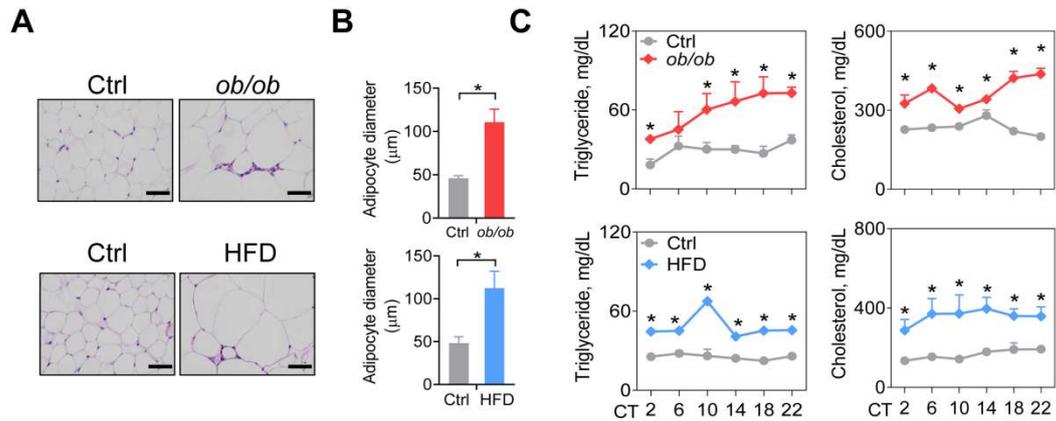
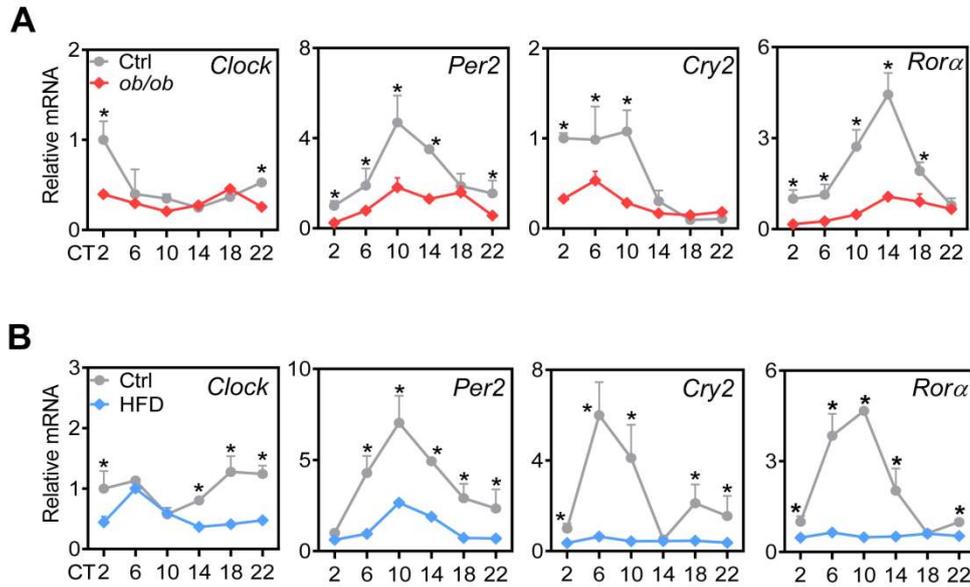


Supplementary Materials for

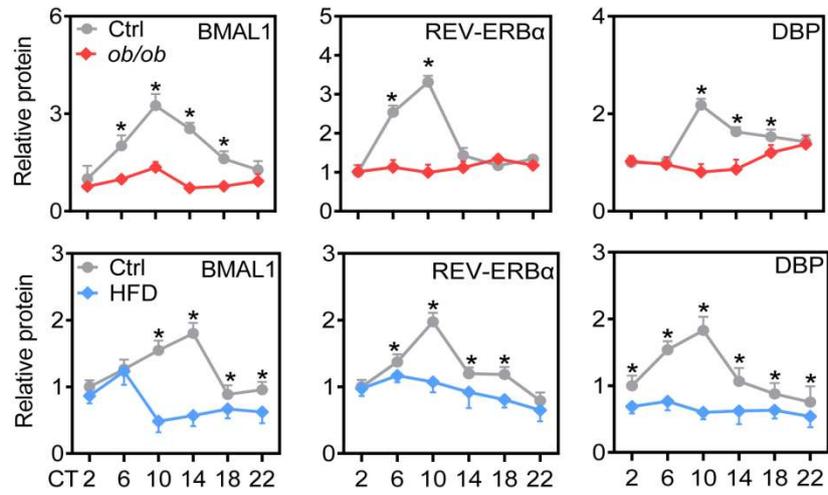
**PPAR- $\gamma$  integrates obesity and adipocyte clock through epigenetic  
regulation of *Bmal1***



