Supplementary Experimental Procedures and Supplementary Table 1 (Masri *et al*.)

Animal housing and experimental procedures. All experiments were performed in accordance to the Institutional animal care and use committee (IACUC) guidelines at UCI. Animals were housed in a 12-hour light/dark paradigm and fed ad libitum. For viral infection, ad5-CMV::FlpO or ad5-CMV::Cre (University of Iowa viral vector core) were used at a titer of $5x10^5$ PFU using intra-tracheal delivery. Mice were sacrificed 4 months post-infection for tissue collection.

DNA microarray analysis. Microarray analysis was performed at the UCI Genomics High throughput Facility. Total RNA was extracted from 3 independent livers of age matched male mice (per genotype and ZT) using Trizol reagent (Gibco BRL Life Technologies, Rockville, MD). The Ambion WT expression kit (Life Technologies, Carlsbad, CA) was used to prepare cDNA, which was hybridized to Affymetrix GeneChip 2.0ST arrays (Affymetrix, Santa Clara, CA). Arrays were scanned using GeneChip Scanner 3000 7G and Command Console Software v. 3.2.3 to produce .CEL intensity files. Probe cell intensity files (.CEL) were analyzed in Affymetrix Expression Console software v1.1.1 using the PLIER algorithm to generate probe level summarization files (.CHP).

Metabolomics analysis. Metabolomics analysis was carried out by Metabolon, Inc. (Durham, NC) as described (Evans et al., 2009; Masri et al., 2014). Briefly, small molecules from 5 independent livers (per genotype and ZT) were methanol extracted and analyzed by ultra-high performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS; positive mode), UPLC-MS/MS (negative mode) and gas chromatography–mass spectrometry (GC-MS). Metabolites were identified by automated comparison of the ion features in the experimental samples to a reference library of chemical standard entries that included retention time, molecular weight (m/z), preferred adducts, and in-source fragments as well as associated MS spectra and curated by visual inspection for quality control using software developed at Metabolon, Inc. (Dehaven et al., 2010).

Bioinformatics and pathway analysis. For analysis of rhythmic genes and metabolites, the non-parametric test, JTK_CYCLE, was used incorporating a window of 20-24 hours for the determination of circadian periodicity (Hughes et al., 2010), including amplitude and phase analysis. A gene was considered circadian, if at least one of its transcripts passed a p-value cutoff of 0.01, while metabolites were considered circadian at a p-value cutoff of 0.05. Heat maps of the circadian transcripts were produced using the R package 'gplots', where row values were normalized and subsequently sorted by phase of circadian expression as determined by JTK_cycle. These analyses were done using modules developed for CircadiOmics (Patel et al., 2015; Patel et al., 2012) and all transcriptomics and metabolomics data is freely accessible at circadiomics.ics.uci.edu. The Database for Annotation, Visualization and Integrated Discovery (DAVID)(Huang da et al., 2009a, b) pathway analysis tool was used to identify GO terms related to biological process. Pathways were ranked by number of genes found annotated using p-value <0.01.

