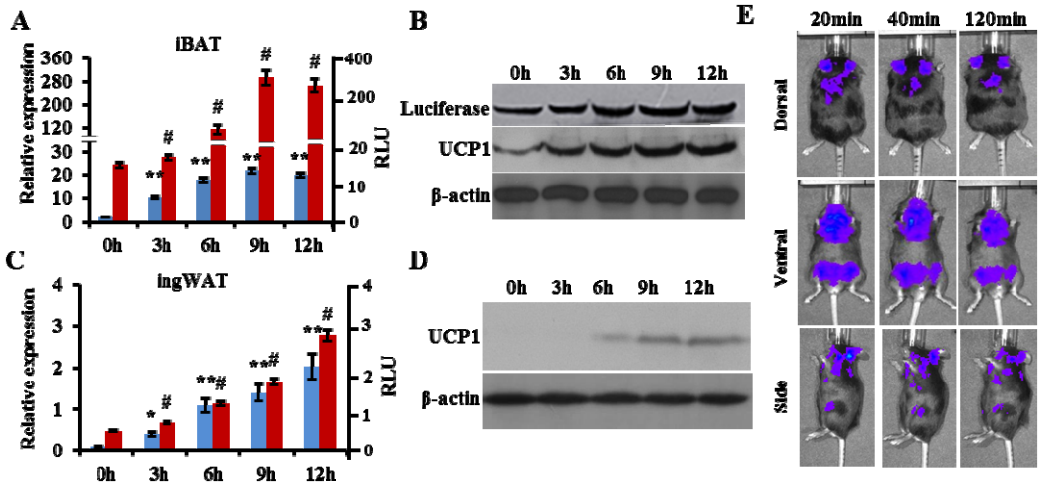
SUPPLEMENTARY DATA

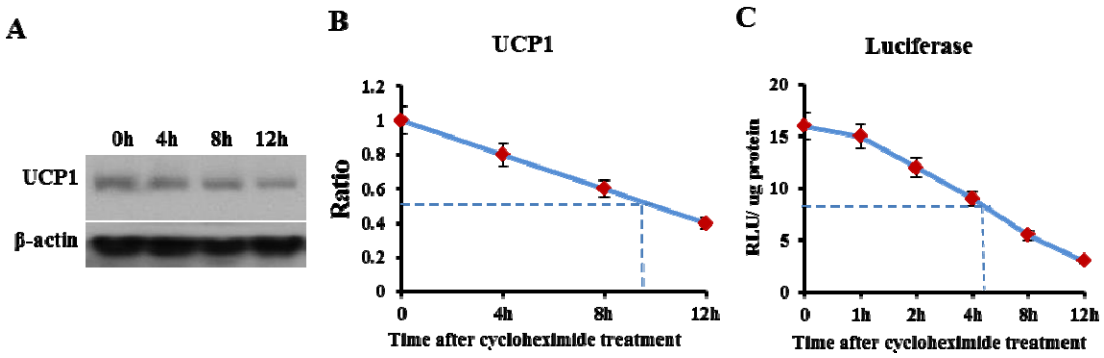
Supplementary Figure S1. UCP1expression level is in concordance with luciferase activity.



(A-D) *Ucp1*-2A-luciferase mice were housed at 4°C for various time periods as indicated. (A) and (C) Relative luciferase activity (RLU) and mRNA level in (A) iBAT and (C) ingWAT; (B) and (D) Western blot analysis of UCP1 and luciferase in (B) iBAT and (D) ingWAT; (E) Representative luminescence images of $UCP1^{+/LUC}$ mice after injection of substrate for 20min, 40min and 120min. n=8, #p<0.05, *p<0.05, **p<0.01.

