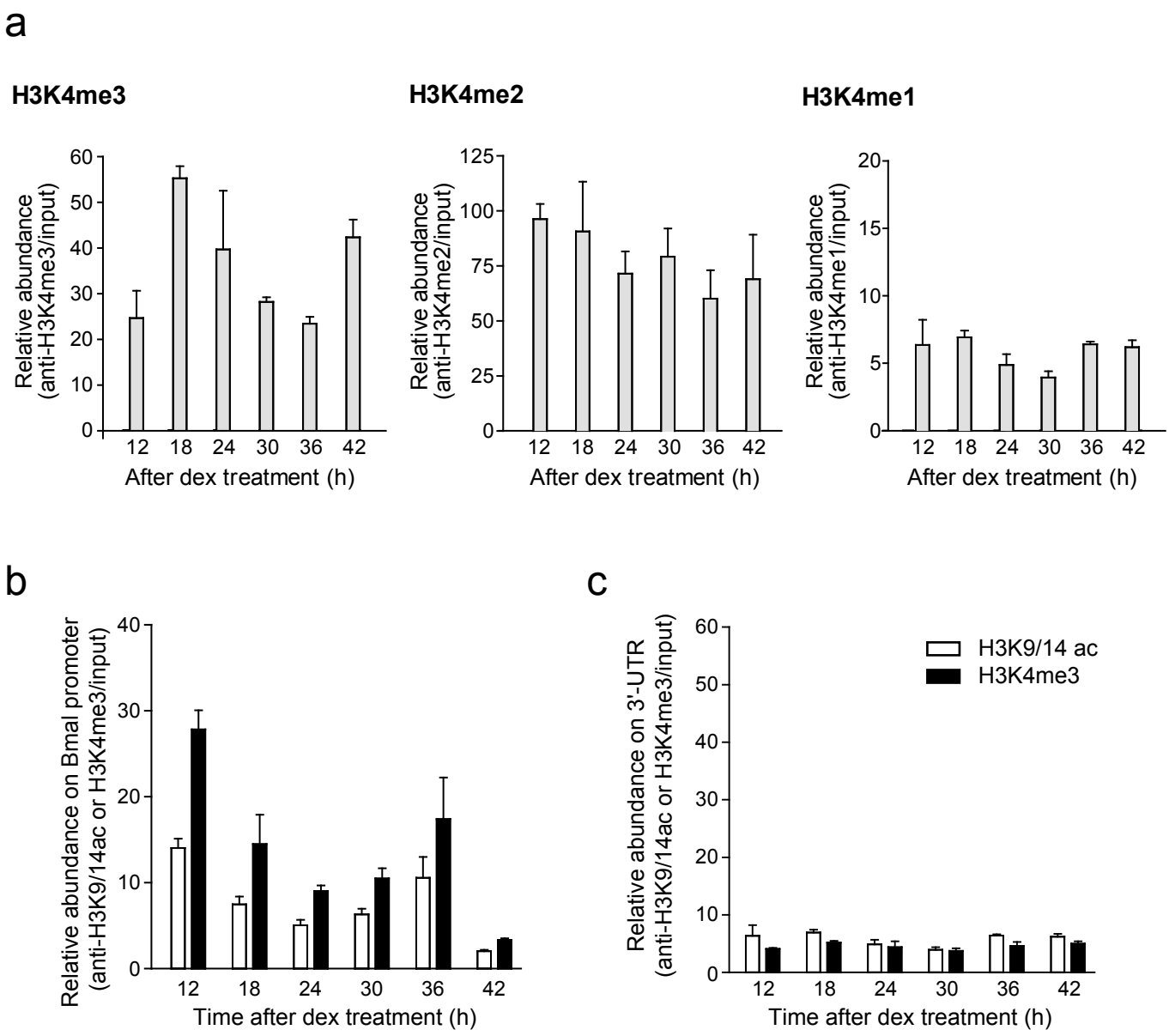
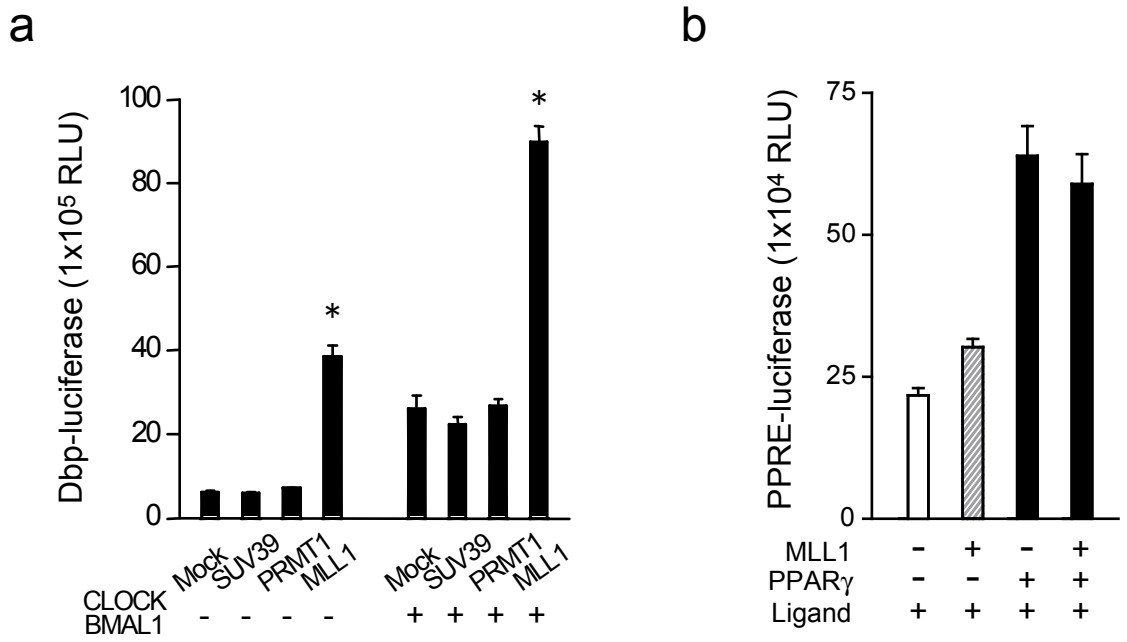
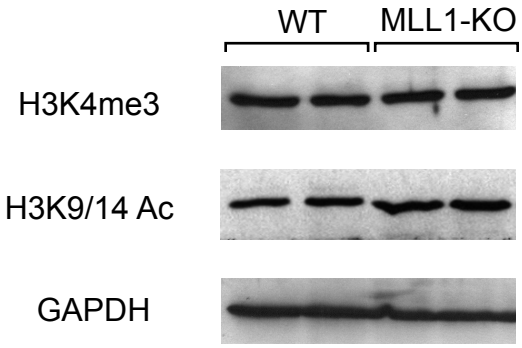


