

Supplementary Files Information:

All Circadian Genes Heatmap Clusters: Directory containing heat map plots of the 12 clusters obtained from the previously identified circadian genes in this dataset

ATACQC_Scores.csv: CSV containing quality control metrics for the ATAC-seq data. First column is sample name, second is the Fractions of reads in Peaks score, third is the Non Redundant Fraction, columns 4 and 5 are the PCR bottlenecking coefficient 1 and 2.

Full_Metascape_Output.zip: Zip file containing full Metascape gene ontology analysis for the WGCNA modules identified from the RNA-seq data

GO_Results: Gene ontology results from Metascape. Last column indicates the WGCNA module.

MetaCycle Results: Directory containing results from meta2d, JTK, ARSER, LS and RAIN analysis.

SLDSC_Enrichment_Results: Directory containing enrichment results from the Stratified linkage disequilibrium score analysis for ADHD, Bipolar disorder, Schizophrenia, Insomnia, MDD, Morningness and PTSD.

TSS QC Summary: PDF file including coverage curved of nucleosome-free and nucleosome signals for each ATAC-seq sample. Transcription Start Site (TSS) Enrichment Score is indicated in bold next to the sample name.

WGCNA_ATAC_Modules_ID.csv: CSV file containing WGCNA module membership results for the ATAC-seq data.

WGCNA_RNA_Modules_ID.csv: CSV file containing WGCNA module membership results for the RNA-seq data.

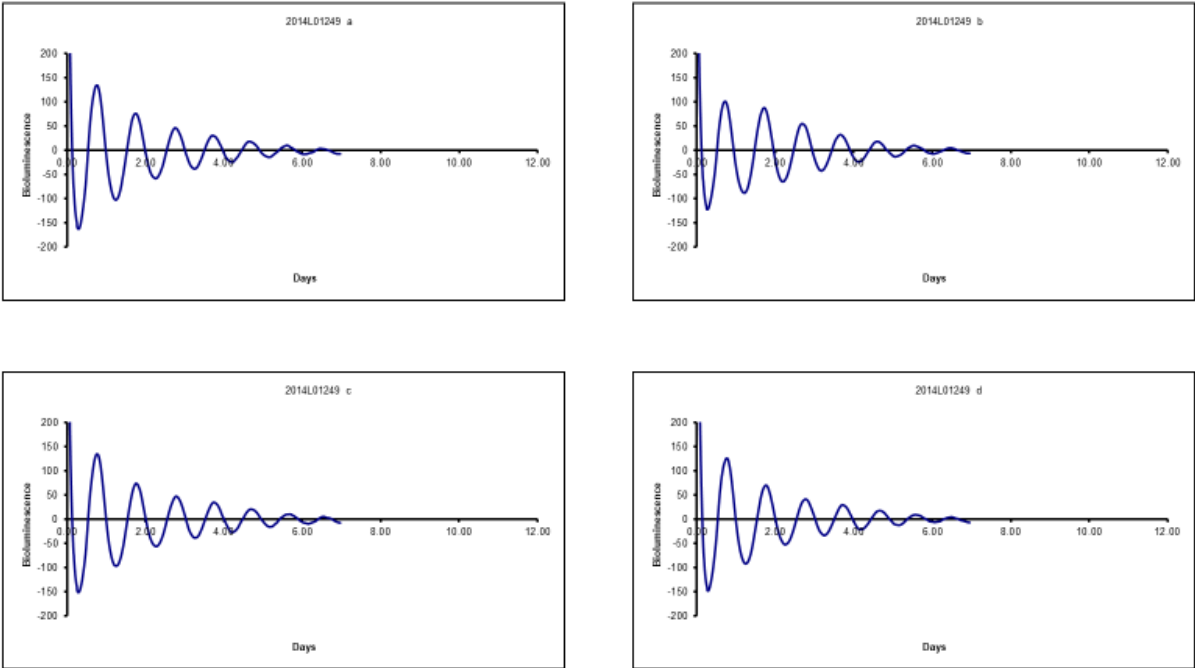
Supplementary Figure 1 Principal component analysis of RNA-seq temporal dataset



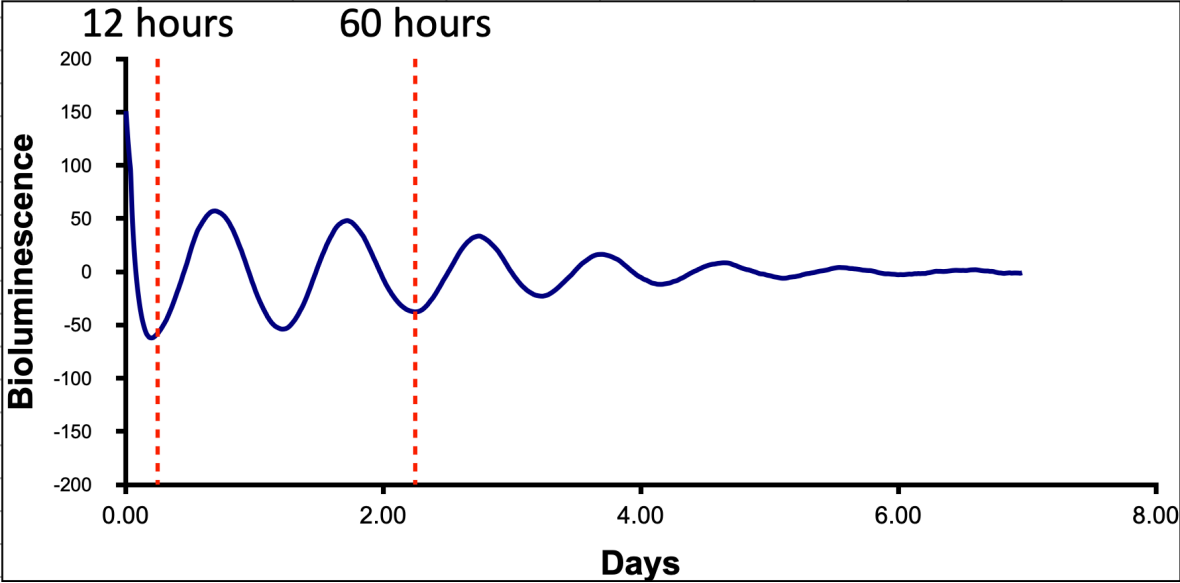
Supplementary Figure 1 Description: Principal component component representation of RNA-seq data after CPM(counts per million) normalization. Colors indicate each individual cell line used in this study. Numbers in the plot indicate the corresponding time point for that cell line.

Supplementary Figure 2 Circadian-bioluminescence transduction experiment results

A



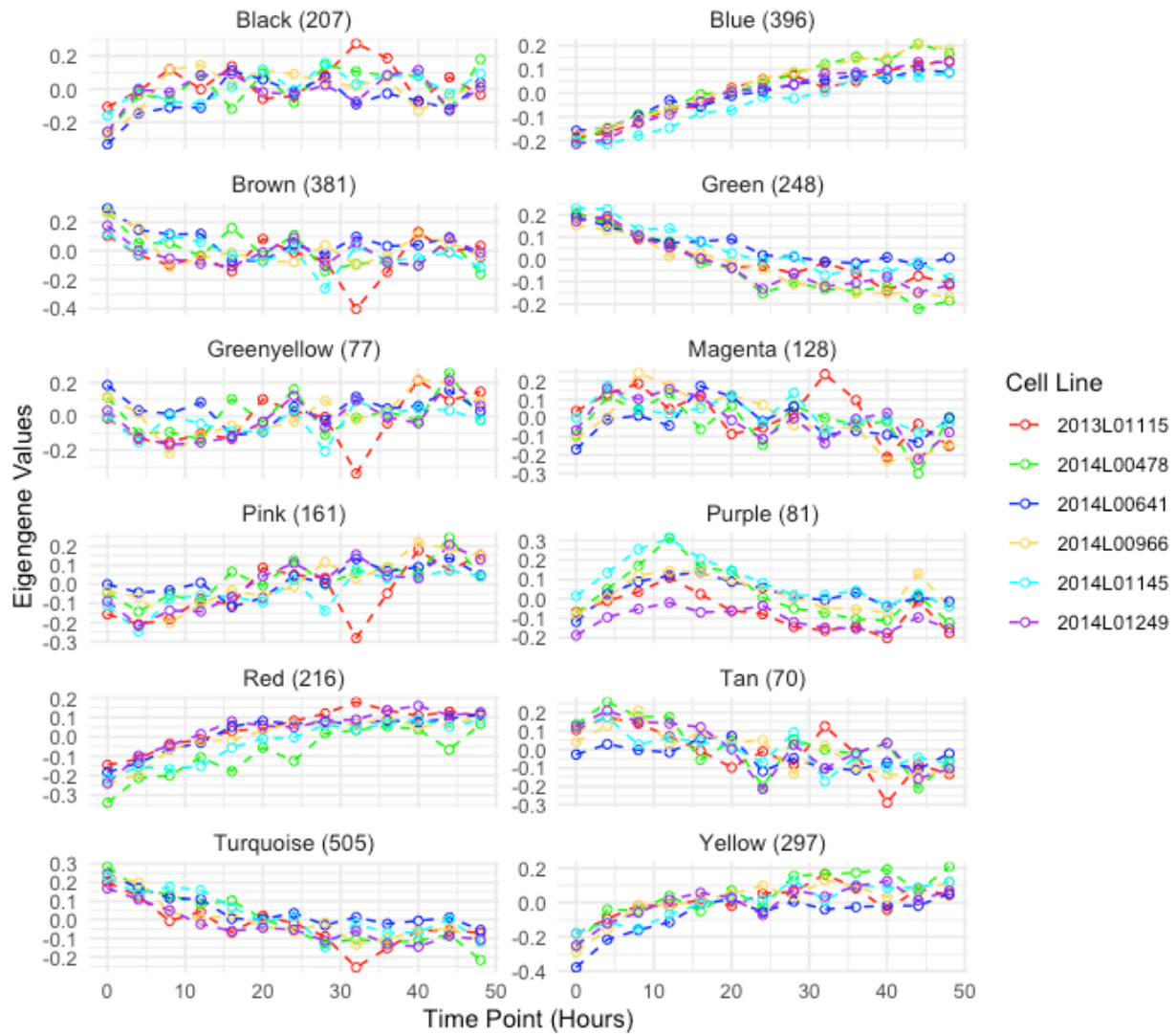
B



Supplementary Figure 2 Description: Example of circadian bioluminescence assay performed using transduced primary fibroblast cell lines with a Bmal1:luc construct, as described previously by Brown, et al. 2005 (The Period Length of Fibroblast Circadian

Gene Expression Varies Widely among Human Individuals). A. Bioluminescence measurements of cell cultures following synchronization with dexamethasone. B. Red lines indicate the time period during which RNA-seq and ATAC-seq data was collected from the cell lines.