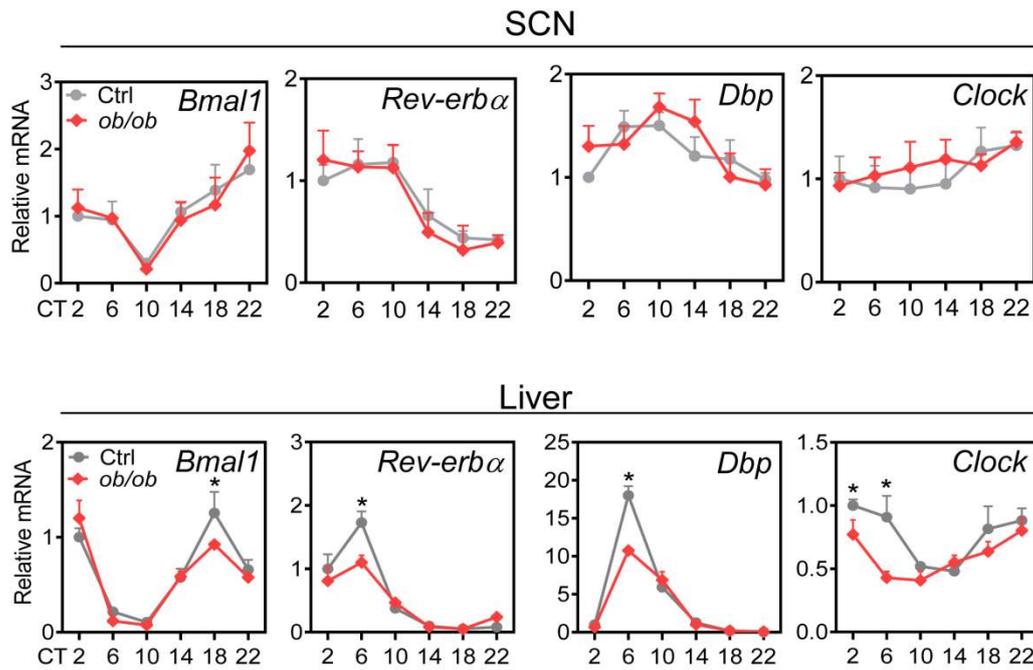
**Fig S1. Validation of two obese models.** (A) H&E staining of WAT derived from *ob/ob*, HFD and control mice. Scale bar: 50  $\mu\text{m}$ . (B) The diameter of adipocytes in WAT from *ob/ob*, HFD and control mice. Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  (t test). (C) Serum triglyceride and cholesterol levels in *ob/ob*, HFD and control mice at 6 circadian time points. Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  at individual time points as determined by two-way ANOVA and Bonferroni post hoc test.



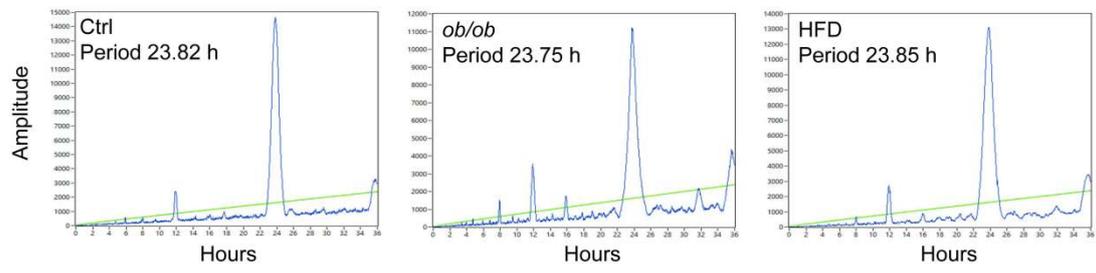
**Fig S2. Disruption of adipocyte clock in obese mice. (A and B)** mRNA expression of clock genes (*Clock*, *Per2*, *Cry2* and *Rora*) in WAT derived from *ob/ob* (A), HFD (B) and control mice at 6 circadian times. Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  at individual time points as determined by two-way ANOVA and Bonferroni post hoc test.