SUPPLEMENTARY DATA

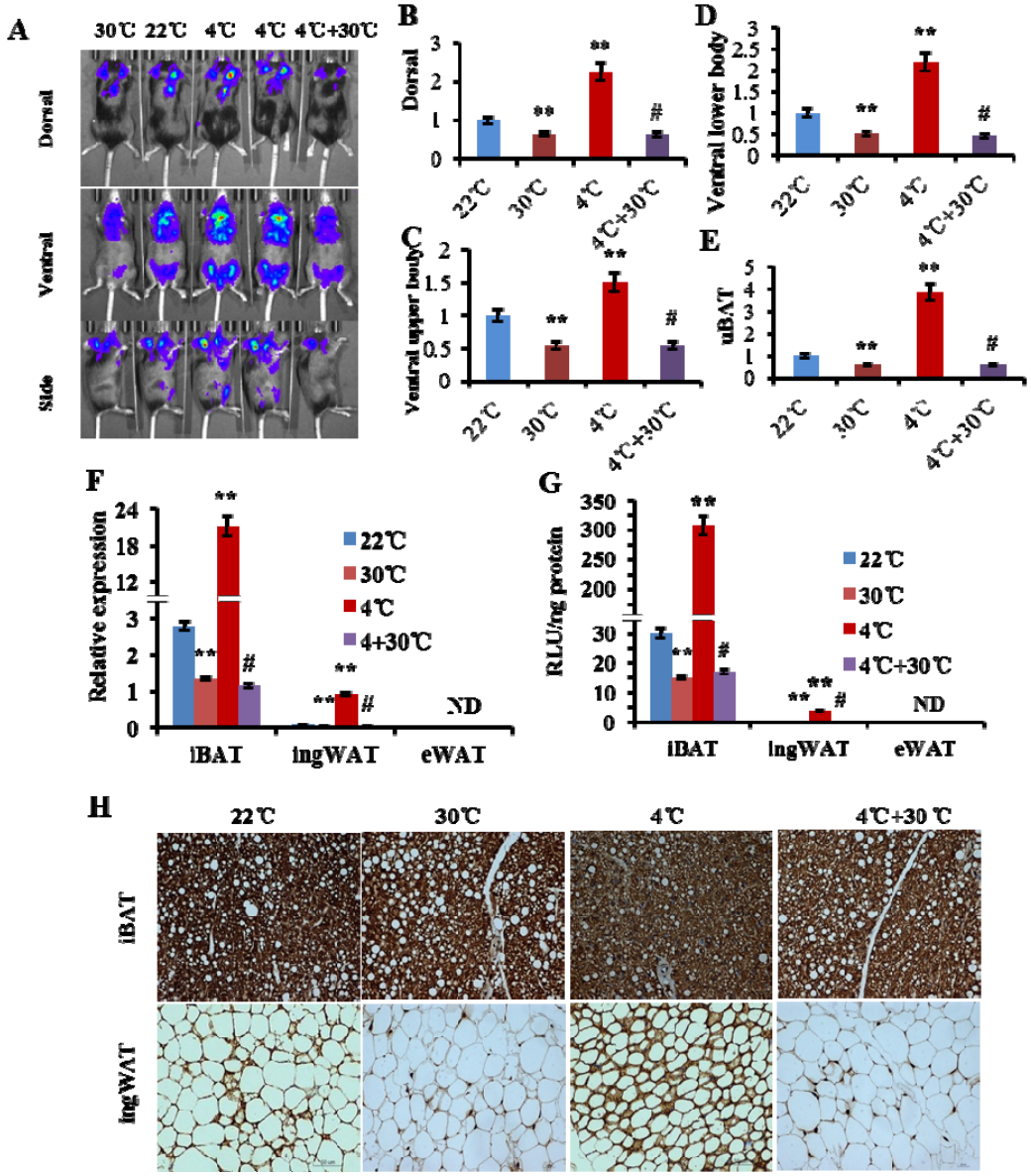
Supplementary Figure S2. Half-lives of UCP1 and luciferase protein.



Brown adipocytes were stimulated with CL316,243 (1 μM) for 2 days, followed by incubation with cycloheximide (10 μM as time zero). The relative protein levels of UCP1 and luciferase were examined. (A) Western blot and (B) densitometry analysis of UCP1 and (C) luciferase activity in treated cells at various time points after cycloheximide treatment. n=6.