Gene expression analysis. Equal amounts of total RNA were reverse-transcribed to cDNA using iScript cDNA synthesis kit (Bio-Rad Laboratories, Hercules, CA), according to manufacturers protocol. cDNA was used for quantitative real-time PCR using iQ SYBR green supermix (Bio-Rad Laboratories). Gene expression was normalized to 18S ribosomal RNA. Primers sequences were designed with Primer3 software (Rozen and Skaletsky, 2000). The following primer sequences were used or previously described (Masri et al., 2014): Srebp2 (For: 5'-TTGACTTCCTTGCTGCAGTG-3'; Rev: 5'-ACCATTTACCAGCCACAGGA-3'), Hmgcs1 (For: 5'-TATGGTTCCCTGGCTTCTGT-3'; Rev: 5'-TGTGGCGTCTTGTGTGACTT-3'), Pmvk (For: 5'-GACCTATCGGAGGGACATGA-3'; Rev: 5'-TAGGCCTCCTGAAACCACTG-3'), Il6ra (For: 5'-ATGCTCCCTGAATGATCACC-3'; Rev: 5'-ACTCACAGATGGCGTTGACA-3'), Il1r1 (For: 5'-TTGGTTTGTACCTGCCAAGG-3'; Rev: 5'-AACACAAGCCAGGGTCATTC-3'), Tnfrsf1b (For: 5'-GGACTGTGAGGCAAGCATGT-3'; Rev: 5'-CACACACTCGGTTCTGCTGT-3'), Stat3 (For: 5'-TCTCCTTCTGGGTCTGGCTA-3'; Rev: 5'-CTGAAGCGCAGTAGGAAGGT-3'), Socs3 (For: 5'-GAGATTTCGCTTCGGGACTA-3'; Rev: 5'-AACTTGCTGTGGGTGACCAT-3'), Socs1 (For: 5'-CTTCTATTGGGGACCCCTGA-3'; 5'-GAAGCCATCTTCACGCTGAG-3'), Socs7 (For: 5'-TCACAGGGTATCACCCATCA-3'; Rev: 5'-AATGAACTCCACCACCGACT-3'), Pck1 (For: 5’-TGTTGGCTGGCTCTCACTGAC-3’; 5’-GGGAACCTGGCGTTGAATGC-3’), Pklr (For: 5'-AATATCACCCAGGTCGTTGC-3'; Rev: 5'-GAAACCACCGTGTTCCACTT-3'), Gck (For: 5’-GATCCGGGAAGAGAAGCAAG-3’; Rev: 5’-GACAGGGATGAGGGACAGAG-3’), Ldha (For: 5'-TTAACCCAGAACTGGGCACT-3'; Rev: 5'-ACCCGCCTAAGGTTCTTCAT-3'), Ldhc (For: 5'-TCTTGGAGAACATGGGGACT-3'; Rev: 5'-CACCACCTGCTTGTGAACAT-3'), Ppara (For: 5’-ACAAGGCCTCAGGGTACCA-3’; Rev: 5’-GCCGAAAGAAGCCCTTACAG-3’), Ehhadh (For: 5'-TCGTTGGAGTTCCTGTTGCT-3'; Rev: 5'-TGGCTTCTTCAACTGGGTCT-3'), Acadm (For: 5’-TGCTTTTGATAGAACCAGACCTACAGT-3’; Rev: 5’- CTTGGTGCTCCACTAGCAGCTT-3’), Acadl (For: 5'-GCGATTTCTGCCTGTGAGTT-3'; Rev: 5'-CCACAAAAGCTCTGGTGACA-3').

References:

Dehaven, C.D., Evans, A.M., Dai, H., and Lawton, K.A. (2010). Organization of GC/MS and LC/MS metabolomics data into chemical libraries. J Cheminform *2*, 9.

Evans, A.M., DeHaven, C.D., Barrett, T., Mitchell, M., and Milgram, E. (2009). Integrated, nontargeted ultrahigh performance liquid chromatography/electrospray ionization tandem mass spectrometry platform for the identification and relative quantification of the small-molecule complement of biological systems. Anal Chem *81*, 6656-6667.

Huang da, W., Sherman, B.T., and Lempicki, R.A. (2009a). Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene lists. Nucleic Acids Res *37*, 1-13.

Huang da, W., Sherman, B.T., and Lempicki, R.A. (2009b). Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. Nat Protoc *4*, 44-57.

Hughes, M.E., Hogenesch, J.B., and Kornacker, K. (2010). JTK_CYCLE: an efficient nonparametric algorithm for detecting rhythmic components in genome-scale data sets. J Biol Rhythms *25*, 372-380.

Masri, S., Rigor, P., Cervantes, M., Ceglia, N., Sebastian, C., Xiao, C., Roqueta-Rivera, M., Deng, C., Osborne, T.F., Mostoslavsky, R.*, et al.* (2014). Partitioning circadian transcription by SIRT6 leads to segregated control of cellular metabolism. Cell *158*, 659-672.

