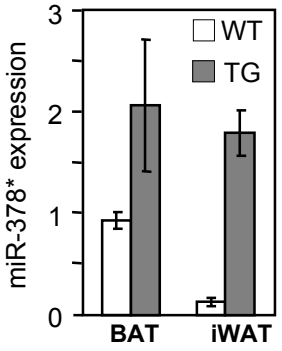
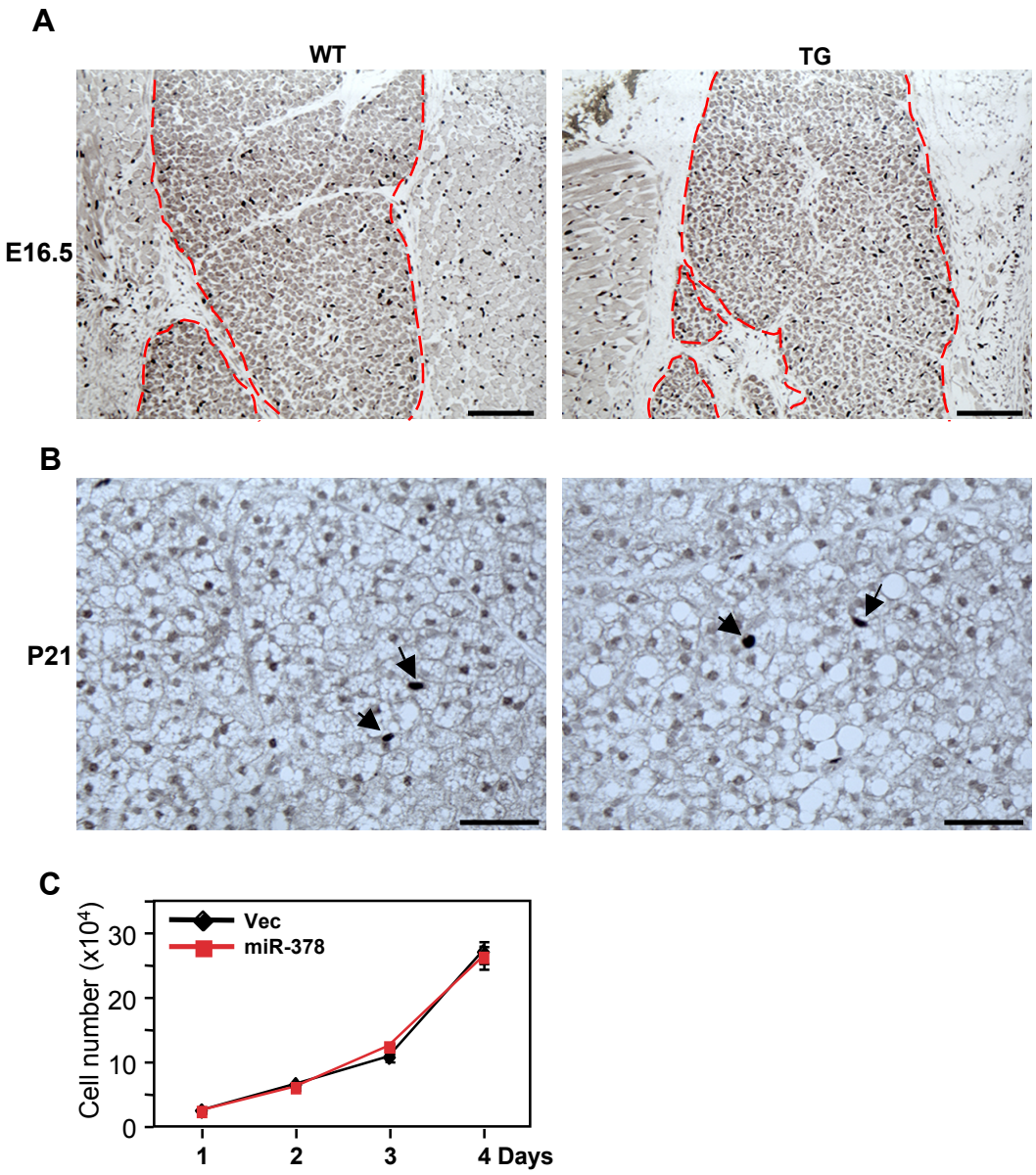
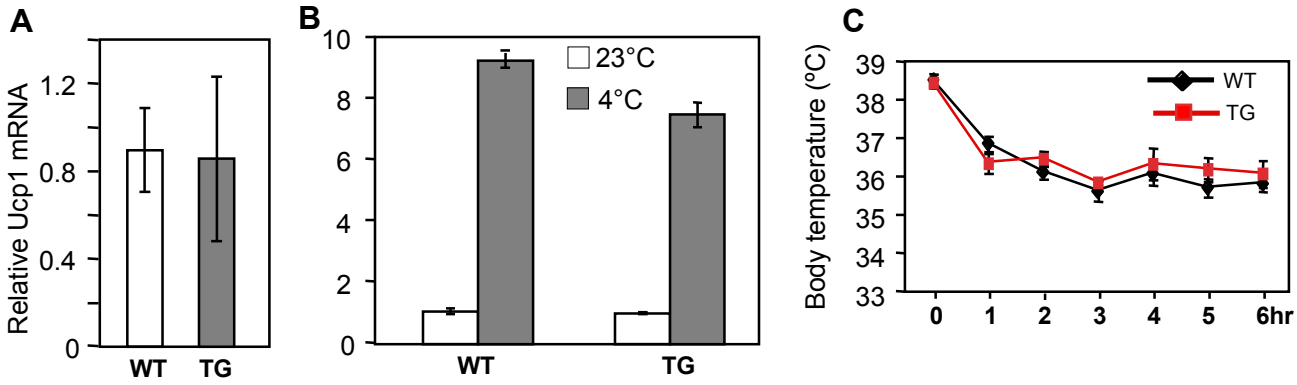