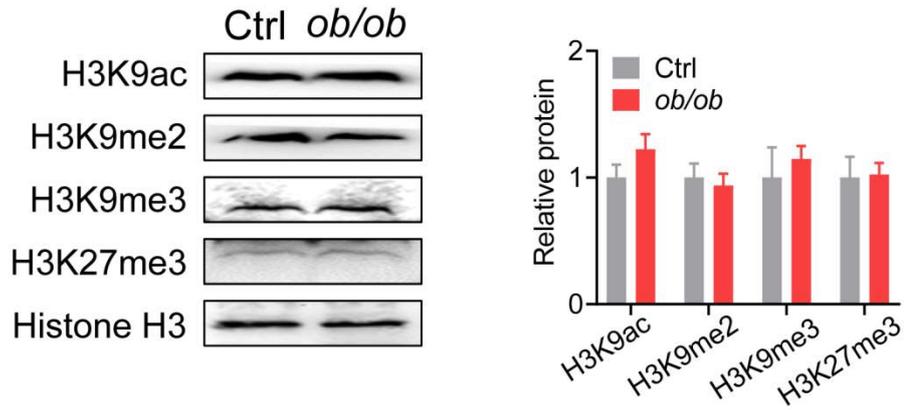
**Fig S3. Quantification data on the protein bands in Fig 1D.** Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  as determined by two-way ANOVA followed by Bonferroni post hoc test.



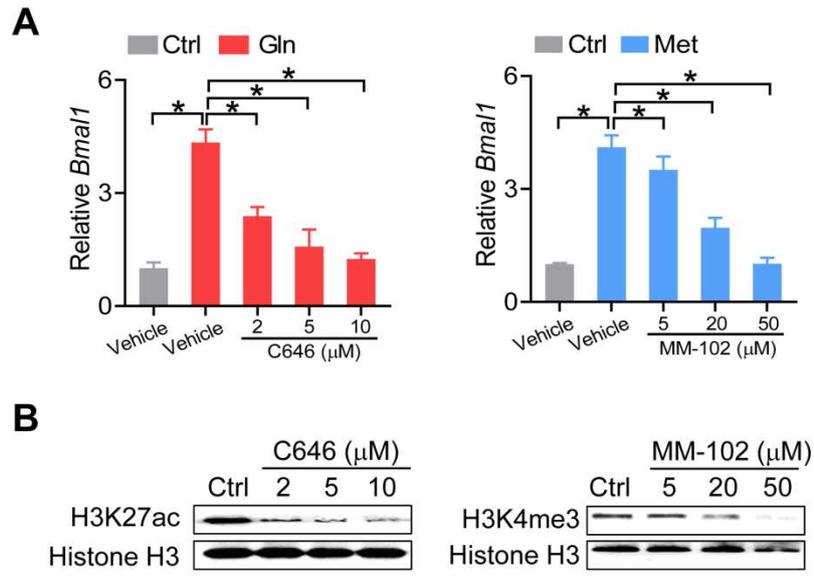
**Fig S4. mRNA expression of clock genes in SCN and liver of obese mice. mRNA expression of clock genes (*Bmal1*, *Rev-erbα*, *Dbp* and *Clock*) in SCN (upper panel) and liver (lower panel) derived from *ob/ob* and control mice at 6 circadian times. Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  at individual time points as determined by two-way ANOVA and Bonferroni post hoc test.**



