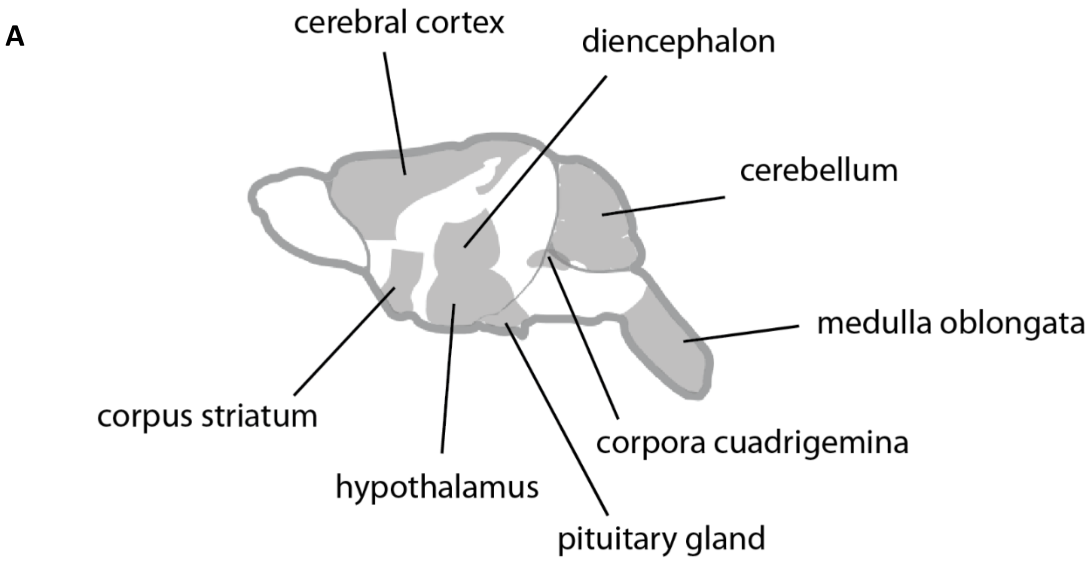
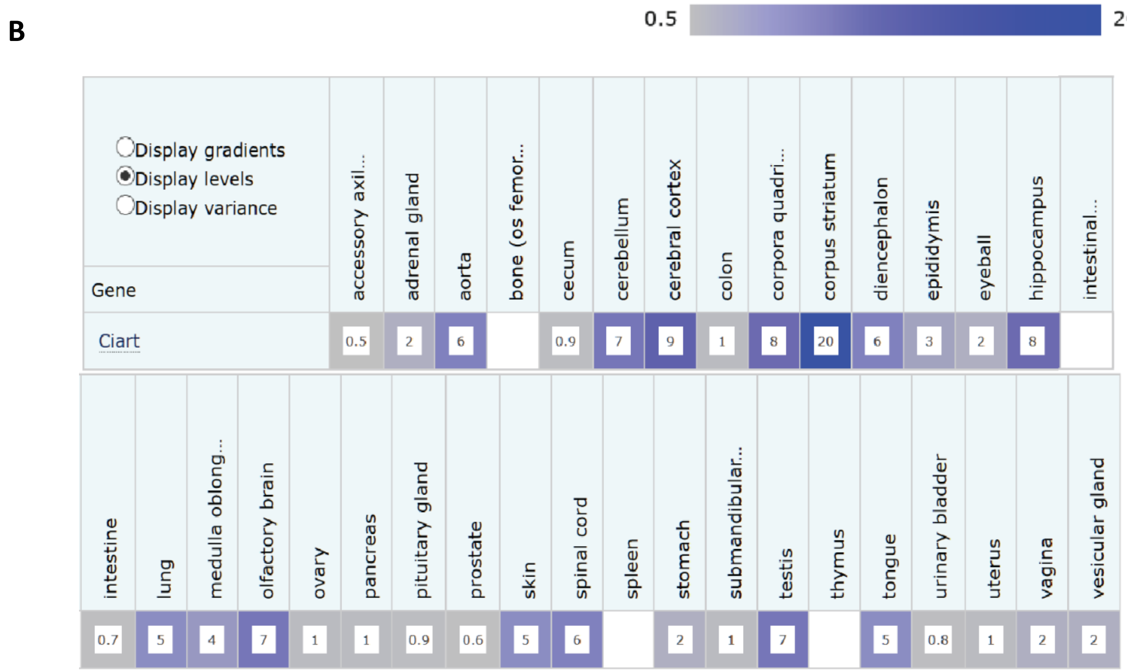
A Circadian Genomic Signature Common to Ketamine and Sleep Deprivation in the Anterior Cingulate Cortex

Supplemental Information





○Display gradients
●Display levels
○Display variance

Gene	accessory axil...	adrenal gland	aorta	bone (os femor...	cecum	cerebellum	cerebral cortex	colon	corpora quadri...	corpus striatum	diencephalon	epididymis	eyeball	hippocampus	intestinal...
Ciart	0.5	2	6		0.9	7	9	1	8	20	6	3	2	8	

intestine	lung	medulla oblong...	olfactory brain	ovary	pancreas	pituitary gland	prostate	skin	spinal cord	spleen	stomach	submandibular...	testis	thymus	tongue	urinary bladder	uterus	vagina	vesicular gland
0.7	5	4	7	1	1	0.9	0.6	5	6		2	1	7		5	0.8	1	2	2

Supplemental Figure S1. *Ciart* (CHRONO or GM129) is highly expressed in the cerebral cortex and striatum. Expression levels of the gene Ciart in different brain areas and peripheral tissues obtained by RNA-seq. A) Gray brain areas denote expression on the *Ciart* gene. B) Relative expression level on different brain areas. The color scale represents the RNA expression level. The data was accessed from the Expression Atlas (https://www.ebi.ac.uk/gxa/home).