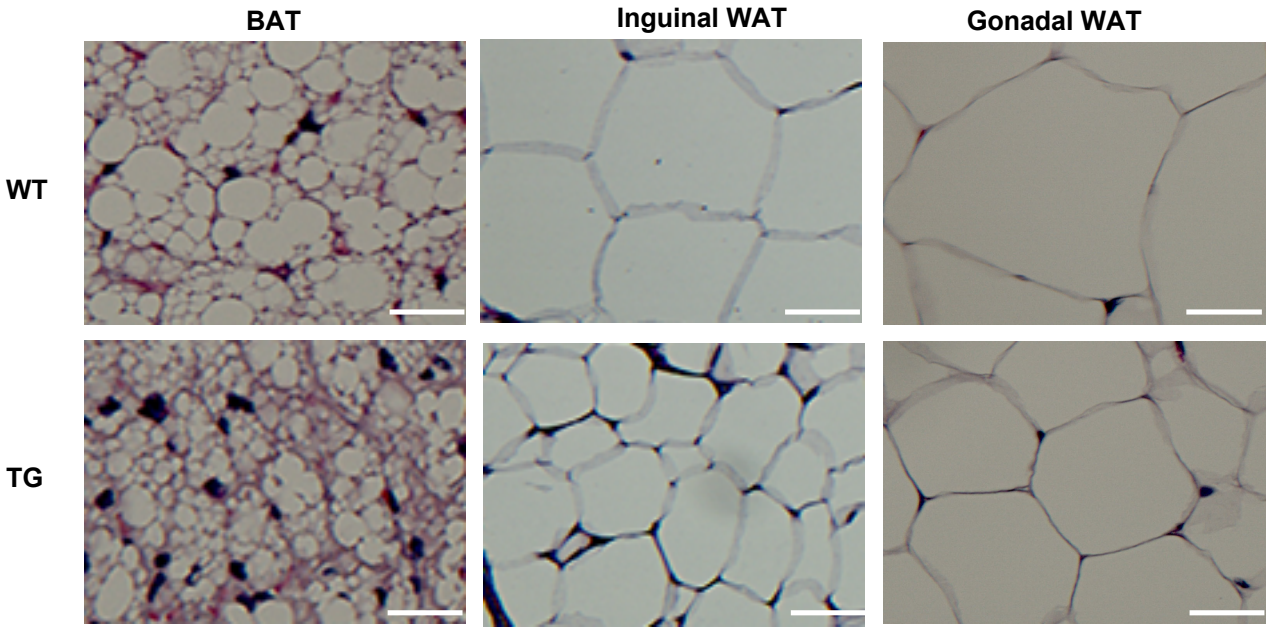
Supplementary Figure 1. miR-378* transgene expression in fat tissues. *n*=2 mice per group (10-week-old male mice).



