SUPPLEMENTARY DATA

Supplementary Table 2. Primer List

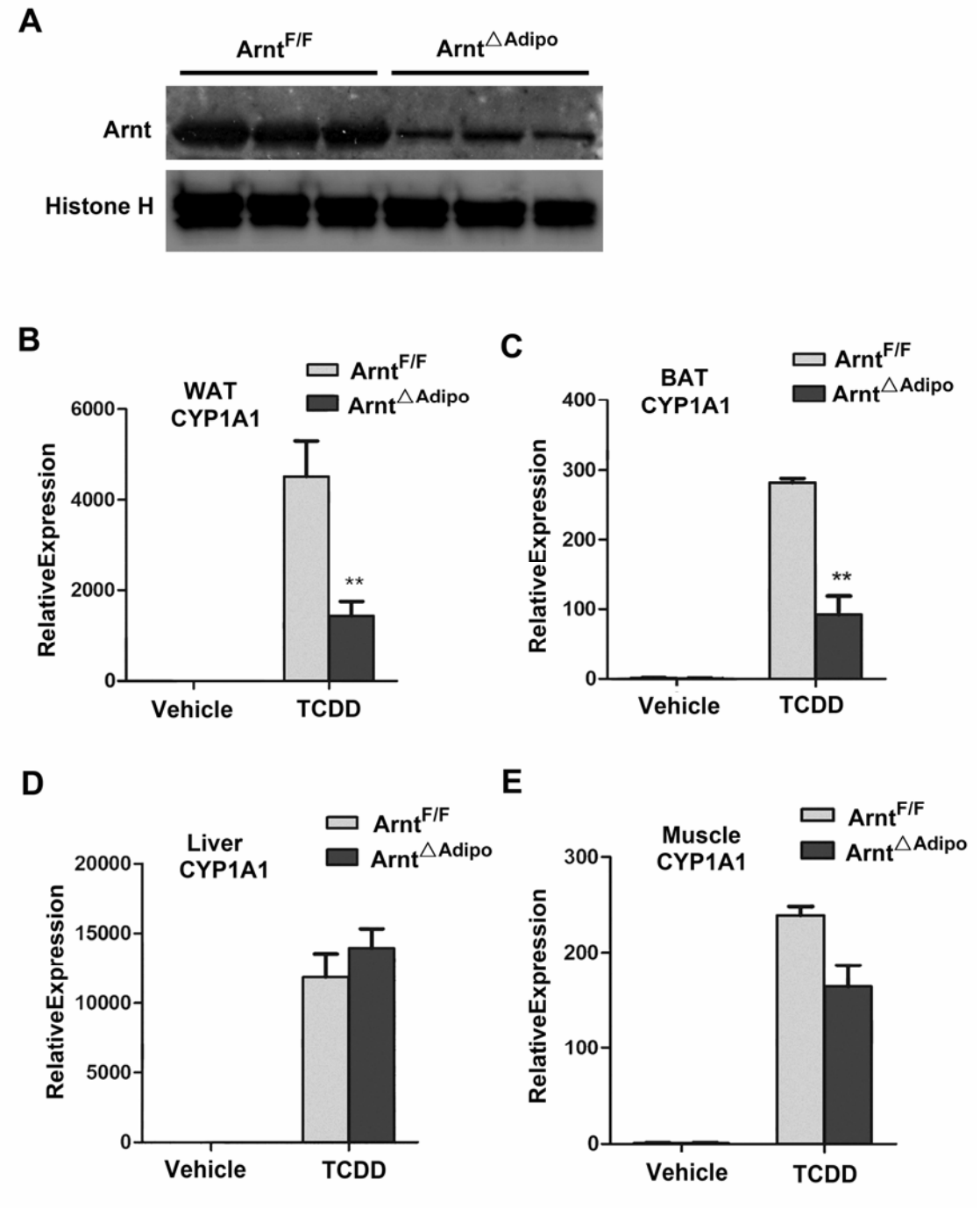
RT-PCR	
ARNT FWD1	5' - ACGCACTACAACACCTGAGCTAA - 3'
ARNT FWD2	5' - TGCCAACATGTGCCACCATGT - 3'
ARNT REV	5' - GCATGCTGGCACATGCCTGTCT - 3'
HIF-1α FWD1	5' - CTGTCTTCCCTGCTTAGGTCTTTCTAAC - 3'
HIF-1α FWD2	5' - GAGATGGAGAAGGAGGTTAGTGTATCC - 3'
HIF-1α REV	5' - ACGTTGGCTCATGGTGTACTTTG - 3'
qPCR	
HIF-1α FWD	5'- ATAGCTTCGCAGAATGCTCAGA -3'
HIF-1α REV	5'- CAGTCACCTGGTTGCTGCAA -3'
ARNT FWD	5'- CAAGCCATCTTTCCTCACTGATC -3'
ARNT REV	5'- ACACCACCCGTCCAGTCTCA -3'
SOCS3 FWD	5'- GCGGGCACCTTTCTTATCC - 3'
SOCS3 REV	5'- TCCCCGACTGGGTCTTGAC - 3'
VEGF FWD	5'- AGACGGACACACATGGAGGT - 3'
VEGF REV	5'- AAAGACTCAATGCATGCCAC - 3'
ADIPOQ FWD	5'- CTCTAAAGATTGTCAGTGGATCTG - 3'
ADIPOQ REV	5'- ACGTCATCTTCGGCATGACT - 3'
GLUT4 FWD	5'- TTTTAAAACAAGATGCCGTCG - 3'
GLUT4 REV	5'- CAGTGTTCCAGTCACTCGCT - 3'
Leptin FWD	5'- TCAAGACCATTGTCACCAGG - 3'
Leptin REV	5' -TGAAGCCCAGGAATGAAGTC - 3'
GLUT-1 FWD	5' - CCAGCTGGGAATCGTCGTT -3'
GLUT-1 REV	5' - CAAGTCTGCATTGCCCATGAT -3'
β-actin FWD	5' - TATTGGCAACGAGCGGTTCC - 3'
β-actin REV	5' - GGCATAGAGGTCTTTACGGATGTC - 3'
PGC1α FWD	5'-TGTAGCGACCAATCGGAAAT - 3'
PGC1α REV	5'- TGAGGACCGCTAGCAAGTTT- 3'
PGC1β FWD	5'-GCTCTCGTCCTTCTTCCTCA - 3'
PGC1β REV	5'- GAGGTCAAGCTCTGGCAAGT- 3'
Resistin FWD	5'- TGAAGCCATCGACAAGAAGA - 3'
Resistin REV	5'- CTTCCCTCTGGAGGAGACTG - 3'
CFD FWD	5'- GCTGTCAGAATGCACAGCTC- 3'
CFD REV	5'- CTCCTGGCCACCCAGAAT- 3'
PPARG FWD	5'- TCTGGGAGATTCTCCTGTTGA -3'
PPARG REV	5'- GGTGGGCCAGAATGGCATCT -3'
C/EBPα FWD	5'- CCAAGAAGTCGGTGGACAAG -3'
C/EBPα REV	5'- TTGTTTGGCTTTATCTCGGC -3'
ATGL FWD	5'- CCACTCACATCTACGGAGCC - 3'
ATGL REV	5'- TAATGTCACCTGCTTCA- 3'
HSL FWD	5'- CCTGCAAGAGTATGTCACGC - 3'
HSL REV	5'- GGAGAGAGTCTGCAGGAACG - 3'