Supplemental Table S1. Overview of gene expression changes on common 64 genes by ketamine or sleep deprivation treated mice.

						Circadian value (JTK)	
Symbol	**Description**	**% change SD**	**% change KT**	**t-test Sal-SD**	**t-test Sal-KT**	**-log (P)**	**-log (q)**
Syne1	synaptic nuclear envelope 1	6.6	-24.9	0.011	0.011	7.6	5.8
Lamp2	lysosomal-associated membrane protein 2	-10.3	-13.9	0.050	0.044	3.8	2.0
Tlr3	toll-like receptor 3	-22.2	-21.2	0.049	0.040	nd	nd
Vprbp	Vpr (HIV-1) binding protein	11.4	10.2	0.048	0.047	nd	nd
Ccdc72	coiled-coil domain containing 72	-15.6	-23.6	0.046	0.024	4.0	2.6
LOC100861909	major urinary protein 2-like	-33.0	-45.5	0.044	0.046	nd	nd
Tob1	transducer of ErbB-2.1	-7.6	-12.2	0.043	0.016	4.9	2.6
4930567K20Rik	RIKEN cDNA 4930567K20 gene	-15.5	-14.8	0.042	0.001	3.1	1.5
Csdc2	cold shock domain containing C2, RNA binding	22.4	4.8	0.041	0.013	2.9	1.3
Kir3dl1	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 1	-40.3	-36.4	0.041	0.018	nd	nd
Fgf1	fibroblast growth factor 1	15.7	15.1	0.040	0.045	10.6	10.6
2900010M23Rik	RIKEN cDNA 2900010M23 gene	-12.6	-19.9	0.040	0.028	4.0	2.6
Tlr8	toll-like receptor 8	-15.8	-27.2	0.040	0.004	nd	nd
Cecr2	cat eye syndrome chromosome region, candidate 2	-10.6	-20.2	0.040	0.001	4.2	1.9
Rps12	ribosomal protein S12	-9.7	-12.7	0.039	0.003	3.5	2.0
1110032A03Rik	RIKEN cDNA 1110032A03 gene	-9.7	-12.2	0.038	0.012	nd	nd
Rps27a	ribosomal protein S27A	-11.5	-12.6	0.036	0.035	3.1	1.8
Ranbp3l	RAN binding protein 3-like	-13.2	-12.1	0.036	0.039	2.6	1.5
Gm129	Circadian-associated repressor of transcription	-33.1	-15.6	0.035	0.004	11.5	7.9
Mylk	myosin, light polypeptide kinase	-7.5	-10.8	0.034	0.037	nd	nd
Gng10	guanine nucleotide binding protein (G protein), gamma 10	-20.6	-9.5	0.033	0.001	3.0	1.7
Olfr194	olfactory receptor 194	32.5	29.5	0.033	0.011	nd	nd
Gm9059	predicted gene 9059	20.6	59.7	0.033	0.034	nd	nd
Rpl37a	ribosomal protein L37a	-15.2	-14.8	0.032	0.014	4.6	2.8
Junb	Jun-B oncogene	-17.4	-27.5	0.032	0.008	4.7	3.3
Fam82a2	family with sequence similarity 82, member A2	16.5	-15.5	0.032	0.035	5.0	3.3
Tmem229b	transmembrane protein 229B	9.4	12.8	0.030	0.013	5.3	2.7
Ssbp3	single-stranded DNA binding protein 3	18.1	5.5	0.029	0.023	2.7	1.3
Alox15	arachidonate 15-lipoxygenase	18.5	22.2	0.029	0.016	5.2	2.7
Gpr183	G protein-coupled receptor 183	-8.8	5.8	0.028	0.002	nd	nd
Gm6249	predicted gene 6249	19.0	33.3	0.028	0.019	nd	nd
Mex3b	mex3 homolog B (C. elegans)	-15.4	-15.1	0.026	0.027	nd	nd
Mir672	microRNA 672	-21.2	-25.1	0.026	0.047	nd	nd
Gabrd	gamma-aminobutyric acid (GABA) A receptor, subunit delta	-10.7	-13.1	0.025	0.004	nd	nd
Slc31a2	solute carrier family 31, member 2	15.4	19.7	0.025	0.006	4.6	3.1
4932441J04Rik	RIKEN cDNA 4932441J04 gene	-15.8	-15.3	0.025	0.033	nd	nd
Snord14e	small nucleolar RNA, C/D box 14E	-45.1	-35.8	0.025	0.040	nd	nd
Vmn1r200	vomeronasal 1 receptor 200	-82.0	-67.0	0.025	0.034	nd	nd
0610007C21Rik	RIKEN cDNA 0610007C21 gene	-12.8	-12.5	0.024	0.042	4.3	2.3
Gm20043	predicted gene, 20043	26.6	43.0	0.023	0.037	nd	nd