Supplementary Figure 3 WGCNA modules obtained from the RNA-seq temporal dataset



Supplementary Figure 3 description: WGCNA modules obtained from n=2,767 genes identified as having a significant effect of time in their expression through cubic splines modeling. Expression values are represented here as eigengene values. Names of the modules were assigned by WGCNA. The number of genes assigned per module is next to the module name.

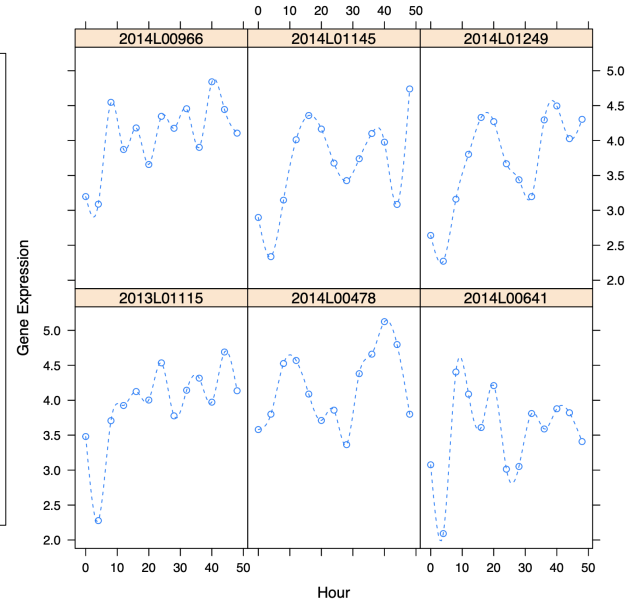
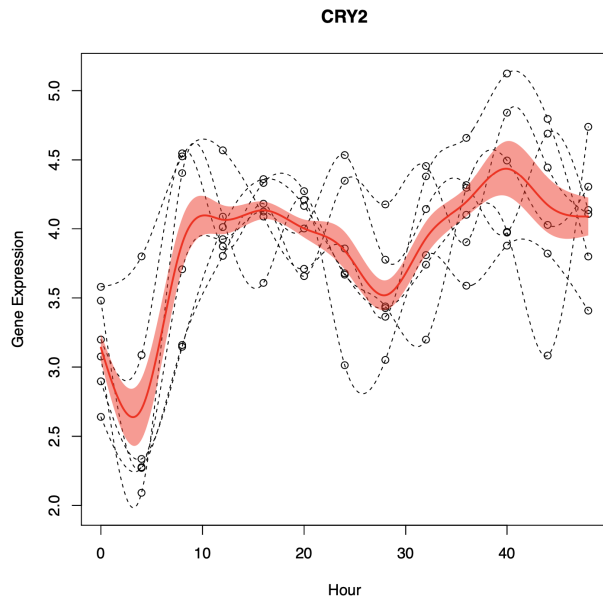
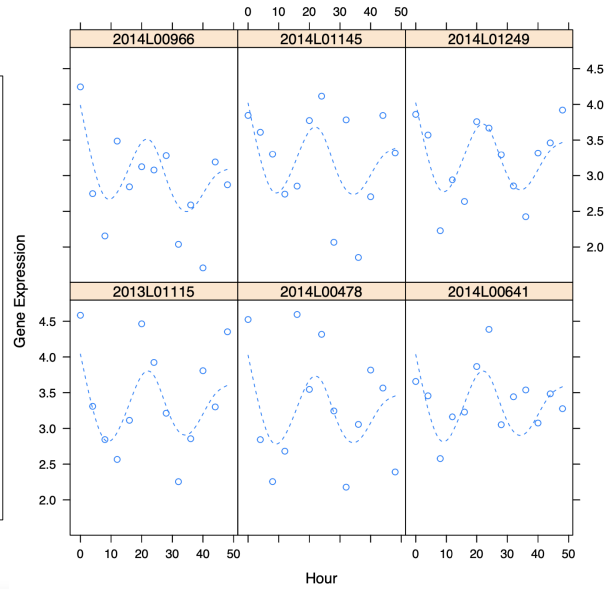
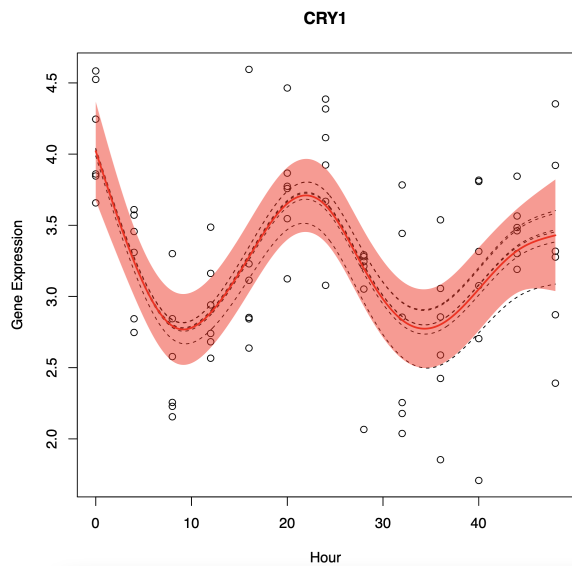
Supplementary Table 1 Gene Ontology Analysis of genes in eigengene modules(Full results in Full_Metaspape_Output.zip)

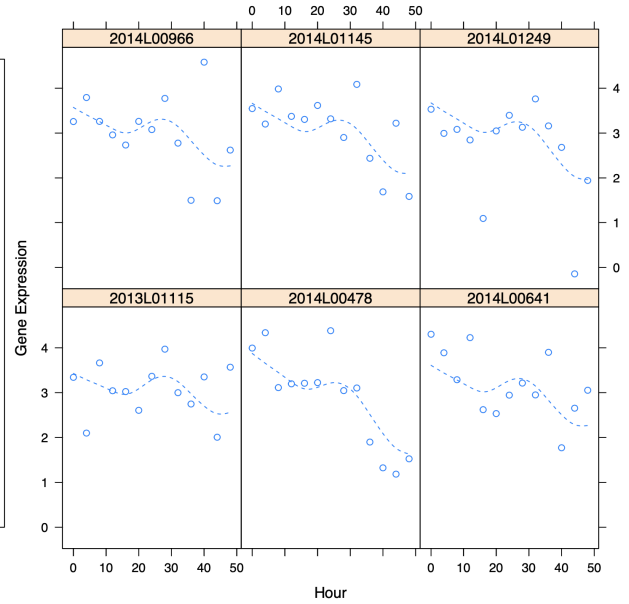
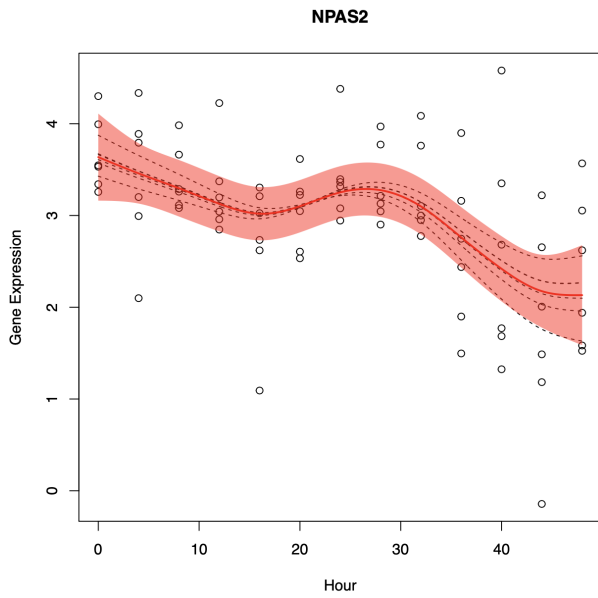
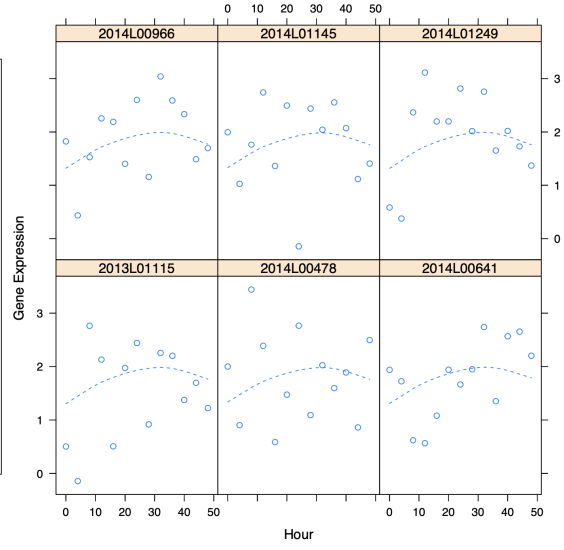
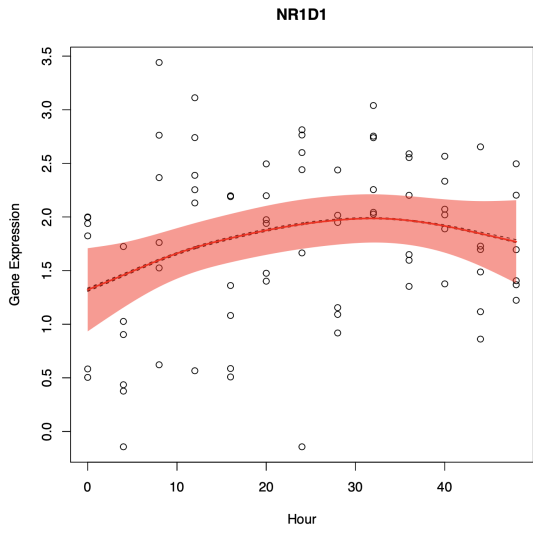
Gene ontology analysis using MetaScape of the genes that belong to the different modules identified by WGCNA

