

Supplementary Materials

Association of Circadian Clock Gene Expression with Glioma Tumor Microenvironment and Patient Survival

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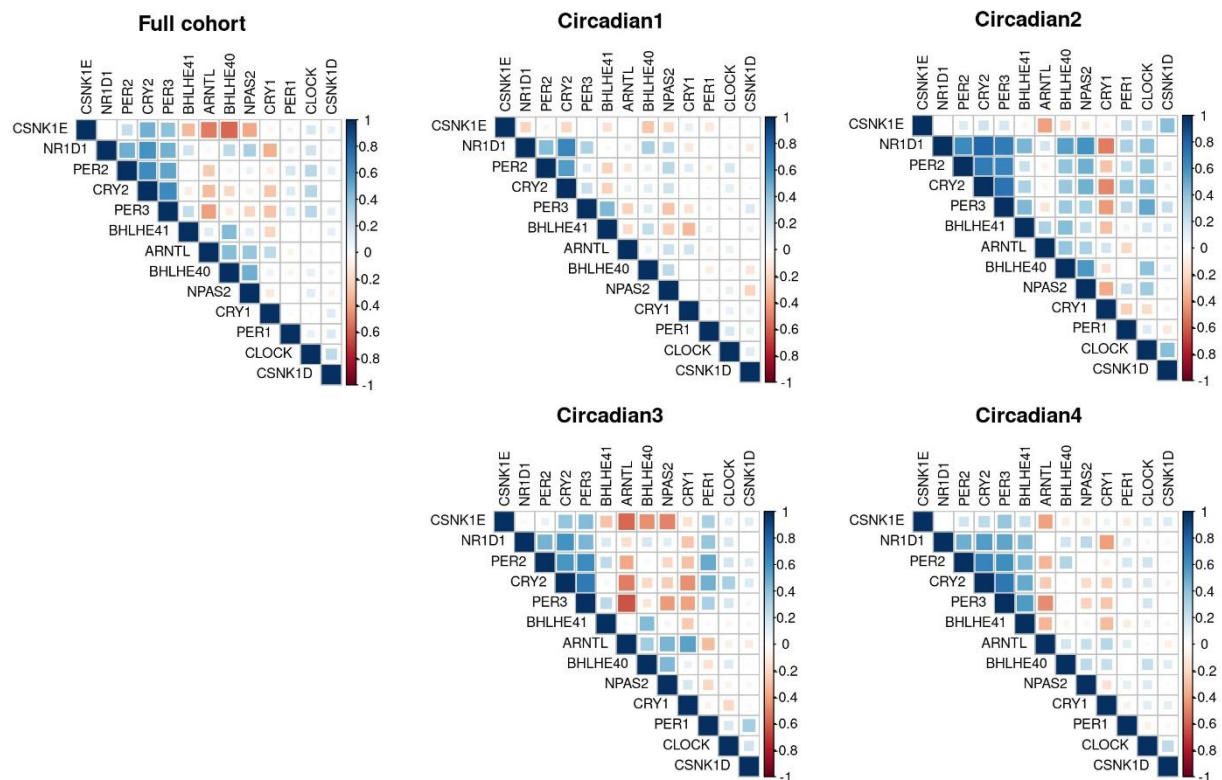


Figure S1. Graphs demonstrating the coordinated patterns of expression of clock genes in the TCGA data and unsupervised consensus clusters.

