# Differential gene expression in Brain and Liver tissue of rats after 9-day Rapid Eye Movement Sleep deprivation

Atul Pandey[1, 2]*, Santosh K Kar[1, 3]*

[1] School of Biotechnology, Jawaharlal Nehru University, New Delhi, India

Present Addresses:

[2] Department of Ecology, Evolution, and Behavior, The Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem, Jerusalem, 91904, Israel.

[3] Nano Herb Research Laboratory, Kalinga Institute of Industrial Technology (KIIT) Technology Bio Incubator, Campus-11, KIIT University Bhubaneswar, Odisha, India.

***Corresponding authors**

Prof. Santosh Kar, e-mail: santoshkariis@rediffmail.com, Phone: +91-9937085111,and

Dr. Atul Pandey, e-mail: atulkuma.pandey@mail.huji.ac.il,Phone: +972-547301848

**Short title:**

REM sleep deprivation of rats for 9days affects the brain and liver differently.

**Keywords:**

Microarray analysis; Rapid eye movement sleep deprivation; Differential Gene expression in brain and liver tissue.

**Highlights of the study**

- Gene expression profile of brain and liver tissues of rats was analysed after REM Sleep deprivation for 9 days by using microarray technique.
- Many of the genes involved in essential physiological processes, such as protein synthesis and neuronal metabolism etc. are affected differently in the brain and liver tissue of rats after 9-day REM sleep deprivation.

**Abstract**

Sleep is essential for the survival of most living beings. Numerous researchers have identified a series of genes that are thought to regulate “sleep-state" or the “deprived state”. As sleep has significant effect on body physiology, we believe that lack of REM sleep for a prolonged period would have a profound impact on various body tissues. Therefore, using microarray method, we have tried to determine which genes are up regulated and which are down regulated in the brain and liver of rats after 9-day REM sleep deprivation. Our results suggest that 9-day REM sleep deprivation differentially affects certain genes in the brain and the liver of the same animal.

## 1. Introduction

Many studies have been conducted by using rodents and primates to find out how sleep promotes survival and why prolonged deprivation is mostly fatal. It has also been analysed in non-mammalian species like the fruit fly (*Drosophila melanogaster*)[1–3], the zebrafish (*Danio rerio*) [4–6], the nematode (*Caenorhabditis elegans*) [7], and bees (Honey bee, *Apis mellifera*, and Bumble bee, (*Bombus terrestris*) [8–11]. Loss of sleep has been shown to have drastic effect on all animals studied thus far [12,13]. The level of physiological changes that sleep loss brings about and the fatality often varies depending upon the nature and duration of sleep deprivation [14,15]. Recent advancement in sleep research has shed light on both, a functional aspect of total sleep in general and rapid eye movement (REM) sleep in particular.

Many theories explain the evolutionary significance and functions of sleep, starting with “null” to “synaptic plasticity” theory [16,17]. Overall, sleep seems to have specific basic standard roles for all species evolved who need it[18]. While the simplest hypothesis advocates that a single basic role cannot be ascribed to sleep, numerous studies links it’s loss to the detrimental effects on metabolism, behavior, immunity, cellular functions and hormonal regulations [19–22]. Sleep is therefore necessary, and a living being cannot be deprived of it for a long time. There is some behavioral plasticity dependent on social or physiological state, with regulation of sleep [23,24]. In the case of drosophila, where not all sleep is considered necessary for survival[23], questions relating to the critical functions of sleep, plasticity and its overall importance has been studied.

REM sleep is an essential part of total sleep, and is present only in avians and mammals, with few exceptions like reptiles[25]. The functional aspect of REM sleep mainly relates to memory consolidation, brain maturation, muscle re-aeration, special memory acquisition, and maintenance of body physiology [26–32]. REM sleep is important for hippocampal, pruning, maintenance of new synapses during development and learning and generation of memory[33–35]. Some recent studies also suggest that lack of REM sleep can actually cause cell death in tissues and neurons [36–38]. Recently, REM sleep deprivation has also been found to be associated with acute phase response of liver, increased synthesis of pro-inflammatory cytokines such as IL1β, IL-6, and IL-12 and increased levels of liver enzymes, alanine transaminase and aspartic transaminase which circulates in the blood [39]. In addition, REM sleep deprivation-induces the production of reactive oxygen species (ROS) and nitric oxide (NO) in hepatocytes, along with an interesting increase in sensitivity to oxidative stress by the hepatocytes [40].

Microarray is a valuable tool for measuring the dynamics of gene expression in a biological system. As a result, microarrays can be used to measure the differences in gene expression

profile in different tissues under the same physiologic conditions[18,41,42]. Most sleep studies have been performed using the entire brain, although there are some recent research where other organs has been used.[43–49].We became interested in comparing the effect on the brain and the liver from the same animal at the same time as our previous studies had indicated that REM sleep may have drastic effect on the liver [37,39,40]. For this purpose, we used the microarray technique to compare gene expression and identify the processes affected in the brain and liver of the same animal after REM sleep deprivation for 9 days. For example, we expected REM sleep loss to affect genes and processes related to circadian rhythm more in the brain and genes related to regeneration and immunity in the liver.

Our findings showed that REM sleep deprivation affected a total of 652 genes in the brain which were different from the 426 genes that were found to be affected in the liver. We found some genes belonging to certain pathways in the brain which were affected by REM sleep deprivation but were not affected in the liver, suggesting that the REM sleep deprivation interestingly affects these two organs differently. We conclude that REM sleep deprivation influences the molecular processes and biological pathways in both brain and liver by affecting different genes, thereby affecting the balance of physiology. Several of these genes identified by us are not recorded in previous studies and therefore taken together, we provide a dataset of genes that have been affected by REM sleep loss in the brain and liver. Our present study could be useful in future work on the detection of candidate genes linked to sleep or sleep loss disorders in general involving a particular organ.

## 2. Material and Methods

We used male Wistar rats weighing between 220-260 gm for this study. We kept the animals in the institutional animal house facility at 12:12hrs L: D cycle (7:00 am lights on) and provided

the rats with food and water ad libitum. We have carried out all the experiments in compliance with the protocol approved by the Institutional Animal Ethics Committee of the University.

### 2.1 REM sleep deprivation procedure

Rats were REM sleep-deprived for nine consecutive days by using the flower pot methods [50,51]. In this method, we keep animals on a small raised platform (6.5 cm in diameter) surrounded by water compared to the control (large platform control, LPC) where the animals are kept on a large platform (12.5 cm in diameter) under identical condition. REM sleep-deprived animals could sit, crouch, and have a NREM-related sleep on this platform. However, due to requirement of atonia of muscle during REM sleep, they are unable to have REM sleep on the small platform. Whenever they try to get REM sleep., they fall into water and next time before the onset of REM sleep, they wake up and are thus deprived of it. Throughout our previous studies, there were no differences between cage control and LPC control group of rats, and thus only the LPC control group as control group was considered in this analysis[40,52]. Further, based on our previous studies we have used 9-day REM sleep deprivation in this study as unlike in the 4 day REM sleep deprivation it significantly affected the acute phase response and caused oxidative stress in the liver. Rats were sacrificed between 10 a.m. and 12 p.m. on day 9 and the total brain and liver were harvested and flash-frozen in liquid nitrogen for further analysis.

### 2.2 RNA extraction and quality analysis

Total RNA was isolated from the entire brain and liver samples using the Qiagen kit. Briefly, rats were anesthetized with isoflurane, and brain and liver samples were immediately dissected and frozen in liquid nitrogen. We isolated the total RNA from the whole brain and liver of each animal using Trizol (Gibco-BRL, Gaithersburg, MD, USA) as directed by the manufacturer. The concentration of total RNA was measured using Nanodrop and the quality was analyzed using Bioanalyzer and the array was performed using good quality samples.

### 2.3 Microarray: labeling, hybridization, and data analysis

For microarrays, we took an equivalent amount of total RNA from the brain and liver. We outsourced Ocimum Biosolutions (USA) genomics facility for microarray analysis. In short, we used Affymetrix Rat Gene 1.0 ST Arrays containing more than 7000 annotated sequences and 18000 expressed sequence tags (ESTs). The Affymetrix Gene Chip Expression Technical Manual (Affymetrix Inc., Santa Clara, CA, USA) was used for the marking, hybridization and expression study of microarrays, mainly as previously reported [45]. The data analysis was performed using Affymetrix Expression Console and Programming Language-R [53,54].

### 2.4 Gene Ontology analysis

The functional annotation of differentially expressed genes was obtained from the Gene Ontology Consortium database, based on their respective biological process, molecular function and cellular component [55]. The overabundance of a particular term was determined on the basis of the number of significant genes in the experiment, the number of significant genes relevant to the term, the total number of genes for the organism, and the number of genes relevant to the term of the organism. We determined the functional categories enriched within genes that varied between control and REMSD. We used a single-tailed Fisher exact probability test based on the hypergeometric distribution to measure the $p$ values. If the term is significant with say $p < 0.05$, it has been enriched with genes.

### 2.5 Pathway analysis

A pathway analysis of microarray data was performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) software. A number of biochemical pathways are identified by physiological processes documented in the KEGG databank. Since rat species-specific functional gene annotations are still few for many biological processes.These considerations make it difficult for the pathways to have a functional analysis of the results of the microarray. We therefore tried to identify general pathways and species-specific pathways. When data from

the rat genome were not available, we looked at other species databases and compared the reference pathways used in the analysis. We used the KEGG map pathway to illustrate the maximum visual impact of REM sleep loss on highly up-regulated genes involved in protein translation processes.