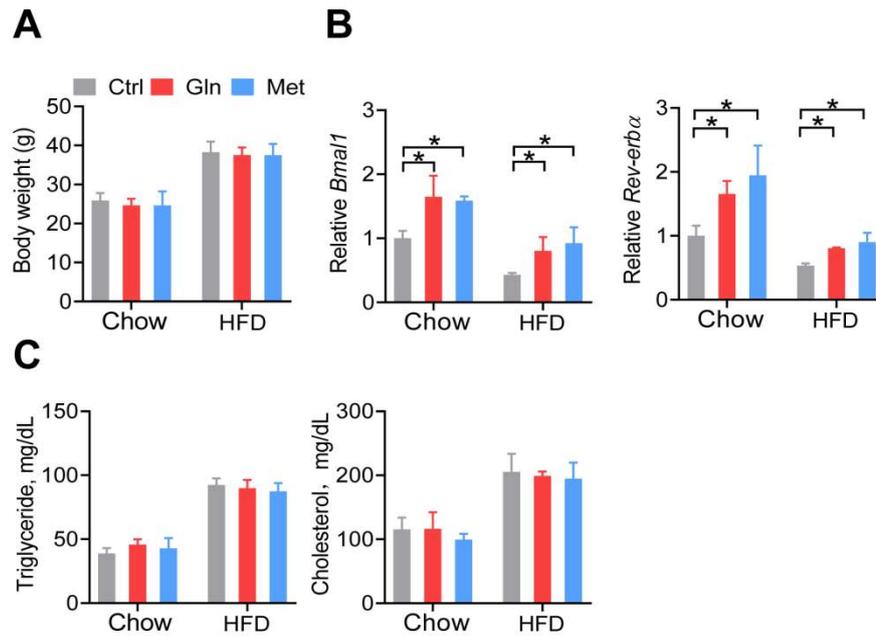
**Fig S5. Free-running periods of *ob/ob*, HFD and control mice.**



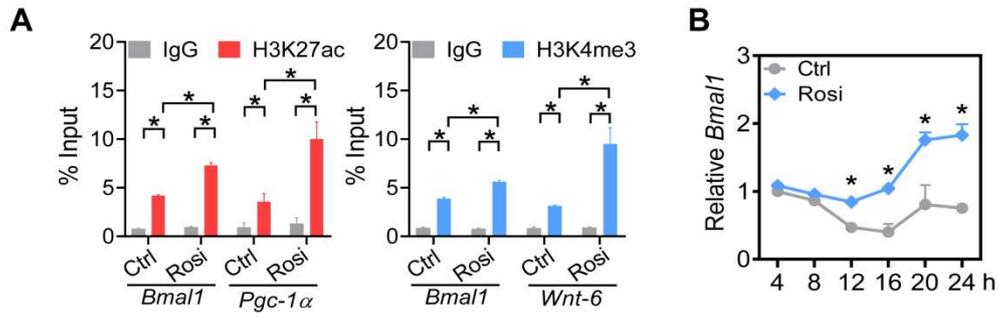
**Fig S6. Protein expression of H3K9ac, H3K9me2, H3K9me3 and H3K27me3 in WAT tissues of *ob/ob* and control mice at CT6. Data are mean  $\pm$  SD ( $n = 5$ ).**



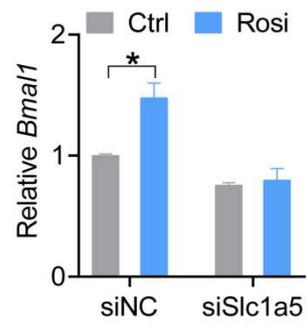
**Fig S7. Effects of C646 and MM-102 on the expression of *Bmal1* (A), H3K27ac and H3K4me3 (B) in 3T3-L1 adipocytes.** Data are mean  $\pm$  SD ( $n = 3$ ). \* $p < 0.05$  (one-way ANOVA and Bonferroni post hoc test).