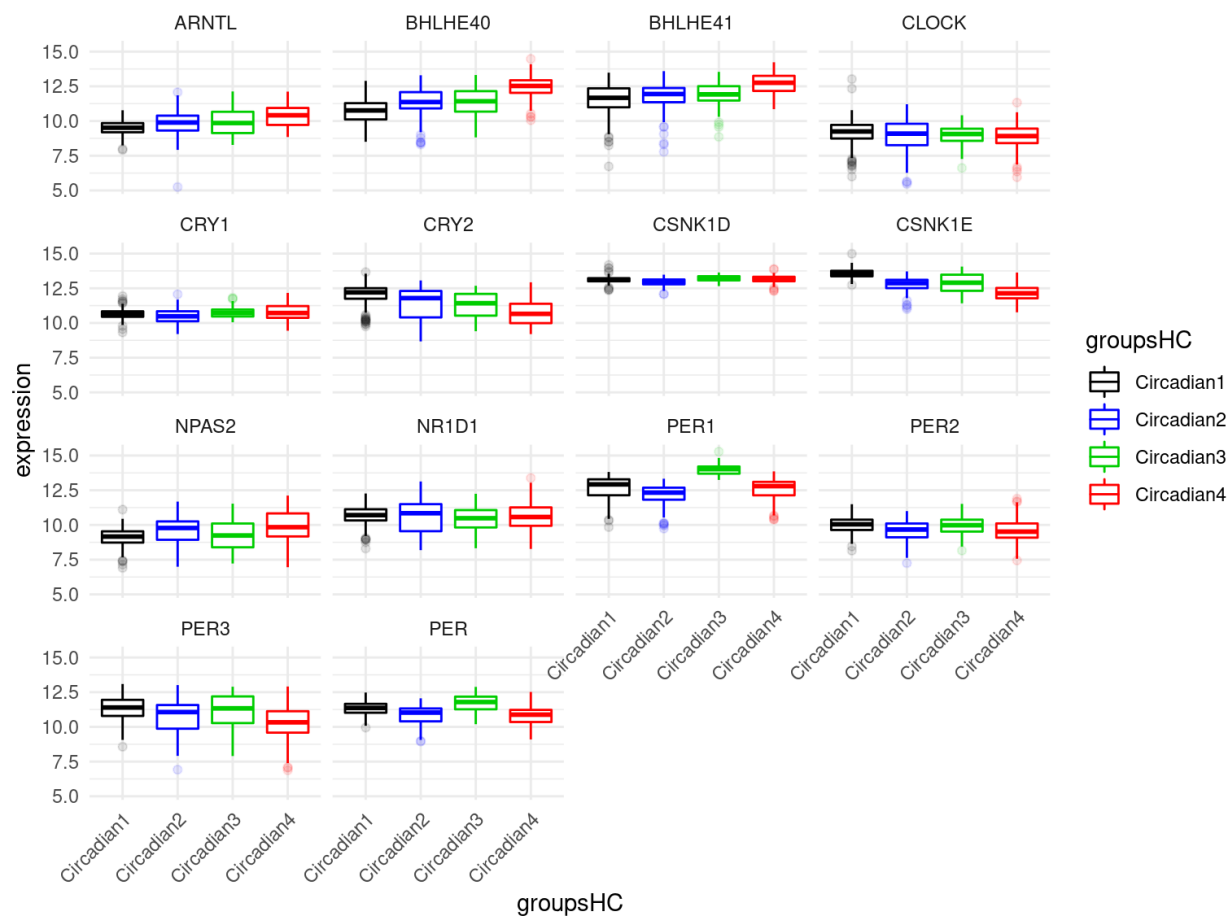


Figure S2. Clock gene expression in the Unsupervised clustering analysis.