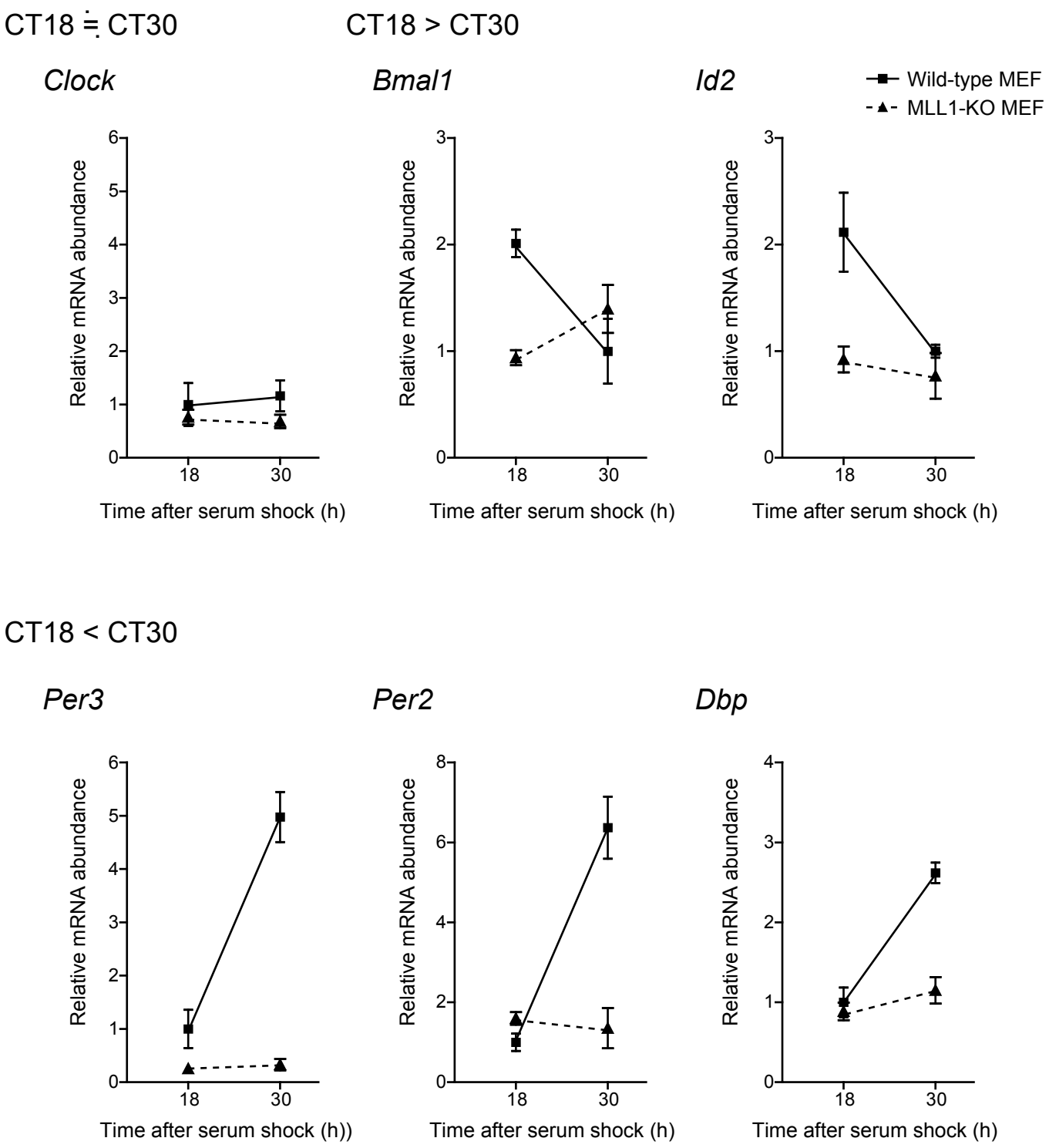
Supplementary Figure 1. H3K4me3 follows circadian rhythmicity on clock controlled gene promoter. (a) H3K4me1, me2, and me3 levels on the dbp promoter E-box region at different time point. ChIP analyses were performed in MEFs after dexamethasone synchronization. (Means SEM of three independent samples) (b, c) Circadian rhythmicity of acetylation of H3K9/14 (white) and H3K4me3 (black) on Bmal promoter E-box region (b), or Dbp promoter 3'-UTR region (c) (Means SEM of three samples).