SUPPLEMENTARY DATA

TNFα FWD	5'- CCACCACGCTCTTCTGTCTAC - 3'
TNFα REV	5'- AGGGTCTGGGCCATAGAACT - 3'
MCP-1 FWD	5'- CCTGCTGTTCACAGTTGCC - 3'
MCP-1 REV	5'- ATTGGGATCATCTTGCTGGT - 3'
Lox FWD	5'- GGAGGACACGTCCTGTGACT - 3'
Lox REV	5' - CTATGTCTGCCGCATAGGTG - 3'
Col1a1 FWD	5' - ACATGTTCAGCTTTGTGGACC -3'
Col1a1 REV	5' - TAGGCCATTGTGTATGCAGC -3'
Col3a1 FWD	5' - GGAACCTGGTTTCTTCTCACC - 3'
Col3a1 REV	5' - TAGGACTGACCAAGGTGGCT - 3'
Loxl FWD	5'- GGGTAGTGTGTACCGACCCA - 3'
Loxl REV	5'- GATGGGCTCTCTGCACGTAT - 3'
CD68 FWD	5'- ATCCCCACCTGTCTCTCTCA - 3'
CD68 REV	5'- ACCGCCATGTAGTCCAGGTA - 3'
F4/80 FWD	5'- GGATGTACAGATGGGGGATG - 3'
F4/80 REV	5'- CATAAGCTGGGCAAGTGGTA - 3'
PAI-1 FWD	5'- GCCTCCTCATCCTGCCTAA- 3'
PAI-1 REV	5'- GCCAGGGTTGCACTAAACAT- 3'
HIF-2α FWD	5'- TGAGTTGGCTCATGAGTTGC - 3'
HIF-2α REV	5'- TATGTGTCCGAAGGAAGCTG - 3'