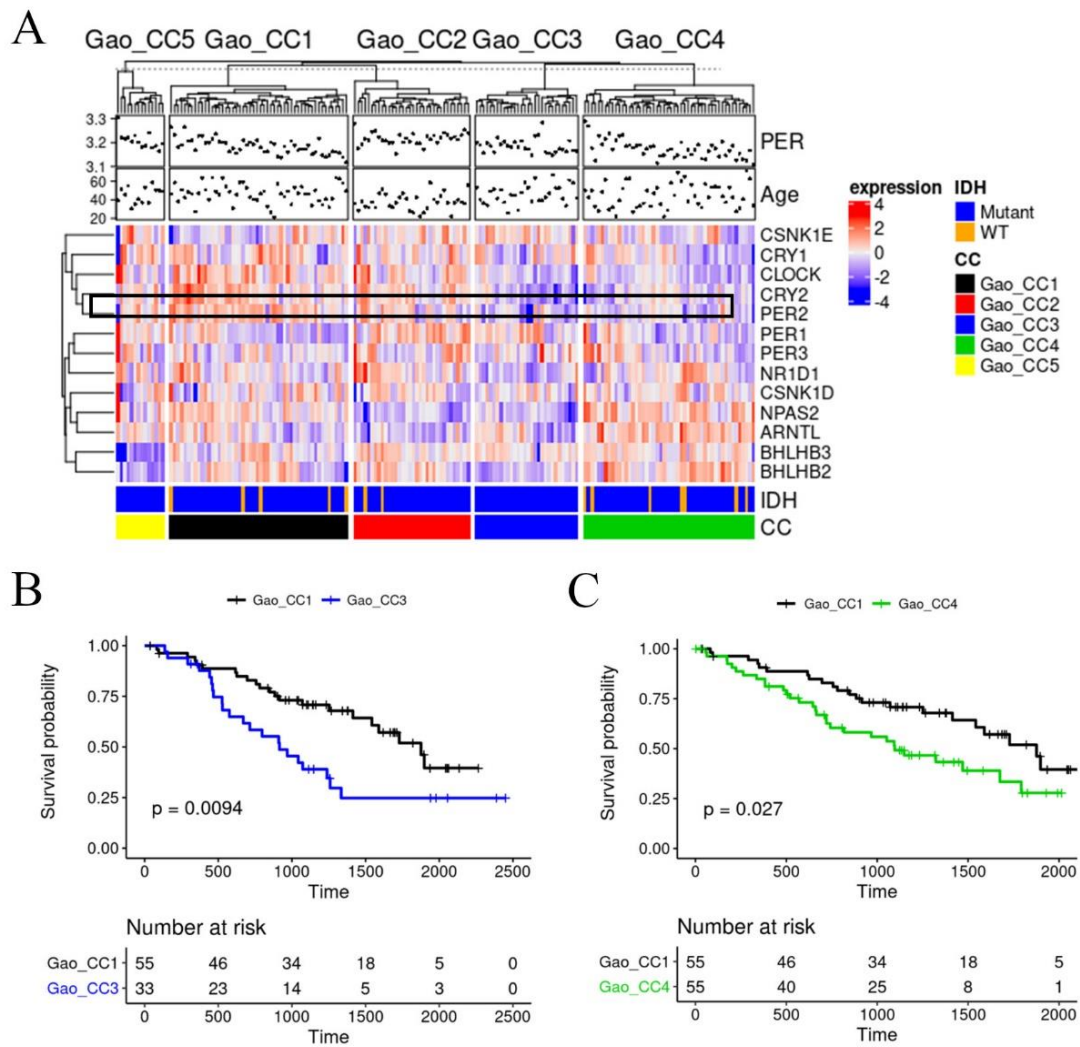


Figure S3. Prognostic relevance of PER in unsupervised clusters for LGG dataset.

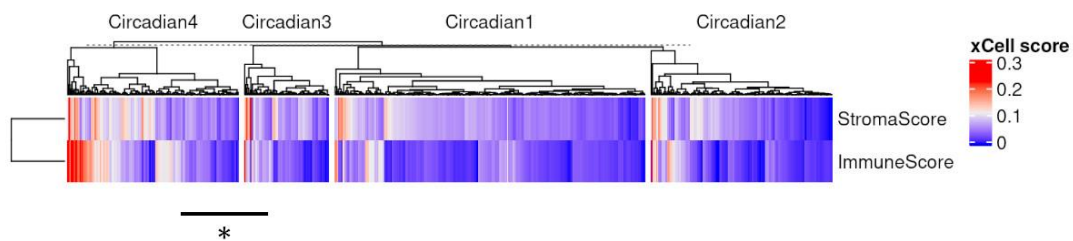


Figure S4. Contribution of different cell types in bulk tumor derived through a transcriptomic deconvolution algorithm.