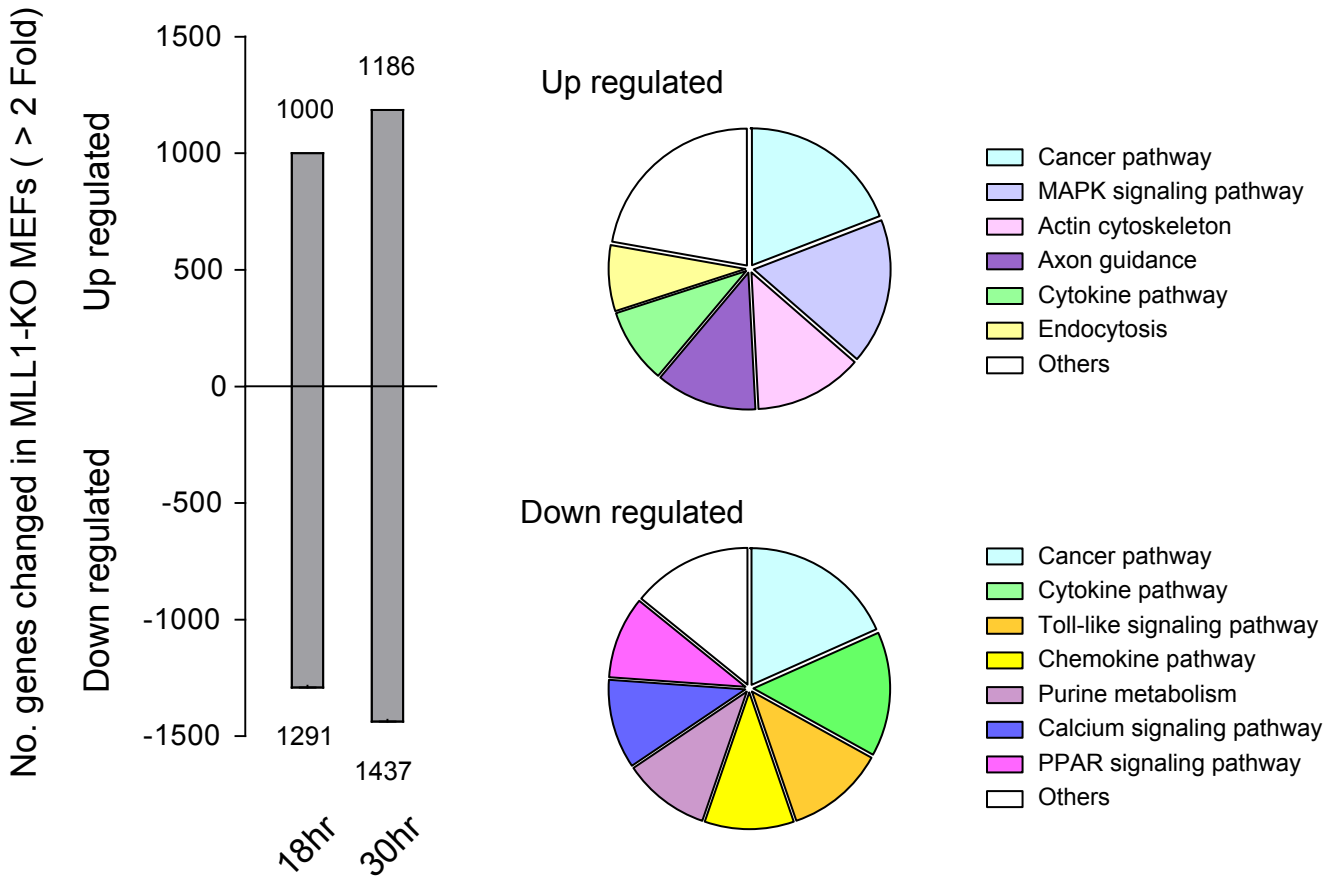
Supplementary Figure 2. MLL1 synergistically activate CLOCK:BMAL1-mediated gene transcription. (a) MLL1 but not other HMTs such as SUV39 and PRMT1 elicited robust increases of transcription collectively with CLOCK:BMAL1. MLL1, SUV39 and PRMT1 were transiently transfected with or without CLOCK:BMAL1 in 293 cells, and luciferase activity was measured post 48 hr using the dbp promoter as a reporter. (Means SEM of four samples). (b) Synergistic transcriptional activation of MLL1 was not observed in combination with PPARγ (peroxisome proliferator-activated receptor γ) on a PPRE-reporter. A PPRE-luciferase reporter plasmid was transfected with PPARγ or MLL1 as indicated in 293 cells. 6hr post transfection, culture media was changed with 5uM of 15-Deoxy-D12, 14-prostaglandin J2 containing medium and cultured for 24hr, then luciferase activity was measured (Means SEM of four