### 2.6 Validation of array expression with Real-Time quantitative qPCR

Following analysis of microarray results, a group of genes was selected for validation by qPCR based on their degree of change in expression. We conducted a correlation study between the effects of the microarray and the qPCR, and statistical significance was calculated (**Fig. 1**). For the microarray, the data input to the correlation study was the Log2 ratio value of the weighted average for each gene on the composite array representing all replicate animals. For qPCR, we used the mean Log2 ratio value stated by qPCR for all replicate animals. We selected six transcripts for validation of microarray analysis using RT-PCR (**Table ST-1**). Controls were established, along with experimental conditions, to rule out any possibilities for external variables to affect our experimental setup. We tested the respective mRNA levels with RT-PCR in real-time. Briefly, samples obtained from total liver and total brain tissue were frozen and stored separately at $-80^0$C before mRNA was quantified. Total RNA was isolated using Trizol methods and re-transcribed using the ABI reverse transcription kit (Applied Biosystems, Catalog number: 4368814). TaqMan gene expression Master Mix (Applied Biosystems, Catalog Number: 4369016) and probes (Applied Biosystems, **Supplementary Table ST1**) used for quantitative analysisof mRNA. Each cDNA sample was analyzed in triplicate. The RT-PCR reactions for all focal genes and Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) were measured from the same cDNA sample and loaded onto the same 96-well analysis plate. We quantified the gene levels using $2^{-\Delta\Delta Ct}$ methods and GAPDH as a reference control gene for expression level normalization.

### 2.7 Statistics

The results of qRT-PCR are presented as a mean of ± SE. We used the Kolmogorov – Smirnov normality test to estimate the data normality. The non-parametric Mann-Whitney U test was used to compare the pairwise expression of the microarray and RT-PCR expression for the respective genes used for liver and brain validation. Expression validation experiments were performed on the basis of five rats per group. The array experiments were analyzed, maintaining a $p<0.5$ significance level. The KEGG bioinformatics map and diagrams used to illustrate findings and discussions. All statistical analyzes considered $p< 0.05$ to be significant and were performed and plotted using Graph Pad 5.1 and Origin 6.0 software.

## 3. Results

### 3.1 General results

In the current analysis, we used the Affymetrix Rat Gene 1.0 ST Array. Primary data analysis was performed using Affymetrix Expression Console and R. A total of 311 up-regulated genes (**Table ST-2, and ST-3A**) and 341 up-regulated genes (**Table ST-2, and ST-3B**) have been found in the brain. In contrast, 209 up-regulated genes (**Table ST-2, and ST-3C**) and 217 genes were down-regulated (**Table ST-2, and ST-3D**) in the liver (**Fig. 2**). Out of this pool, we found a set of genes that were commonly affected, either in the same or opposite direction, between the brain and the liver. For example, 4 of the 11 genes identified (**Table ST-4A,** namely ***WEE1 G2 Checkpoint Kinase (Wee1, NM 001012742), Solute Carrier Family 2 Member 12 (Slc2a12, NM 001107451), Harakiri, BCL2 Interacting Protein (Hrk, NM 057130),*** and ***Family With Sequence Similarity 110 Member B (Fam 110b, NM 001024341.1)*** were negatively affected in both the brain and liver tissues (Fig. 2). Similarly, only 3 of the 6 genes identified (**Table ST-4B**; namely ***Hemoglobin Subunit Alpha 1*** (***Hba-a1, NM 013096.2), Hemoglobin Subunit Alpha 2 (Hba-a2, NM 013096),*** and ***Major urinary protein 5 (Mup5, NM 203325.1)*** were up-regulated in the brain and down-regulated in the liver (**Fig. 2**).In addition, we identified 3 genes (**Table, ST-4C;** namely ***Histocompatibility 2, class II DR***

***alpha* (*RT1-Da,*** NM 001008847), ***Zinc Finger And BTB Domain Containing 6*** (***Zbtb6,*** NM 001108953), and ***Transmembrane protein 106B*** (***Tmem* 106a,** NM 001004267) out of a total of 4 genes that were up-regulated in the liver and down-regulated in the brain (**Fig. 2**). These findings underpinned our hypothesis that REM sleep loss will affect different tissues differently. In order to further explore and refine this, we continued with the study of gene ontology and KEGG pathway analysis.

**3.2 Gene Ontology analysis**

Functional categories within genes that vary between regulation and REM sleep deprivation in the brain and liver have been established. We also grouped all processes and components into three main groups, namely biological processes, molecular functions, and cellular components (**Fig. 3-5**). In addition, we classified each group into two subcategories based on their direction of regulation (upregulation and downregulation), e.g. biological processes (**Fig.3, A-D**), molecular functions (**Fig. 4, A-D**) and cellular components (**Fig. 5, A-D**).In our analysis, we used only significantly *($p<0.05$)* affected processes. They were plotted on 3 dimensional graphs considering their p-values, the affected genes (node count) and the total genes in the database (database count, log-transformed). This gave us a better understanding of the processes most profoundly affected and the nature of regulation.

The top five brain-regulated processes / functions included translational elongation, translation, anatomical rRNA processing and erythrocyte differentiation (**Fig. 3A**, Biological Processes), structural components of ribosomes, protein binding, rRNA binding, translation regulator activity, and mRNA binding (**Fig. 4A,** molecular function) and ribosomes, cytosols, intracellular, small ribosomal subunits, and nucleolus (**Fig. 5A,** cellular component).While REM sleep loss negatively affected processes in brain related to behavioral fear response, locomotive behavior, dopamine receptor signaling pathway, dopamine synaptic transmission, and brain visual learning (**Fig. 3B**, biological processes), protein binding, serotonin receptor

activity, serotonin binding, drug binding and G-protein coupled receptor activity (**Fig . 4B,** molecular function), plasma membrane, axon, membrane, dendrite, and extracellular space (**Fig. 5B,** cellular component). Similarly, the liver was positively affected by Sarcoma, Gluconeogenesis, triglyceride metabolic process, negative regulation of fatty acid biosynthetic process and response to an organic cyclic substance (**Fig. 3C,** biological processes), pyridoxal phosphate binding, structural constituents of the cytoskeleton, identical protein binding, protein binding, and dimethyl arginase activity (**Fig. 4C,** molecular function), and endoplasmic reticulum, plasma membrane, membrane, lysosome, and cytosol (**Fig. 5C,** cellular component). Although pore complex assembly, circadian rhythm, erythrocyte development, positive regulation of interleukin-1 beta secretion, and oxygen transport (**Fig. 3D,** biological processes), oxygen binding, oxygen transport activity, extracellular ATP-gated cation channel activity, Iron-ion binding, and Interleukin-8 binding (**Fig. 4D,** molecular function), and hemoglobin complex, extracellular space, soluble fraction, extracellular region, and mast cell granules (**Fig. 5D,** cellular component) were got downregulated in the liver.

**3.3 Pathway analysis**

We have used the KEGG analysis to evaluate the pathways affected by REM sleep loss. We also categorized positive and negatively affected pathways in the brain and liver. They were plotted against their significance level ($p<0.05$), database count, and multiple genes affected by each pathway (node count).We illustrated up-regulated and down-regulated pathways in the brain (**Fig. 6**) and up-regulated pathways in the liver (**Fig. 7A**) and down-regulated pathways (**Fig. 7B**). Based on these analyzes, we selected some of the most significantly affected pathways in each tissue. We further described them by illustrating the affected genes on the KEGG pathway map ( **Fig. SF 1-4**), which allowed us to visualize the components, proteins, and genes most affected by the process and further helped us in our discussion. We used subunits of ribosomes most strongly negatively regulated (**Fig. SF1**) and neuroactive legend-

receptor interaction pathways (**Fig. SF2**) that were positively regulated in the brain. We also identified the cancer pathway (**Fig. SF3**) and glycerophospholipid metabolism pathway (**Fig. SF4**) that were negatively and positively regulated due to REM sleep loss. We further expanded and examined our results in the light of the available literature and tried to conclude our findings.

## 4. Discussion

The 9-day REM sleep loss study showed that many biological, cellular, and molecular processes were differentially affected in the brain and liver. These findings are consistent with our hypothesis and prediction that different body tissues will respond differently to REM sleep loss. Out of the hundreds of genes found to be significantly affected in the brain and liver, we identified few genes that were mainly shared between the tissues examined and the direction of regulation. Of the 11 genes widely regulated in the brain and liver, only four were identified as ***Wee1, slc2a12, Hrk***, and ***Fam110b*** (**Fig. 2 and Table, ST-4A**). The GO term analysis of molecular / biological functions illustrates the involvement of protein tyrosine kinase activity, carbohydrate transmembrane transport activity, and processes such as apoptosis (**Table, ST-4A**). Recent preprints and other studies support this concept of REM sleep deprivation that effectively results in the apoptotic death of neuronal and hepatocytic cells [36–38]. We could not identify any common genes between brain and liver which are positively affected (out of 2 probes).In addition, a total of 3 genes (out of 6 differentially expressed probes) that were up-regulated in the brain and down-regulated in the liver were found to be ribosomal proteins (***Hba-a1, Hba-a2 & Mup5)*** responsible for drug transport, oxidoreductase activity, heme binding, fatty acid biosynthesis processes and catalytic activity (**Table, ST-4B**).Usually hemoglobin denaturation occurs in the REM sleep period, but we cannot explain how REM sleep loss can affect the hemoglobin saturation status. Similarly, close association was identified with cerebral hypoxemia and obstructive sleep apnea [56,57]. We assume that REM

sleep loss is causing a cerebral hypoxia-like condition in the brain, and the ***Hba-a2*** gene has been induced to respond to it as found in our array studies. The explanation why it has been regulated in the liver is difficult to explain and requires a more detailed study.

Sleep restriction study showing an increase in free fatty acids in healthy men provided us to speculate that REM sleep deprivation can affect genes such as ***Mup5*** which is involved in fatty acid biosynthetic processes differently under REM sleep deprivation condition.[58]. Genes that were found to be up-regulated in the liver and at the same time down-regulated in the brain (***RT1Da, Zbtb6***, and ***Tmem 106b***) were associated with GO term function linked to stimulus response (**Table, ST-4C**). ***Zbtb6*** is a homologous gene of zinc finger protein containing the BTB domain in mammals with unknown functions. ***Tmem 106b*** is found to be associated with lesser known functions except protein binding, dendrite morphogenesis, and lysosomal transport [58,59]. A recent research shows the dementia-related functions of ***Tmem 106b***, regulated by microRNAs[60].

In addition, our analysis of biological, molecular and cellular processes in response to REM sleep loss showed that many of the important processes that are associated with maintenance functions linked to protein translations required for damage control are differentially effected in the brain and liver (**Fig. 2-4**). Overall, it shows that brain processes are mainly up-regulated in response to REM sleep loss. At the same time, the liver becomes more actively involved in energy conservation. Therefore, negative responses indicate that REM sleep loss influences processes linked to the brain's fear response and locomotive activity related to the peripheral circadian clock, hemoglobin level, and transport of oxygen throughout the liver.