Category	CategoryID	GO	Description	PARENT_GO
GO Biological Processes	19	GO:0006325	chromatin organization	19_GO:0009987 cellular process
Reactome Gene Sets	6	R-HSA-5617833	Cilium Assembly	
Reactome Gene Sets	6	R-HSA-1852241	Organelle biogenesis and maintenance	
WikiPathways	27	WP3651	Pathways affected in adenoid cystic carcinoma	
GO Biological Processes	19	GO:0006351	DNA-templated transcription	19_GO:0008152 metabolic process
GO Biological Processes	19	GO:0097659	nucleic acid-templated transcription	19_GO:0008152 metabolic process
Reactome Gene Sets	6	R-HSA-5620912	Anchoring of the basal body to the plasma membrane	
GO Biological Processes	19	GO:0032774	RNA biosynthetic process	19_GO:0008152 metabolic process
GO Biological Processes	19	GO:0006338	chromatin remodeling	19_GO:0009987 cellular process
Reactome Gene Sets	6	R-HSA-2565942	Regulation of PLK1 Activity at G2/M Transition	
GO Biological Processes	19	GO:0008380	RNA splicing	19_GO:0008152 metabolic process
GO Biological Processes	19	GO:0099111	microtubule-based transport	19_GO:0051179 localization
GO Biological Processes	19	GO:0010970	transport along microtubule	19_GO:0051179 localization
Reactome Gene Sets	6	R-HSA-380284	Loss of proteins required for interphase microtubule organization from the centrosome	
Reactome Gene Sets	6	R-HSA-380259	Loss of Nlp from mitotic centrosomes	
Reactome Gene Sets	6	R-HSA-8854518	AURKA Activation by TPX2	
Reactome Gene Sets	6	R-HSA-380270	Recruitment of mitotic centrosome proteins and complexes	
Reactome Gene Sets	6	R-HSA-380287	Centrosome maturation	
Reactome Gene Sets	6	R-HSA-68877	Mitotic Prometaphase	
GO Biological Processes	19	GO:0030705	cytoskeleton-dependent intracellular transport	19_GO:0051179 localization
GO Biological Processes	19	GO:0000226	microtubule cytoskeleton organization	19_GO:0009987 cellular process
Reactome Gene Sets	6	R-HSA-380320	Recruitment of NuMA to mitotic centrosomes	
GO Biological Processes	19	GO:0031023	microtubule organizing center organization	19_GO:0009987 cellular process
GO Biological Processes	19	GO:0006366	transcription by RNA polymerase II	19_GO:0008152 metabolic process

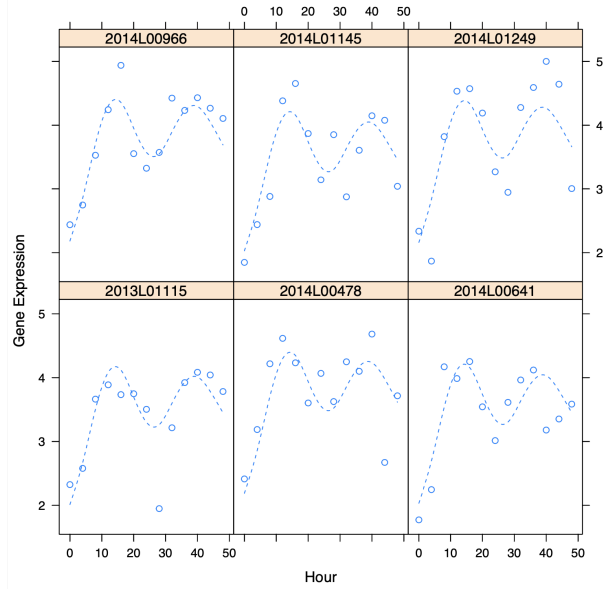
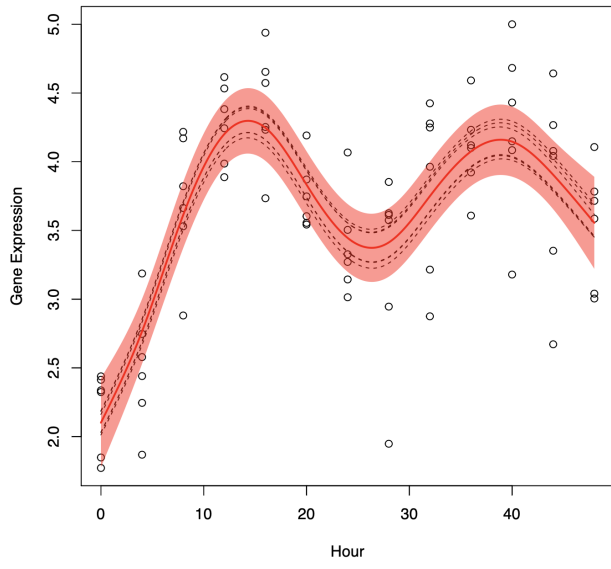
Supplementary figure 4 Mixed non-linear modeling of circadian genes

A

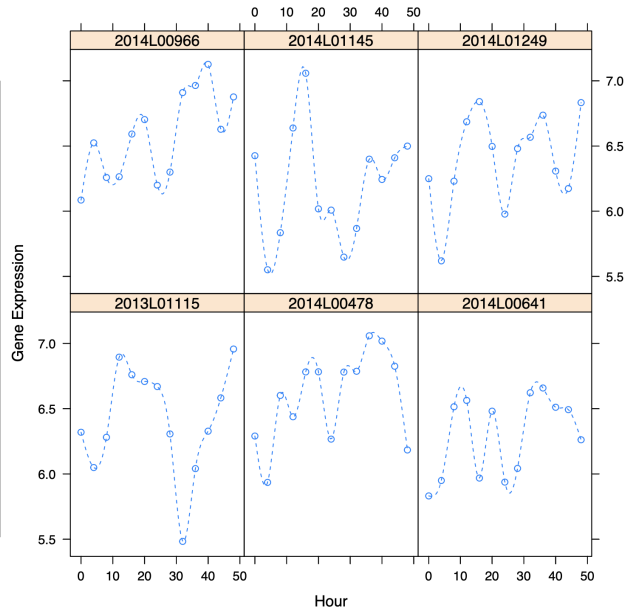
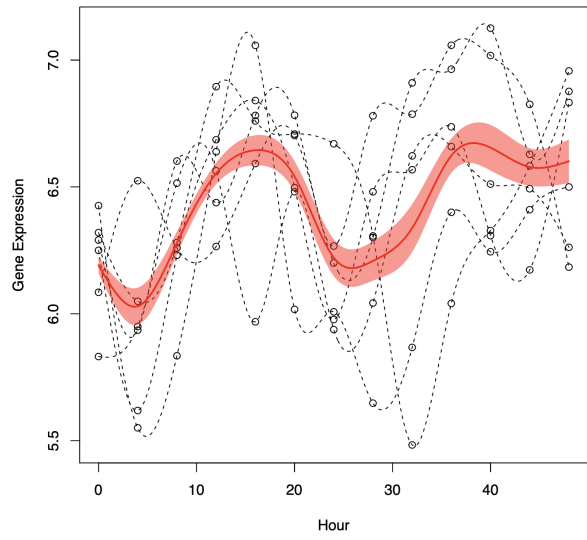




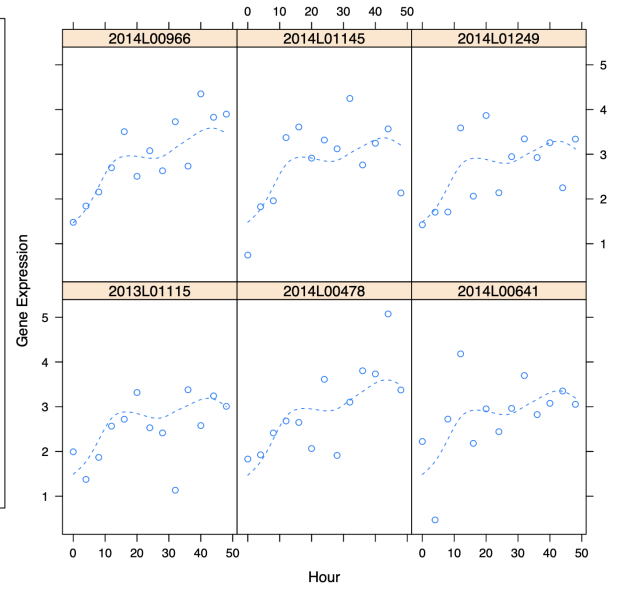
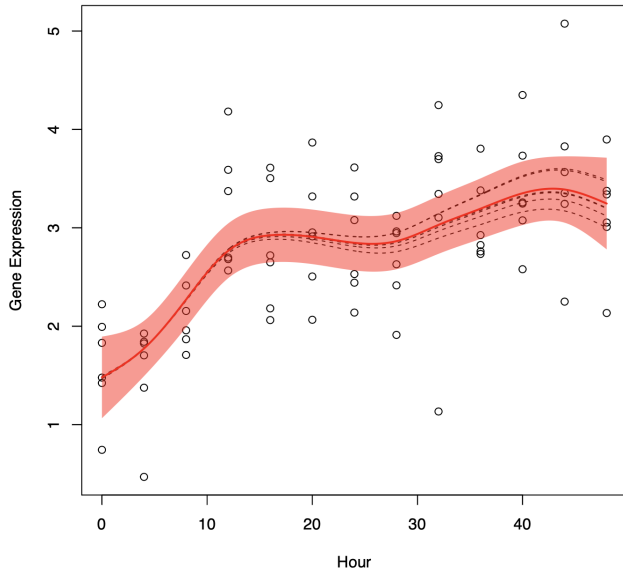
TEF



