTACCAGAT
	R	CCTTGAAGAAGCGACCTTTG
FoxO1	F	AAGGATAAGGGCGACAGCAA
	R	TCCACCAAGAACTCTTTCCA
FoxO3a	F	CTTCAAGGATAAGGGCGACAG
	R	CCTCGGCTCTTGGTGTACTTG
pgc1a	F	AAGTGTGGAACTCTCTGGAACTG
	R	GGGTTATCTTGGTTGGCTTTATG
pgc1b	F	TGGAGACTGCTCTGGAAGGT
	R	TGCTGCTGTCCTCAAATACG
ppard	F	AATGCGCTGGAGCTCGATGAC
	R	ACTGGCTGTCAGGGTGGTTG
g6pase	F	CCGGATCTACCTTGCTGCTCACTTT
	R	TAGCAGGTAGAATCCAAGCGCGAAAC
pepck	F	CCACAGCTGCTGCAGAACA
	R	GAAGGGTCGCATGGCAAA
ucp1	F	CTTTGCCTCACTCAGGATTGG
	R	ACTGCCACACCTCCAGTCATT

cidea	F	TGCTCTTCTGTATCGCCCAGT
	R	GCCGTGTTAAGGAATCTGCTG
prdm16	F	TGGCCTTCATCACCTCTCTGAA
	R	TTTCTGATCCACGGCTCCTGTGA
dio2	F	AGAGTGGAGGCGCATGCT
	R	GGCATCTAGGAGGAAGCTGTTC
pparg	F	ATGGGTGAAACTCTGGGAGATTCT
	R	CTTGGAGCTTCAGGTCATATTTGTA
cox2	F	GTTGATAACCGAGTCGTTCTGC
	R	CCTGGGATGGCATCAGTTTT
hk2	F	GCCAGCCTCTCCTGATTTTAGTGT
	R	GGGAACACAAAAGACCTCTTCTGG

Western Blot quantification

Figure 1A



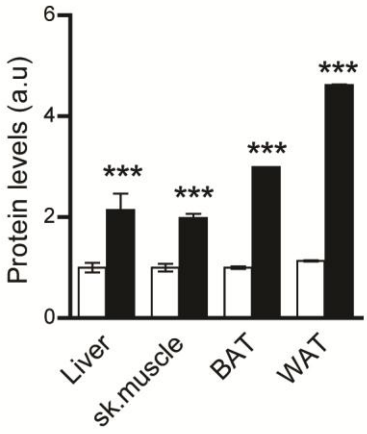
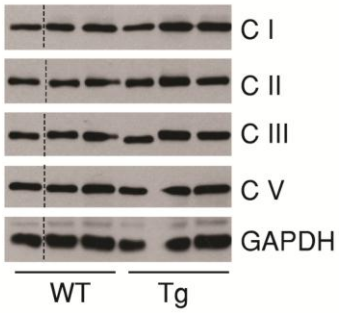


Figure 3F



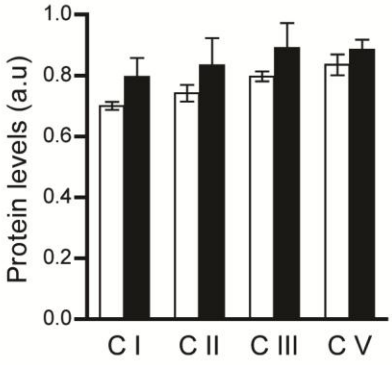
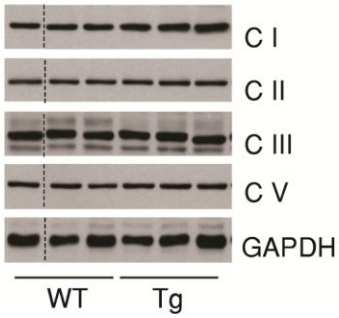