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Cst3	cystatin C	-7.5	-7.7	0.022	0.012	4.1	1.8
Rpl23a	ribosomal protein L23A	-11.7	-10.4	0.022	0.029	2.2	1.4
Clip3	CAP-GLY domain containing linker protein 3	9.5	11.3	0.021	0.011	nd	nd
Olfr32	olfactory receptor 32	42.1	61.7	0.021	0.007	nd	nd
Adamts1	a disintegrin-like and metallopeptidase (reprolysin type) with thrombospondin type 1 motif, 1	17.1	-18.5	0.020	0.039	3.8	2.2
Pcdhb4	protocadherin beta 4	-11.1	-9.9	0.018	0.029	nd	nd
Bhlhe41	basic helix-loop-helix family, member e41	-21.2	-14.0	0.018	0.030	8.0	5.2
Sec61b	Sec61 beta subunit	-19.0	-18.7	0.017	0.015	3.4	2.1
Mir669k	microRNA 669k	-25.6	-26.6	0.015	0.007	nd	nd
6030419C18Rik	RIKEN cDNA 6030419C18 gene	7.8	-10.9	0.011	0.012	2.5	1.5
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.055	3.6	2.0
Gm17756	predicted gene, 17756	25.4	13.5	0.010	0.048	nd	nd
Lrrc2	leucine rich repeat containing 2	-12.3	-6.8	0.010	0.034	4.1	2.1
Pigp	phosphatidylinositol glycan anchor biosynthesis, class P	-7.5	-15.6	0.009	0.050	nd	nd
Pitx1	paired-like homeodomain transcription factor 1	-15.8	-16.1	0.009	0.033	nd	nd
Zfp58	zinc finger protein 58	-13.0	-12.9	0.008	0.007	nd	nd
Fos	FBJ osteosarcoma oncogene	-23.9	-25.9	0.008	0.007	5.3	2.3
Gm8158	predicted gene 8158	-9.6	-10.2	0.004	0.039	nd	nd
Mup4	major urinary protein 4	462.1	437.1	0.003	0.046	3.3	1.8
Grcc10	gene rich cluster, C10 gene	-8.4	-5.9	0.001	0.040	3.2	1.8
Shd	src homology 2 domain-containing transforming protein D	-22.2	-12.1	0.000	0.007	nd	nd
Ammecr1l	AMME chromosomal region gene 1-like	14.4	-8.0	0.042	0.020	2.9	1.5
Gm10408	predicted gene 10408	-11.5	-13.7	0.045	0.017	nd	nd
Hist2h3b	histone cluster 2, H3b	-37.4	-39.3	0.047	0.005	11.3	9.0

Supplemental Table S2. Overview of gene expression changes in the cingulate cortex of ketamine and sleep deprivation treated mice.

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Nervous system development							
Mef2c	myocyte enhancer factor 2C	-9.7	-7.2	0.022	0.189	ns	ns
Ina	internexin neuronal intermediate filament protein, alpha	16.6	0.9	0.021	0.865	4.6	1.9
Nrp1	neuropilin 1	29.3	0.5	0.011	0.956	4.2	2.4
Mdga1	MAM domain containing glycosylphosphatidylinositol anchor 1	42.8	0.6	0.002	0.945	ns	ns
Scn2a1	sodium channel, voltage-gated, type II, alpha 1	-9.7	-4.1	0.007	0.385	3.8	2.2
Ttll7	tubulin tyrosine ligase-like family, member 7	-15.0	-7.9	0.029	0.232	ns	ns
Nrxn1	neurexin I	-9.1	-5.4	0.018	0.063	4.3	1.8
Sufu	suppressor of fused homolog (Drosophila)	10.5	2.7	0.047	0.374	4.1	2.7
Slc11a2	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	-9.3	-11.5	0.019	0.050	4.3	3.0
Pfn1	profilin 1	16.1	8.3	0.042	0.092	3.1	1.7
Myt1l	myelin transcription factor 1-like	10.9	-4.4	0.026	0.307	2.2	1.4
Epha7	Eph receptor A7	-11.3	-17.3	0.038	0.149	2.8	1.5
Slitrk4	SLIT and NTRK-like family, member 4	-12.5	-3.6	0.028	0.669	ns	ns
Btg2	B cell translocation gene 2, anti-proliferative	-25.7	-12.1	0.038	0.185	4.4	1.9
Sema7a	sema domain, immunoglobulin domain (Ig), and GPI membrane anchor, (semaphorin) 7A	13.8	-6.7	0.014	0.366	4.0	2.4
Sema3e	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3E	29.2	-1.2	0.007	0.945	4.9	2.2
Myo16	myosin XVI	-28.2	-15.4	0.035	0.090	ns	ns
Etv1	ets variant gene 1	-23.9	-3.8	0.007	0.603	5.0	3.1
Cntn4	contactin 4	-13.4	-10.4	0.020	0.123	3.5	1.7
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.055	3.6	2.0
Fgf5	fibroblast growth factor 5	-0.3	-16.2	0.970	0.004	ns	ns
Ush1g	Usher syndrome 1G	1.1	24.1	0.883	0.006	ns	ns
Nr2e1	nuclear receptor subfamily 2, group E, member 1	-4.9	-18.1	0.635	0.031	5.1	2.3
Ttc3	tetratricopeptide repeat domain 3	-3.0	-7.1	0.178	0.010	2.9	1.6
Ckb	creatine kinase, brain	-4.9	-9.0	0.210	0.001	5.0	3.1
Otp	orthopedia homolog (Drosophila)	1.8	12.7	0.768	0.040	3.1	1.7
Lamb2	laminin, beta 2	5.1	-6.4	0.123	0.035	3.8	1.6
Hoxa3	homeobox A3	-9.8	15.9	0.432	0.037	ns	ns
Bag1	BCL2-associated athanogene 1	-6.1	-18.1	0.390	0.013	4.6	2.8
Crb1	crumbs homolog 1 (Drosophila)	9.9	20.9	0.169	0.012	2.3	1.4
Atg7	autophagy related 7	4.8	4.2	0.528	0.036	2.9	1.8
Tlx2	T cell leukemia, homeobox 2	2.9	18.4	0.781	0.032	2.7	1.6
Etv4	ets variant gene 4 (E1A enhancer binding protein, E1AF)	-5.1	9.3	0.472	0.003	ns	ns
Tes	testis derived transcript	0.5	-17.7	0.948	0.045	3.8	2.0
Dvl2	dishevelled 2, dsh homolog (Drosophila)	-4.0	8.6	0.581	0.007	3.5	1.9
Irs2	insulin receptor substrate 2	14.2	-16.8	0.156	0.006	4.3	2.5
Scd2	stearoyl-Coenzyme A desaturase 2	1.0	9.2	0.786	0.000	6.8	4.3
Nkx2-6	NK2 transcription factor related, locus 6 (Drosophila)	19.1	6.7	0.125	0.684	2.9	1.7
Foxa1	forkhead box A1	-0.2	26.9	0.988	0.045	ns	ns
Grin1	glutamate receptor, ionotropic, NMDA1 (zeta 1)	-0.8	-3.8	0.632	0.000	3.3	1.4
Efnb2	ephrin B2	-5.5	-8.2	0.115	0.013	ns	ns
Sphk1	sphingosine kinase 1	9.4	15.9	0.450	0.011	4.2	2.5
Emx2	empty spiracles homolog 2 (Drosophila)	-3.5	-14.7	0.747	0.025	ns	ns
Neurog1	neurogenin 1	-21.1	35.3	0.229	0.005	2.9	1.4
Dll1	delta-like 1 (Drosophila)	-2.3	12.8	0.780	0.114	ns	ns
Nkx6-1	NK6 homeobox 1	8.7	22.0	0.170	0.012	4.7	2.2
Tacc2	transforming, acidic coiled-coil containing protein 2	3.9	-6.0	0.700	0.016	5.3	3.3