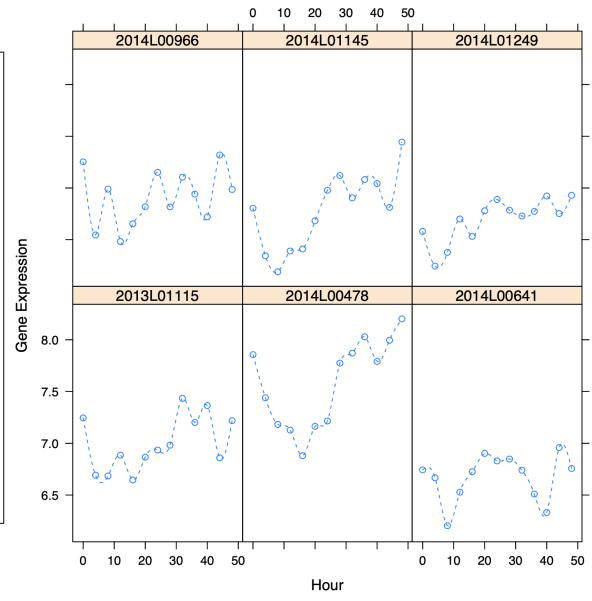
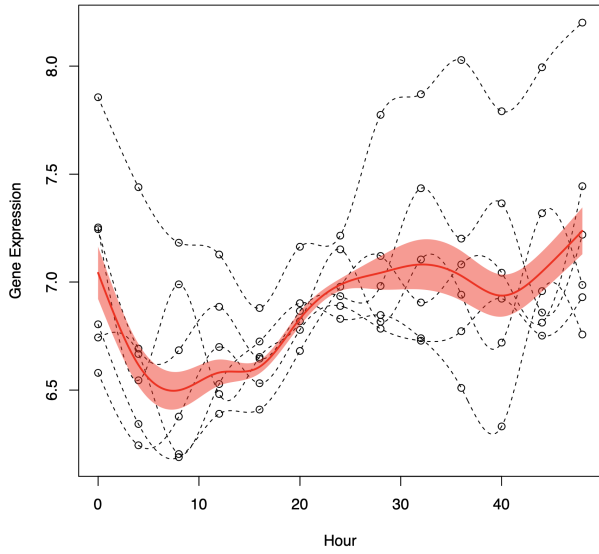
PER1



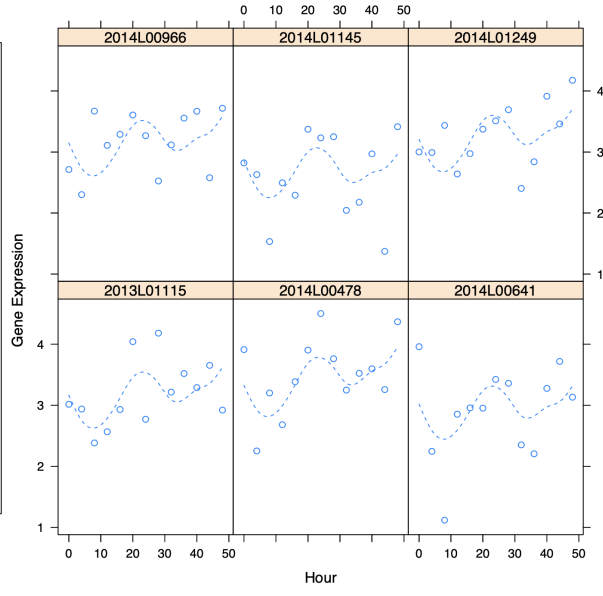
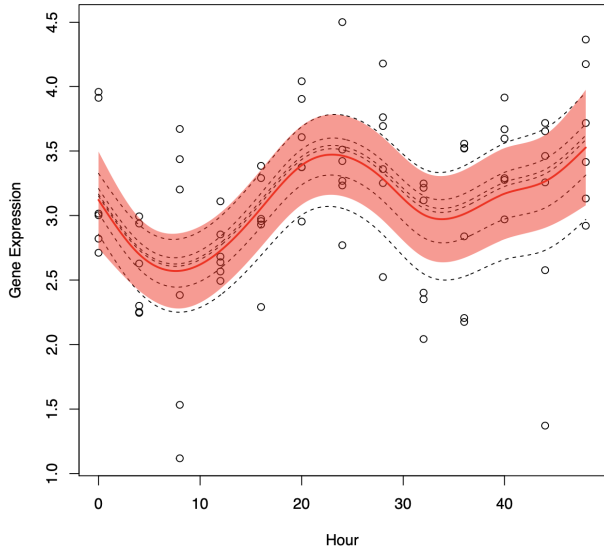
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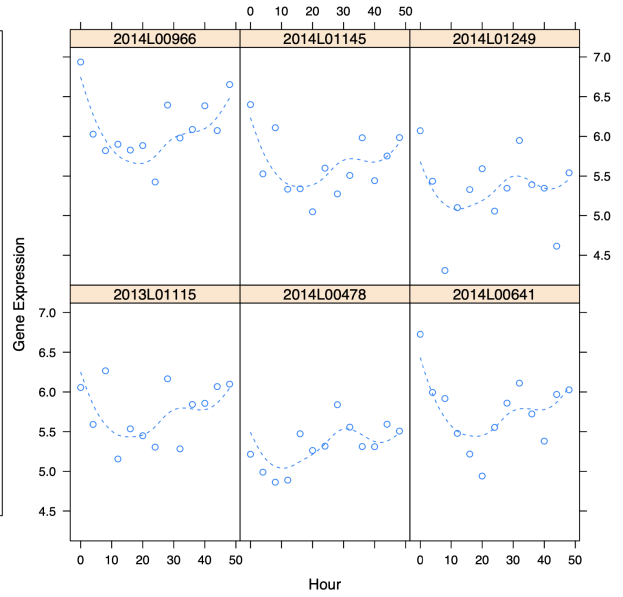
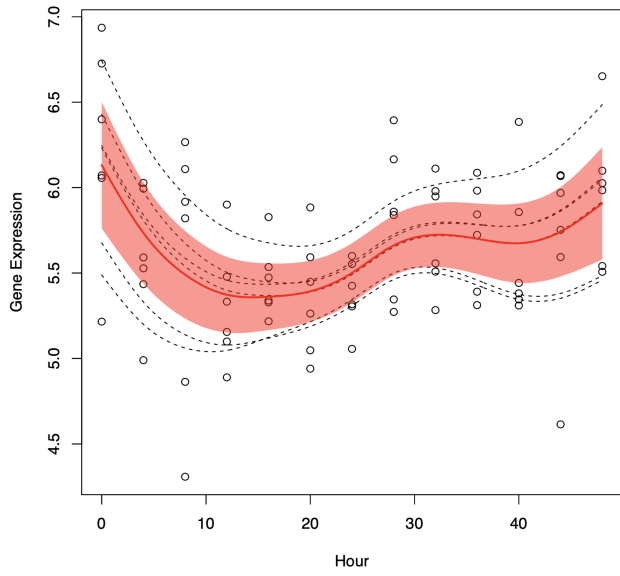
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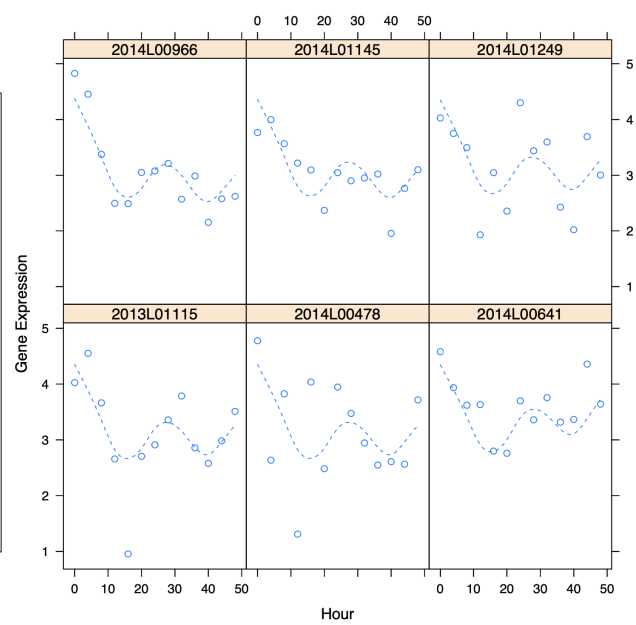
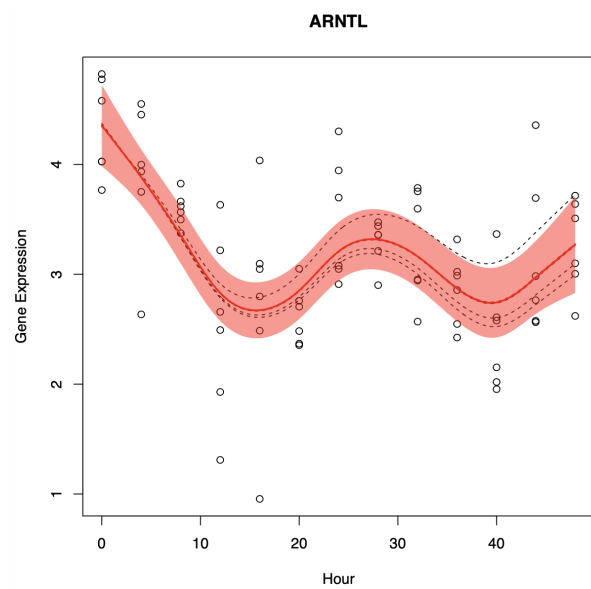
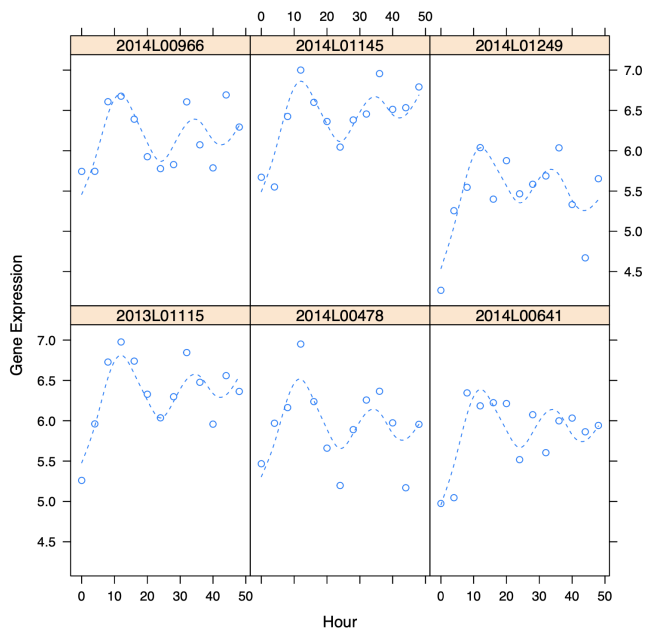
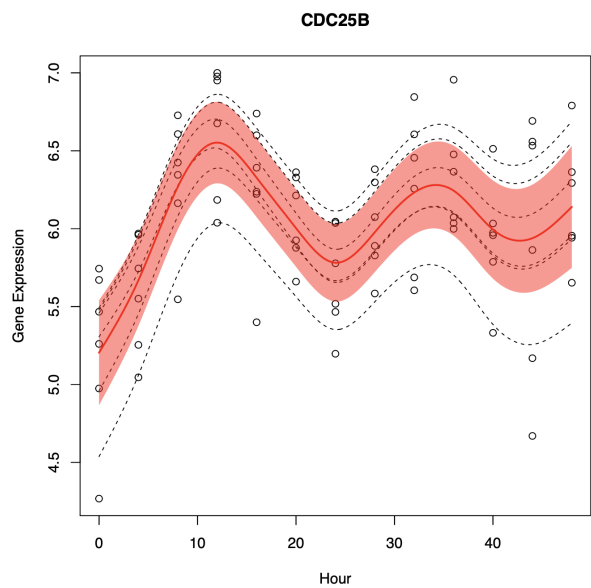