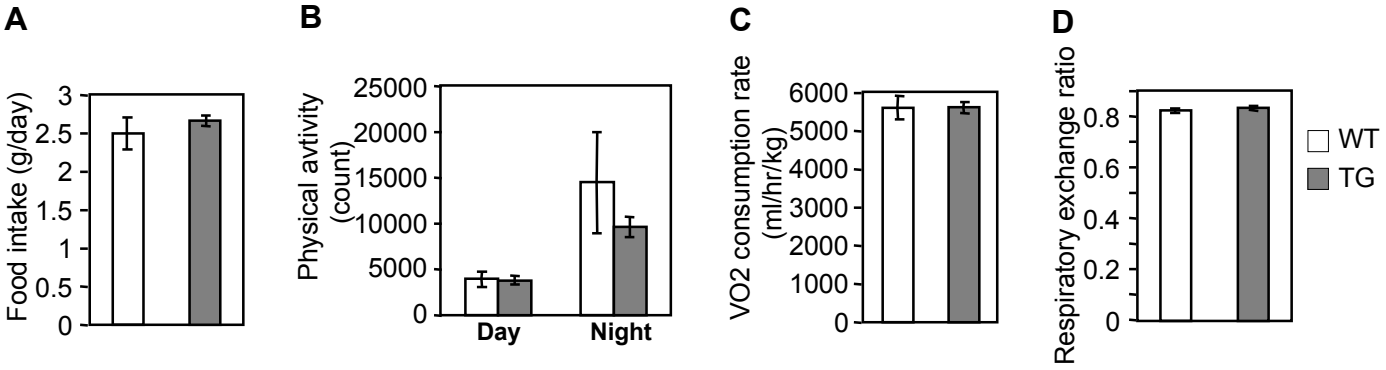
Supplementary Figure 2. (**A** and **B**) Ki67 immunohistochemical staining (dark brown, and indicated by arrows in **B**) of BAT at embryonic E16.5 and postnatal 21 day (P21). Red lines define brown fat. Scale bar, 100 μm. (**C**) Overexpression of miR-378 in immortalized brown preadipocytes does not affect cell proliferation. Brown preadipocytes overexpressing miR-378 or control cells were plated in 24-well plates at 4.8×10^4 per well. Cells were trypsinized and counted on a hemocytometer every 24 hr. n=4.



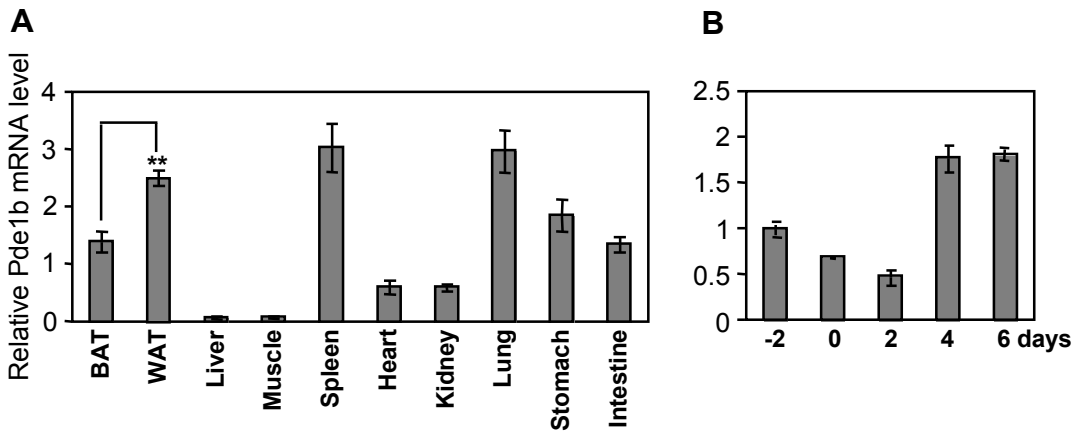
Supplementary Figure 3. (**A**) Levels of *Ucp1* mRNA in gonadal WAT from mice maintained at 23°C. *n*=4-6 mice per group (10-week-old male mice). (**B**) *Ucp1* expression is induced in BAT of both WT and TG mice after cold exposure for 6 hr. *n*=3-6 mice per group (10-week-old male mice). (**C**) Body temperature was measured during cold challenge. *n*=5-10 mice per group (12-week-old male mice).



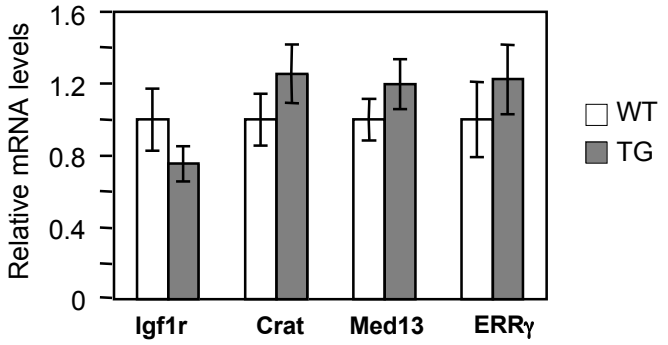
Supplementary Figure 4. H&E-stained histological sections of fat pads from TG and WT mice after 13 week of HFD. Scale bar, 50 μm.