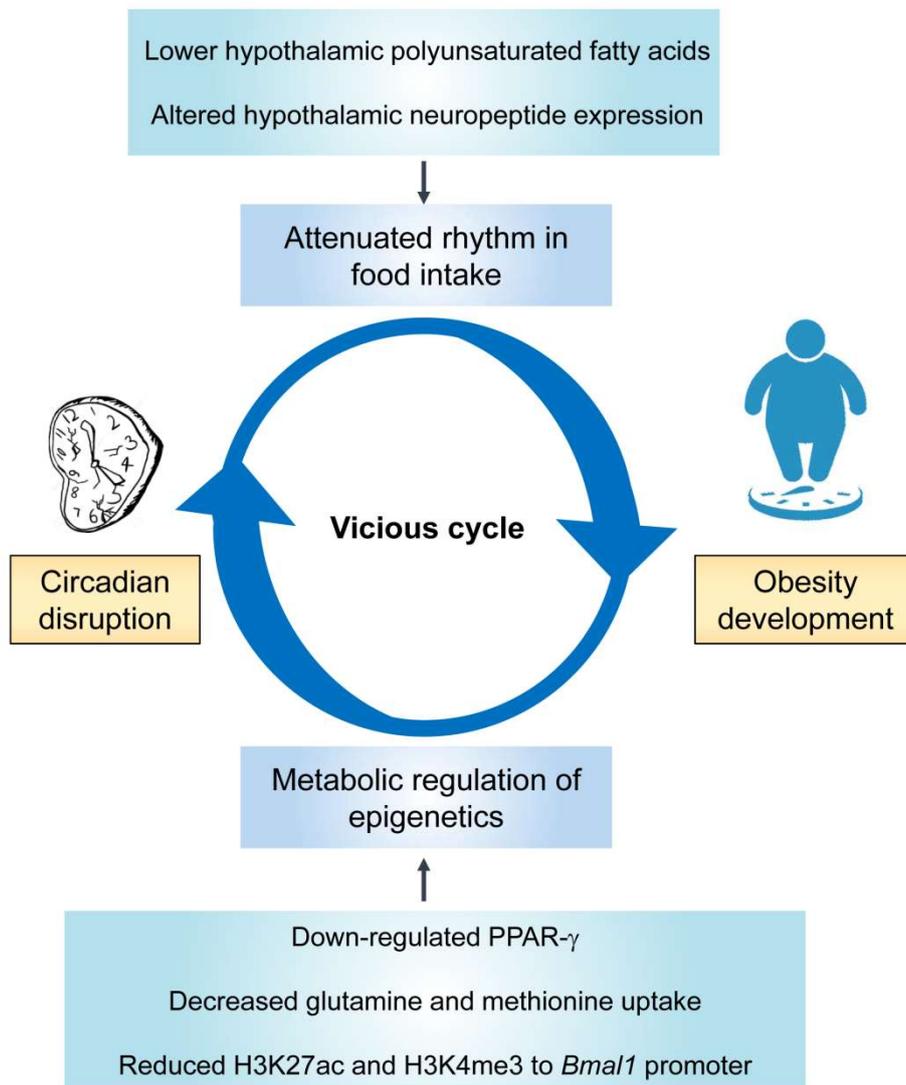
**Fig S8. Short-term (two weeks) treatment of glutamine or methionine enhances *Bmal1* expression independent of body weight.** (A) Body weight of HFD- and chow-fed mice treated with glutamine or methionine. (B) mRNA expression of *Bmal1* and *Rev-erbα* in WAT in HFD- and chow-fed mice treated with glutamine or methionine. (C) Serum triglycerides and cholesterol in HFD- and chow-fed mice treated with glutamine or methionine. All data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  (one-way ANOVA and Bonferroni post hoc test).



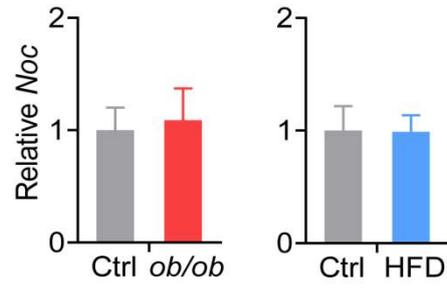
**Fig S9. Effects of rosiglitazone (Rosi) on enrichments of H3K27ac and H3K4me3 at the *Bmal1* promoter (A) and on *Bmal1* expression (B) in 3T3-L1 adipocytes.** Data are mean  $\pm$  SD ( $n = 3$ ). \* $p < 0.05$  (two-way ANOVA and Bonferroni post hoc test).



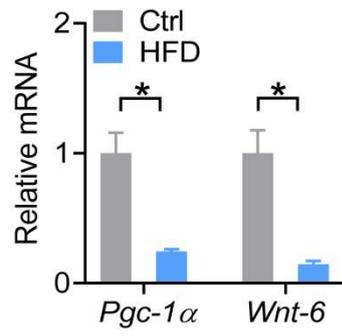
**Fig S10. Effects of rosiglitazone (Rosi) on mRNA expression of *Bmal1* in 3T3-L1 adipocytes transfected with siSlc1a5 or control (siNC).** Data are mean  $\pm$  SD ( $n = 3$ ). \* $p < 0.05$  (t-test).