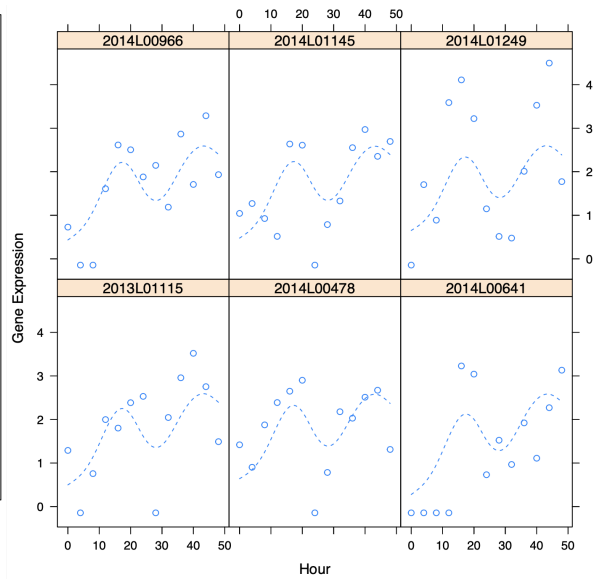
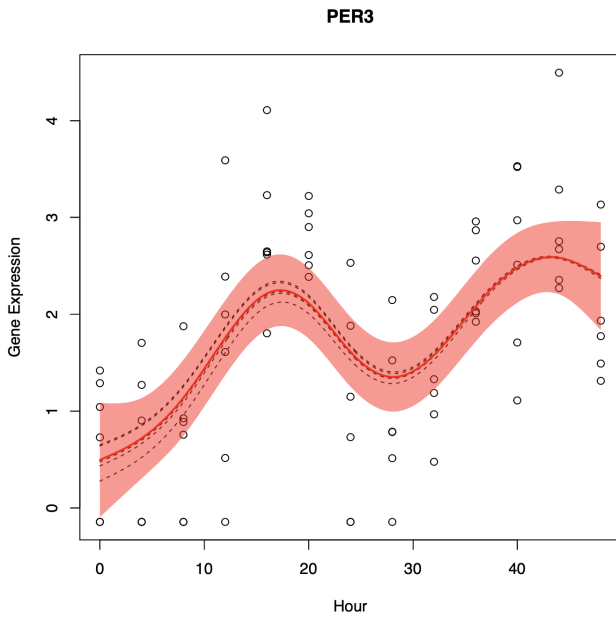
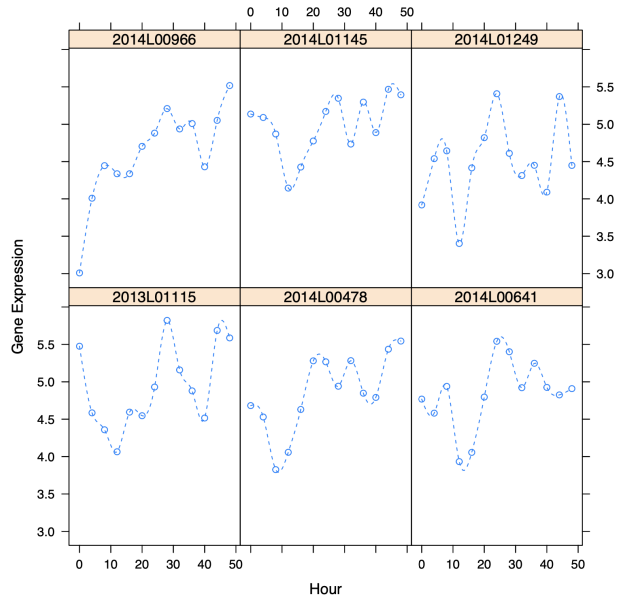
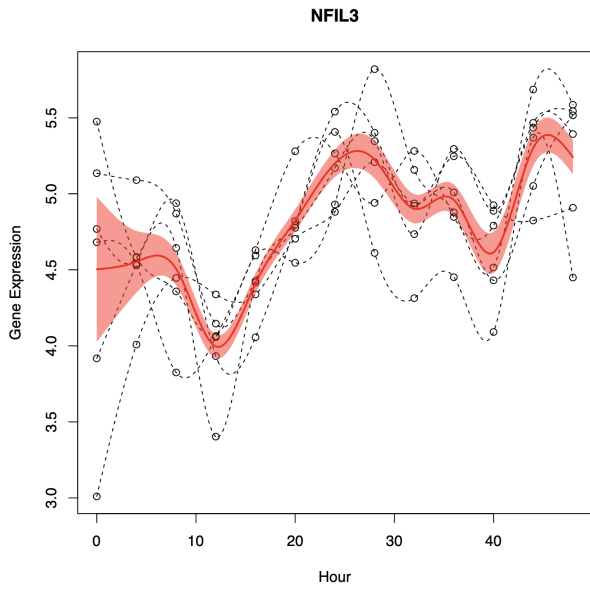
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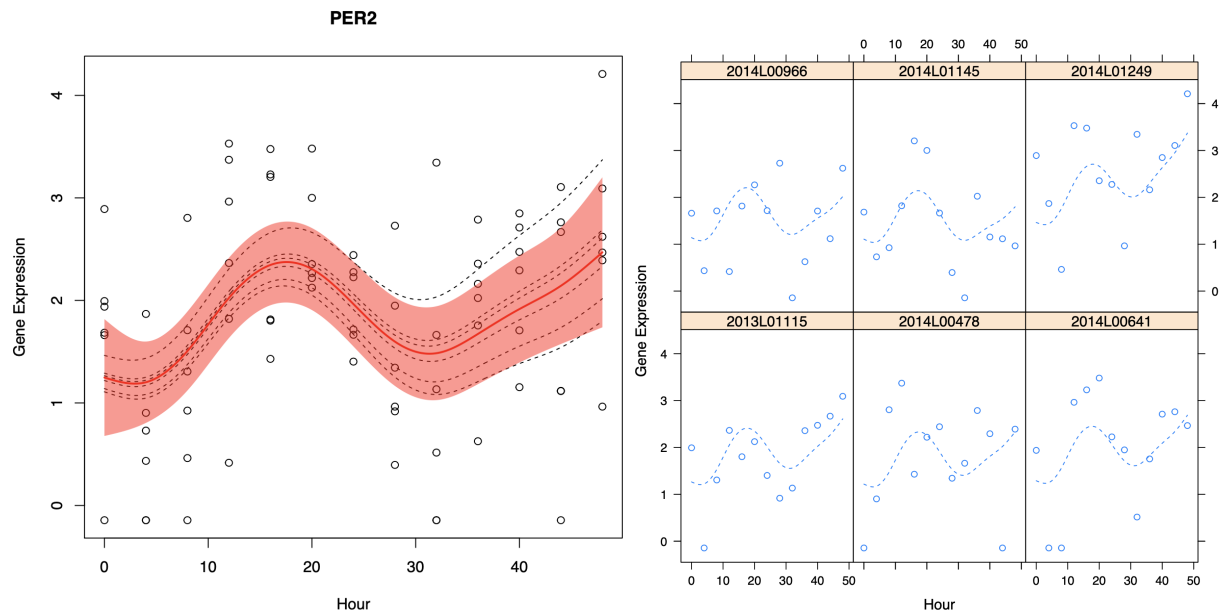