Now, we have identified pathways that have been significantly influenced either positively or negatively using the threshold values ($p<0.05$) and have illustrated it (**Fig. 6, 7A & 7B**).

We further defined some of the pathways most affected in either direction due to REM sleep loss in the brain and liver to visually explain the effects using the KEGG pathway map (**Fig.**

**SF 1-4**). We found that many of the ribosomal proteins involved in protein synthesis processes were positively affected in response to REM sleep loss in brain (**Fig. SF1**). Similarly, long-term sleep loss has been found to control several genes in the brain linked to DNA binding / regulation of transcription, immunoglobulin synthesis , and stress response [61,62]. Irrespective of the notion that ***Homer-1a*** is a key brain molecule in response to sleep loss in the mouse model, no substantial modulation of Homer's gene expression was found in our studies involving REM sleep loss in rats[48].

Additionally, REM sleep loss negatively affected several genes linked to neuroactive ligand-receptor interaction pathways in brain, primarily related to gamma-Aminobutyric acid, Human Thrombin receptor, and associated receptor signaling dopamine (**Fig. SF2**). A recent research reviewed sleep and protein-dependent synaptic plasticity, indicating that sleep deprivation impairs many of the related biological and physiological processes[63]. We have found that many of the pathways in the liver which have been upregulated are linked to metabolism, immunity, and depression (**Fig. 7A**). On the other hand, only a few downregulated pathways in liver have been established which includes nitrogen metabolism and circadian rhythm (**Fig. 7B**). These findings further indicate that REM sleep deprivation may affect the different set of genes as measured in our study compared to the total sleep loss studies in mice. It is also important to understand the species-specific and sleep phase-specific response of the loss of sleep function in order to understand its consequences.

REM sleep loss also affected several genes such as ***prostaglandin-endoperoxide synthase*** (***Ptgs2***), ***B-cell lymphoma 2*** (***Bcl-2***), Proto-Oncogene, ***Tyrosine Kinase receptor (Kit), KRAS Proto-Oncogene (K-Ras)*** and ***Fos Proto-Oncogene (Fos)*** which are marked in cancer pathways (**Fig. SF 3**). A number of recent studies have shown that sleep dysfunction / loss and cancer processes are very related [64–70]. However, some emerging evidence also suggests that sleep loss / insomnia prior to the onset of cancer is independently associated with cancer

risk [65,69,71,72]. ***Ptgs2***, an enzyme, plays a key role in various pathological processes by catalyzing conversion of arachidonic acid to prostaglandins[73]. Studies have shown that overexpression of ***Ptgs2*** is associated with angiogenesis, metastases, and immunosuppression [75,76]. ***Pgst2*** is also found to be associated with the chemoresistance of some malignant tumors, including liver, pancreatic, lung, esophageal, and gastric cancers [77–79]. Inhibition of ***Ptgs2*** effectively increased the sensitivity of tumors to drugs[74]. Similarly, ***Bcl-2, Kit, K-Ras***, and ***Fos*** genes have been found associated with cancer [75–78]. These genes play an important role in the sleep-wake cycle regulation and are shown to be correlated with sleep [36,37,79–81]. At the same time, glycerophospholipid metabolism pathway was found significantly upregulated in liver (**Fig. SF 4**). This includes the genes ***Phospholipase, PLa2g*** (NM_001004277), ***Phosphatidylcholine 2-Acylhydrolase 12A Pla2g12a*** (NM_001108565), ***Glycerol-3-Phosphate Dehydrogenase 2, Gpd2*** (NM_012736), ***CDP-Diacylglycerol Synthase 2, Cds2*** (NM_053643), and ***Phospholipid Phosphatase 2, Plpp2*** (NM_139252). The ***PLa2g*** associates with neurodegeneration and elevated mitochondrial lipid peroxidation and dysfunction [82–84] The ***PLa2g*** is further found positively associated with sleep loss and psoriasis in humans [85,86] Similarly, ***Gpd2*** gene is found associated with intellectual disability in humans [87] and positively affected due to circadian desynchrony in mouse [88]. The chronic sleep deprivation in rats affected the protein profile of ***Gpd2*** in hypothalamic Astrocytes [89] The functional aspect of other genes affected (e.g., ***Pla2g12a, Cds2*** and ***Plpp2)*** is lacking and needs further exploration.

Studies are very inconsistent with REM sleep deprivation and the behavior of locomotives in rodents. Several studies have shown that REM sleep loss induces locomotor activity [51,90,91] while others have shown decreased locomotor activity [92]. We consider these ambiguities to be related to procedural changes or the degree of REM sleep loss. To illustrate this, few studies used multiple pots compared to our classic single flower pot method for deprivation, and other

studies have used less time for deprivation (72-96 hrs.) compared to ours, which was ~216 hrs. Recent research supporting that REM sleep deprivation can affect locomotor activity in rats in an inverted-U manner has been published [93,94].The widely accepted view in the scientific community is that sleep deprivation decreases the pain tolerance and increases the transmission of pain in multiple chronic pain conditions [95–100]. We also found conflicting reports on the sensory perception of pain that were negatively affected in our studies relative to others [101,102]. There are few studies indicating that it is only total sleep deprivation that raises the intensity to pain rather than REM sleep deprivation [103,104]. Nonetheless, selective REM sleep deprivation is correlated with enhanced placebo analgesia effects[105].

Furthermore, there are some report describing individual variations in REM sleep loss and its association with the perception of pain [106]. We assume that total and short-term sleep deprivation could lower the pain threshold, while long-term sleep deprivation increases it. REM sleep deprivation and pain is also found to be significantly correlated with environmental conditions (e.g. dry or wet conditions). Whereas pain sensitivity was found to be enhanced in dry test conditions and no difference in wet conditions. [107]. This suggests that further work is needed to understand deeply the relationship between experience of pain and lack of sleep. Reports suggest that chronic REM sleep deprivation is associated with increased metabolic rate in brown adipose tissue [108]. Several studies are suggesting that there is a strong correlation between sleep loss and an increased risk of obesity and diabetes [109–111].

Our approach to GO term and KEGG pathway analysis is quite relevant in the current era of genomics and sequencing, but it also involves discrepancies in gene function across organisms, distributed biases and biases linked to positive and negative annotations (more information in 56–58). Like GO term analysis, KEGG analysis also has its limitations, apart from reducing the complexity of the data and helping to increase the explanatory power. One of the key disadvantages of KEGG is the independent consideration of pathways, even though crosses

and overlaps occur in the natural system [115–118]. Therefore, the findings of our current study indicate that REM sleep deprivation affects the physiology of different tissues and organs differently. We therefore need further research into sleep deprivation to determine stage and tissue-specific effects in order to explain particular effects and to evaluate the influence of sleep deprivation in related disorders.

## 5. Conclusion

Our microarray analysis found that many of the physiological processes and the genes involved in the pathways are regulated differently in the brain and liver tissues in response to REM sleep loss. This supports the general concept of the body reacting to the stress induced by REM sleep loss, where the liver helps to combat the body's stress response. In general, brain cells have been shown to be more receptive and influence processes such as apoptosis, learning and memory, oxidative stress, and circadian rhythms in response to REM sleep loss. On the other hand, hepatocytes were found to be more affected by processes such as protein synthesis, stress balance and detoxification. Our study provides an excellent platform for visualizing the effects of REM sleep loss in the body and can be used as the underlying basis for further studies on sleep deprivation.

## 6. Acknowledgments

This research was carried out and funded by a laboratory grant from the SKK Laboratory at the School of Biotechnology, Jawaharlal Nehru University, New Delhi, India. AP received funding from the Research Fellowship of the University Grants Commission (2008-2012), India and afterward supported by planning and budgeting committee (PBC) outstanding postdoctoral fellowship of Israel to Chinese and Indian citizens (2014-2017)

## 7. Conflict of Interests

The authors have no conflict of interest and all funding and scientific contributions are fully recognized.

**Figures and figure legends:**

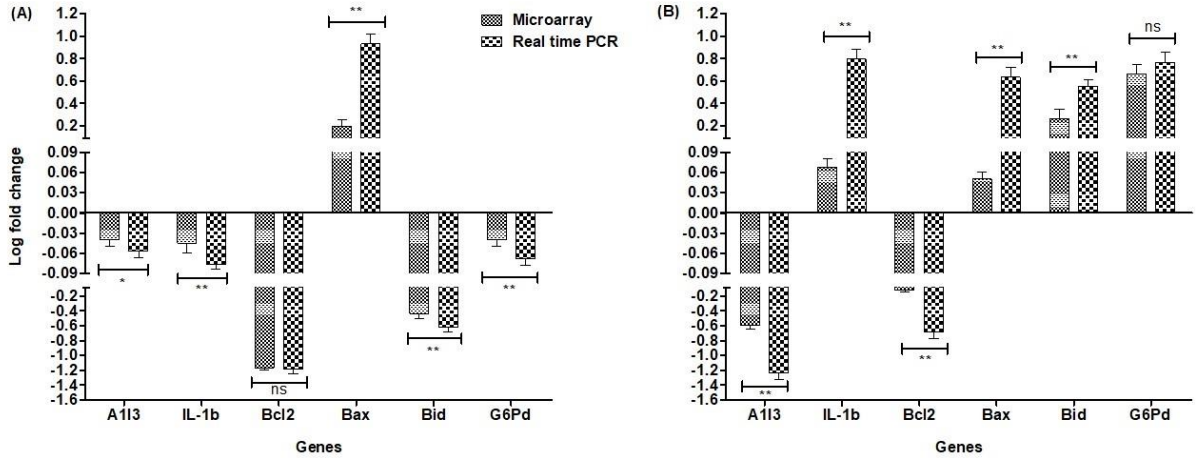



**Figure 1:** Relative expression of six candidate genes from the brain and liver tissue using real-time PCR and Microarray. (A) the comparative expression of genes in the brain; (B) the comparative expression of genes in the liver. Relative gene expressions were normalized by comparison with the expression of the Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene, while results were analyzed using the 2−ΔΔCT method. For each gene, all RT-qPCRs used five biological replicates, with three technological replicates per experiment. The non-parametric Mann-Whitney U test was used to compare the pairwise expression of the microarray and the RT-PCR expression for the respective genes.We evaluated the normality of the data using the Kolmogorov-Smirnov normality test. Error bars indicate a ±SE value.