Patel, V.R., Ceglia, N., Zeller, M., Eckel-Mahan, K., Sassone-Corsi, P., and Baldi, P. (2015). The pervasiveness and plasticity of circadian oscillations: the coupled circadian-oscillators framework. Bioinformatics.

Patel, V.R., Eckel-Mahan, K., Sassone-Corsi, P., and Baldi, P. (2012). CircadiOmics: integrating circadian genomics, transcriptomics, proteomics and metabolomics. Nat Methods *9*, 772-773.

Rozen, S., and Skaletsky, H. (2000). Primer3 on the WWW for general users and for biologist programmers. Methods Mol Biol *132*, 365-386.

Supplementary Table 1 (Related to Figure 5): Overlapping known STAT3 target genes with WT and TB-specific gene lists. Mean replicate values of gene expression of known STAT3 target genes in WT and TB liver transcriptomics analysis over the circadian cycle. Official gene symbol is provided.

Supplementary Table 1 (Related to Figure 5): Overlapping known STAT3 target genes with WT and TB-specific gene lists.

Mean												
WT ZT 0	WT ZT 4	WT ZT 8	WT ZT 12	WT ZT 16	WT ZT 20	TB ZT 0	TB ZT 4	TB ZT 8	TB ZT 12	TB ZT 16	TB ZT 20	GeneSym
349.22	394.58	352.08	309.69	286.24	288.03	283.22	321.96	231.83	261.51	293.58	278.64	Stat1
23.77	25.18	26.28	19.39	25.79	21.47	24.29	28.47	30.48	28.04	27.85	25.04	Il10
22.37	207.23	905.52	811.76	157.07	33.33	27.55	299.39	775.25	694.02	77.13	34.95	Rgs16
3841.29	3330.23	3571.38	3871.27	3390.85	3070.32	3692.13	3934.18	4343.63	4353.22	4195.21	3401.36	Fn1
209.44	201.32	185.28	186.02	140.26	199.77	208.28	173.23	163.68	166.94	189.68	158.33	Fcer1g
396.58	460.38	365.90	295.13	290.10	345.72	368.60	378.99	287.03	237.14	288.81	359.14	Capn2
441.92	515.94	322.73	288.14	321.22	312.82	353.80	384.78	245.21	201.95	279.89	354.65	Cited2
72.17	60.77	66.28	74.21	56.68	69.25	80.13	79.55	75.10	65.93	75.61	66.34	Itgb2
154.00	158.43	166.55	128.02	118.18	138.99	191.13	182.21	135.23	143.25	163.77	129.65	Lcp2
120.39	111.07	130.97	111.13	89.34	99.14	119.44	122.03	112.82	100.87	114.48	117.49	Irf1
294.12	285.29	355.83	447.50	405.35	275.49	255.06	248.44	290.14	393.16	318.16	266.10	Map2k3
49.26	61.41	56.27	53.52	37.47	46.86	49.84	47.16	43.30	39.40	41.47	38.68	Myh10
26.43	26.32	28.77	22.78	25.61	28.89	34.01	26.44	23.76	31.47	25.01	24.45	Ccl2
960.66	702.14	634.78	731.64	587.86	617.19	1016.22	1006.31	901.37	998.53	983.02	814.84	Stat3
116.97	45.10	102.72	66.95	39.76	40.36	111.61	104.03	153.37	120.58	111.82	61.94	Socs3
23.87	37.68	44.36	39.52	46.65	31.67	28.58	26.75	54.45	46.36	27.48	25.71	Dact1
119.05	48.97	36.92	44.24	38.21	52.53	43.97	42.16	46.01	56.81	59.97	50.27	Fos