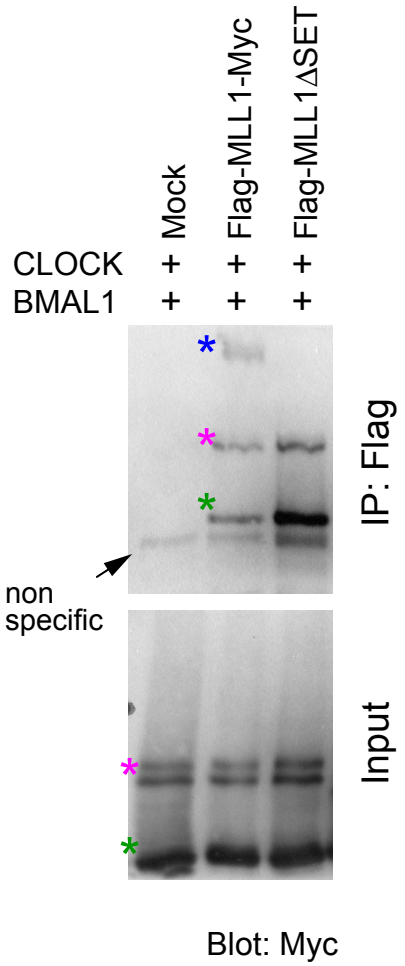
Supplementary Figure 3. Global histone H3K4me3 and H3K9/14 acetylation levels in MLL1-KO MEFs were not changing. Proteins were extracted from wild type (WT) or MLL1-KO MEFs at CT0 and H3K4me3 (upper) or H3K9/14 acetylation (middle) levels were measured by western blot using each antibody. The amount of GAPDH (lower panel) was used as a loading control.