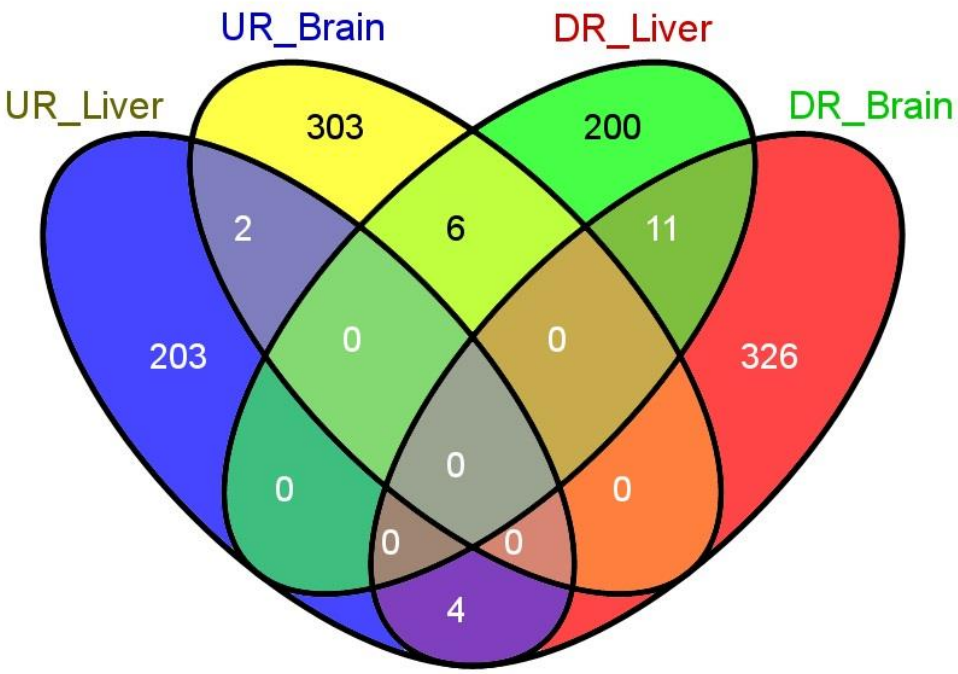



**Figure 2:** Venn diagram showing the graphical representation of the regulated genes in the liver and brain after a rapid eye movement of sleep deprivation for 9 days in the rat. The Venn diagram shows overlapping genes of the UR_Liver: up-regulated liver; UR_Brain: up-regulated brain; DR_Liver: down-regulated liver; DR_Brain: down-regulated brain. Number in separate shaded panels reflects the genes typically affected in both tissues, either in a similar direction or in the opposite direction.

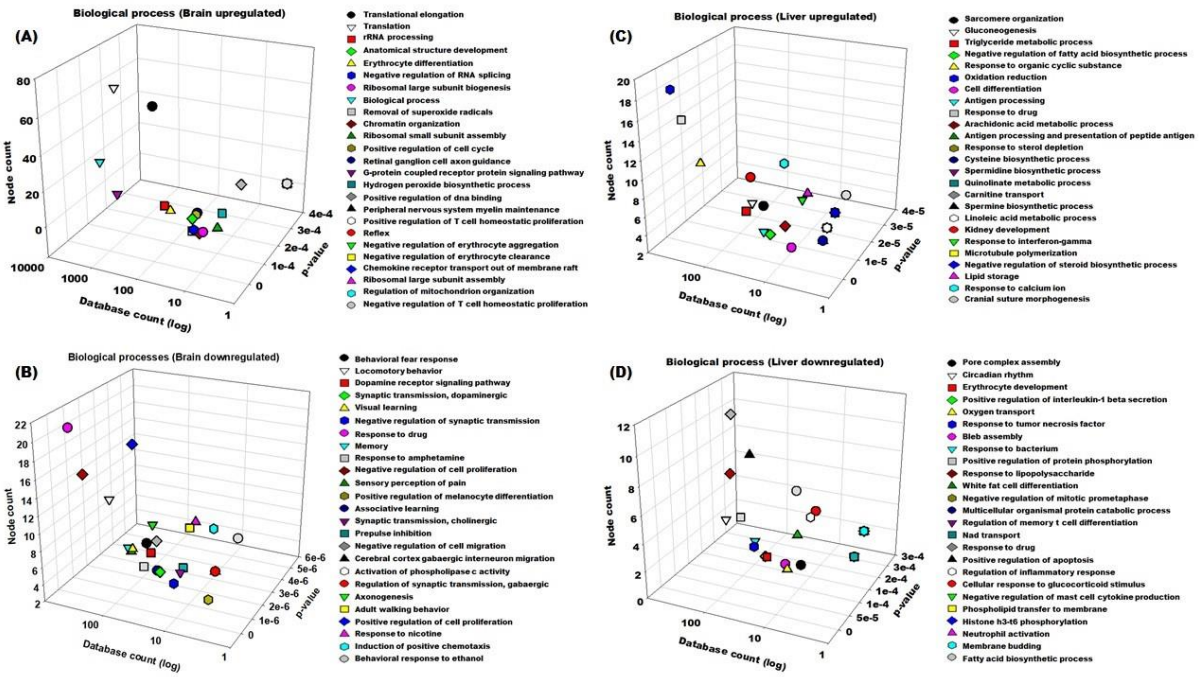



**Figure 3:** GO term analysis representation of biological processes that have been shown to be up-regulated in the brain (A), down-regulated in the brain (B), up-regulated in the liver (C) and down-regulated in the liver (D) following rapid eye movements sleep deprivation in rats. The x-axis is a *p*-value. The y-axis is the number of nodes affected. The z-axis displays the total number of log-transformed databases for the respective biological processes. The first 25 most important biological processes have been chosen for inclusion. See Supplementary Tables 3A-D for more information on the genes affected.

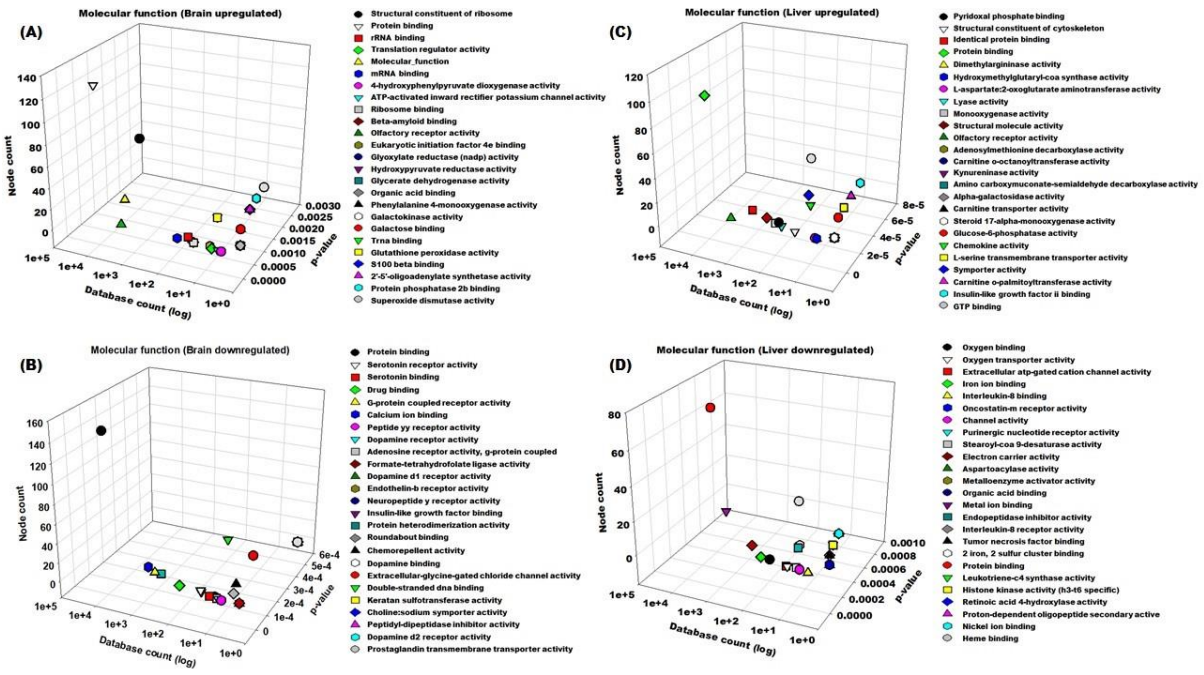



**Figure 4:** GO term analysis of the representation of molecular functions that were up-regulated in the brain (A), down-regulated in the brain (B), up-regulated in the liver (C) and down-regulated in the liver (D) following rapid eye movement sleep deprivation in rats. The x-axis is a *p*-value. The y-axis is the number of nodes affected. The z-axis displays the total number of database numbers (log-transformed) for the respective molecular function. The first 25 most important functions have been chosen for representation. See Supplementary Tables 3A-D for more information on the genes affected.