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Pcdh18	protocadherin 18	-1.0	-7.1	0.519	0.023	5.1	3.1
Hes1	hairy and enhancer of split 1 (Drosophila)	13.3	-9.1	0.200	0.033	2.2	1.4
Hoxb3	homeobox B3	9.5	17.8	0.493	0.288	ns	ns
Eya1	eyes absent 1 homolog (Drosophila)	-6.5	-9.4	0.306	0.005	5.8	3.7
Hes5	hairy and enhancer of split 5 (Drosophila)	-3.7	23.2	0.665	0.032	ns	ns
Zic5	zinc finger protein of the cerebellum 5	-4.9	2.9	0.505	0.652	ns	ns
Cx3cr1	chemokine (C-X3-C) receptor 1	0.7	4.7	0.881	0.027	3.9	2.3
Bmp7	bone morphogenetic protein 7	-2.1	-7.1	0.621	0.003	3.0	1.9
Lrp2	low density lipoprotein receptor-related protein 2	4.1	14.9	0.646	0.010	3.3	1.8
Tbx19	T-box 19	-3.8	18.1	0.683	0.027	5.1	2.7
Transmembran receptor protein tyrosine kinase signaling pathway							
Epha7	Eph receptor A7	-11.3	-17.3	0.038	0.149	2.8	1.5
Epha6	Eph receptor A6	-19.9	-9.6	0.011	0.174	5.7	2.6
Nrp1	neuropilin 1	29.3	0.5	0.011	0.956	4.2	2.4
Sorbs1	sorbin and SH3 domain containing 1	18.2	2.5	0.033	0.601	11.2	8.9
Flt3	FMS-like tyrosine kinase 3	-13.3	-8.1	0.013	0.372	2.8	1.6
Epha8	Eph receptor A8	-14.6	2.1	0.010	0.511	ns	ns
Grb2	growth factor receptor bound protein 2	12.8	1.4	0.048	0.761	ns	ns
Ctgf	connective tissue growth factor	13.8	-0.8	0.045	0.858	10.2	6.8
Zfand5	zinc finger, AN1-type domain 5	-7.8	-8.2	0.059	0.046	4.8	2.9
Ddr1	discoidin domain receptor family, member 1	-17.6	-10.1	0.031	0.013	ns	ns
Fgf5	fibroblast growth factor 5	-0.3	-16.2	0.970	0.004	ns	ns
Irs2	insulin receptor substrate 2	14.2	-16.8	0.156	0.006	4.3	2.5
Musk	muscle, skeletal, receptor tyrosine kinase	-13.2	25.2	0.051	0.018	ns	ns
Csrnp1	cysteine-serine-rich nuclear protein 1	10.6	-25.9	0.425	0.048	3.6	1.6
Tiparp	TCDD-inducible poly(ADP-ribose) polymerase	-10.7	-30.9	0.414	0.014	4.6	2.2
Angpt1	angiopoietin 1	-17.6	-4.7	0.171	0.734	2.7	1.3
Zfp640	zinc finger protein 640 // zinc finger protein 640	60.7	-80.4	0.515	0.009	ns	ns
Fgf4	fibroblast growth factor 4	-2.1	15.1	0.764	0.018	3.1	1.7
Cell motion							
Epha7	Eph receptor A7	-11.3	-17.3	0.038	0.149	2.8	1.5
Nrp1	neuropilin 1	29.3	0.5	0.011	0.956	4.2	2.4
Ctgf	connective tissue growth factor	13.8	-0.8	0.045	0.858	10.2	6.8
Mdga1	MAM domain containing glycosylphosphatidylinositol anchor 1	42.8	0.6	0.002	0.945	ns	ns
Etv1	ets variant gene 1	-23.9	-3.8	0.007	0.603	5.0	3.1
Nup85	nucleoporin 85	8.7	-0.7	0.031	0.860	3.4	2.2
Cx3cl1	chemokine (C-X3-C motif) ligand 1	16.1	1.3	0.017	0.703	4.3	2.3
Itga4	integrin alpha 4	-16.2	-8.6	0.030	0.234	ns	ns
Scg2	secretogranin II	31.3	-7.5	0.005	0.149	ns	ns
Elmo1	engulfment and cell motility 1, ced-12 homolog (C. elegans)	8.8	-2.4	0.032	0.677	5.3	2.3
Zfand5	zinc finger, AN1-type domain 5	-7.8	-8.2	0.059	0.046	4.8	2.9
Apoa1	apolipoprotein A-I	16.7	20.9	0.293	0.023	ns	ns
Nup62	nucleoporin 62	6.6	8.8	0.326	0.005	10.9	8.6
Emx2	empty spiracles homolog 2 (Drosophila)	-3.5	-14.7	0.747	0.025	ns	ns
Cx3cr1	chemokine (C-X3-C) receptor 1	0.7	4.7	0.881	0.027	3.9	2.3
Myh9	myosin, heavy polypeptide 9, non-muscle	16.8	-13.4	0.178	0.023	ns	ns
Bmp7	bone morphogenetic protein 7	-2.1	-7.1	0.621	0.003	3.0	1.9
Zfp640	zinc finger protein 640 // zinc finger protein 640	60.7	-80.4	0.515	0.009	ns	ns
Nr2e1	nuclear receptor subfamily 2, group E, member 1	-4.9	-18.1	0.635	0.031	5.1	2.3
Tnp2	transition protein 2 // transition protein 2	6.3	31.9	0.304	0.012	4.4	2.2
Etv4	ets variant gene 4 (E1A enhancer binding protein, E1AF)	-5.1	9.3	0.472	0.003	ns	ns