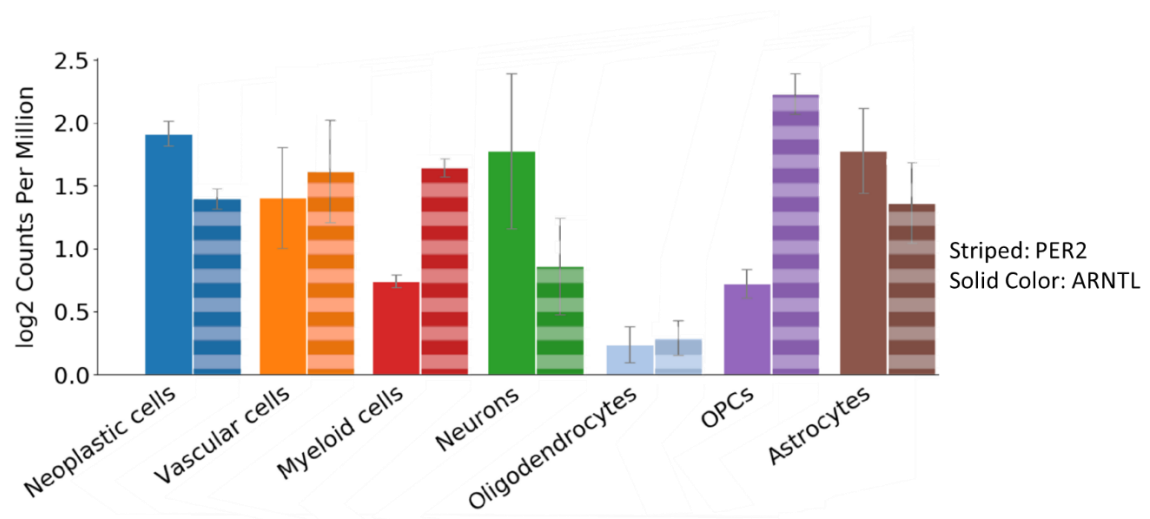


Figure S5. Differences in PER2 and ARNTL expression patterns between different cells of the tumor microenvironment.