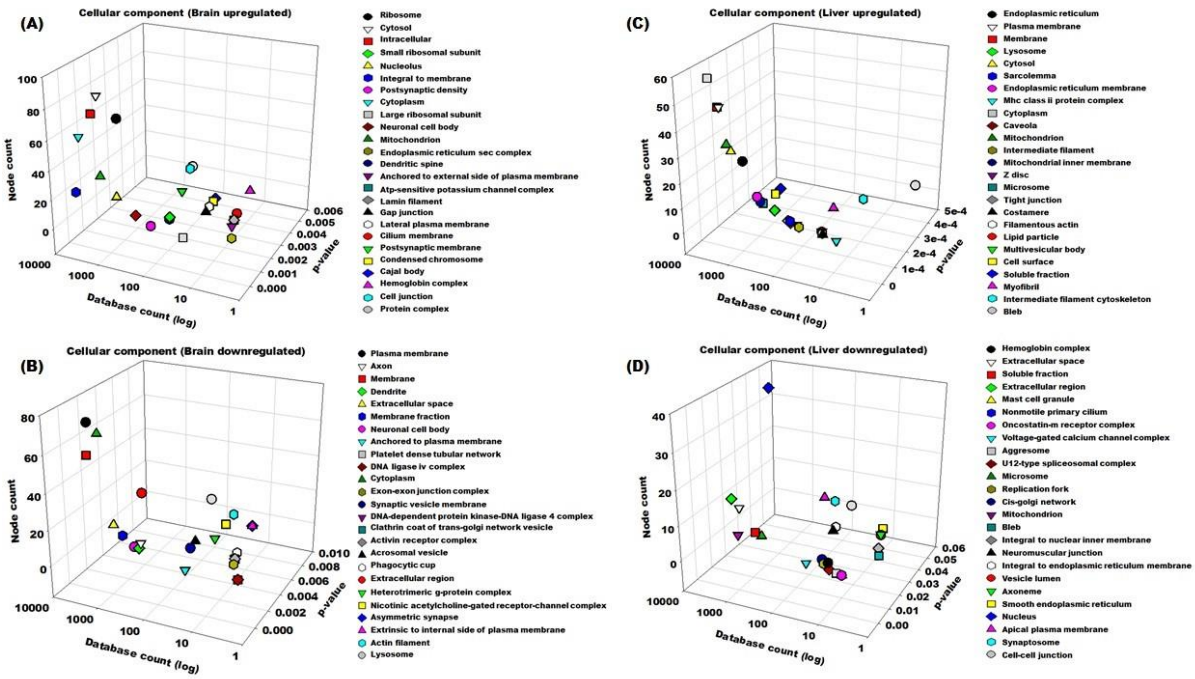



**Figure 5:** GO term study of cellular components that were up-regulated in the brain (A), down-regulated in the brain (B), up-regulated in the liver (C) and down-regulated in the liver (D) following rapid eye movements of sleep deprivation in rats. The x-axis is a *p*-value. The y-axis is the number of nodes affected. The z-axis shows the total number of database numbers (log-transformed) for the respective cellular portion. The first 25 most significant cellular components were selected for representation. See Supplementary Tables 3A-D for more information on the genes affected.

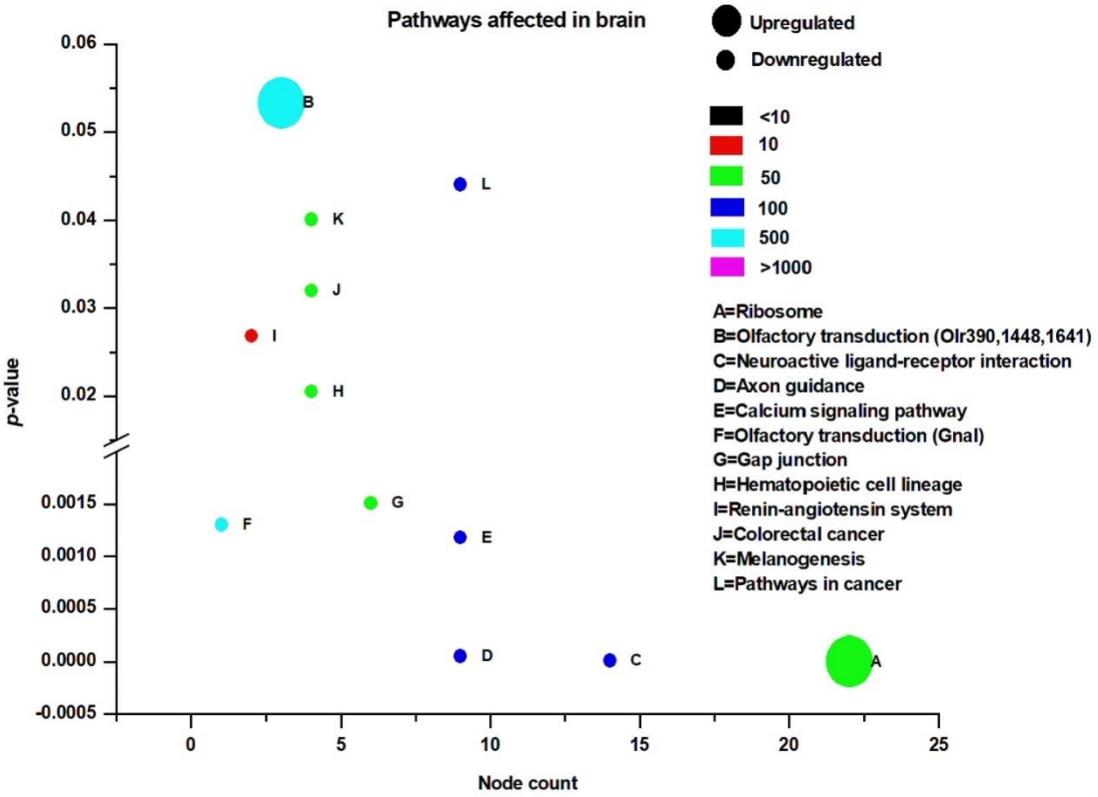



**Figure 6:** KEGG pathways affected by rapid eye movement sleep deprivation in rats in the brain. The x-axis is the number of nodes affected, while the y-axis is the *p*-value ($p<0.05$). Color coding is the epitome of the total number of database nodes evaluated. The size of the circle indicates the direction of the regulation.

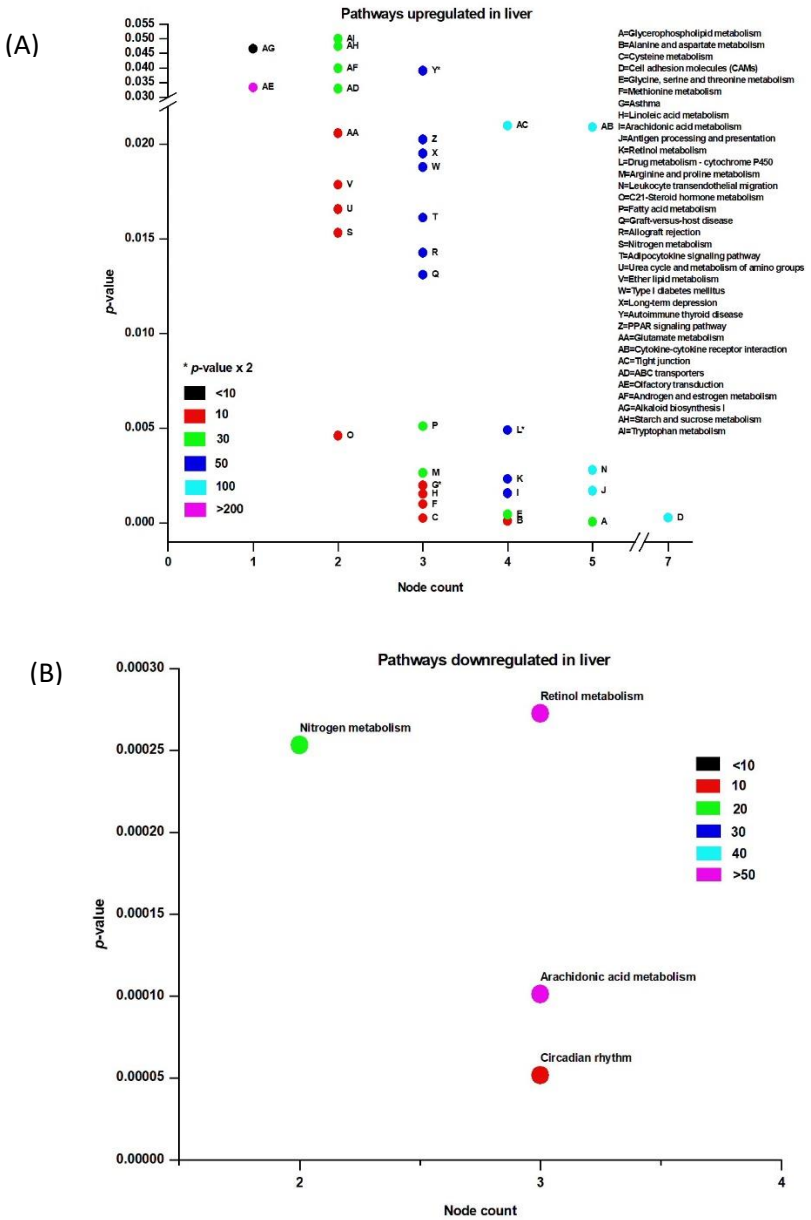
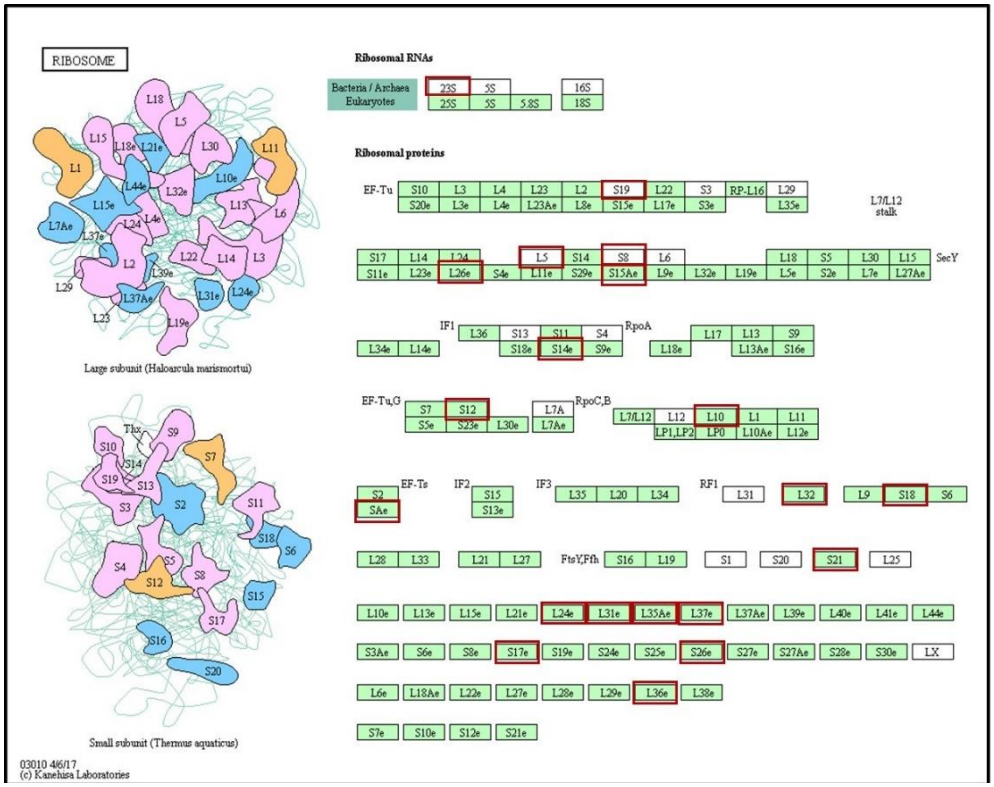
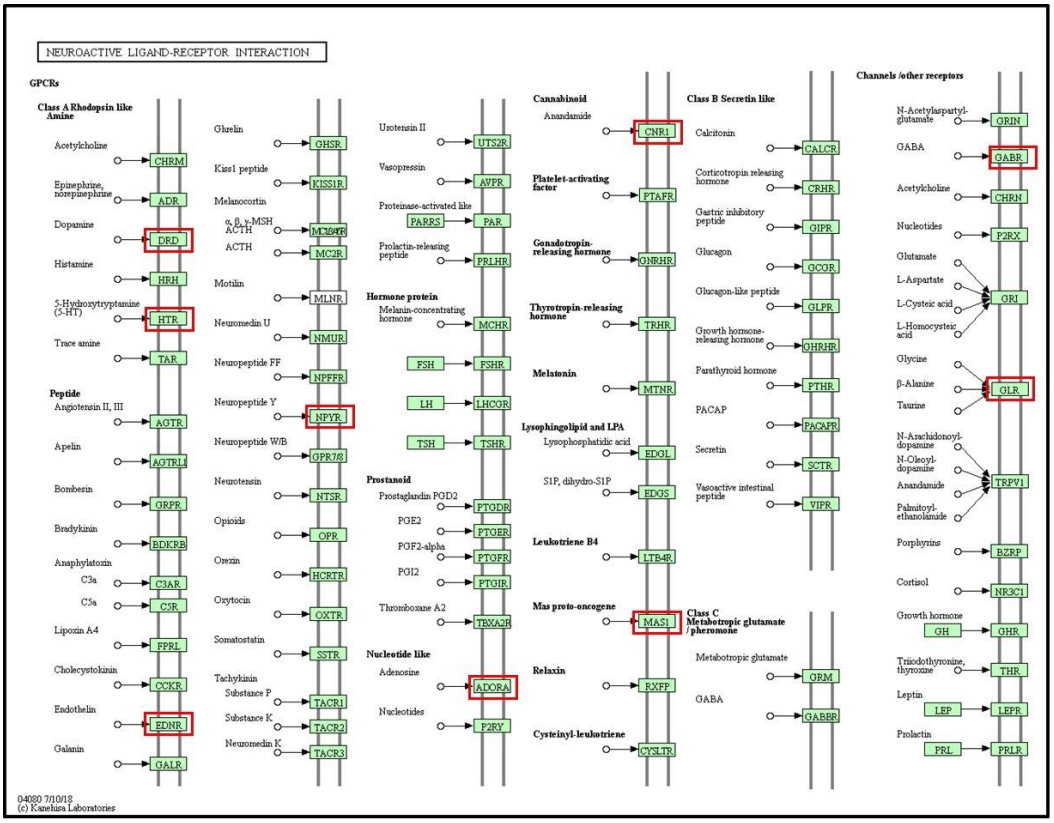