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Tes	testis derived transcript	0.5	-17.7	0.948	0.045	3.8	2.0
Cholinergic synapse							
Camk2g	calcium/calmodulin-dependent protein kinase II gamma	-10.0	-5.8	0.000	0.146	11.5	7.9
Camk4	calcium/calmodulin-dependent protein kinase IV	-9.4	-10.9	0.053	0.219	ns	ns
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.057	3.6	2.0
Creb3l3	cAMP responsive element binding protein 3-like 3	4.2	29.9	0.770	0.040	3.4	2.2
Fos	FBJ osteosarcoma oncogene	-23.9	-25.9	0.008	0.007	5.3	2.3
Gng3	guanine nucleotide binding protein (G protein), gamma 3	-4.7	12.8	0.510	0.077	2.2	1.4
Itpr2	inositol 1,4,5-triphosphate receptor 2	-0.4	-7.1	0.961	0.031	5.1	3.4
Kcnj3	potassium inwardly-rectifying channel, subfamily J, member 3	-13.2	-4.0	0.003	0.442	6.8	4.4
Kcnq2	potassium voltage-gated channel, subfamily Q, member 2	16.1	-1.1	0.063	0.732	ns	ns
Kcnq4	potassium voltage-gated channel, subfamily Q, member 4	-5.1	14.5	0.059	0.022	ns	ns
Kcnq5	potassium voltage-gated channel, subfamily Q, member 5	-6.4	-7.0	0.049	0.199	2.9	1.7
Pik3r2	phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 2 (p85 beta)	-4.2	-7.8	0.518	0.006	3.3	1.8
Plcb4	phospholipase C, beta 4	-9.8	-13.3	0.072	0.181	5.5	3.5
Cell morphogenesis involved in neuron differentiation							
3110039M20Rik	RIKEN cDNA 3110039M20 gene	17.2	-4.2	0.012	0.602	ns	ns
Slc11a2	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	-9.3	-11.5	0.019	0.050	5.4	3.1
Slitrk4	SLIT and NTRK-like family, member 4	-12.5	-3.6	0.028	0.669	ns	ns
Epha7	Eph receptor A7	-11.3	-17.3	0.038	0.149	2.8	1.5
Nrp1	neuropilin 1	29.3	0.5	0.011	0.956	4.2	2.4
Etv1	ets variant gene 1	-23.9	-3.8	0.007	0.603	5.0	3.1
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.057	4.4	2.2
Hes1	hairy and enhancer of split 1 (Drosophila)	13.3	-9.1	0.200	0.033	2.2	1.4
Lamb2	laminin, beta 2	5.1	-6.4	0.123	0.035	3.8	1.6
Bmp7	bone morphogenetic protein 7	-2.1	-7.1	0.621	0.003	3.0	1.9
Nr2e1	nuclear receptor subfamily 2, group E, member 1	-4.9	-18.1	0.635	0.031	5.1	2.3
Etv4	ets variant gene 4 (E1A enhancer binding protein, E1AF)	-5.1	9.3	0.472	0.003		
Notch signaling pathway							
Dvl2	dishevelled 2, dsh homolog (Drosophila)	-4.0	8.6	0.581	0.007	3.5	1.9
Hes1	hairy and enhancer of split 1 (Drosophila)	13.3	-9.1	0.200	0.033	2.2	1.4
Notch2	notch 2	-2.1	-11.6	0.800	0.022	3.9	2.1
Mfng	MFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	-16.0	6.7	0.038	0.551	4.5	2.1
Hes5	hairy and enhancer of split 5 (Drosophila)	-3.7	23.2	0.665	0.032	ns	ns
Aph1a	anterior pharynx defective 1a homolog (C. elegans)	9.8	-2.7	0.681	0.815	5.2	3.7
Dll1	delta-like 1 (Drosophila)	-2.3	12.8	0.780	0.114	ns	ns
Maml3	mastermind like 3 (Drosophila)	38.4	0.2	0.021	0.976	ns	ns
Numbl	numb-like	2.2	-11.5	0.691	0.005	4.0	2.4
Neuroactive ligand-receptor interaction							
Taar7e	trace amine-associated receptor 7E	-1.8	24.1	0.935	0.028	ns	ns
Glra1	glycine receptor, alpha 1 subunit	16.4	10.2	0.044	0.289	3.3	1.8
Gabra4	gamma-aminobutyric acid (GABA) A receptor, subunit alpha 4	-12.5	-7.0	0.014	0.194	ns	ns
Drd5	dopamine receptor D5	-4.6	-3.2	0.576	0.740	ns	ns
Gabra6	gamma-aminobutyric acid (GABA) A receptor, subunit alpha 6	-7.8	30.6	0.566	0.010	ns	ns
Grin1	glutamate receptor, ionotropic, NMDA1 (zeta 1)	-0.8	-3.8	0.632	0.000	3.3	1.4
Grin3b	glutamate receptor, ionotropic, NMDA3B	-3.2	15.3	0.795	0.021	ns	ns
Gria3	glutamate receptor, ionotropic, AMPA3 (alpha 3)	-7.5	-5.1	0.000	0.430	5.8	3.7
Plg	plasminogen	-12.2	40.0	0.549	0.004	ns	ns
Hcrtr1	hypocretin (orexin) receptor 1	-9.9	8.7	0.296	0.023	ns	ns