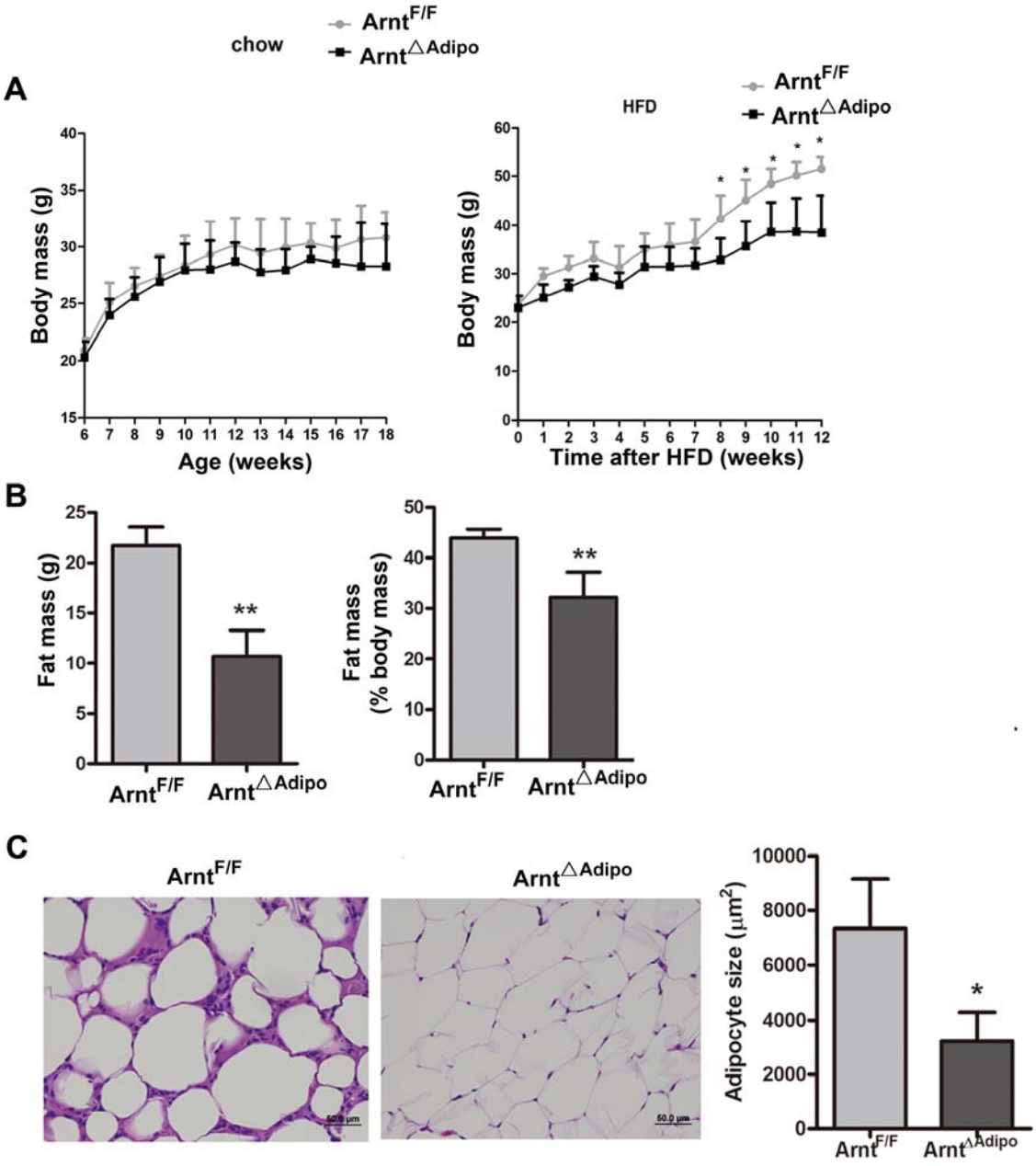
SUPPLEMENTARY DATA

Supplementary Figure 1. Adipocyte-specific Disruption of ARNT via Cre-loxP-mediated Recombination. (A) Western blot analysis measuring *Arnt* expression in WAT from $Arnt^{F/F}$ or $Arnt^{\Delta Adipo}$ mice. (B)-(E) qPCR analysis of CYP1A1 mRNA induction by TCDD treatment in WAT, BAT, liver and skeletal muscle of $Arnt^{F/F}$ or $Arnt^{\Delta Adipo}$ mice. For qPCR analysis the expression was normalized to β-actin. Data are mean ± SD. **P<0.01 compared to floxed littermates.