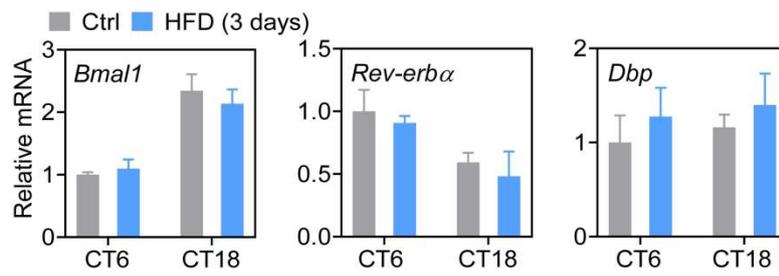
**Fig S11. Schematic diagram showing a vicious circle between circadian disruption and obesity development.**



**Fig S12. mRNA expression of *nocturnin* (Noc) in WAT tissues in HFD-induced obese and control mice. Data are mean  $\pm$  SD ( $n = 5$ ).**



**Fig S13.** mRNA expression of non-clock genes (*Pgc-1α* and *Wnt-6*) in WAT tissues in HFD-induced obese and control mice. Data are mean  $\pm$  SD ( $n = 5$ ). \* $p < 0.05$  (t test).



**Fig S14. Effects of HFD feeding for 3 days on expression of clock genes (*Bmal1*, *Rev-erbα* and *Dbp*) in WAT. Data are mean  $\pm$  SD ( $n = 5$ ).**

Fig 1D

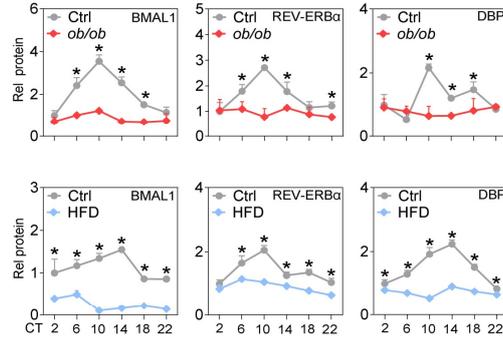


Fig 4B

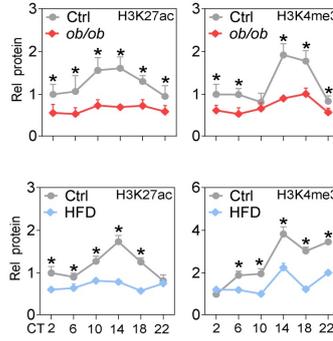


Fig 5B

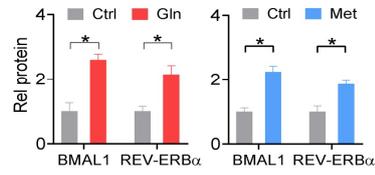


Fig 5D

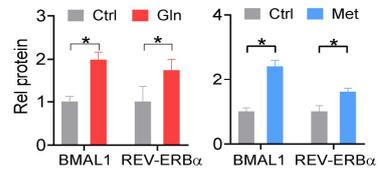


Fig 6B

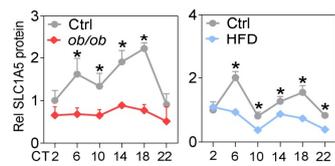


Fig 6D

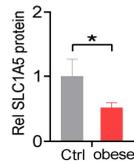
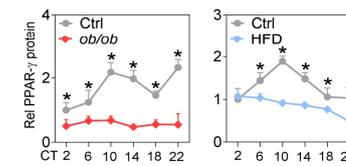


Fig 7B



**Figure S15. Quantification data generated from Western blots in this study. Data are mean ± SD. \*p < 0.05.**

**Table S1.** Characteristics of obese and lean subjects.

<b>Subjects</b>	<b>Obese</b>	<b>Lean</b>
Number	13	10
Age	28.5 ± 5.1	35.4 ± 14.6
Gender (F/M)	10/3	6/4
BMI	40.2 ± 7.1	20.8 ± 1.8

BMI, body mass index; F, female; M, male.