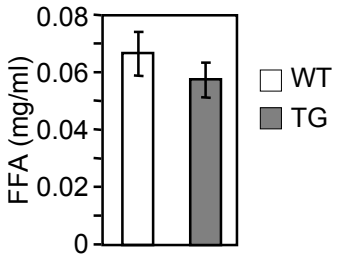
Supplementary Figure 5. Metabolic cage studies of miR-378 transgenic (TG) and wild type (WT) mice with a 3-day HFD. (**A**) WT and TG mice consumed similar amount of high fat diet daily measured with metabolic cages. (**B**) Physical activity. (**C**) Oxygen consumption rate normalized with lean mass. (**D**) Respiratory exchange ratio. *n*=5 mice per group (4-month-old female mice). Note, similar results were obtained on a normal chow.



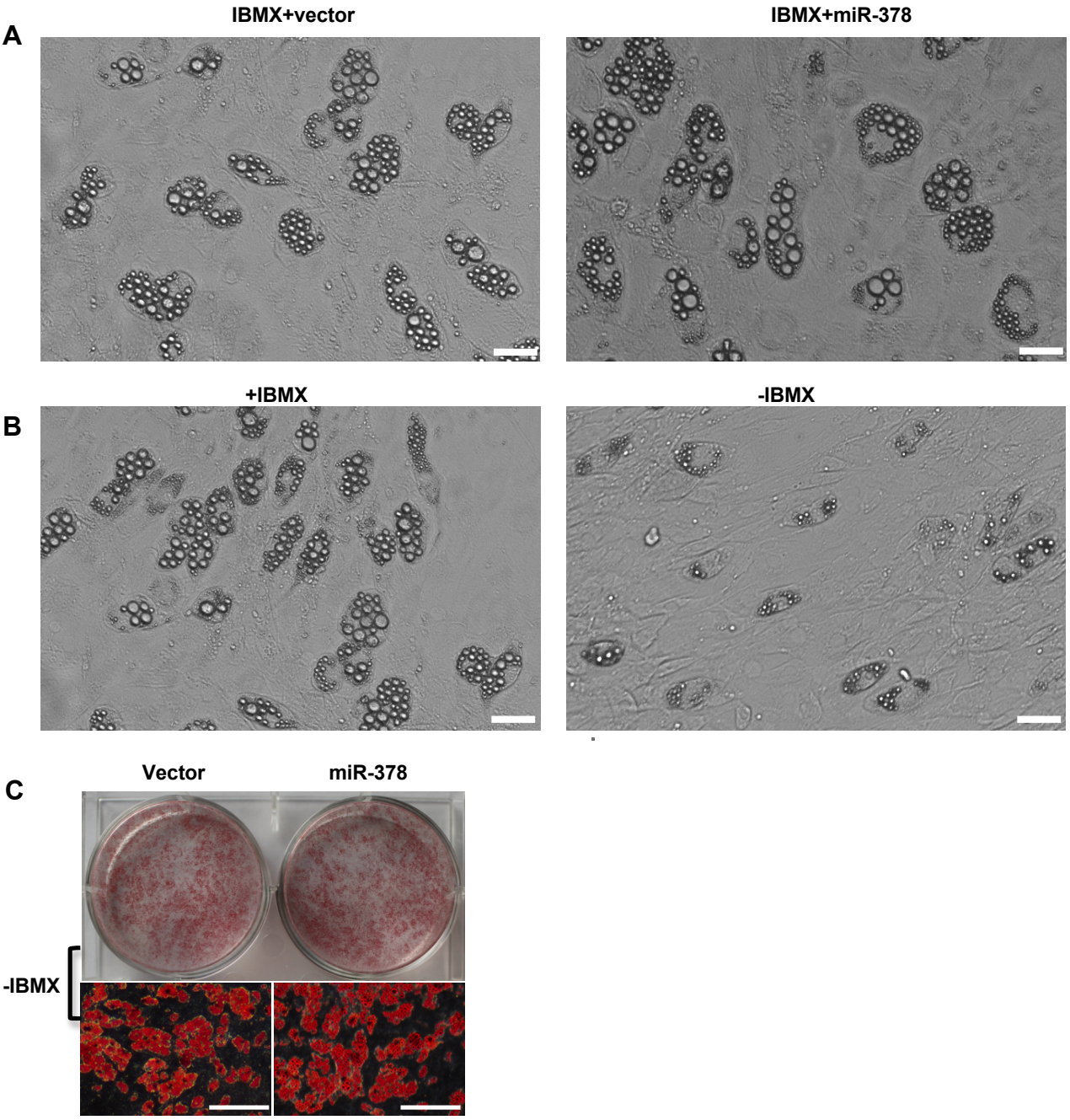
Supplementary Figure 6. **(A)** *Pde1b* expression in different tissues (n=4, 10-week-old male mice). **P=0.004 (two-tailed Student's t-test). **(B)** *Pde1b* expression during brown adipogenesis.