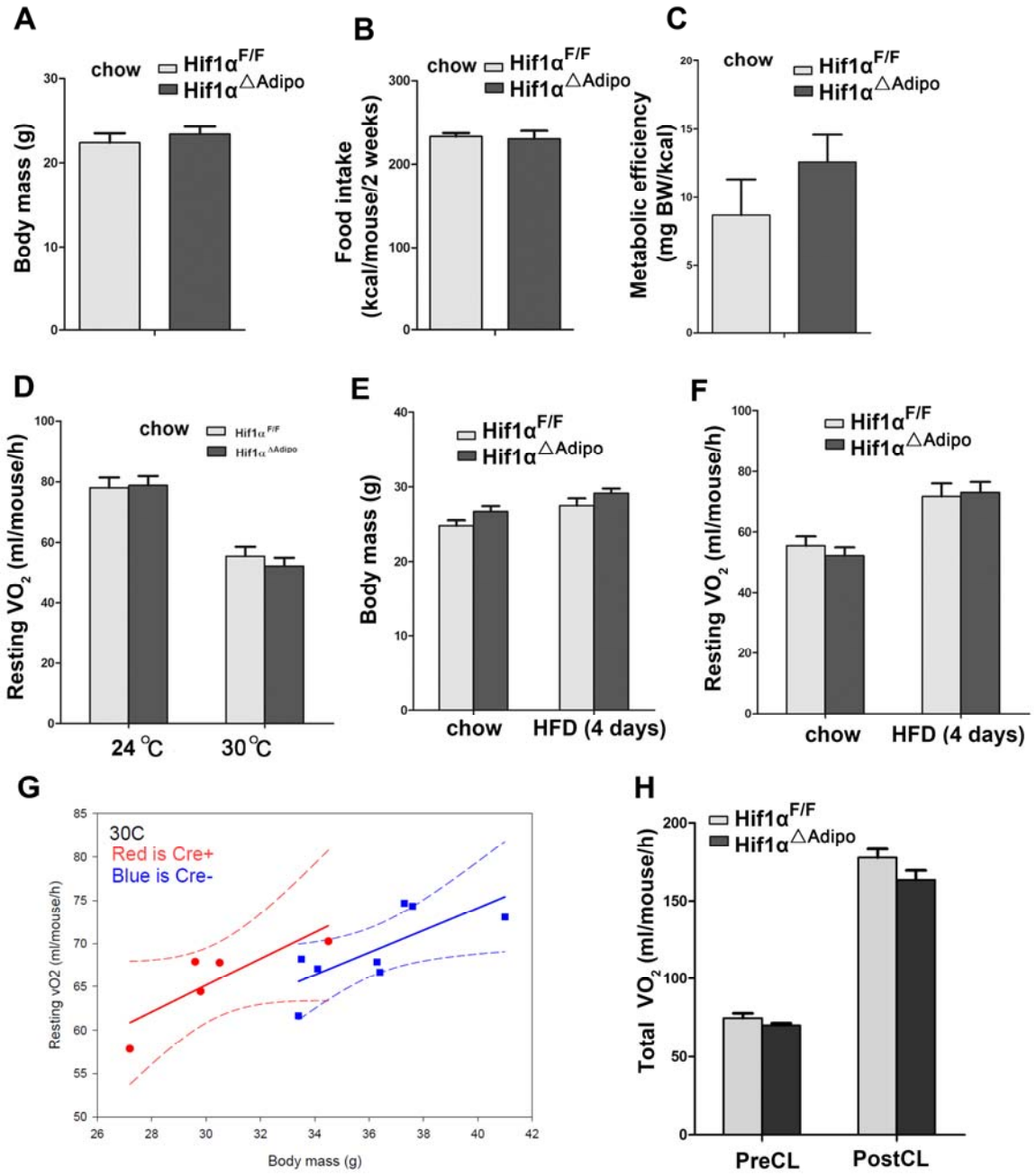
SUPPLEMENTARY DATA

Supplementary Figure 2. Disruption of ARNT Protected Mice from High-fat Diet-induced Obesity. (A) Typical growth curves of *Arnt*$^{F/F}$ and *Arnt*$^{\Delta Adipo}$ mice maintained on chow diet (left panel) or high-fat diet (HFD, right panel). (B) Body composition by NMR to show the fat mass and fat mass ratio in *Arnt*$^{F/F}$ and *Arnt*$^{\Delta Adipo}$ mice after 12 weeks of HFD. (C) Representative H&E-stained WAT sections and quantification of adipocyte size from *Arnt*$^{F/F}$ and *Arnt*$^{\Delta Adipo}$ mice after 12 weeks of HFD (n = 5/group). Data are mean ± SD. **P<0.01 compared to floxed littermates.