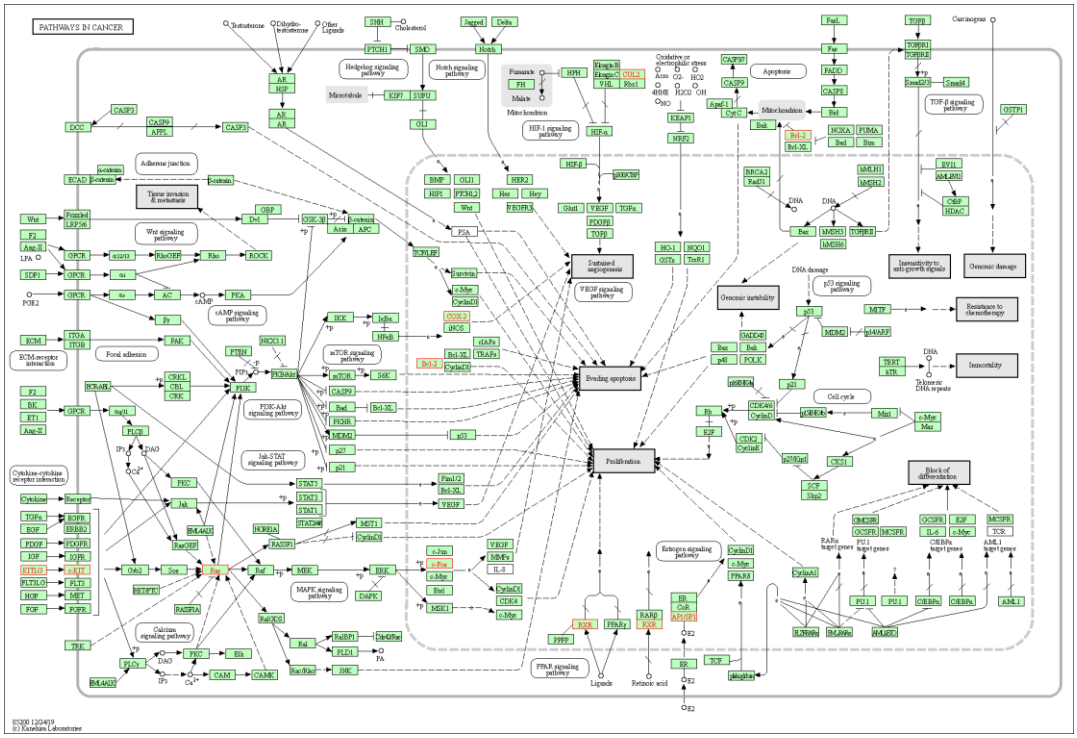

**Figure 7:** KEGG pathways affected by rapid eye movement sleep deprivation in rats in the liver. (A) Up-regulated, (B) Down-regulated. The x-axis is the number of nodes affected. The y-axis is the *p*-value ($p<0.05$). Color coding reflects the total number of nodes evaluated in the database.



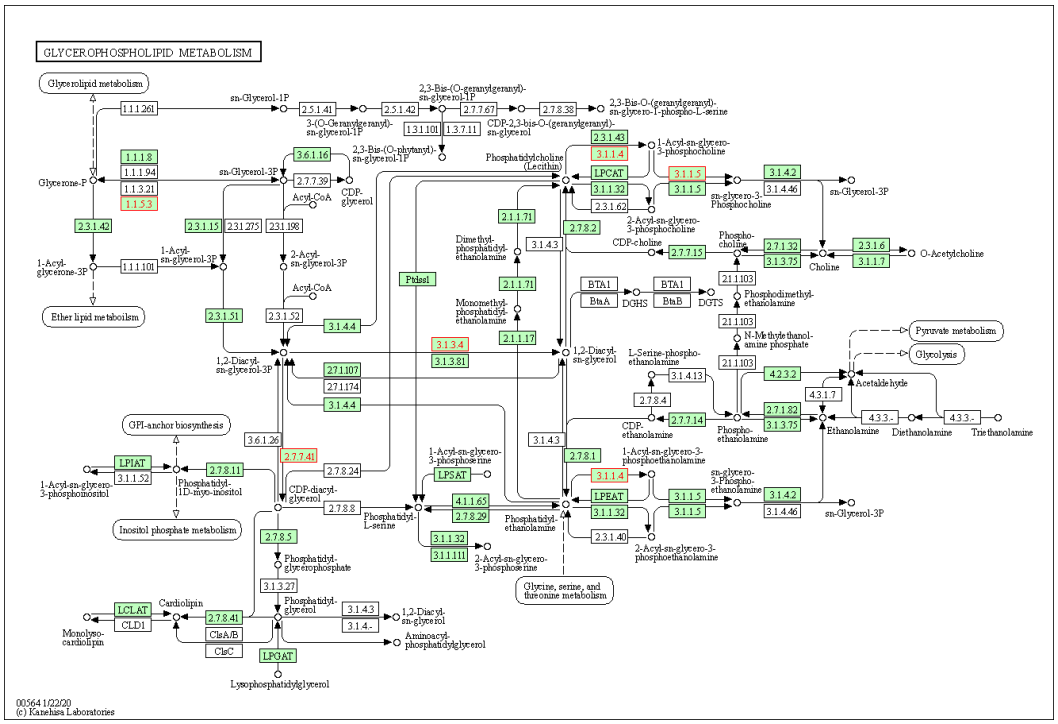

**Supplementary Figure 1:** Impact of REM sleep deprivation on ribosome proteins. The number of protein translational ribosomal subunits was found to be regulated (marked in dark red) in the entire brain of REM sleep-deprived rats. We used the bioinformatics map of KEGG for illustrative purposes.




**Supplementary Figure 2.** Influence of REM sleep deprivation on the function of the neuroactive legend-receptor. The number of genes found to be negatively affected (marked in light red) in the entire brain of REM sleep-deprived rats. We used the bioinformatics map of KEGG for illustrative purposes.




**Supplementary Figure 3:** The effect of REM sleep loss on the progression of cancer. The number of genes observed to be negatively affected (marked in light red) in liver samples of REM sleep-deprived rats. We used the bioinformatics map of KEGG for illustrative purposes.



**Supplementary Figure 4:** The effect of REM sleep loss on the metabolism process of glycerophospholipids. The number of genes observed to be negatively affected (marked in light red) in liver samples of REM sleep-deprived rats. We used the bioinformatics map of KEGG for illustrative purposes.

