



Figure S1. Hypothalamic gene expression in transgenic compared to WT mice. (A) The distributions (number of probes) of normalized fold change (Log_2) in expression of all detected hypothalamic probes between $Per3^{4/4}$ compared to WT (black line) and $Per3^{5/5}$ compared to WT (red line). The percentage of these detected probes that were significantly differentially expressed are also indicated with the right-hand axis (black bars = $Per3^{4/4}$, red bars = $Per3^{5/5}$). (B) Horizontal bars (black = $Per3^{4/4}$, red = $Per3^{5/5}$) indicate the up- and down-regulated fold changes (Log_2) in the differential expression (compared to WT) of five genes associated with sleep homeostasis (top), and a core set of circadian clock genes (bottom). The vertical grey dashed lines in panels A and B indicate the maximal fold change observed in the clock gene transcripts, which were all non-significant. (C) Gene ontology analysis of biological process, molecular function, and cellular component terms that were associated with differentially expressed hypothalamic genes in $Per3^{5/5}$ compared with WT (number of observed probes contributing to each term, enrichment score, percentage of differentially expressed genes contributing to each term and adjusted P value are indicated). Gene ontology analysis did not reveal significant terms for the differential expression in the $Per3^{4/4}$ mice due to the smaller number of probes analyzed.

| ProbeName | GeneSymbol | Per3 ^{4/4} vs.Per3 ^{5/5} | WT vs Per3 ^{4/4} and/or Per3 ^{5/5} | Per3 ^{5/5} | Per3 ^{4/4} | WT |
|--------------|----------------|---|---|---------------------|---------------------|----------|
| A_52_P267651 | <i>Arntl</i> | | | -0.12898 | 0.10941 | -0.04331 |
| A_51_P272553 | <i>Bhlhe40</i> | | | -0.01092 | -0.04802 | 0.04374 |
| A_51_P451176 | <i>Bhlhe41</i> | | P = 0.0052 | 0.16994 | 0.06284 | -0.31015 |
| A_52_P618912 | <i>Bhlhe41</i> | | | 0.26348 | 0.07570 | -0.23859 |
| A_52_P161365 | <i>Clock</i> | | | 0.11360 | -0.15249 | -0.01458 |
| A_52_P279391 | <i>Clock</i> | | | 0.11598 | -0.07711 | 0.00522 |
| A_52_P334670 | <i>Clock</i> | | P = 0.0262 | 0.05596 | -0.14214 | 0.29667 |
| A_52_P334677 | <i>Clock</i> | | | -0.05199 | -0.14977 | 0.20162 |
| A_51_P302204 | <i>Cry1</i> | | | -0.25761 | 0.06965 | -0.06256 |
| A_52_P420500 | <i>Cry1</i> | | P = 0.0458 | -0.68362 | -0.50719 | 0.31876 |
| A_51_P135542 | <i>Cry2</i> | | P = 0.0055 | 0.00655 | 0.08840 | -0.49925 |
| A_52_P248378 | <i>Cry2</i> | | P = 0.0434 | 0.06761 | 0.06106 | -0.16752 |
| A_51_P136277 | <i>Csnk1d</i> | | P = 0.0245 | 0.09405 | 0.32989 | -0.33567 |
| A_51_P359813 | <i>Csnk1d</i> | | | -0.12066 | -0.04088 | 0.10839 |
| A_52_P11576 | <i>Csnk1d</i> | | | 0.11080 | 0.18629 | -0.16877 |
| A_52_P477369 | <i>Csnk1d</i> | | P = 0.0161 | 0.22056 | 0.36733 | -0.37472 |
| A_51_P429197 | <i>Csnk1e</i> | | | 0.16857 | -0.02134 | -0.01003 |
| A_52_P542419 | <i>Csnk1e</i> | | | -0.00284 | 0.04857 | 0.00023 |
| A_51_P180492 | <i>Dbp</i> | | P = 0.0102 | 0.02481 | 0.08902 | -0.29256 |
| A_52_P534749 | <i>Npas2</i> | | P = 0.6067 | -0.00435 | -0.06607 | -0.17249 |
| A_51_P223776 | <i>Nr1d1</i> | | P = 0.0245 | 0.08307 | 0.12696 | -0.46491 |
| A_52_P130952 | <i>Nr1d1</i> | | | 0.11137 | 0.30631 | -0.36408 |
| A_52_P130961 | <i>Nr1d1</i> | | | -0.41301 | 0.11641 | -0.34571 |
| A_52_P303891 | <i>Nr1d2</i> | | P = 0.0363 | -0.08817 | -0.09040 | 0.23406 |
| A_52_P79889 | <i>Per1</i> | | | 0.09700 | 0.02805 | -0.01378 |
| A_51_P282760 | <i>Per2</i> | | | -0.09000 | -0.02738 | 0.09985 |
| A_52_P536869 | <i>Per2</i> | | | -0.12907 | 0.32956 | -0.13785 |
| A_51_P258493 | <i>Per3</i> | | P = 0.0372 | 0.25613 | -0.03558 | -0.21079 |
| A_51_P477779 | <i>Rora</i> | | | 0.15948 | -0.09179 | 0.16905 |
| A_52_P652442 | <i>Rora</i> | | | 0.23779 | -0.04323 | 0.01108 |
| A_52_P652950 | <i>Rora</i> | | | 0.35369 | -0.05030 | 0.04104 |