						Circadian value (JTK)	
Symbol	**Description**	**% change SD**	**% change KT**	**t-test Sal-SD**	**t-test Sal-KT**	**-log (P)**	**-log (q)**
P2ry10	purinergic receptor P2Y, G-protein coupled 10	62.9	38.2	0.012	0.023	3.0	1.5
Sstr2	somatostatin receptor 2	12.1	4.6	0.033	0.290	ns	ns
Grm3	glutamate receptor, metabotropic 3	-12.3	-1.8	0.022	0.735	2.2	1.4
Adrb1	adrenergic receptor, beta 1	-8.5	-7.0	0.097	0.021	2.8	1.5
Sstr3	somatostatin receptor 3	7.6	17.8	0.223	0.006	4.8	2.2
Gria2	glutamate receptor, ionotropic, AMPA2 (alpha 2)	-3.7	-2.4	0.021	0.570	ns	ns
Grin2c	glutamate receptor, ionotropic, NMDA2C (epsilon 3)	2.9	-9.9	0.750	0.155	4.4	2.2
Galr3	galanin receptor 3	21.1	43.5	0.066	0.002	ns	ns
Hrh4	histamine receptor H4	-2.6	-11.9	0.818	0.003	ns	ns
Ghsr	growth hormone secretagogue receptor	12.1	19.2	0.421	0.042	ns	ns
Nmbr	neuromedin B receptor	13.3	10.6	0.162	0.020	ns	ns
Ctsg	cathepsin G	-0.7	26.2	0.961	0.046	ns	ns
Glp1r	glucagon-like peptide 1 receptor	19.3	32.3	0.089	0.014	ns	ns
Htr5b	5-hydroxytryptamine (serotonin) receptor 5B	32.8	-2.0	0.009	0.781	ns	ns
Glycine, serine and threonine metabolism							
Alas2	aminolevulinic acid synthase 2, erythroid	28.3	4.3	0.001	0.693	ns	ns
Gcat	glycine C-acetyltransferase (2-amino-3-ketobutyrate-coenzyme A ligase)	-8.5	-6.7	0.003	0.277	6.4	4.7
Agxt2	alanine-glyoxylate aminotransferase 2	0.2	16.1	0.989	0.010	ns	ns
Gnmt	glycine N-methyltransferase	-0.1	24.0	0.991	0.008	2.2	1.4
Sardh	sarcosine dehydrogenase	1.3	5.3	0.783	0.191	4.0	2.0
Cbs	cystathionine beta-synthase	14.5	-3.9	0.014	0.267	14.8	12.0
MAPK signaling pathway							
Mef2c	myocyte enhancer factor 2C	-9.7	-7.2	0.022	0.189	ns	ns
Fgf5	fibroblast growth factor 5	-0.3	-16.2	0.970	0.004	ns	ns
Grb2	growth factor receptor bound protein 2	12.8	1.4	0.048	0.761	ns	ns
Fgf14	fibroblast growth factor 14	-15.0	-7.8	0.009	0.116	3.7	2.0
Fgf17	fibroblast growth factor 17	-3.1	24.0	0.852	0.032	3.7	2.0
Fgf11	fibroblast growth factor 11	12.5	5.7	0.046	0.403	3.8	1.9
Elk1	ELK1, member of ETS oncogene family	22.3	0.9	0.013	0.823	ns	ns
Hspa1b	heat shock protein 1B	37.7	-11.6	0.016	0.391	3.3	2.2
Mapkapk2	MAP kinase-activated protein kinase 2	3.0	-9.7	0.660	0.021	6.1	3.7
Ppm1b	protein phosphatase 1B, magnesium dependent, beta isoform	-0.9	-10.8	0.729	0.034	11.5	9.2
Hspa1l	heat shock protein 1-like	4.8	34.7	0.673	0.033	3.4	1.9
Nfatc4	nuclear factor of activated T cells, cytoplasmic, calcineurin dependent 4	13.9	32.2	0.375	0.004	2.2	1.4
Fas	Fas (TNF receptor superfamily member 6)	16.6	12.5	0.214	0.008	5.7	3.8
Fgf4	fibroblast growth factor 4	-2.1	15.1	0.764	0.018	3.1	1.7
Relb	avian reticuloendotheliosis viral (v-rel) oncogene related B	-4.6	8.5	0.365	0.021	3.6	1.9
Cacna2d3	calcium channel, voltage-dependent, alpha2/delta subunit 3	13.2	-13.6	0.012	0.042	3.9	2.2
Dusp5	dual specificity phosphatase 5	15.1	-27.7	0.191	0.010	2.6	1.5
Dusp1	dual specificity phosphatase 1	-5.6	-11.2	0.542	0.007	4.6	2.5
Gadd45g	growth arrest and DNA-damage-inducible 45 gamma	-22.2	-20.2	0.127	0.003	3.6	2.0
Pla2g6	phospholipase A2, group VI	-7.0	-4.9	0.118	0.012	5.1	2.3
Rap1b	RAS related protein 1b	-2.6	-9.7	0.754	0.022	5.3	3.0
Gadd45b	growth arrest and DNA-damage-inducible 45 beta	-16.0	-22.6	0.158	0.023	5.2	2.8
Dusp8	dual specificity phosphatase 8	-2.5	-10.8	0.704	0.031	ns	ns
Ppp5c	protein phosphatase 5, catalytic subunit	-5.4	-10.2	0.140	0.026	3.5	1.4
Dusp6	dual specificity phosphatase 6	7.4	-19.0	0.229	0.005	3.3	1.5
Pathways in cancer							
Bid	BH3 interacting domain death agonist	-0.8	9.6	0.894	0.039	4.9	3.5
Fgf5	fibroblast growth factor 5	-0.3	-16.2	0.970	0.004	ns	ns