FKBP5



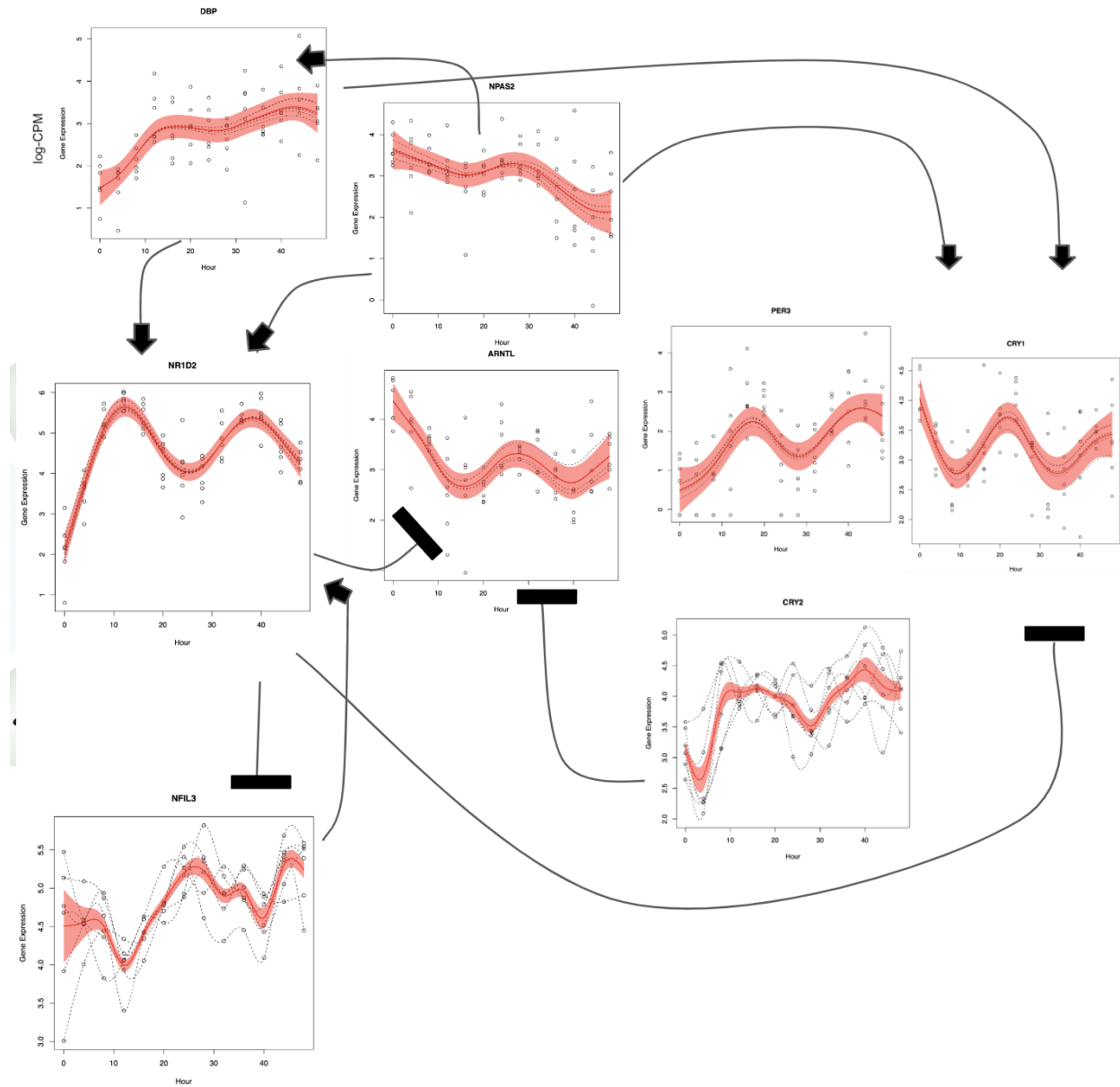






Supplementary figure 4 description: A, Smoothing-splines mixed-effect models of circadian gene expression across previously reported circadian genes in skin. Red line indicates the average fitted model across cell lines, with the red area representing a 95% confidence interval.

Supplemental figure 5 Known interactions between circadian genes present identified in this dataset



Supplemental figure 5 description: Known gene expression relationships of core circadian genes. Arrows indicate a gene inducing in the expression of another gene. The black bar indicates a gene repressing the expression of another gene.

Supplementary table 2: Results for circadian analysis tools ARSER, JTK, LS and metacycle ARSER (Full results in MetaCycle Results folder)

CycID	meta3d_Pvalue	meta3d_BH.Q	meta3d_Period	meta3d_Phase	meta3d_Base	meta3d_AMP	meta3d_rAMP
NR1D2	1.213429e-11	1.335258e-07	24.77884	12.3604684	4.587153	1.1940252	0.26131517
TEF	1.715038e-09	9.436137e-06	23.77328	13.5969101	3.699635	0.8258222	0.22327689
CRY1	2.518402e-07	9.237500e-04	23.53269	21.9876554	3.224590	0.7364189	0.22766198
TECPR1	8.314857e-07	2.287417e-03	23.10611	13.2858023	4.907502	0.4514711	0.09187609
CDC25B	2.614718e-06	5.754472e-03	21.75986	12.1292808	6.138671	0.4665738	0.07624382
HNRNPU	4.643564e-06	8.516295e-03	23.89180	22.2422183	8.048284	0.1775919	0.02208631
COG8	8.449688e-06	1.109890e-02	23.42245	2.8576798	1.871940	0.9216777	0.51115138
YBEY	9.077615e-06	1.109890e-02	23.81287	20.9649802	3.579168	0.4444663	0.12770498
ANGPTL2	8.758998e-06	1.109890e-02	21.93092	18.0668207	6.473876	0.4057508	0.06259919
PER3	1.238981e-05	1.239431e-02	24.56212	16.2925841	1.839917	1.2330494	0.65617035
KIAA1244	1.221822e-05	1.239431e-02	23.66213	12.9676442	2.154037	0.7363603	0.38380775
RGS4	1.420238e-05	1.302358e-02	21.36553	20.9752510	3.487784	0.6029858	0.18236976
CCDC22	1.565106e-05	1.324802e-02	24.96972	22.8001950	3.048887	0.6679597	0.21892731
RASSF4	2.297644e-05	1.805948e-02	22.03420	10.8342720	3.589962	0.5734768	0.16243627
LRP12	2.669229e-05	1.958146e-02	22.66092	21.0085194	5.286893	0.3908946	0.07430898
MRPS25	2.907814e-05	1.999849e-02	23.27449	1.8402432	6.042704	0.2289662	0.03786866
TRIT1	5.205274e-05	3.017278e-02	24.63071	22.7026574	3.092441	0.7523076	0.24757035
TRAF3IP3	5.483965e-05	3.017278e-02	24.18468	8.6541727	1.986866	0.5518161	0.28633139
NEAT1	5.003333e-05	3.017278e-02	25.64616	9.2529887	8.313655	0.2999881	0.03629947
CPM	5.357480e-05	3.017278e-02	21.85298	9.7703230	7.692930	0.3817325	0.04931089
DFFB	6.756078e-05	3.128110e-02	24.20344	19.7974604	2.767652	0.6863324	0.25005403

JTK

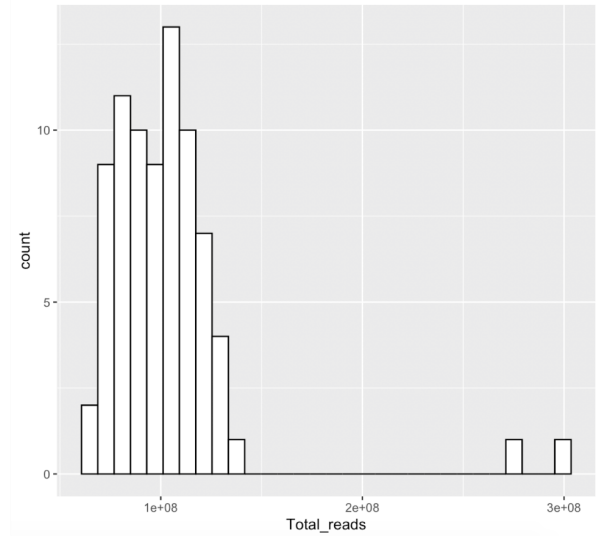
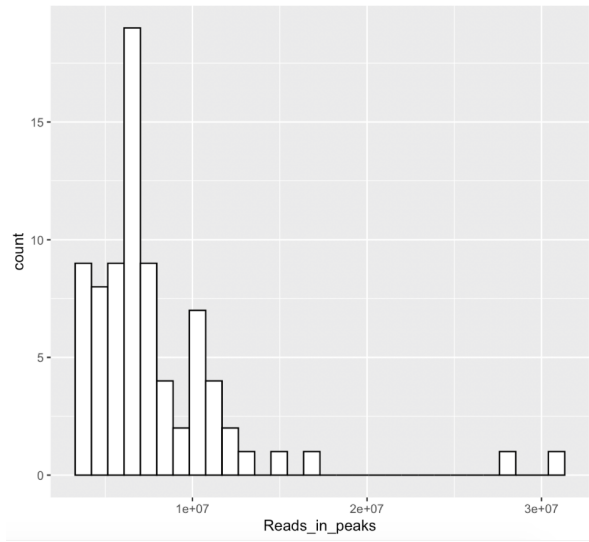
CycID	meta3d_Pvalue	meta3d_BH.Q	meta3d_Period	meta3d_Phase	meta3d_Base	meta3d_AMP	meta3d_rAMP
NR1D2	9.595880e-12	1.055931e-07	27.68920	1.334773e+01	4.4620012	1.18082732	0.265828928
TEF	2.655185e-05	1.460883e-01	25.84020	1.566192e+01	3.6157010	0.77420363	0.213709662
LOC102723897	9.999611e-01	1.000000e+00	20.00000	1.400000e+01	2.7681907	0.44691374	0.161446154
LINC01128	9.570960e-01	1.000000e+00	23.04465	6.284749e+00	2.5484198	0.50800380	0.201301191
NOC2L	7.292068e-01	1.000000e+00	26.89478	1.041780e+01	1.9934585	0.56383520	0.290242126

LS

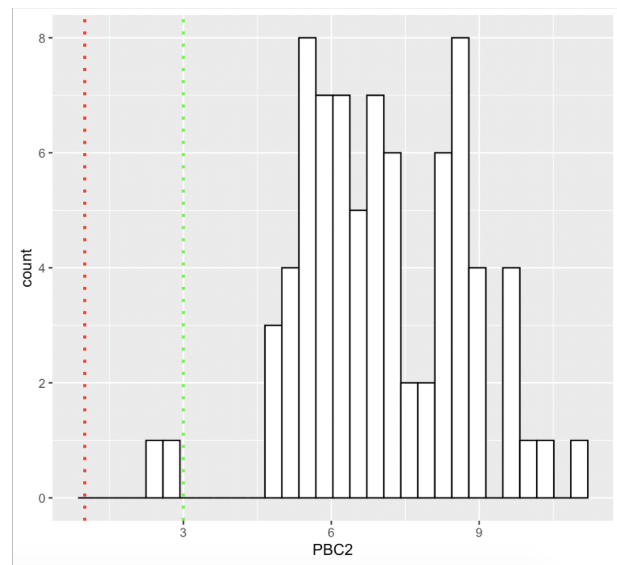
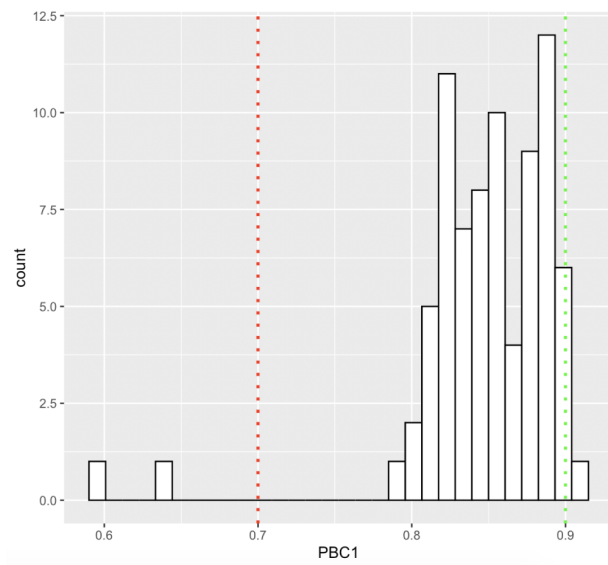
CycID	meta3d_Pvalue	meta3d_BH.Q	meta3d_Period	meta3d_Phase	meta3d_Base	meta3d_AMP	meta3d_rAMP
NR1D2	0.01633951	1	25.64740	12.87639324	4.5440208	1.2277886	0.27153134
TEF	0.05023642	1	24.95835	15.27871444	3.6363365	0.8011303	0.22052088
PER3	0.12094754	1	25.61226	17.01255748	1.8317137	1.2665310	0.67639039
ZNF772	0.20681331	1	25.37394	1.94345724	3.2468177	0.6224801	0.19051836
COG8	0.21600155	1	23.46244	2.96438099	1.8183856	0.9070828	0.51457672
CRY1	0.23380311	1	23.53425	21.96794674	3.2583237	0.7522083	0.23038240