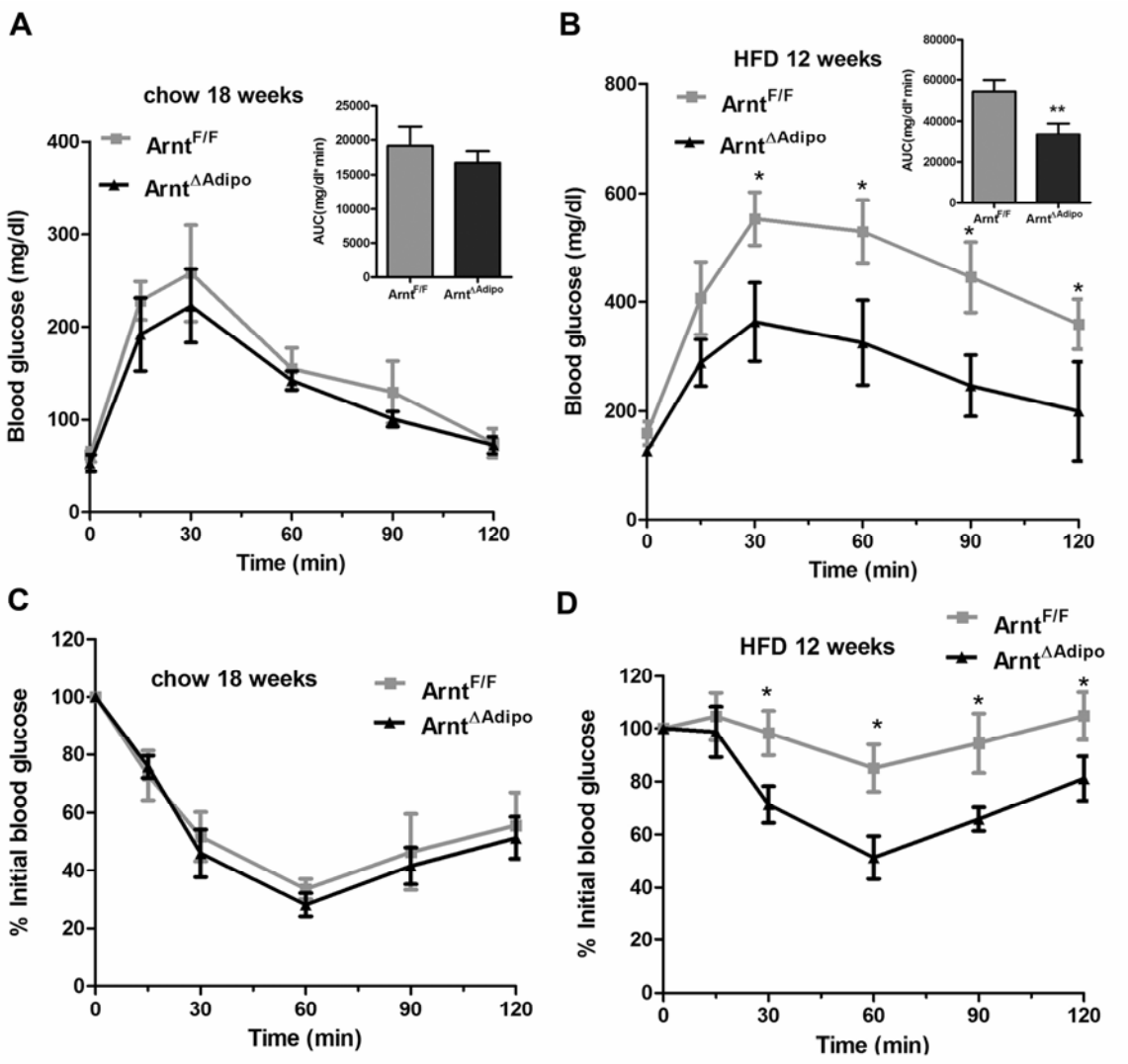
SUPPLEMENTARY DATA

Supplementary Figure 3. Energy Balance in *Hif1α*$^{F/F}$ and *Hif1α*$^{\Delta Adipo}$ Mice. (A)- (C) Body weight, cumulative food intake and metabolic efficiency in 6 to 8 week old mice maintained on chow diet. (D) Total O_2 consumption measured in 9 week old mice fed chow diet. (E) and (F) Body weight and resting O_2 consumption in 9 week old mice before and after a 4 day exposure to HFD. (A)-(F) Experiments were performed on the same set of mice (n=5/group). (G) Resting O_2 consumption and body weight after 7 weeks of HFD at 30°C by multiple regression. (H) Total O_2 consumption after 7 weeks of HFD before and after β3-adrenergic agonist CL316243. (G-H) Used the same set of mice (n=6-8/group). Data are mean ± SEM.