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Grb2	growth factor receptor bound protein 2	12.8	1.4	0.048	0.761	ns	ns
Fgf14	fibroblast growth factor 14	-15.0	-7.8	0.009	0.116	3.7	2.0
Fgf17	fibroblast growth factor 17	-3.1	24.0	0.852	0.032	3.7	2.0
Fgf11	fibroblast growth factor 11	12.5	5.7	0.046	0.403	3.8	1.9
Sufu	suppressor of fused homolog (Drosophila)	10.5	2.7	0.047	0.374	5.1	2.7
Lamb2	laminin, beta 2	5.1	-6.4	0.123	0.035	3.8	1.6
Cdkn2a	cyclin-dependent kinase inhibitor 2A	3.4	10.9	0.650	0.034	ns	ns
Itgav	integrin alpha V	-9.9	-10.1	0.017	0.140	2.4	1.4
Nkx3-1	NK-3 transcription factor, locus 1 (Drosophila)	2.9	22.9	0.780	0.030	ns	ns
Flt3l	FMS-like tyrosine kinase 3 ligand // FMS-like tyrosine kinase 3 ligand	9.0	23.7	0.427	0.033	4.2	2.7
Fas	Fas (TNF receptor superfamily member 6)	16.6	12.5	0.214	0.008	5.7	3.8
Csf2ra	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	6.8	13.3	0.048	0.048	ns	ns
Pik3r2	phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 2 (p85 beta)	-4.2	-7.8	0.518	0.006	3.3	1.8
Fgf4	fibroblast growth factor 4	-2.1	15.1	0.764	0.018	3.1	1.7
Fn1	fibronectin 1	21.5	-7.4	0.016	0.157	2.5	1.5
Cebpa	CCAAT/enhancer binding protein (C/EBP), alpha	-8.0	-2.6	0.036	0.759	8.0	4.7
Fzd9	frizzled homolog 9 (Drosophila)	-0.5	18.3	0.953	0.021	4.0	2.2
Dvl2	dishevelled 2, dsh homolog (Drosophila)	-4.0	8.6	0.581	0.007	3.5	1.9
Wnt10b	wingless related MMTV integration site 10b	-2.8	11.6	0.824	0.028	2.2	1.4
Flt3	FMS-like tyrosine kinase 3	-13.3	-8.1	0.013	0.372	2.8	1.6
Birc5	baculoviral IAP repeat-containing 5	7.5	38.3	0.479	0.007	ns	ns
Rad51	RAD51 homolog (S. cerevisiae)	-9.4	8.2	0.470	0.001	ns	ns
Jup	junction plakoglobin	22.3	2.7	0.004	0.632	2.3	1.4
Plcg1	phospholipase C, gamma 1	12.5	4.1	0.039	0.569	4.0	2.6
Tceb2	transcription elongation factor B (SIII), polypeptide 2	-4.4	-1.4	0.133	0.433	3.9	1.4
Ptch2	patched homolog 2	3.9	19.0	0.752	0.008	2.2	1.4
Cytokine-cytokine receptor interaction							
Il18r1	interleukin 18 receptor 1	0.3	23.4	0.955	0.018	8.0	5.2
Il2rb	interleukin 2 receptor, beta chain	1.8	11.1	0.862	0.004	2.5	1.4
Acvrl1	activin A receptor, type II-like 1	15.1	2.8	0.018	0.559	3.0	1.4
Osmr	oncostatin M receptor	20.6	-9.1	0.030	0.275	ns	ns
Flt3	FMS-like tyrosine kinase 3	-13.3	-8.1	0.013	0.372	2.8	1.6
Gm2564	predicted gene 2564 // predicted pseudogene 2457 // predicted gene 12407 // predicted gene 2023 // chemokine (C-C motif) ligand 19	-0.5	-15.1	0.954	0.021	ns	ns
Cntfr	ciliary neurotrophic factor receptor	17.7	12.8	0.089	0.026	8.5	5.0
Cx3cl1	chemokine (C-X3-C motif) ligand 1	16.1	1.3	0.017	0.703	4.8	2.5
Cxcl11	chemokine (C-X-C motif) ligand 11	-3.4	31.6	0.785	0.019	ns	ns
Gm614	predicted gene 614	10.3	35.6	0.368	0.003	ns	ns
Amh	anti-Mullerian hormone	-15.5	14.5	0.033	0.198	ns	ns
Cxcl16	chemokine (C-X-C motif) ligand 16	0.5	-9.8	0.827	0.004	3.6	2.1
Ccr2	chemokine (C-C motif) receptor 2	10.2	9.9	0.285	0.009	2.5	1.3
Cx3cr1	chemokine (C-X3-C) receptor 1	0.7	4.7	0.881	0.027	3.9	2.3
Fas	Fas (TNF receptor superfamily member 6)	16.6	12.5	0.214	0.008	5.7	3.8
Pdgfd	platelet-derived growth factor, D polypeptide	2.9	-10.1	0.694	0.033	4.0	1.8
Flt3l	FMS-like tyrosine kinase 3 ligand // FMS-like tyrosine kinase 3 ligand	9.0	23.7	0.427	0.033	4.2	2.7
Xcl1	chemokine (C motif) ligand 1	9.6	18.7	0.535	0.023	ns	ns
Bmp7	bone morphogenetic protein 7	-2.1	-7.1	0.621	0.003	3.0	1.9
Csf2ra	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	6.8	13.3	0.048	0.048	ns	ns
Il2	interleukin 2	25.4	6.7	0.032	0.504	ns	ns
Circadian Clock							