**Table S2.** Sequences of primers for qPCR analysis

<b>Name</b>	<b>Forward (5'-3' sequence)</b>	<b>Reverse (5'-3' sequence)</b>
<i>mBmal1</i>	CTCCAGGAGGCAAGAAGATTC	ATAGTCCAGTGGAAGGAATG
<i>mClock</i>	CCAGAGGGAGAACATTCA	TGGCTCCTTTGGGTCTAT
<i>mRev-erba</i>	TTTTTCGCCGGAGCATCCAA	ATCTCGGCAAGCATCCGTTG
<i>mRev-erb<math>\beta</math></i>	GGAGTTCATGCTTGTGAAGGCT	CAGACACTTCTTAAAGCGGCAC
<i>mPer1</i>	GAAAGAAACCTCTGGCTGTTCC	GCTGACGACGGATCTTTCTTG
<i>mPer2</i>	CCACACTTGCCTCCGAAATA	ACTGCCTCTGGACTGGAAGA
<i>mCry1</i>	CCCAGGCTTTTCAAGGAATGGA	GCAGGGAGTTTGCATTCATTG
<i>mCry2</i>	GATGCCGATTTCAAGTGTGAATG	GGCAGTAGCAGTGGAAAGAAT
<i>mDbp</i>	ACATCTAGGGACACACCCAGTC	AAGTCTCATGGCCTGGAATG
<i>mRor<math>\alpha</math></i>	GAGACCCCGCTGACCCA	TGACTGAGATACCTCGGCTG
<i>mSlc1a5</i>	CATGTAAAATACCGCAATCCTGT	GACGATAGCGAAGACCACCA
<i>mSlc38a1</i>	ATCTTCGGAGCCACCTCTCT	TGCATCCTCCTCTCCCATGA
<i>mSlc38a2</i>	CATCCCGCTGTTCTTCCCAT	AAAGAGAGCAGCGAGCAAGT
<i>mBhmt</i>	TTAGAACGCTTAAATGCCGGAG	GATGAAGCTGACGAACTGCCT
<i>mMtr</i>	TCCTCCTCGGCCTATCTTTATTT	GGTCCGAATGAGACACGCT
<i>mMat2a</i>	GGTCATTGTCAGGGATCTGGA	ACCAAAGTGCCATAGGCTG
<i>mGlul</i>	AGGCACCAGTACCACATTG	CACCGGCAGAAAAGTCGTTG
<i>mGls</i>	GCAGCGGGATTATGACTCCA	ATTCCACCTGTCCTTGGGGA
<i>mGls2</i>	AGTTCACCACGGCTCTGAAG	TGCTGCTCACACACTTTTGG
<i>mPpar-<math>\gamma</math></i>	AACCCACAACCAAATCCACAC	ATCACGGAGAGGTCCACAGA
<i>mPgc-1<math>\alpha</math></i>	GCACGCAGCCCTATTCATTG	TGAGTCTCGACACGGAGAGT
<i>mWnt-6</i>	GCAGGACATCCGAGAGACAG	TGGAACAGGCTTGAGTGACC
<i>mGapdh</i>	CAAGGAGTAAGAAACCCTGGA	CGAGTTGGGATAGGGCCTCT
<i>mNoc</i>	CGCGTCCTGGTGCCTAATCT	GAGCGCGTGTCTGGGAGAA
<i>hBMAL1</i>	ACTTCCCCTCTACCTGCTCA	ATCCAGCCCATCTTTGTGG
<i>hREV-ERB</i>	GACATGACGACCCTGGACTC	GCTGCCATTGGAGTTGTCAC
<i>hDBP</i>	CCGCTATCTTTCTATTAAGTAC	TCAACCAGCTACAAAAGCATG
<i>hSLC1A5</i>	AGGCTTTCTCTGGCTGGTAA	ACCCAGGCTCTTAGGTCCG
<i>hGAPDH</i>	CATGAGAAGTATGACAACAGCC	AGTCCTTCCACGATACCAAAGT

m: mouse    h: human

**Table S3.** Sequences of primers for CHIP assays

<b>Name</b>	<b>Forward (5'-3' sequence)</b>	<b>Reverse (5'-3' sequence)</b>
<i>Bmal1</i> _H3K27ac	GTAGGTCAGGGACGGAGGT	GCAGCCATGCCGACACTCA
<i>Pgc-1<math>\alpha</math></i> _H3K27ac	CAAAGCTGGCTTCAGTCAC	AAAAGTAGGCTGGGCTGTCA
<i>Bmal1</i> _H3K4me3	AGAGATGCGGCGTTTTCTC	GTGACTGCCTCTCAGCTCTC
<i>Wnt-6</i> _H3K4me3	CTTCCTTCCCCCAAAGAAAT	GTCCAACAGCTCTTCCCTACCTATC
<i>Slc1a5</i> _PPRE	TTCCTTCTCCAACAAGCCCT	GTCTGTTCTACCAGGCGCTC