Supplemental table S1A: Clock gene expression in hypothalamic samples

| ProbeName | GeneSymbol | Per3 ^{4/4} vs.Per3 ^{5/5} | WT vs Per3 ^{4/4} and/or Per3 ^{5/5} | Per3 ^{5/5} | Per3 ^{4/4} | WT |
|--------------|----------------|---|---|---------------------|---------------------|----------|
| A_52_P267651 | <i>Arntl</i> | | | -0.06289 | 0.14908 | -0.01202 |
| A_51_P272553 | <i>Bhlhe40</i> | | | -0.02212 | -0.07854 | -0.06550 |
| A_51_P451176 | <i>Bhlhe41</i> | | P = 0.0032 | 0.18719 | 0.05677 | -0.24150 |
| A_52_P618912 | <i>Bhlhe41</i> | | | 0.09504 | 0.14551 | -0.26483 |
| A_52_P161365 | <i>Clock</i> | | | 0.08955 | -0.02715 | 0.05125 |
| A_52_P279391 | <i>Clock</i> | | | 0.07064 | -0.15654 | -0.07816 |
| A_52_P334670 | <i>Clock</i> | | | 0.05231 | -0.09172 | 0.21352 |
| A_52_P334677 | <i>Clock</i> | | P = 0.0377 | -0.02105 | -0.19695 | 0.10035 |
| A_51_P302204 | <i>Cry1</i> | | | -0.05304 | 0.16666 | -0.09487 |
| A_52_P420500 | <i>Cry1</i> | | P = 0.0071 | -0.53089 | -0.47892 | 0.57222 |
| A_51_P135542 | <i>Cry2</i> | | P = 0.0017 | 0.26195 | 0.13782 | -0.45281 |
| A_52_P248378 | <i>Cry2</i> | | P = 0.0078 | 0.08495 | 0.18414 | -0.16797 |
| A_51_P136277 | <i>Csnk1d</i> | | P = 0.0094 | 0.01389 | 0.27917 | -0.39669 |
| A_51_P359813 | <i>Csnk1d</i> | | | -0.01190 | -0.04583 | -0.01672 |
| A_52_P11576 | <i>Csnk1d</i> | | P = 0.0019 | 0.01862 | 0.20343 | -0.43821 |
| A_52_P477369 | <i>Csnk1d</i> | | P = 0.0015 | 0.02986 | 0.20707 | -0.64890 |
| A_51_P429197 | <i>Csnk1e</i> | | | 0.15034 | -0.05504 | 0.00226 |
| A_52_P542419 | <i>Csnk1e</i> | | | -0.02476 | -0.03711 | -0.01421 |
| A_51_P180492 | <i>Dbp</i> | | | 0.09361 | 0.10192 | -0.18879 |
| A_52_P79889 | <i>Npas2</i> | | P = 0.0418 | 0.13054 | 0.03951 | -0.21103 |
| A_51_P223776 | <i>Nr1d1</i> | | | 0.17853 | 0.19377 | -0.22922 |
| A_52_P130952 | <i>Nr1d1</i> | | | -0.01569 | 0.24713 | -0.35349 |
| A_52_P130961 | <i>Nr1d1</i> | | | -0.22156 | 0.01417 | -0.34439 |
| A_52_P303891 | <i>Nr1d2</i> | | P = 0.0109 | 0.00165 | -0.09362 | 0.13994 |
| A_52_P79889 | <i>Per1</i> | | P = 0.0412 | 0.14551 | 0.04336 | -0.12888 |
| A_51_P282760 | <i>Per2</i> | | | 0.10941 | -0.02899 | -0.01415 |
| A_52_P536869 | <i>Per2</i> | | | 0.03497 | 0.22631 | -0.15680 |
| A_51_P258493 | <i>Per3</i> | | P = 0.008 | 0.22901 | -0.04939 | -0.45997 |
| A_51_P477779 | <i>Rora</i> | | | 0.00057 | -0.16541 | 0.01888 |
| A_52_P652442 | <i>Rora</i> | | | 0.05234 | -0.04869 | -0.05583 |
| A_52_P652950 | <i>Rora</i> | | | 0.10809 | -0.05947 | -0.07725 |