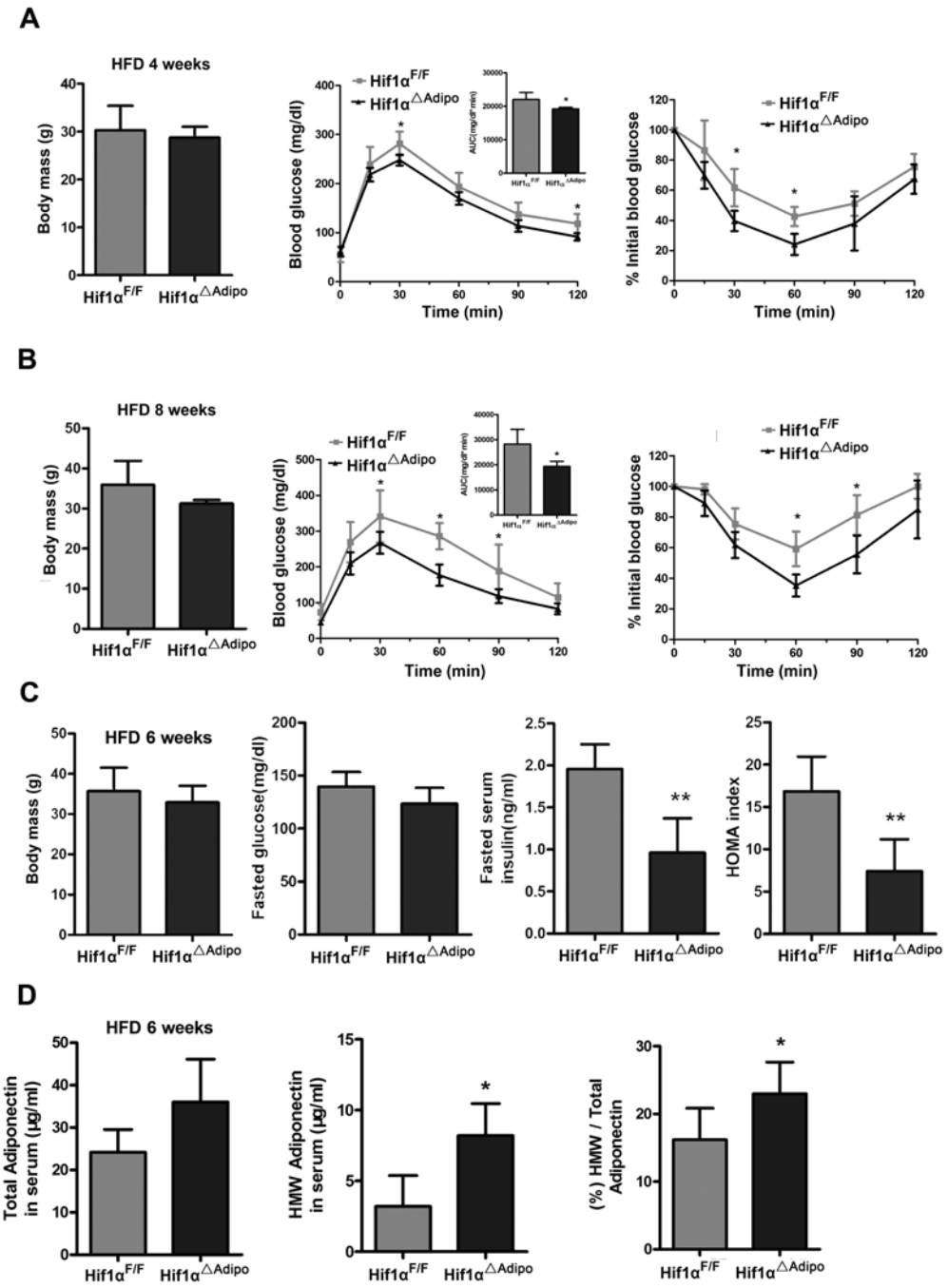
SUPPLEMENTARY DATA

Supplementary Figure 4. ARNT Deficiency in Adipocytes Improved HFD-induced Glucose Intolerance and Insulin Resistance. (A) and (B) Glucose tolerance test (GTT) 18 weeks old on chow diet and 11 weeks after HFD. Inset graphs in **(**A) and (B) depict the respective analysis of the area under the curve (AUC). (C) and (D) Insulin tolerance test (ITT) 18 weeks old on chow diet and 12 weeks after HFD (n =5/group). Data are mean ± SD. *P<0.05 compared to *Arnt*$^{\Delta Adipo}$ littermates.



