PPAR-γ 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 μm. (B) The diameter of adipocytes in WAT from ob/ob, HFD and control mice. Data are mean ± 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 ± 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 Rorα) in WAT derived from ob/ob (A), HFD (B) and control mice at 6 circadian times. Data are mean ± 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 ± 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 ± 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 ± 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 ± 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 \textit{Bmal1} expression independent of body weight. (A) Body weight of HFD- and chow-fed mice treated with glutamine or methionine. (B) mRNA expression of \textit{Bmal1} and \textit{Rev-erba} 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 ± 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 ± 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 ± 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 ± 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 ± SD (n = 5). *p < 0.05 (t test).
Fig S14. Effects of HFD feeding for 3 days on expression of clock genes ($Bmal1$, $Rev-erb\alpha$ and $Dbp$) in WAT. Data are mean ± SD ($n = 5$).
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.

| Subjects     | Obese       | Lean       |
|--------------|-------------|------------|
| 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

| Name       | Forward (5'-3' sequence)          | Reverse (5'-3' sequence)          |
|------------|-----------------------------------|-----------------------------------|
| mBmal1     | CTCCAGGAGGCAAGAAGATTC             | ATAGTCCAGTGGAAGGAATG              |
| mClock     | CAACAGGAGGAGAACATTTCA             | TGGCTCCTTTGGGTCTAT               |
| mRev-erb   | TTTTTCGCCGGGAGACTCCCAA            | ATCTCGGGAAGGACATCCGGTTG          |
| mRev-erbβ  | GAAGATCGATCTTGTAGAGGT             | CAGACACTTCTAAAGGGCGGCAC          |
| mPer1      | GAAAGAACAAGTGCTGTGGTTG            | GCTGACGAGAGGAGCTTTTG             |
| mPer2      | CACACTTGCTCCGAAGATA               | ACTGCTCCTTGAGACTGGAAGA           |
| mCry1      | CCCAGGCTTTTCCAGGAGTGGGA          | CGCGGAGTGGTCTTCTATCCGGTTG        |
| mCry2      | GATGCCGATCTCAGTGAGATG             | GGCAGTACAGTGGAAGGAGA             |
| mDbp       | CAATCTGGGAAACAACACCTCCTGG         | AAGCTCCTAGCCGGAGGAGA             |
| mRorα      | GAGACCCCGCAGACACCGGGC            | TGACTGAGATACCTCCGGCT             |
| mSlc1a5    | CATGTAAAGATACGAGATCTGTA           | GACGATACGAGAGGAGGAA             |
| mSlc38a1   | ATCCTTGAGGACCACCTCTCT            | TGGCATCCTCTCCCTCAGTGA            |
| mSlc38a2   | CATCCGCTCTTGCTTTCTCCCTG          | AAAGAGAGACACGAGGAGAA            |
| mBhmt      | TTAGAAAGCTCTAAATGGCCGGAG          | GATGAAGCTGAGAAGCTGCT             |
| mMtr       | TCCTCCCTGCGCCTATCTCTATTT          | GCGGAGGATACGAGAGGAGA             |
| mMat2a     | GGCTTTGCTAGGAGATCTGGA            | ACCAAATGGGCAACTAAGGGC            |
| mGlu       | AGGCAGTGGAGTACGAGATCTGGA         | AACGAGGAGAGGAGGAGGAGA            |
| mGls       | GCACGGGAGGATTGACTGCA             | ATCCTCGCTTGGCTCTTGGGGA           |
| mGls2      | AGTTCACGAGGCTCTGAGAAGGA          | TGGCTCCTACACCTCCTCCGGTT          |
| mPpar-γ    | AACCAGACACAAATCCACAC             | ATCAGGAGAGGAGGAGGAGA             |
| mPgc-1α    | GCACGGAGGCTATCTCCATTGGA          | TGGGAGGAGGAGGAGGAGGAGA           |
| mWnt-6     | GCACCGAGATCCCGAGAGACAG           | TGGACAGGCTGGAGATGGACC            |
| mGapdh     | CAAGGAGTAAAGAACGCTCTGGAA        | CGAGTGGGAGTGGCCGCTCT             |
| mNoc       | CGCGTCTCGTGCTGGCTATCTA           | GAGCGCAGTCTTGCTGGGAAGG           |
| hBMAL1     | ACTTCCCTCTCATTGCTCAA             | ATCCAGGCCCCATCTTTGGG             |
| hREV-ERB   | GACCTGAGACAGCCCTGGACTC           | GGTGCCATTGGAGATTGTCAC            |
| hDBP       | CCGTACGAGGCTTTTATAGGACTG         | TCAAAGCGGATACCAAGACCATGA         |
| hSLC1A5    | AGGCTTTCTCTGGCTGGTAA             | ACCACGCAGTTAGGGTCTCCG            |
| hGAPDH     | CATGAGAATGATGACACAGGC           | ATCGCTCCACGATACCAAGG             |

m: mouse  h: human
**Table S3.** Sequences of primers for ChIP assays

| Name              | Forward (5'-3' sequence)     | Reverse (5'-3' sequence)         |
|-------------------|------------------------------|----------------------------------|
| Bmal1_H3K27ac     | GTAGGTCAAGGACGGAGGT          | GCAGCCATGCGGACACTCA              |
| Pgc-1α H3K27ac    | CAAAGCTGGCTTCAGTCAC          | AAAAGTGGGCTGGGCTGTCA             |
| Bmal1_H3K4me3     | AGAGATGCGGGCTTTTCTC          | GTGACTGCTCCTCAGCTCTC             |
| Wnt-6_H3K4me3     | CTTCCTTCCTCCCAAAGAAAT        | GTTCAACAGCTTTCCCTACCTATCT        |
| Slc1a5_PPRE       | TTCTTTCTCCAAGAAAGCCCT        | GTGCTTTTCTACAGGCGCTC             |