Supplemental Figure 6 Quality Control for ATAC-seq data

A

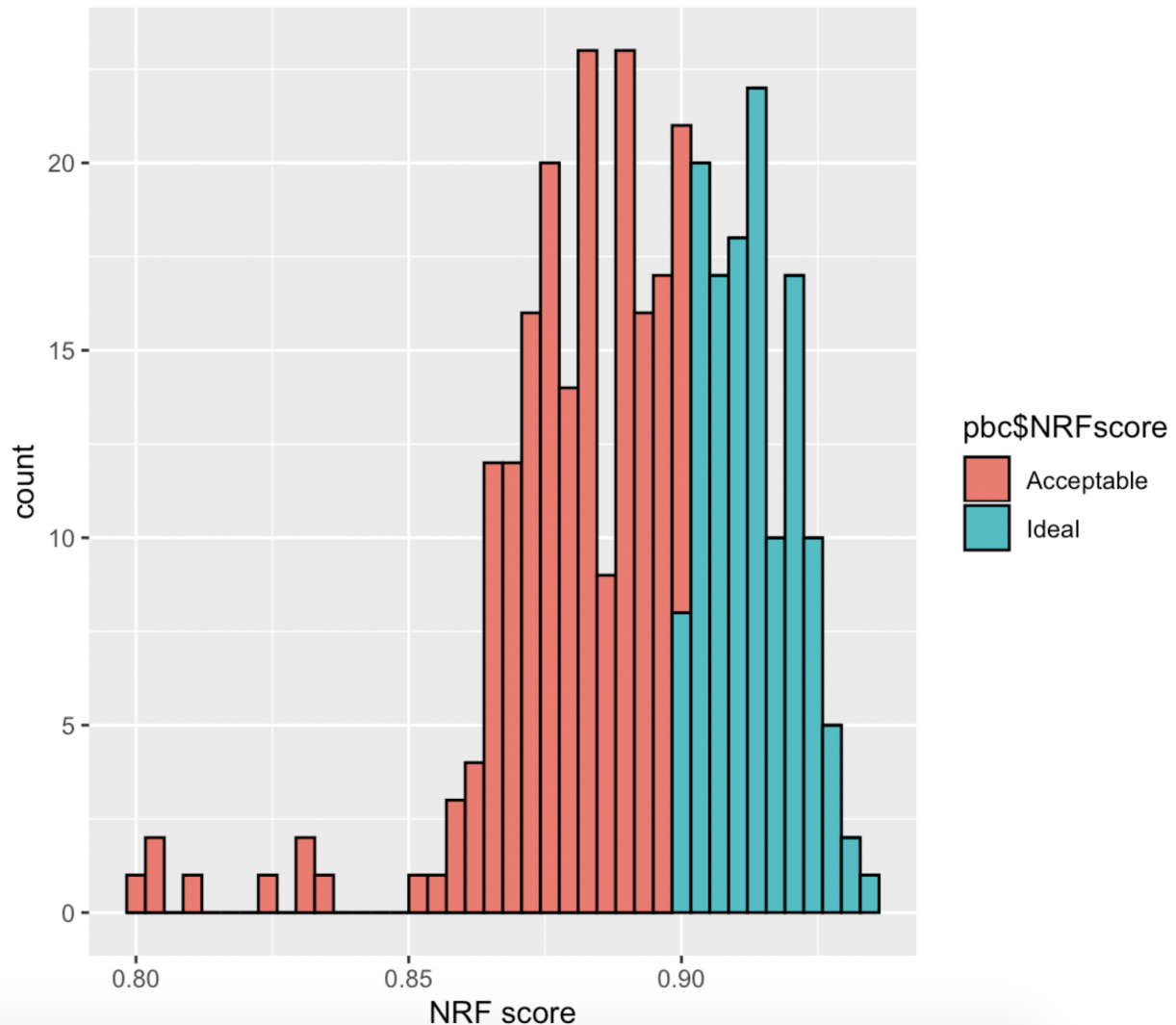


B



c

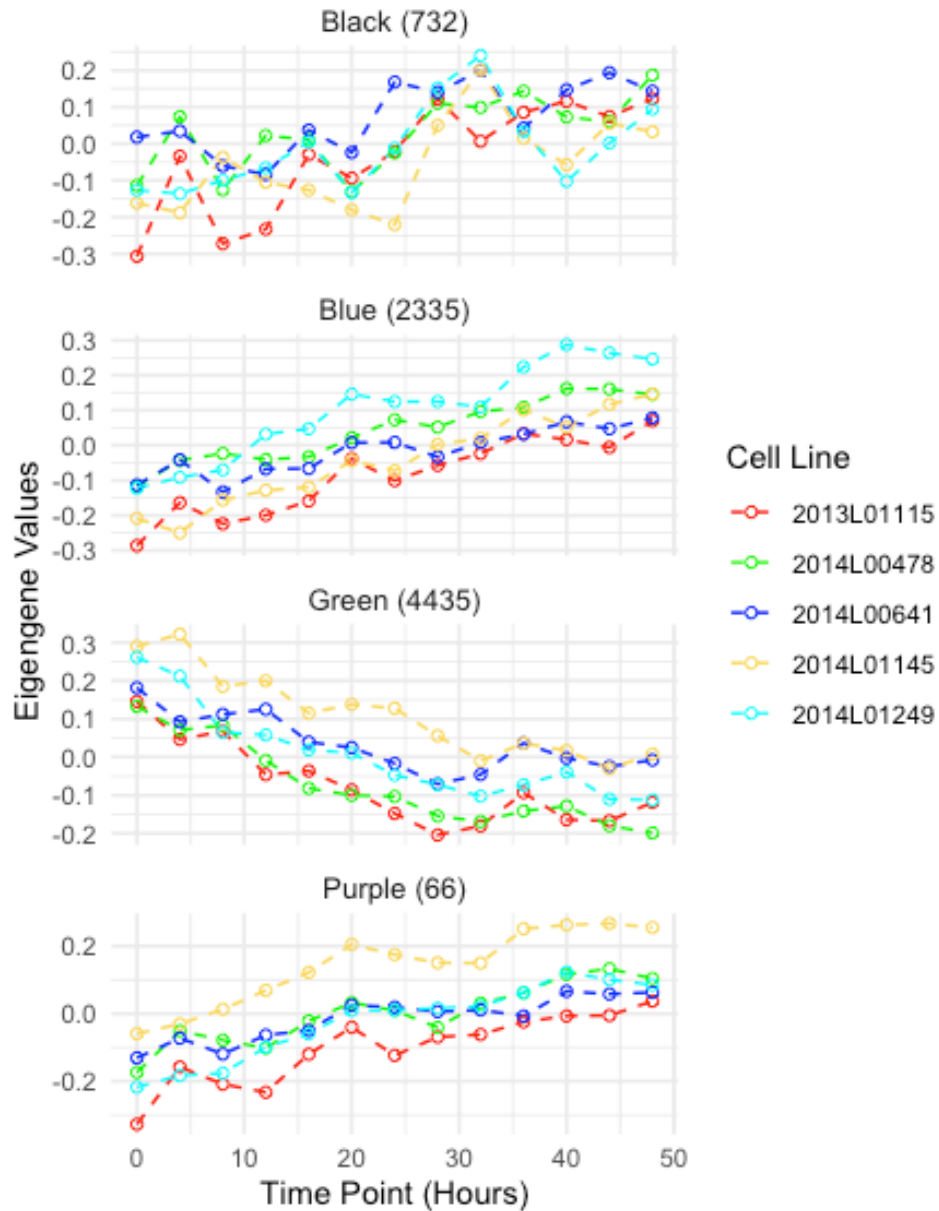
Distribution of Non-Redundant Fraction (NRF) scores



Supplementary Figure 6 Description: Quality control metrics, using the thresholds provided by the standard ENCODE Pipeline for the identification of open chromatin regions (OCRs) of the genome. A shows distribution of all reads present in the peaks identified in the ATAC-seq dataset, as well as the distribution of all the reads by sample. B shows library complexity metrics of PCR Bottlenecking Coefficients (PBC), measured as $PBC1 = \frac{[\# \text{ of positions with exactly 1 read mapped}]}{[\# \text{ of positions with 1 or more reads mapped}]}$ and $PBC2 = \frac{[\# \text{ of positions with exactly 1 read mapped}]}{[\# \text{ of positions with 2 reads mapped}]}$. Red cutoff color indicates severe PCR bottlenecking threshold (<0.7 for PBC1, <1 for PBC2), green cutoff corresponds to no PCR bottleneck (>0.9 for PBC1, >3 for PBC2). C shows the distribution of Non-redundant Fraction(NRF) scores. Values within 0.7 and 0.9

are considered acceptable. The outlying samples across QC were from the 2014L00966 cell line, time points 20 and 0.