Figure 4H



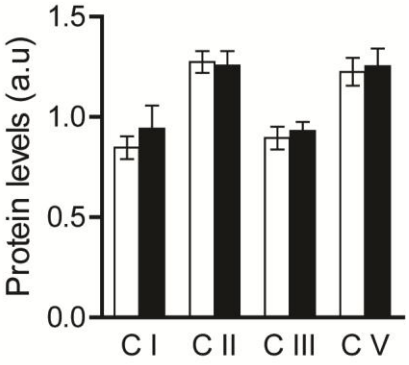


Figure 5E

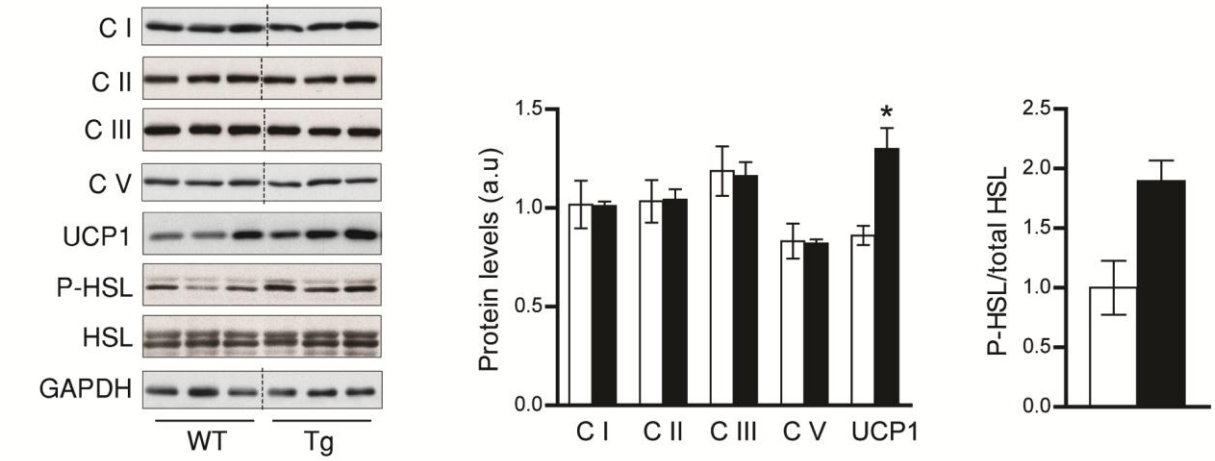


Figure 5K

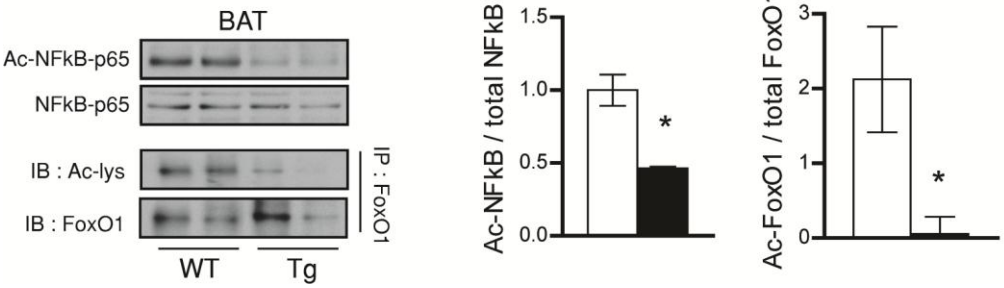


Figure 6D

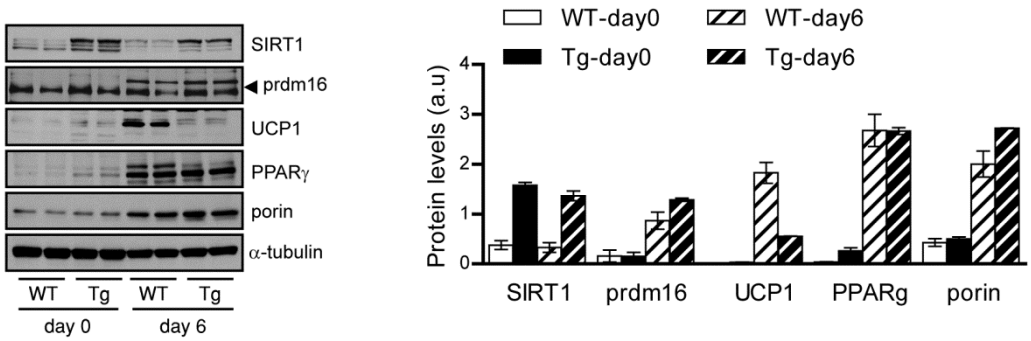


Figure 6F

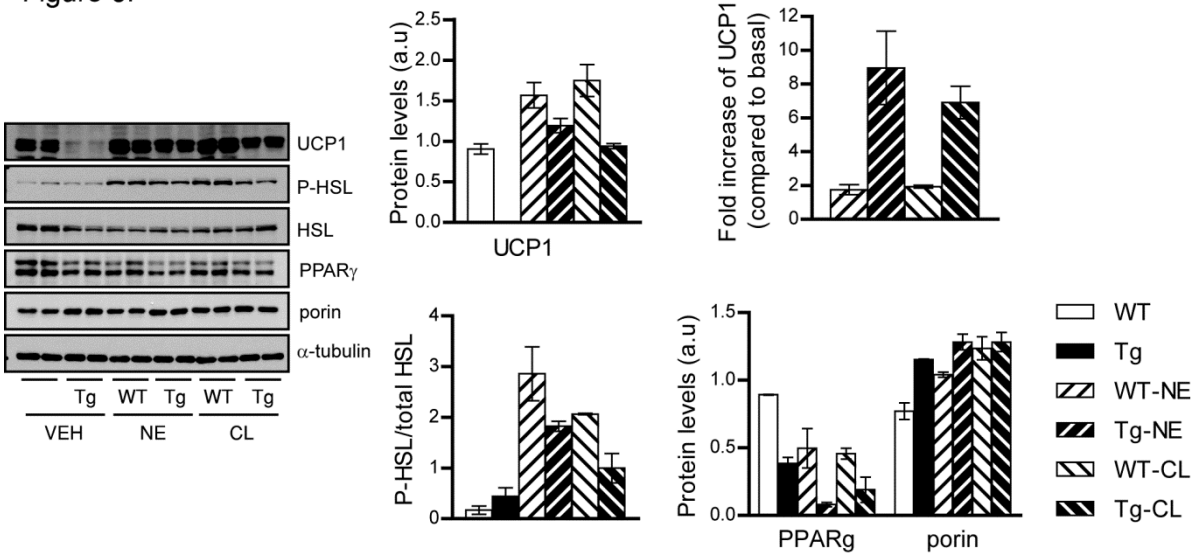


Figure 7I