SUPPLEMENTARY DATA

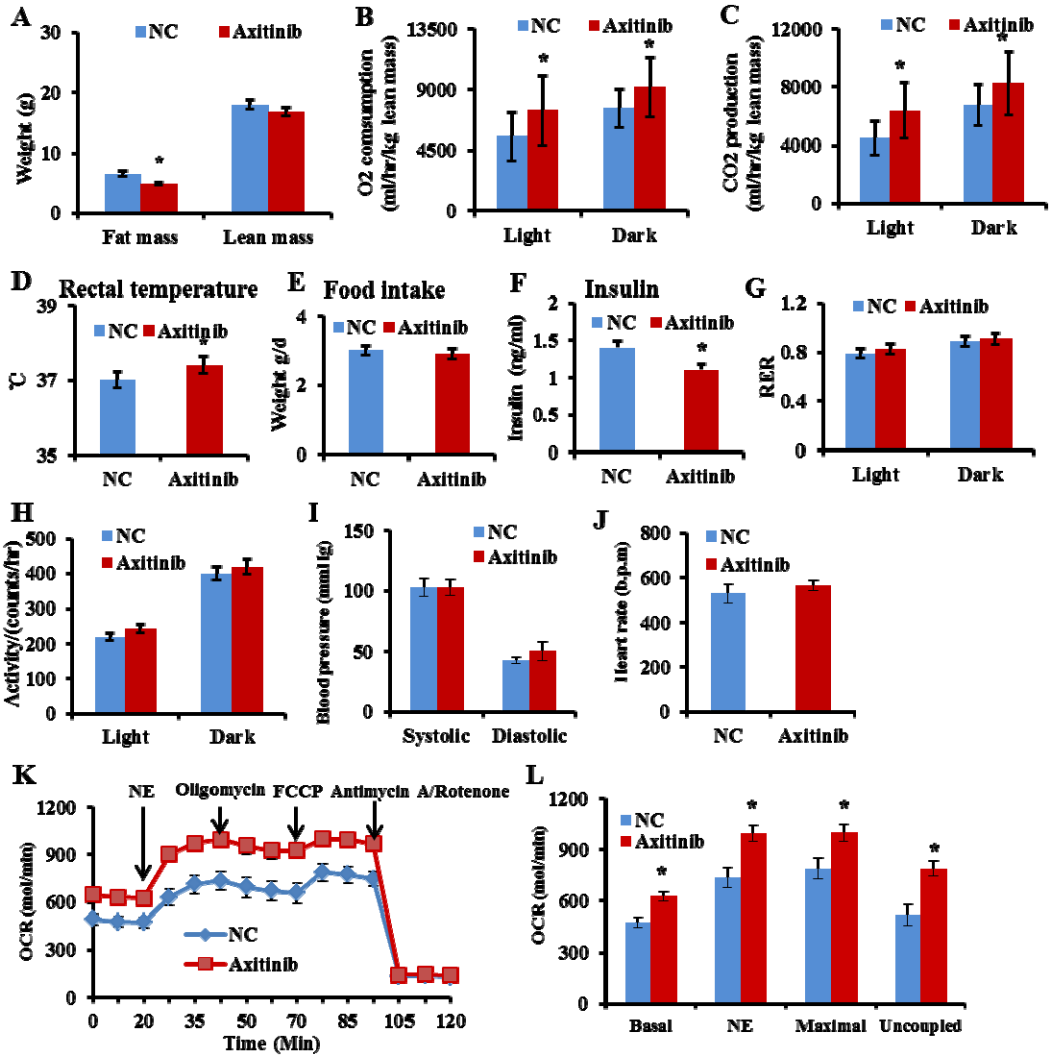
Supplementary Figure S3. UCP1 expression was reduced upon thermoneutrality.



Ucp1-2A-luciferase mice were housed at 4°C or 22°C for 12 h, and then housed at 30°C for 48 h. (A) Luminescence images of mice; (B-E) Quantification of luminescence in (A) at various parts of the mice; (F) Relative levels of *Ucp1* mRNA and (G) relative luciferase activity in different adipose tissues of the mice; (H) Immunostaining of UCP1 in iBAT and iWAT. n=8. #p<0.05, *p<0.05, **p<0.01, ND, not detected.

SUPPLEMENTARY DATA

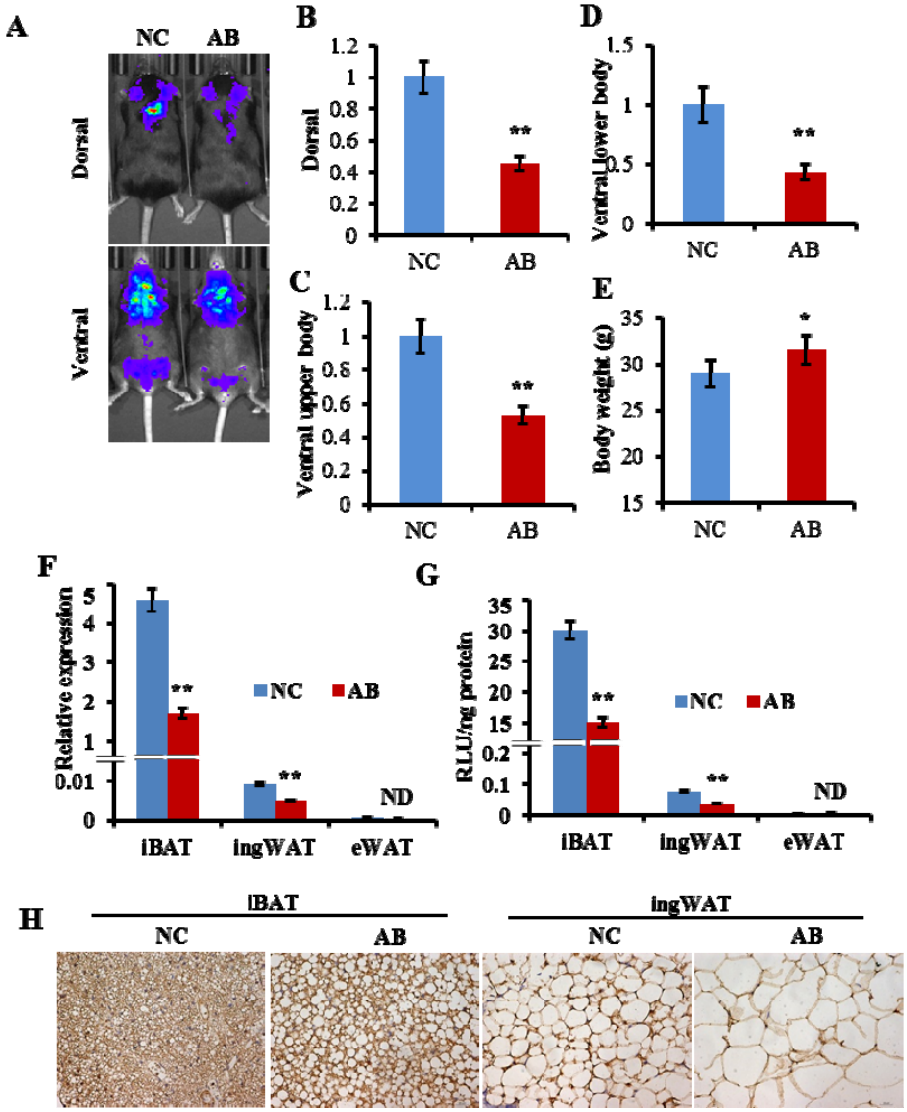
Supplementary Figure S4. Axitinib promotes energy expenditure *in vivo* and *in vitro*.