**Supplementary Tables:**

**Supplementary table (ST1): List of real time PCR gene primers used in microarray validation experiments.**

| S. N | **Primer/probe** | **Primer/probe sequence ID's** |
|---|---|---|
| 1 | Alpha 1 inhibitor 3 | Rn00440636-m1 |
| 2 | Interleukin-1b | Rn00580432_m1 |
| 3 | TP53 | Rn00755717_m1 |
| 4 | Bcl2 | Rn99999125_m1 |
| 5 | Bax | Rn02532082_g1 |
| 6 | Bid | Rn01459517_m1 |
| 7 | G6pD | Rn01529640_g1 |
| 8 | GAPDH | Rn01749022_g1 |
| 9 | Master mix | Cat. 4304437 |

**Supplementary table (ST2): Number of genes getting either up-regulated or down-regulated more than 1.8-fold compared to control.**

| S. No | Comparison | Fold Change | # Up-regulated Genes | # Down-regulated Genes |
|---|---|---|---|---|
| 1 | Control vs Sleep Deprived Liver | 1.8 | 209 | 217 |
| 2 | Control vs Sleep Deprived Brain | 1.8 | 311 | 341 |

**Supplementary table (ST3A): List of genes upregulated in brain**

| Probe Set ID | Control Brain | Sleep Deprived Brain | Log Fold Change | Fold Change | Entrez ID | Gene Symbol | Accession |
|---|---|---|---|---|---|---|---|
| 10701797 | 5.09 | 5.98 | 0.89 | 1.85 | 680891 | Sf3b5 | NM_001126092 |
| 10701825 | 4.66 | 5.69 | 1.03 | 2.05 | 361453 | Deadc1 | NM_001115028 |
| 10702286 | 6.52 | 7.54 | 1.01 | 2.02 | 65139 | Rps12 | NM_031709 |
| 10702306 | 2.93 | 3.79 | 0.86 | 1.81 | 252856 | Tcf21 | NM_001032397 |
| 10702361 | 3.80 | 4.81 | 1.01 | 2.01 | 155430 | Hey2 | NM_130417 |
| 10702592 | 7.46 | 8.37 | 0.90 | 1.87 | 683872 | LOC683872 | ENSRNOT00000031807 |
| 10704411 | 6.75 | 7.69 | 0.94 | 1.92 | 29287 | Rps19 | NM_001037346 |
| 10704452 | 4.48 | 5.53 | 1.05 | 2.08 | 361514 | Meis3 | NM_001108472 |
| 10705414 | 6.97 | 8.33 | 1.35 | 2.55 | 361528 | Ttc9b | NM_001108478 |
| 10705511 | 9.06 | 10.12 | 1.06 | 2.08 | 140655 | Rps16 | ENSRNOT00000026576 |
| 10705753 | 5.28 | 6.17 | 0.89 | 1.85 | 114004 | Ppp1r14a | NM_130403 |
| 10706571 | 5.53 | 6.71 | 1.18 | 2.27 | 292876 | Josd2 | NM_001106256 |
| 10710771 | 7.00 | 7.97 | 0.97 | 1.96 | 117053 | Rps15a | NM_053982 |
| 10713538 | 5.99 | 6.89 | 0.90 | 1.87 | 24913 | Pla2g16 | NM_017060 |
| 10716085 | 6.70 | 7.84 | 1.13 | 2.19 | 65139 | Rps12 | NM_031709 |
| 10716373 | 3.40 | 4.45 | 1.05 | 2.07 | 25702 | Pnlip | NM_013161 |
| 10717434 | 7.73 | 8.83 | 1.10 | 2.15 | 287417 | Rpl26 | NM_001105788 |
| 10722005 | 4.04 | 5.20 | 1.16 | 2.23 | 83535 | Kcnj11 | NM_031358 |
| 10722084 | 7.07 | 8.13 | 1.05 | 2.08 | 365243 | Sergef | ENSRNOT00000015352 |
| 10723233 | 7.22 | 8.45 | 1.23 | 2.34 | 29286 | Rps17 | NM_017152 |
| 10725078 | 3.48 | 4.50 | 1.02 | 2.02 | 499249 | Plekha7 | NM_001144861 |
| 10726477 | 3.85 | 4.94 | 1.09 | 2.13 | 309095 | Nkx6-2 | NM_001107558 |
| 10728312 | 6.40 | 7.34 | 0.94 | 1.92 | 293702 | Fkbp2 | NM_001134429 |
| 10731729 | 8.40 | 9.28 | 0.88 | 1.84 | 363248 | Rpl37a | NM_001100994 |
| 10732439 | 4.86 | 6.28 | 1.41 | 2.66 | 685451 | Gng13 | NM_001135918 |
| 10733888 | 4.80 | 5.92 | 1.12 | 2.17 | 287336 | Olr1448 | NM_001000019 |
| 10734817 | 7.35 | 8.39 | 1.05 | 2.07 | 287417 | Rpl26 | NM_001105788 |
| 10736053 | 9.03 | 9.98 | 0.94 | 1.92 | 81770 | Rpl37 | NM_031106 |
| 10736232 | 8.78 | 9.71 | 0.93 | 1.90 | 360572 | Rpl23a | NM_001108283 |
| 10737445 | 9.98 | 10.97 | 0.99 | 1.98 | 688136 | LOC688136 | XM_001081257 |
| 10738657 | 5.82 | 6.80 | 0.98 | 1.98 | 303577 | Acbd4 | NM_001012013 |
| 10739395 | 9.56 | 10.47 | 0.91 | 1.88 | 689284 | Rpl38 | NM_001077592 |
| 10739994 | 2.84 | 3.86 | 1.02 | 2.03 | 303735 | Rnf213 | ENSRNOT00000004904 |
| 10741529 | 4.91 | 5.93 | 1.02 | 2.03 | 287151 | Metrn | NM_001009962 |
| 10741756 | 7.65 | 9.22 | 1.57 | 2.98 | 25632 | Hba-a2 | NM_013096 |
| 10741778 | 7.39 | 8.85 | 1.45 | 2.74 | 25632 | Hba-a2 | NM_013096 |
| 10745595 | 2.70 | 3.65 | 0.95 | 1.94 | 303378 | Slfn8 | NM_001013970 |
| 10746952 | 7.41 | 8.31 | 0.90 | 1.87 | 57809 | Rpl35a | NM_021264 |
| 10749058 | 6.94 | 7.91 | 0.96 | 1.95 | 294282 | Rps18 | NM_213557 |
| 10749061 | 4.93 | 5.87 | 0.93 | 1.91 | 287835 | Galk1 | NM_001008282 |
| 10751767 | 4.53 | 5.54 | 1.02 | 2.03 | 27139 | Rps26 | NM_013224 |
| 10752146 | 6.99 | 7.86 | 0.87 | 1.82 | 117053 | Rps15a | NM_053982 |
| 10753005 | 7.85 | 8.88 | 1.03 | 2.04 | 24786 | Sod1 | NM_017050 |
| 10756054 | 5.11 | 6.41 | 1.30 | 2.46 | 65131 | Cldn5 | NM_031701 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10756455 | 4.06 | 4.97 | 0.91 | 1.88 | 140635 | Flt3 | NM_001100822 |
| 10756546 | 9.69 | 10.57 | 0.88 | 1.84 | 690441 | Atp5j2 | ENSRNOT00000033537 |
| 10758457 | 4.37 | 5.35 | 0.98 | 1.97 | 29531 | Hpd | NM_017233 |
| 10758777 | 2.96 | 4.04 | 1.08 | 2.12 | 192281 | Oas1a | NM_138913 |
| 10760018 | 7.59 | 8.47 | 0.87 | 1.83 | 57809 | Rpl35a | NM_021264 |
| 10761299 | 6.29 | 7.22 | 0.93 | 1.90 | 498173 | Auts2 | ENSRNOT00000044800 |
| 10762537 | 6.27 | 7.29 | 1.02 | 2.03 | 83620 | Cit | NM_001029911 |
| 10766797 | 3.83 | 4.74 | 0.90 | 1.87 | 364081 | Irf6 | NM_001108859 |
| 10767371 | 8.85 | 9.86 | 1.01 | 2.01 | 27139 | Rps26 | NM_013224 |
| 10770117 | 4.99 | 5.99 | 1.01 | 2.01 | 289264 | Grem2 | NM_001105974 |
| 10771040 | 5.24 | 6.17 | 0.93 | 1.90 | 689919 | LOC689919 | ENSRNOT00000061643 |
| 10771592 | 3.88 | 4.77 | 0.89 | 1.85 | 289501 | Ankrd56 | ENSRNOT00000002995 |
| 10772655 | 7.26 | 8.49 | 1.23 | 2.35 | 124323 | Rps23 | NM_078617 |
| 10772901 | 9.84 | 10.70 | 0.86 | 1.82 | 29507 | Cox7a2 | NM_022503 |
| 10772982 | 5.59 | 6.48 | 0.88 | 1.84 | 58927 | Rpl36 | NM_022504 |
| 10772984 | 5.59 | 6.48 | 0.88 | 1.84 | 58927 | Rpl36 | NM_022504 |
| 10774359 | 9.55 | 10.49 | 0.94 | 1.92 | 689284 | Rpl38 | NM_001077592 |
| 10774372 | 7.68 | 8.72 | 1.04 | 2.06 | 691531 | Rps28 | NM_001105730 |
| 10774894 | 8.32 | 9.57 | 1.25 | 2.37 | 124440 | Rpl41 | NM_139083 |
| 10776237 | 9.05 | 10.15 | 1.10 | 2.15 | 360572 | Rpl23a | NM_001108283 |
| 10778058 | 4.63 | 5.48 | 0.85 | 1.81 | 681091 | Ccdc157 | ENSRNOT00000006911 |
| 10778918 | 6.18 | 7.05 | 0.87 | 1.82 | 29287 | Rps19 | NM_001037346 |
| 10780979 | 6.51 | 7.55 | 1.04 | 2.06 | 360572 | Rpl23a | NM_001108283 |
| 10781984 | 5.99 | 6.95 | 0.97 | 1.96 | 306157 | Gpc5 | NM_001107285 |
| 10782041 | 5.80 | 7.10 | 1.31 | 2.48 | 306170 | RGD1560050 | ENSRNOT00000057567 |