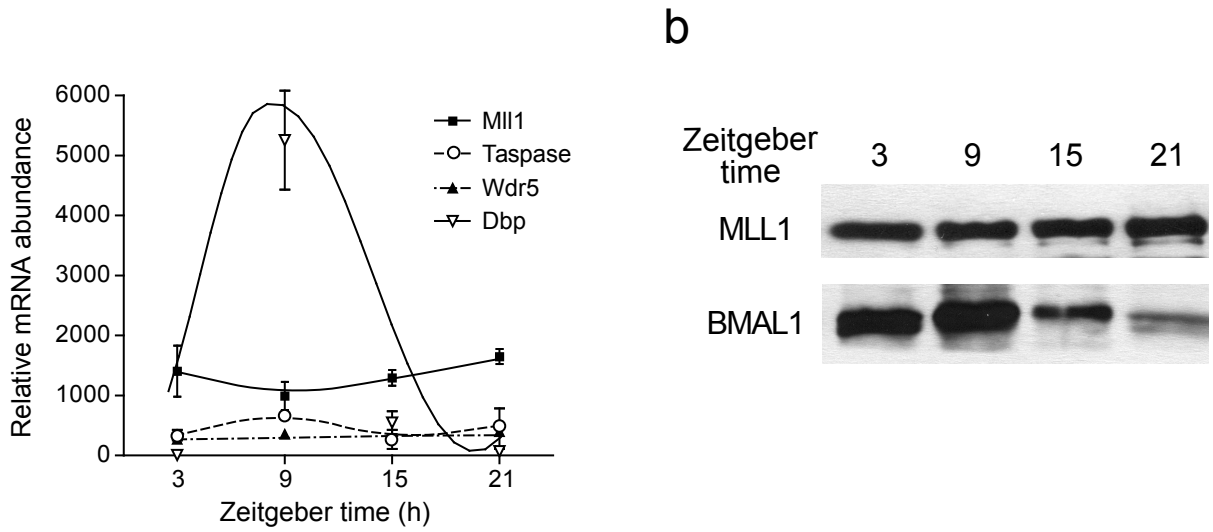
Supplementary Figure 4. Confirmation of array experiments by quantitative real-time RT-PCR. mRNA was extracted from wild type or MLL1-KO MEFs at 18hr or 30hr after serum shock, and reverse transcription reaction was performed. The Chromo4 real time detection system (BIO-RAD) was used to measure the expression of each gene (Means SEM of three samples).



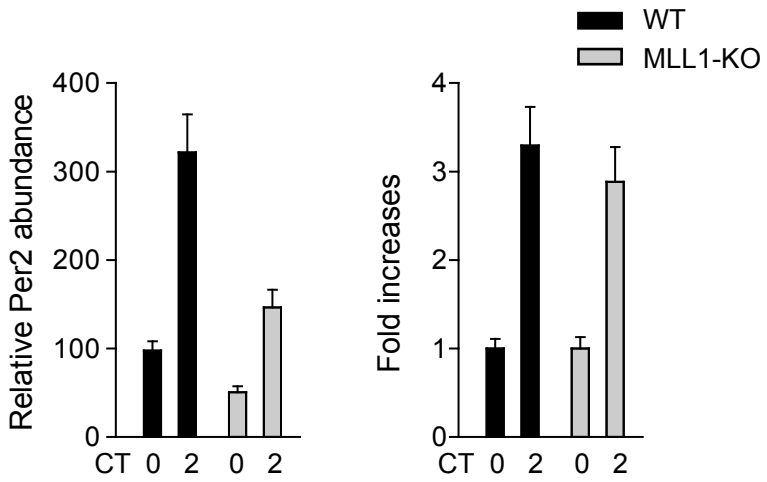
Supplementary Figure 5. Global analysis of gene expression profile in MLL1-KO MEFs. Bar graphs represent the number of genes whose expression change > 2-fold between WT and MLL1-KO MEFs in each time point. Pie charts represent functional categories of up regulated or down regulated genes in MLL1-KO MEFs.



Supplementary Figure 6. CLOCK and BMAL1 interact with the SET domain deleted mutant of MLL1 (MLL1ΔSET). 293 cells were transfected with Myc-tagged CLOCK and BMAL1 expression vectors together with Mock or Flag-MLL1-Myc or Flag-MLL1ΔSET. Flag-tagged fragments were immunoprecipitated by Flag-Agar, and coimmunoprecipitated proteins were determined by western blot using anti-Myc antibody. Myc-BMAL1 (green star) and Myc-CLOCK (pink star) and Myc-tagged C-terminal fragments of MLL1 (blue star) proteins were coimmunoprecipitated with MLL1 N-terminal fragments. Lower panel shows the results of total cell lysates as an input.