(A-I) *Ucp1*-2A-luciferase mice were orally gavaged with axitinib (10 mg/kg body weight) or PBS daily for 8 weeks. (A) Body compostion, (B) O2 consumption, (C) CO2 production, (D) Rectal temperature and (E) Food intake, (F) Serum insulin (G) RER, (H) activity, (I) blood pressure and (J) heart rate in normal control (NC) and Axitinib-treated mice. (K-L) SVF-derived mature adipocytes were treated with DMSO or axitinib (1μM) for 24 h. The oxygen consumption rate (OCR) of the cells was measured by Seahorse bioanalyzer. (K) OCRs upon sequential compound injections measuring basal, stimulated (10μM norepinephrine, NE), ATP production (2μM Oligomycin), maximal (2μM FCCP) and non-mitochondrial (1μM Antimycin A and 3μM Rotenone) respiration. (L) Basal, stimulated, maximal and uncoupled OCRs. Uncoupled OCR was calculated as the difference between stimulated and non-mitochondrial OCRs.*p<0.05, ND, not detected, n=4.

SUPPLEMENTARY DATA

Supplementary Figure S5. Browning is reduced in female mice after birth to baby.



(AB). (A) Luminescence images of virgin mice and AB mice at the same age; (B-D) Quantification of luminescence in (A) at various parts; (E) Body weight, (F) Relative levels of *Ucp1 m*RNA, (G) luciferase activity in various adipose tissues of the mice; (H) UCP1 immunostaining in iBAT and ingWAT. *p<0.05, **p<0.01, ND, not detected, n=6.

SUPPLEMENTARY DATA

Supplementary Table 1. Primers used for gene expression

Gene	Accession number		Primers
Tbx1	AF349658.1	F	GGCAGGCAGACGAATGTTC
		R	TTGTCATCTACGGGCACAAAG
PRDM16	NM_027504	F	CAGCACGGTGAAGCCATTC
		R	GCGTGCATCCGCTTGTG
Tmem26	NM_177794.3	F	ACCCTGTCATCCCACAGAG
		R	TGTTTGGTGGAGTCCTAAGGTC
Cidea	BC096649.1	F	TGCTCTTCTGTATCGCCCAGT
		R	GCCGTGTTAAGGAATCTGCTG
Cd137	DQ832278.1	F	CGTGCAGAACTCCTGTGATAAC
		R	GTCCACCTATGCTGGAGAAGG
Ucp1	NM_009463	F	GGCATTCAGAGGCAAATCAGCT
		R	CAATGAACACTGCCACACCTC
Zic1	BC060247.1	F	AACCTCAAGATCCACAAAAGGA
		R	CCTCGAACTCGCACTTGAA
Hoxc8	NM_010466.2	F	GTCTCCCAGCCTCATGTTTC
		R	TCTGATACCGGCTGTAAGTTTGT
18S	NM_013536.2	F	GTAACCCGTTGAACCCCATT
		R	CCATCCAATCGGTAGTAGCG