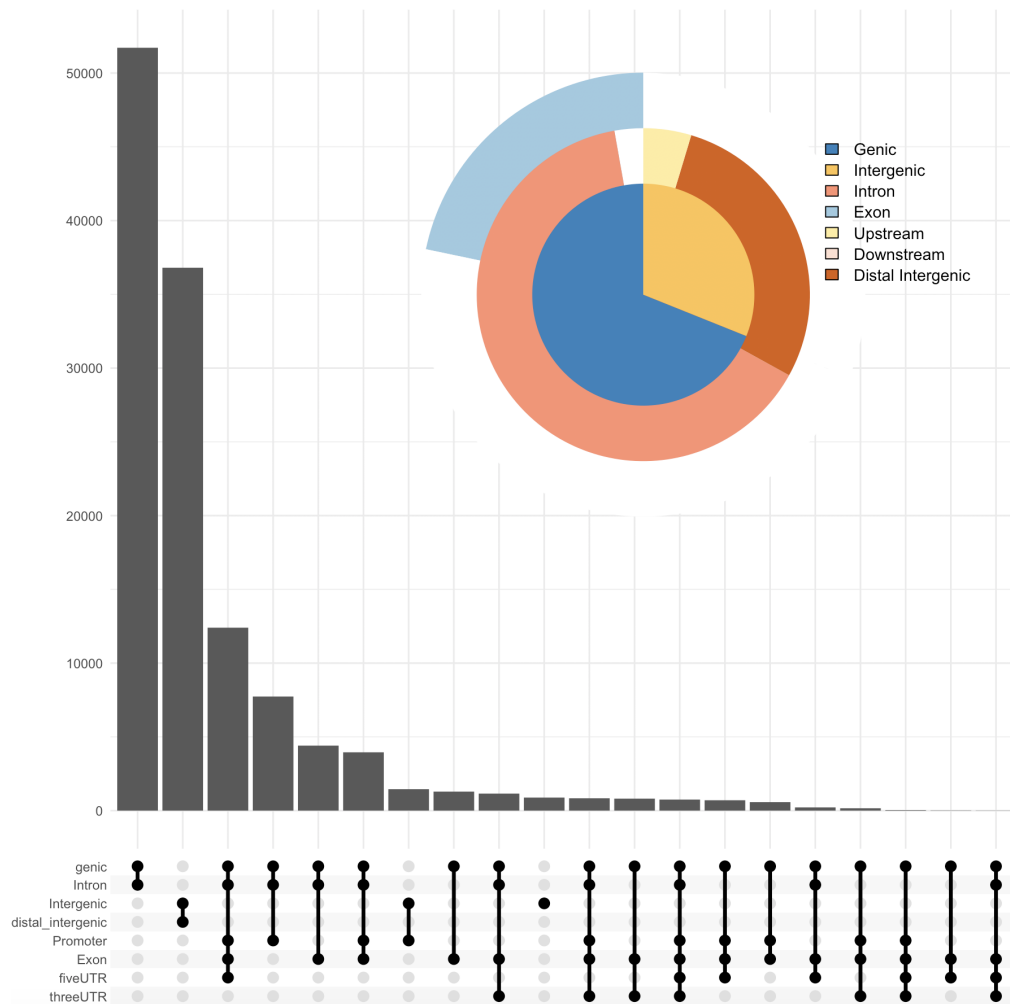
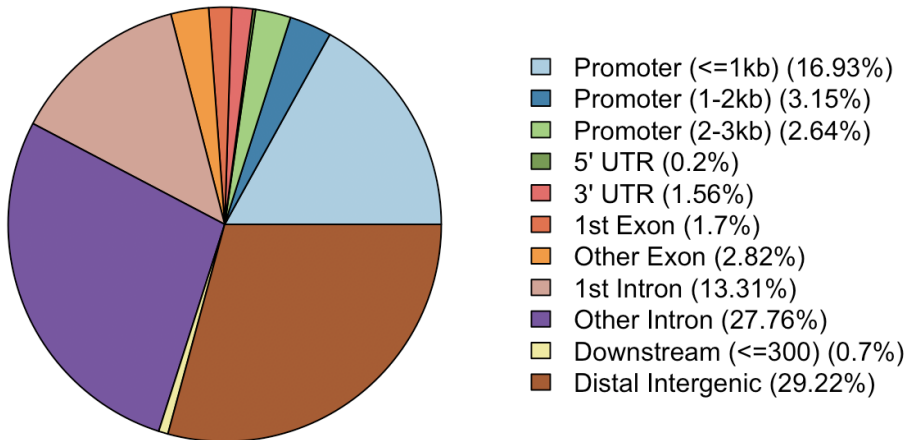
Supplemental Figure 7 Eigengene values for ATAC-seq modules obtained from WGCNA



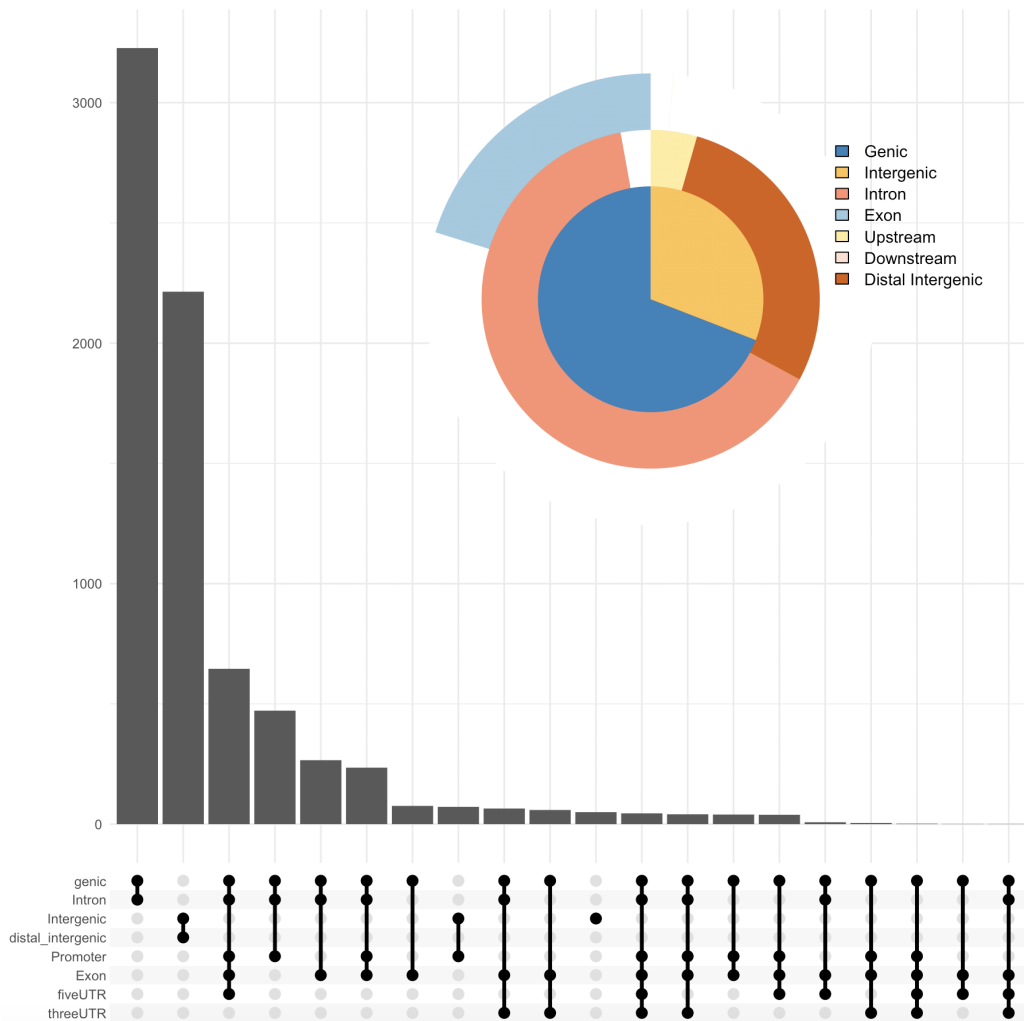
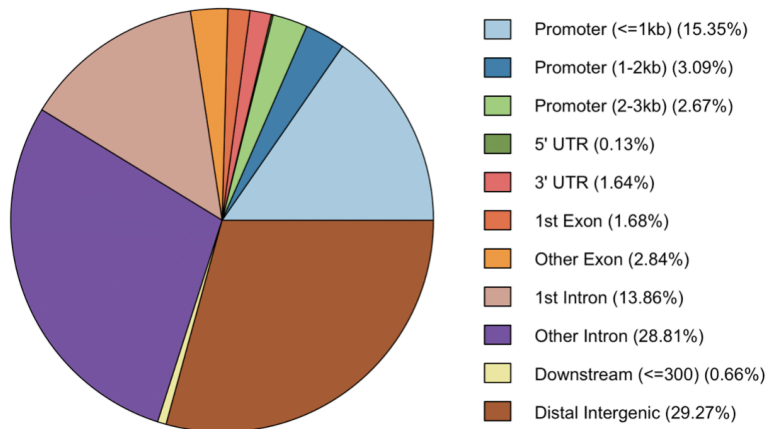
Supplemental Figure 7 Description: Eigengene modules from WGCNA of the longitudinal chromatin accessibility patterns of ATAC-seq data collected every 4 hours for a 48 hour period. Each color represents a fibroblast cell culture from a different individual. The number of chromatin accessible regions assigned per module is indicated next to the module name.

Supplementary Figure 8 Genomic annotation of the consensus peak regions and selected time significant regions

A. All consensus regions

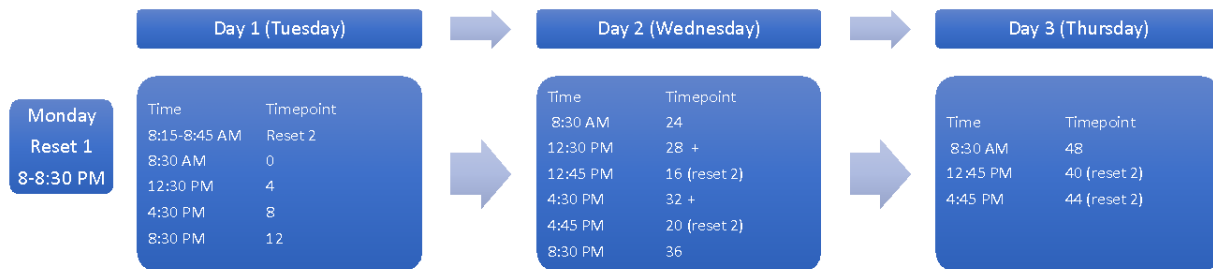


B. Time significant regions



Supplementary Figure 8 description: ChIPseeker annotations for peak regions. A. Genomic annotations for all n=126,057 consensus peak regions. B. Genomic annotations for the n=7,568 peaks that had a significant change over time in their accessibility.

Supplementary figure 9 Schematic of synchronization and collection times



Supplementary Figure 9 description: Collection scheme for both RNA-seq and ATA-seq fibroblast cell culture samples. Cells were reset 12 hours before the first collection. In order to collect RNA or cells every 4 hours for 48 hours, cells were split into two batches, which were reset 12 hours apart.