Supplementary Figure 7. The transcript levels of MLL1 do not oscillate in a circadian manner. (a) mRNA expression of Dbp (clock controlled gene) (inverted triangle), MLL1 (square), Taspase1 (an endopeptidase which cleaves MLL1) (diamond) and Wdr5 (a core MLL1 component) (triangle) in each time point of liver were measured by quantitative RT-PCR. (Means SEM of three independent samples). (b) A protein amount of MLL1 dose not change throughout the day. Proteins were extracted from each time point of liver and MLL1 expression levels were detected using anti-MLL antibodies. Bmal1 expression patterns of lower panel ensure circadian rhythmicity of each sample.



Supplementary Figure 8. Dexamethazone induced rapid induction of per2 mRNA in MLL1-KO MEFs. Per2 mRNA accumulation in wild type and MLL1-KO MEFs after 2 hr post dexamethazone shock was measured by quantitative real-time PCR. (Means SEM of three samples).

Supplementary table1. Forty one genes that showed different expression level between two time points (CT18 and 30) in wild type MEFs

Gene Description	Fold change in WT MEF	Fold change in MLL1-KO
gamma glutamyltransferase 5 (Ggt5)	- 2.23	1.04
Period homolog 3 (mPer3)	- 2.14	- 1.13
N-myc downstream regulated gene 2 (Ndrg2)	- 2.08	- 1.40
D site albumin promoter binding protein (Dbp)	- 2.04	- 1.22
Sorbin and SH3 domain containing 2 (Sorbs2)	- 1.97	- 1.03
Drosophila period homolog 2 (mPer2)	- 1.93	- 1.03
Enolase 2 gamma neuronal (Eno2)	- 1.86	- 1.51
Heparanase (Hpse)	- 1.85	- 2.13
Placenta-specific 8 (Plac8)	- 1.82	- 3.13
Interferon induced transmembrane protein 6 (Ifitm6)	- 1.78	- 1.12
alpha 1,4-galactosyltransferase (A4galt)	- 1.78	- 1.81
Yippee-like 4 (Ypel4)	- 1.74	- 1.22
Peptidase inhibitor 15 (Pi15)	- 1.73	- 1.78
Semaphorin 4g (Sema4g)	- 1.73	- 1.61
Ectonucleotide pyrophosphatase/phosphodiesterase 3 (Enpp3)	- 1.71	- 1.31
Thyrotroph embryonic factor (Tef)	- 1.69	1.02
Olfactory receptor 1314 (Olfr1314)	- 1.67	- 1.03
Major histocompatibility complex (Mr1)	- 1.67	- 2.23
WNT1 inducible signaling pathway protein 2 (Wisp2)	- 1.65	1.07
Fibrinogen-like protein 1 (Fgl1)	- 1.61	- 1.14
Cell division cycle 6 (Cdc6)	1.62	- 1.02
Serine (or cysteine) peptidase inhibitor (Serpinb9d)	1.63	1.79
Minichromosome maintenance deficient 5 (Mcm5)	1.64	1.04
Activating transcription factor 3 (Atf3)	1.64	- 2.15
Serine (or cysteine) peptidase inhibitor (Serpinb9c)	1.64	1.02
Serine (or cysteine) peptidase inhibitor (Serpinb9g)	1.64	- 1.25
Leucine rich repeat containing 8 (Lrrc8b)	1.66	1.03
DNA replication helicase 2 (Dna2)	1.66	1.60
Dihydrofolate reductase (Dhfr)	1.67	- 1.04
tRNA splicing endonuclease 15 (Tsen15)	1.67	1.20
Aryl hydrocarbon receptor nuclear translocator (BMAL1)	1.67	- 1.48
Histone cluster 1 (Hist1h2a)	1.68	1.35
Cation transport regulator-like (Chac1)	1.69	- 1.25
Serine (or cysteine) peptidase inhibitor (Serpinb9f)	1.69	- 1.01
Inhibitor of DNA binding 2 (Id2)	1.72	- 1.15
Serine peptidase inhibitor (Serpinb9g)	1.72	- 1.25
Serine peptidase inhibitor (Serpinb9e)	1.83	1.11

Tumor necrosis factor receptor superfamily (Tnfrsf12a)	1.91	1.29
Nnephronectin (Npnt)	1.91	- 1.17
Histone cluster 1 (Hist1h2ab)	1.96	1.30
Actin alpha (Acta2)	4.45	1.42