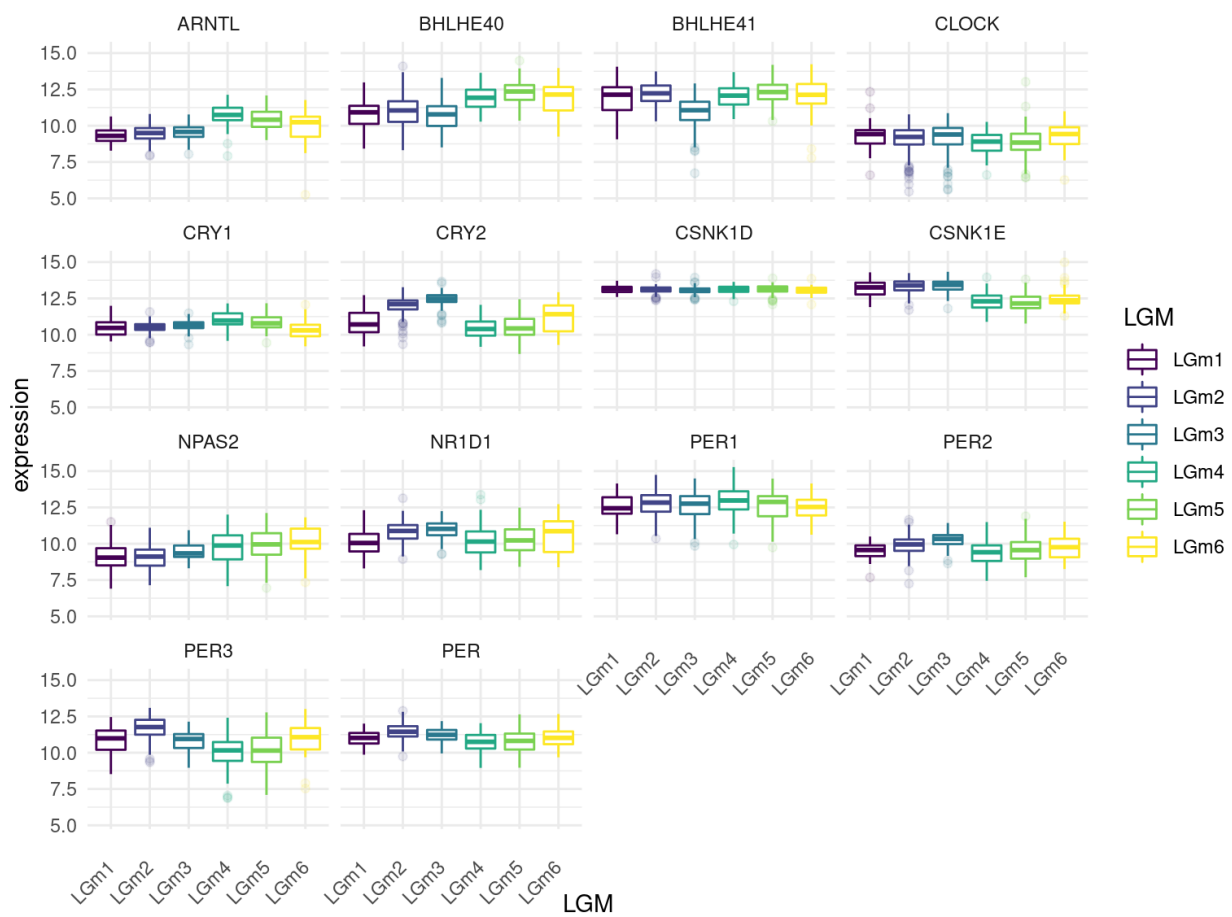


Figure S6. Clock gene expression in the subgroups separated by methylation status.

Table S1. Differences in clock gene expression between high and low PER expressing circadian clusters with predominantly IDH mutant or wild-type.

Circadian2 vs Circadian1				
gene	logFC	logCPMLR	PValue	FDR
ARNTL	0.5099157	4.36970964.5409047	0.00000000.0000000	
BHLHE40	0.6679979	5.78967669.4056474	0.00000000.0000000	
BHLHE41	0.1215525	6.5048872.0096113	0.15630540.1934536	
CLOCK	-0.07549723.9439700.6899571		0.40617900.4585456	
CRY1	-0.06993245.2135172.5647545		0.10926950.1395630	
CRY2	-0.48407696.62015535.6831852		0.00000000.0000000	
CSNK1D	-0.16271057.63195841.1579738		0.00000000.0000000	
CSNK1E	-0.74571537.924245358.51435130.00000000.0000000			
NPAS2	0.6526307	4.11445176.4362739	0.00000000.0000000	
NR1D1	0.1313123	5.4331082.6794321	0.10165200.1305154	
PER1	-0.52350857.24654552.0496282		0.00000000.0000000	
PER2	-0.39771074.54651643.1780577		0.00000000.0000000	
PER3	-0.43930305.95998824.5644610		0.00000070.0000018	
Circadian4 vs Circadian3				
gene	logFC	logCPMLR	PValue	FDR
ARNTL	0.2986951	5.0003976.9924615	0.00818540.0188575	
BHLHE40	1.0120603	6.98270666.7986798	0.00000000.0000000	
BHLHE41	0.7587220	7.21510046.0548514	0.00000000.0000000	
CLOCK	-0.04067913.7042230.1349282		0.71337610.7818568	
CRY1	0.0928333	5.4390471.3343710	0.24802910.3373284	
CRY2	-0.57610735.76364522.8909132		0.00000170.0000122	
CSNK1D	-0.03150967.7583610.6148198		0.43297880.5304049	
CSNK1E	-0.79490897.11890094.6417929		0.00000000.0000000	
NPAS2	0.6088404	4.66425017.8250353	0.00002420.0001207	
NR1D1	0.3253224	5.4129506.1109049	0.01343500.0289239	
PER1	-1.29913807.870965211.71432270.00000000.0000000			
PER2	-0.25103324.5195525.1130381		0.02374670.0471488	
PER3	-0.68638625.67600819.5286806		0.00000990.0000556	