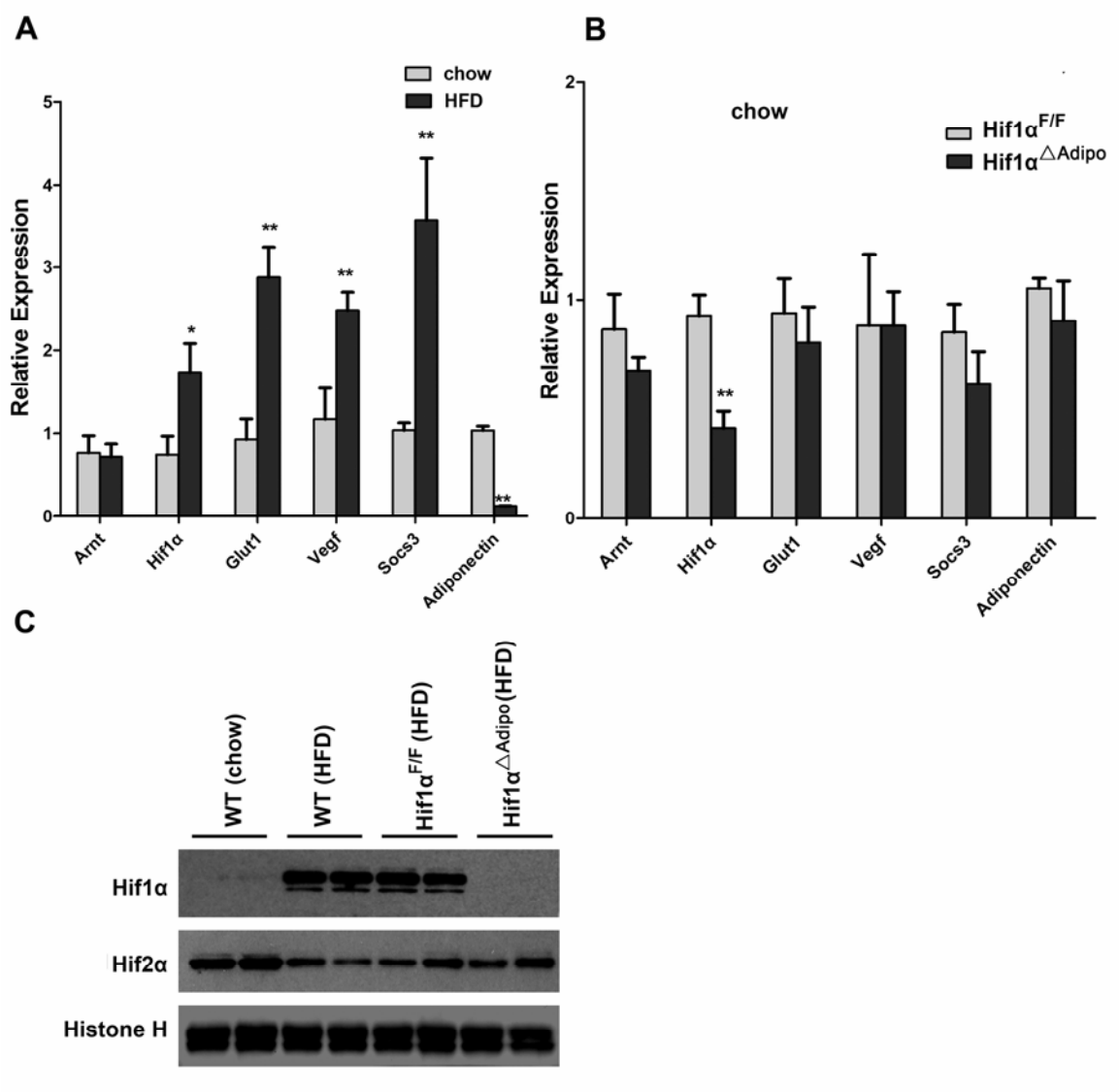
SUPPLEMENTARY DATA

Supplementary Figure 5. HIF1α Deficiency in Adipocytes Improves HFD-induced Glucose Intolerance and Insulin Resistance. (A)-(B) Body weight, GTT and ITT of *Hif1α*$^{F/F}$ and *Hif1α*$^{\Delta Adipo}$ mice. 4 weeks and 8 weeks after HFD. *P<0.05 compared to *Hif1α*$^{\Delta Adipo}$ littermates. Inset graphs in **(**A) and (B) depict the respective analysis of the area under the curve (AUC). (C) Body weight, fasted glucose, fasted serum insulin levels and HOMA index of *Hif1a*$^{F/F}$ and *Hif1α*$^{\Delta Adipo}$ mice after 6 weeks of HFD. (D) Serum total adiponectin levels, HMW adiponectin and the ratio of HMW to total adiponectin of *Hif1α*$^{F/F}$ and *Hif1α*$^{\Delta Adipo}$ mice after 6 weeks of HFD. Data are mean ± SD. *P<0.05, **P<0. 01 compared to *Hif1α*$^{F/F}$ littermates. (n =5/group).