Supplemental table S1B: Clock gene expression in cortical samples

| <i>Per3</i> ^{4/4} | | <i>Per3</i> ^{5/5} | |
|----------------------------|-------------|----------------------------|-------------|
| Gene/Probe | Fold change | Gene/Probe | Fold change |
| <i>Ccl21a</i> | -3.39 | <i>Lct</i> | -3.38 |
| <i>Gdpd3</i> | 2.76 | <i>A_52_P788961</i> | 2.81 |
| <i>Lcn12</i> | -2.32 | <i>Grn</i> | -2.38 |
| <i>Pttg1</i> | 2.31 | <i>8430429K09Rik</i> | 2.25 |
| <i>Prl</i> | -2.18 | <i>Dsp</i> | -2.20 |
| <i>Dyrk4</i> | -2.17 | <i>Neurod6</i> | -1.98 |
| <i>LOC674214</i> | -1.95 | <i>Sln</i> | -1.96 |
| <i>Slx1b</i> | -1.81 | <i>A_51_P311235</i> | -1.90 |
| <i>Ugt2b38</i> | -1.78 | <i>Agxt</i> | -1.87 |
| <i>Apoc4</i> | 1.77 | <i>Hamp</i> | -1.62 |
| <i>Tsix</i> | 1.68 | <i>Neurod2</i> | -1.62 |
| <i>Gm3893</i> | -1.56 | <i>Thbs4</i> | -1.61 |
| <i>Wfdc2</i> | 1.27 | <i>Ccl21a</i> | -1.57 |
| <i>A930018M24Rik</i> | -1.23 | <i>Fam105a</i> | 1.54 |
| <i>AU023762</i> | -1.19 | <i>Grin2a</i> | -1.53 |
| <i>Gh</i> | -1.19 | <i>A_52_P348256</i> | -1.52 |
| <i>Sln</i> | 1.13 | <i>Egr3</i> | -1.49 |
| <i>A_52_P36261</i> | 1.10 | <i>Thbs4</i> | -1.49 |
| <i>Myh1</i> | 1.10 | <i>Spink8</i> | -1.47 |
| <i>Folr1</i> | 1.06 | <i>9430091E24Rik</i> | -1.43 |
| <i>Sult1c2</i> | 0.99 | <i>Wipf3</i> | -1.42 |
| <i>Tmem72</i> | 0.93 | <i>Fabp1</i> | -1.39 |
| <i>A_51_P417257</i> | -0.93 | <i>Mup5</i> | -1.38 |
| <i>Chi3l4</i> | -0.89 | <i>2310002F09Rik</i> | -1.36 |
| <i>Tns1</i> | -0.89 | <i>Tnfrsf25</i> | -1.36 |
| <i>Cd38</i> | 0.88 | <i>Kcne2</i> | -1.33 |
| <i>Myh4</i> | 0.88 | <i>Itпка</i> | -1.33 |
| <i>Defb22</i> | -0.87 | <i>Hormad1</i> | -1.32 |
| <i>Mpl</i> | -0.84 | <i>Egr4</i> | -1.30 |
| <i>Eif2a</i> | -0.83 | <i>Dusp18</i> | 1.24 |

Table S2: Top 30 fold change probes for each genotype compared to WT in the hypothalamus during the ultradian light-dark cycle.