29.56	33.93	30.23	35.71	36.83	29.73	32.92	29.71	36.35	40.98	36.64	34.46	Dact1
1269.46	1039.69	1062.19	1141.42	1120.68	1083.58	1423.06	1292.13	1433.47	1658.71	1510.91	1349.29	Il6st
343.53	220.62	76.54	140.31	201.08	230.68	349.25	210.90	112.62	128.80	232.88	276.31	Nfil3
161.09	284.86	222.86	145.51	136.76	139.17	197.52	218.56	222.65	138.86	163.68	167.82	Ocln
10.53	13.10	20.31	16.54	16.11	11.55	15.55	14.31	14.51	15.20	17.48	15.44	Angpt1
15.09	20.06	16.86	15.20	20.38	18.09	20.45	16.08	20.44	19.30	17.91	18.45	Has2
53.01	66.50	193.42	75.44	78.70	80.14	63.43	52.44	76.27	103.17	59.02	40.67	Myc
86.30	70.13	75.69	111.64	65.31	72.27	156.43	119.61	119.26	142.49	137.75	97.71	Osmr
29.24	28.99	29.12	120.95	32.80	40.14	30.64	30.60	28.17	30.55	34.60	38.09	Angpt1
77.50	90.17	87.86	87.01	69.64	74.28	78.39	62.00	77.73	77.53	75.31	72.83	Has2
337.94	304.75	200.69	394.65	196.08	207.30	273.50	189.03	235.23	140.83	189.31	263.96	Ly6a
53.60	44.98	49.30	71.91	50.41	40.11	67.52	50.39	81.58	67.21	65.52	43.70	Ier3
46.32	46.69	51.37	44.65	43.32	51.83	50.59	49.81	42.13	45.98	48.08	39.82	Vav1
2634.99	2034.84	1899.71	2353.75	1899.74	1968.48	2480.59	2836.92	2782.32	3216.11	3006.51	2243.41	C4b
48.06	64.31	93.72	65.93	64.19	44.45	52.43	62.69	75.47	68.59	63.72	74.57	Npc1
102.27	148.16	67.15	44.14	38.31	79.34	128.00	161.67	60.98	75.77	62.81	95.99	Egr1
384.45	453.80	490.43	402.96	311.01	456.01	469.31	512.16	425.58	519.36	545.38	427.56	Cd74
195.36	181.20	172.94	171.17	122.32	173.61	208.17	176.78	165.27	168.51	180.43	165.18	Csf1r
38.62	37.00	36.42	30.35	41.59	38.44	40.02	35.74	41.05	44.28	41.54	40.93	Pmaip1
422.02	620.50	1091.07	814.01	591.70	460.45	470.53	646.27	940.11	778.86	547.62	465.66	Npc1
280.72	289.81	313.67	503.12	292.78	287.52	351.57	333.80	271.55	281.88	320.07	271.16	Vim
22.87	25.91	19.67	28.86	24.77	24.15	26.75	25.04	30.69	30.00	25.70	22.94	Thbs1
86.60	72.93	70.36	79.10	59.46	67.95	78.94	79.20	59.63	88.28	92.63	69.26	Hck
287.98	428.56	338.75	376.65	284.21	295.04	269.20	335.06	310.67	406.45	225.37	271.50	Slc25a25
51.13	40.97	43.36	39.09	45.43	46.41	41.72	49.80	43.54	55.26	51.97	39.33	Dlx2
7493.71	6456.86	6042.21	5943.14	5466.46	6126.29	6977.72	7169.51	6989.13	6629.08	6706.52	6466.39	Fgg
29.52	34.87	27.60	23.46	19.83	29.06	28.83	37.78	29.61	36.66	39.62	37.24	Gbp1
361.92	257.43	212.27	198.41	176.28	190.03	225.79	204.47	170.97	155.56	188.08	222.00	Cyr61
130.22	146.05	180.86	165.19	144.04	148.30	176.76	210.54	182.61	207.19	174.97	163.17	Ugcg
192.04	85.62	71.63	106.92	83.86	103.10	73.55	66.97	46.37	81.43	111.45	71.40	Jun