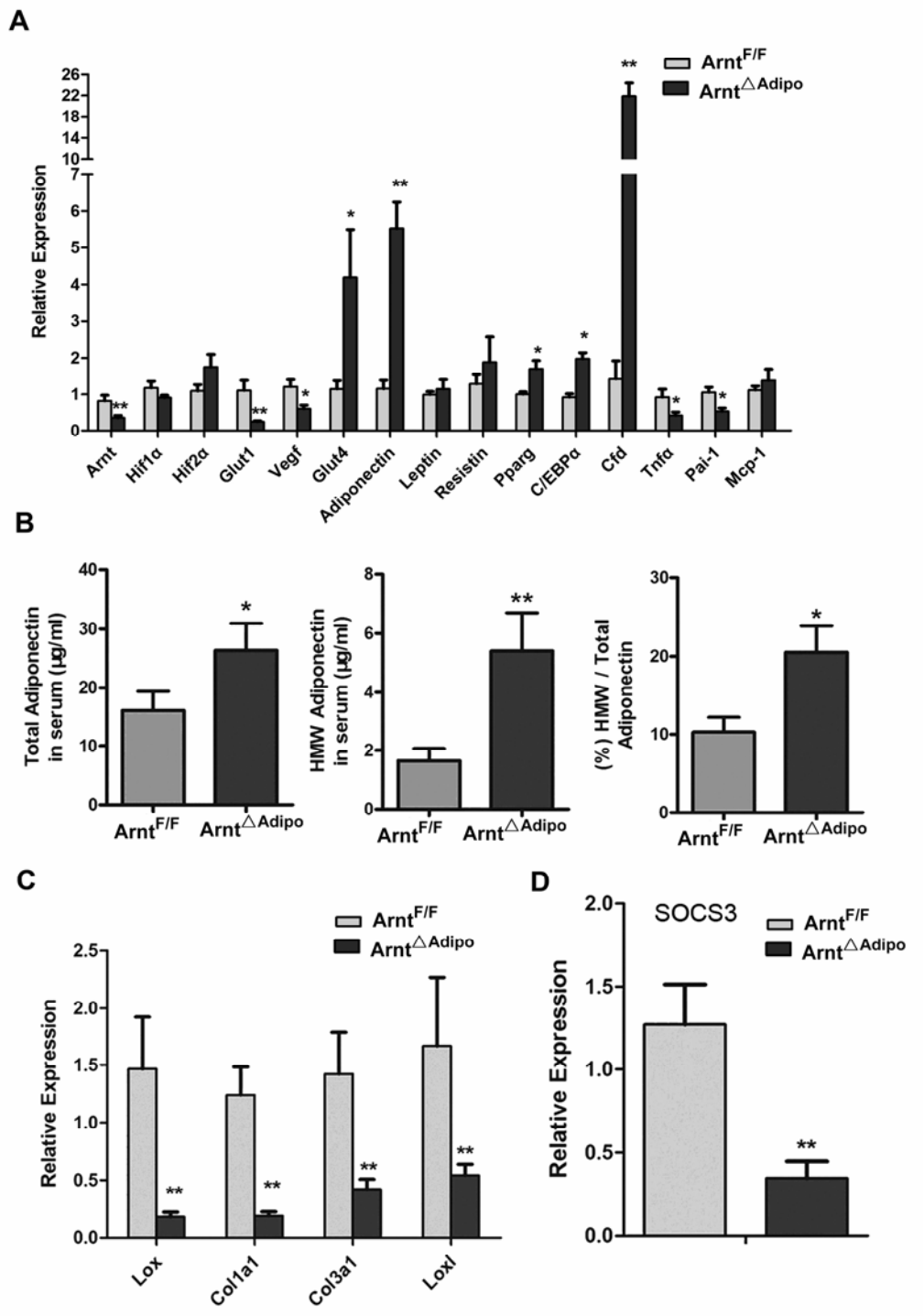
SUPPLEMENTARY DATA

Supplementary Figure 6. HIF1α Expression was Induced in WAT on a HFD. (A) Gene expression in the WAT of chow and 12 weeks of HFD-treated wild type (WT) C57BL/6 mice. *P<0.05, **P<0.01 compared to chow-treated mice. (B) Gene expression in the WAT of 10 weeks old *Hif1α*$^{F/F}$ and *Hif1α*$^{\Delta Adipo}$ mice on a chow diet. (n =5/group). For qPCR analysis, expression was normalized to β-actin. Data are mean ± SD. (C) Western blot analysis measuring HIF1α and HIF2α expression. The nuclear protein was extracted from WAT.*P<0.05, **P<0.01 compared to *Hif1α*$^{F/F}$ littermates.



SUPPLEMENTARY DATA

Supplementary Figure 7. Expression of Genes Related to Insulin Resistance in ARNT Disrupted White Adipose Tissue. (A) and (B) qPCR analysis of gene expression in WAT. (C) *Arnt*$^{\Delta Adipo}$ mice exhibited higher serum total adiponectin levels, HMW adiponectin and the ratio of HMW to total adiponectin after 12 weeks of HFD. (D) qPCR analyses of fibrosis related gene expression in WAT. (E) qPCR analyses of *Socs3* expression in WAT. For qPCR analysis, expression was normalized to β-actin. Data are mean ± SD. *P<0.05, **P<0.01 compared to floxed littermates.



SUPPLEMENTARY DATA

Supplementary Figure 8. Disruption of HIF1 Reduced Macrophage Infiltration to WAT after HFD. (A) and (B) Representative images of macrophage marker F4/80 by immunohistochemistry staining (left panel) and qPCR analysis of F4/80 and CD68 mRNA (right panel) in adipose tissue in $Arnt^{F/F}$ and $Arnt^{\Delta Adipo}$, or $Hif1\alpha^{F/F}$ and $Hif1\alpha^{\Delta Adipo}$ mice after 12 weeks of HFD. The expression was normalized to β-actin. Data are mean ± SD. **P<0.01 compared to floxed littermates.