Supplementary Figure 7. Expression of other known miR-378/378* targets in BAT of miR-378 transgenic mice. *n*=6 mice per group (9-week-old male mice).



Supplementary Figure 8. Serum free fatty acids level after 13-week high fat diet feeding. *n*=6 mice per group.



Supplementary Figure 9. (**A**) Ectropic expression of miR378/378* has little stimulatory effect on the adipogenesis of C3H10T1/2 cells in the presence of IBMX. Scale bar, 50 μm. (**B**) Removal of IBMX abolishes adipogenesis of C3H10T1/2 cells. Scale bar, 50 μm. (**C**) Overexpression of miR-378/378* does not affect the adipogenesis of iWAT preadipocytes in the absence of IBMX. Scale bar, 50 μm.

Supplementary Table 1 Gene full names and sequences of primers used in this study.

	Gene full name	Sequences for QPCR assays and shRNA target
		Primers used for real-time QPCR
Ucp1	Uncoupling protein 1 (mitochondrial, proton carrier)	F: GGATTGGCCTCTACGACTCA R: TGCCACACCTCCAGTCATTA
Pgc-1α	Peroxisome proliferative activated receptor, gamma, coactivator 1 alpha	F: AACCACACCCACAGGATCAGA R: TCTTCGCTTTATTGCTCCATGA
Pgc-1β	Peroxisome proliferative activated receptor, gamma, coactivator 1 beta	F: CCGAGCTCTTCCAGATTGACA R: CGTAAGCGCAGCCAAGAGA
Prdm16	PR domain containing 16	F: CAGCACGGTGAAGCCATTC R: GCGTGCATCCGCTTGTG
Cox7a1	Cytochrome c oxidase subunit VIIa 1	F: CAGCGTCATGGTCAGTCTGT R: AGAAAACCGTGTGGCAGAGA
Pparγ	Peroxisome proliferative activated receptor gamma	F: CAAGAATACCAAAGTGCGATCAA R: GAGCTGGGTCTTTTCAGAATAATAAG
aP2	Fatty acid binding protein 4, adipocyte	F: GGCGTGACTTCCACAAGAGTTTA R: GCCTCTTCCTTTGGCTCATG
Resistin	Resistin	F: CAACTCCCTGTTTCCAAATGC R: GTCCAGCAATTTAAGCCAATGTT
Leptin	Leptin	F: TTCACACACGCAGTCGGTAT R: GCTGGTGAGGACCTGTTGAT
Agt	Angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	F: CAGACAGCACCCTACTTTTCAA R: CAGACACCGAGATGCTGTTG
C/EBPβ	CCAAT/enhancer binding protein (C/EBP), beta	F: CAAGCTGAGCGACGAGTACA R: GACAGCTGCTCCACCTTCTT
Pde1b	Phosphodiesterase 1B, $Ca2^{+}$-calmodulin dependent	F: CGCTCTGAGGACCATTGTTT R: TCCCATAGCCTGTCTCCAAG
Igf1r	Insulin-like growth factor I receptor	F: GACAACTGCCCTGATATGCT R: GAAGGAGACCTCCTGGAAGC
Crat	Carnitine acetyltransferase	F: AACGCCTACAGAAGGGACTG R: GGGCTGGAGTAGATGACCAC
Med13	Mediator complex subunit 13	F: GCGAGATCAAAGACCTGGAA R: AGGCCATTCTCCCATACTCC
ERRγ	Estrogen-related receptor gamma	F: ACTTGGCTGACCGAGAGTTG R: GCAAGGGACAGTGTGGAGAA
U36B4	Ribosomal protein, large, P0	F: AGATGCAGCAGATCCGCA R: GTTCTTGCCCATCAGCACC
		shRNA target sequence
Pde1b	Phosphodiesterase 1B, $Ca2^{+}$-calmodulin dependent	CCTTCTTTAGATGTGGACGTA