Symbol	Description	% change SD	% change KT	t-test Sal-SD	t-test Sal-KT	Circadian value (JTK)	
						-log (P)	-log (q)
Gm129	Circadian-associated repressor of transcription	-33.1	-15.6	0.009	0.003	11.5	7.9
Per1	period homolog 1 (Drosophila)	1.8	-3.9	0.843	0.489	4.8	3.4
Per2	period homolog 2 (Drosophila)	1.2	-9.3	0.927	0.074	18.0	14.0
Per3	period homolog 3 (Drosophila)	-3.4	-5.3	0.565	0.089	13.3	8.9
Arntl	aryl hydrocarbon receptor nuclear translocator-like	14.3	-7.4	0.091	0.287	18.7	14.3
Cry1	cryptochrome 1 (photolyase-like)	-6.1	-10.5	0.393	0.085	18.4	14.9
Cry2	cryptochrome 2 (photolyase-like)	-3.4	-7.2	0.595	0.131	8.5	5.7
Clock	circadian locomotor output cycles kaput	6.9	-3.1	0.118	0.540	14.1	11.4
Npas1	neuronal PAS domain protein 1	4.8	0.1	0.318	0.984	3.3	1.8
Npas2	neuronal PAS domain protein 2	9.6	-0.8	0.306	0.884	13.9	10.2
Npas3	neuronal PAS domain protein 3	3.3	-6.8	0.742	0.367	2.7	1.6
Npas4	neuronal PAS domain protein 4	-22.5	-17.8	0.001	0.087	3.1	1.5
Dbp	D site albumin promoter binding protein	-22.6	1.0	0.031	0.804	21.0	16.4
Rora	RAR-related orphan receptor alpha	-2.4	-11.7	0.540	0.238	6.5	4.9
Nr1d2	nuclear receptor subfamily 1, group D, member 2	-7.4	-5.4	0.083	0.358	19.0	14.3
Rorb	RAR-related orphan receptor beta	-20.9	-6.2	0.054	0.486	4.6	2.0
Cholinergic synapse							
Camk2g	calcium/calmodulin-dependent protein kinase II gamma	-10.0	-5.8	0.000	0.146	11.5	7.9
Camk4	calcium/calmodulin-dependent protein kinase IV	-9.4	-10.9	0.053	0.219	ns	ns
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.057	ns	ns
Chrnb2	cholinergic receptor, nicotinic, beta polypeptide 2 (neuronal)	-11.8	-4.7	0.013	0.057	4.4	2.2
Creb3l3	cAMP responsive element binding protein 3-like 3	4.2	29.9	0.770	0.040	3.4	2.2
Fos	FBJ osteosarcoma oncogene	-23.9	-25.9	0.008	0.007	5.3	2.3
Gng3	guanine nucleotide binding protein (G protein), gamma 3	-4.7	12.8	0.510	0.077	2.2	1.4
Itpr2	inositol 1,4,5-triphosphate receptor 2	-0.4	-7.1	0.961	0.031	5.1	3.4
Kcnj3	potassium inwardly-rectifying channel, subfamily J, member 3	-13.2	-4.0	0.003	0.442	6.8	4.4
Kcnq2	potassium voltage-gated channel, subfamily Q, member 2	16.1	-1.1	0.063	0.732	ns	ns
Kcnq4	potassium voltage-gated channel, subfamily Q, member 4	-5.1	14.5	0.059	0.022	ns	ns
Kcnq5	potassium voltage-gated channel, subfamily Q, member 5	-6.4	-7.0	0.049	0.199	2.9	1.7
Pik3r2	phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 2 (p85 beta)	-4.2	-7.8	0.518	0.006	3.3	1.8
Plcb4	phospholipase C, beta 4	-9.8	-13.3	0.072	0.181	5.5	3.5

Supplemental Table S3. Primers used in the real-time PCR

Gene names	Symbol	MGI accession	Forward	Reverse
RAR-related orphan receptor beta	Rorb	MGI:1343464	GGCAGACCCACACCTACGA	CAGAGCCTCCCTGGACTTG
D site albumin promoter binding protein	Dbp	MGI:94866	AATGACCTTTGAACCTGATCCCGCT	GCTCCAGTACTTCTCATCCTTCTGT
Neuronal PAS Domain Protein 2	Npas2	MGI:109232	CACTCGGAAAATGGACAAAACC	TGAGACTTCATTGTGTTTCTGCAA
Period circadian clock 1	Per1	MGI:1098283	CCTCCAGAGCAGCCATCC	GCCTGAAGCGGTTGACATC
Cryptochrome 2	Cry2	MGI:1270859	CAACACAGGCCCCAGAGCACTATC	TCAGGAGTCCTTGCTTGCTGGCTC
Neuronal PAS Domain Protein 4	Npas4	MGI:2664186	ACTACCCTATCAGTGACACG	CTAGGACATAGGCTGCCTG
Period circadian clock 2	Per2	MGI:1195265	CGCCTAGAATCCCTCCTGAGA	CCACCGGCCTGTAGGATCT
Circadian Associated Repressor Of Transcription	Ciart	MGI:2684975	AAGCAAGCACTTTCCCAG	GTGTTTGGCCCATCTTCTC
Neurogenic locus notch homolog protein 2	Notch 2	MGI:97364	CCTGAACGGGCAGTACATTT	GCGTAGCCCTTCAGACACTC
Beta actin	Actinb	MGI:87904	GGCTGTATTCCCCTCCATCG	CCAGTTGGTAACAATGCCATGT