Table S2. Kaplan-Meier analysis of overall survival between unsupervised consensus clusters.

	Circadian1	Circadian4	Circadian2
Circadian4	2×10^{-16}	-	-
Circadian2	4.9×10^{-7}	1.1×10^{-6}	-
Circadian3	1.3×10^{-6}	6.3×10^{-4}	0.7800

Table S3. Summary of full Cox model of the 13 core clock gene expression and reduced model of significant clock genes.

Full model					
	coef	exp(coef)	se(coef)	z	Pr(> z)
IDHWT	1.355	3.877	0.307	4.407	<0.001
age	0.046	1.047	0.007	6.255	<0.001
sexmale	-0.182	0.833	0.161	-1.133	0.257
ARNTL	0.157	1.169	0.115	1.366	0.172
BHLHE40	0.131	1.140	0.105	1.251	0.211
BHLHE41	0.027	1.027	0.108	0.251	0.802
CLOCK	0.097	1.102	0.104	0.937	0.349
CRY1	-0.171	0.842	0.185	-0.927	0.354
CRY2	-0.194	0.824	0.146	-1.328	0.184
CSNK1D	0.862	2.368	0.306	2.817	0.005
CSNK1E	0.028	1.028	0.168	0.164	0.869
NPAS2	-0.114	0.892	0.099	-1.154	0.248
NR1D1	0.117	1.125	0.135	0.872	0.383
PER1	0.093	1.097	0.086	1.081	0.280
PER2	-0.425	0.654	0.148	-2.881	0.004
PER3	-0.080	0.923	0.106	-0.751	0.452
Reduced model					
	coef	exp(coef)	se(coef)	z	Pr(> z)
IDHWT	1.671	5.318	0.214	7.821	<0.001
age	0.045	1.046	0.006	6.925	<0.001
sexmale	-0.130	0.878	0.157	-0.829	0.407
CSNK1D	0.942	2.565	0.299	3.151	0.002
PER2	-0.498	0.608	0.111	-4.491	<0.001

Table S4. Tumor composition analysis by deconvolution.

A) Immune Score				
Comparison	Diff	lwr	upr	padj
Circadian4-Circadian1	0.0513	0.0391	0.0634	0.0000
Circadian2-Circadian1	0.0024	-0.0096	0.0144	0.9550
Circadian3-Circadian1	0.0083	-0.0073	0.0240	0.5175
Circadian2-Circadian4	-0.0489	-0.0625	-0.0352	0.0000
Circadian3-Circadian4	-0.0429	-0.0599	-0.0260	0.0000
Circadian3-Circadian2	0.0059	-0.0109	0.0228	0.7996
B) Stroma Score				
Comparison	Diff	lwr	upr	padj
Circadian4-Circadian1	0.0244	0.0144	0.0344	0.0000
Circadian2-Circadian1	-0.0061	-0.0159	0.0038	0.3875
Circadian3-Circadian1	0.0141	0.0013	0.0270	0.0250
Circadian2-Circadian4	-0.0305	-0.0417	-0.0193	0.0000
Circadian3-Circadian4	-0.0103	-0.0242	0.0037	0.2303
Circadian3-Circadian2	0.0202	0.0064	0.0340	0.0011