| 10783353 | 6.26 | 7.12 | 0.86 | 1.82 | 29287 | Rps19 | NM_001037346 |
| 10783357 | 2.60 | 3.51 | 0.92 | 1.89 | 290050 | Olr1641 | NM_001000100 |
| 10784117 | 4.22 | 5.46 | 1.24 | 2.36 | 394266 | Gjb2 | NM_001004099 |
| 10784512 | 2.85 | 3.79 | 0.94 | 1.92 | 498534 | RGD1565212 | NM_001109103 |
| 10787085 | 2.59 | 3.71 | 1.12 | 2.17 | 25331 | Mat1a | NM_012860 |
| 10788293 | 2.23 | 3.07 | 0.85 | 1.80 | 290757 | F11 | NM_001047848 |
| 10790471 | 4.76 | 5.81 | 1.05 | 2.07 | 64347 | Sncg | NM_031688 |
| 10790525 | 9.55 | 10.49 | 0.94 | 1.92 | 689284 | Rpl38 | NM_001077592 |
| 10791497 | 2.81 | 3.84 | 1.03 | 2.04 | 29395 | Hmgb2 | NM_017187 |
| 10792163 | 5.13 | 5.98 | 0.85 | 1.80 | 116636 | Eif4ebp1 | NM_053857 |
| 10795546 | 6.25 | 7.15 | 0.90 | 1.86 | 29287 | Rps19 | NM_001037346 |
| 10796677 | 9.55 | 10.41 | 0.86 | 1.82 | 81770 | Rpl37 | NM_031106 |
| 10796991 | 5.32 | 6.27 | 0.95 | 1.93 | 290963 | Npepo | NM_001012346 |
| 10797469 | 5.11 | 6.00 | 0.89 | 1.85 | 25461 | Hrh2 | NM_012965 |
| 10798499 | 7.02 | 8.00 | 0.98 | 1.98 | 64627 | Hist1h4b | NM_022686 |
| 10800426 | 3.36 | 4.23 | 0.88 | 1.84 | 24856 | Ttr | NM_012681 |
| 10801821 | 4.50 | 5.35 | 0.85 | 1.80 | 116685 | Lmnb1 | NM_053905 |
| 10802128 | 8.53 | 9.64 | 1.11 | 2.17 | 124323 | Rps23 | NM_078617 |
| 10803025 | 4.32 | 5.58 | 1.25 | 2.38 | 361354 | Fbxo15 | NM_001108436 |
| 10805996 | 4.79 | 5.89 | 1.10 | 2.14 | 64364 | Pllp | NM_022533 |
| 10806210 | 2.61 | 3.69 | 1.07 | 2.10 | 29225 | Es22 | NM_031565 |
| 10807044 | 4.69 | 5.95 | 1.26 | 2.39 | 688429 | Arhgap10 | NM_001109501 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10807514 | 6.79 | 7.90 | 1.12 | 2.17 | 65139 | Rps12 | NM_031709 |
| 10807542 | 2.52 | 3.77 | 1.25 | 2.38 | 83502 | Cdh1 | NM_031334 |
| 10808107 | 3.72 | 4.66 | 0.93 | 1.91 | 498954 | RGD1563834 | XR_085682 |
| 10809402 | 7.21 | 8.71 | 1.50 | 2.83 | 117038 | Mt3 | NM_053968 |
| 10810299 | 7.25 | 8.21 | 0.96 | 1.94 | 361385 | Ndufb7 | NM_001108442 |
| 10812416 | 8.60 | 9.62 | 1.02 | 2.03 | 124323 | Rps23 | NM_078617 |
| 10812899 | 9.01 | 10.01 | 1.00 | 1.99 | 360572 | Rpl23a | NM_001108283 |
| 10813330 | 8.98 | 9.94 | 0.96 | 1.94 | 81770 | Rpl37 | NM_031106 |
| 10813951 | 5.20 | 6.16 | 0.95 | 1.94 | 619558 | Fam134b | ENSRNOT00000014423 |
| 10814540 | 6.08 | 7.19 | 1.11 | 2.16 | 310269 | RGD1307225 | NM_001107663 |
| 10816675 | 2.94 | 3.80 | 0.85 | 1.81 | 24651 | Pklr | NM_012624 |
| 10821695 | 7.01 | 7.94 | 0.93 | 1.91 | 117053 | Rps15a | NM_053982 |
| 10822005 | 4.65 | 5.54 | 0.88 | 1.85 | 78961 | Golph3 | NM_023977 |
| 10822929 | 2.77 | 3.67 | 0.89 | 1.86 | 207120 | Nudt6 | NM_181363 |
| 10824689 | 5.30 | 6.19 | 0.88 | 1.84 | 295214 | S100a1 | NM_001007636 |
| 10825236 | 9.55 | 10.49 | 0.94 | 1.92 | 689284 | Rpl38 | NM_001077592 |
| 10825238 | 1.68 | 2.60 | 0.92 | 1.89 | 365885 | Olr390 | NM_001000558 |
| 10825768 | 2.68 | 3.69 | 1.00 | 2.00 | 310771 | Chi3l4 | XM_001069770 |
| 10828433 | 7.49 | 8.53 | 1.04 | 2.06 | 294282 | Rps18 | NM_213557 |
| 10828737 | 7.31 | 8.18 | 0.86 | 1.82 | 81729 | Rpl10a | NM_031065 |
| 10830624 | 6.65 | 7.54 | 0.89 | 1.85 | 25145 | Cd24 | NM_012752 |
| 10832847 | 3.57 | 4.44 | 0.87 | 1.83 | 309902 | Tet1 | NM_001107643 |
| 10833564 | 4.24 | 5.36 | 1.13 | 2.19 | 499454 | RGD1560095 | ENSRNOT00000040584 |
| 10834310 | 7.11 | 8.00 | 0.89 | 1.85 | 296570 | Edf1 | NM_001106557 |
| 10839400 | 8.99 | 9.86 | 0.86 | 1.82 | 28298 | Rpl32 | NM_013226 |
| 10839443 | 3.88 | 4.95 | 1.07 | 2.11 | 65192 | Slc27a2 | NM_031736 |
| 10839876 | 6.77 | 7.92 | 1.15 | 2.23 | 65139 | Rps12 | NM_031709 |
| 10840783 | 3.65 | 4.60 | 0.95 | 1.93 | 311536 | RGD1304644 | BC099097 |
| 10841484 | 5.64 | 6.74 | 1.11 | 2.15 | 679572 | Romo1 | ENSRNOT00000026856 |
| 10842436 | 8.85 | 9.73 | 0.89 | 1.85 | 689284 | Rpl38 | NM_001077592 |
| 10842667 | 4.55 | 5.43 | 0.88 | 1.84 | 64307 | Rpl24 | NM_022515 |
| 10842805 | 8.48 | 9.72 | 1.24 | 2.37 | 81775 | Rps21 | NM_031111 |
| 10842971 | 5.31 | 6.30 | 0.99 | 1.99 | 362288 | Rtel1 | ENSRNOT00000055030 |
| 10844327 | 6.85 | 7.93 | 1.08 | 2.12 | 499780 | RGD1561113 | ENSRNOT00000034930 |
| 10844946 | 7.17 | 8.33 | 1.15 | 2.23 | 29286 | Rps17 | NM_017152 |
| 10851386 | 8.32 | 9.31 | 0.99 | 1.98 | 81765 | Rpl13 | NM_031101 |
| 10851650 | 3.10 | 5.10 | 2.00 | 4.01 | 296369 | Tnnc2 | NM_001037351 |
| 10853871 | 2.28 | 3.49 | 1.21 | 2.31 | 24255 | Cftr | NM_031506 |
| 10854386 | 2.69 | 3.57 | 0.88 | 1.84 | 296968 | RGD1308226 | NM_001106589 |
| 10857231 | 3.78 | 4.87 | 1.09 | 2.12 | 685999 | Uroc1 | ENSRNOT00000038251 |
| 10861676 | 9.43 | 10.31 | 0.89 | 1.85 | 689284 | Rpl38 | NM_001077592 |
| 10863218 | 4.07 | 5.08 | 1.01 | 2.01 | 83730 | Vamp8 | NM_031827 |
| 10863664 | 5.00 | 5.91 | 0.91 | 1.88 | 312504 | RGD1566130 | NM_001107871 |
| 10863679 | 5.96 | 7.29 | 1.33 | 2.52 | 114020 | Cml5 | NM_080884 |
| 10864121 | 4.38 | 5.53 | 1.16 | 2.23 | 171571 | Grip2 | NM_138535 |
| 10864425 | 5.51 | 6.40 | 0.89 | 1.85 | 297481 | Eif4e3 | NM_001106612 |
| 10864769 | 9.59 | 10.54 | 0.95 | 1.93 | 28298 | Rpl32 | NM_013226 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10865630 | 3.83 | 4.84 | 1.00 | 2.01 | 362438 | Ncapd2 | ENSRNOT00000025889 |
| 10866505 | 8.90 | 9.85 | 0.95 | 1.93 | 690830 | LOC690830 | XM_001075809 |
| 10868673 | 4.81 | 5.82 | 1.01 | 2.01 | 680021 | Grhpr | NM_001113754 |
| 10870043 | 6.60 | 7.45 | 0.85 | 1.80 | 294282 | Rps18 | NM_213557 |
| 10871071 | 2.78 | 3.71 | 0.93 | 1.91 | 313507 | Tal1 | NM_001107958 |
| 10871169 | 7.97 | 8.92 | 0.95 | 1.93 | 366448 | Uqcrh | NM_001009480 |
| 10872015 | 3.84 | 4.99 | 1.16 | 2.23 | 362597 | Fam176b | BC167091 |
| 10872093 | 7.21 | 8.08 | 0.88 | 1.84 | 57809 | Rpl35a | NM_021264 |
| 10872139 | 6.41 | 7.28 | 0.87 | 1.83 | 286923 | Dlgap3 | NM_173138 |
| 10873322 | 10.01 | 10.92 | 0.90 | 1.87 | 287005 | Camk2n1 | NM_173337 |
| 10874691 | 6.17 | 7.06 | 0.88 | 1.85 | 117053 | Rps15a | NM_053982 |
| 10875089 | 4.87 | 5.73 | 0.85 | 1.81 | 362472 | Cspp1 | ENSRNOT00000008480 |
| 10876652 | 3.62 | 4.71 | 1.09 | 2.12 | 362515 | Anks6 | NM_001015028 |
| 10877372 | 2.63 | 4.04 | 1.41 | 2.65 | 298107 | Mup5 | AB039828 |
| 10878428 | 9.57 | 10.45 | 0.87 | 1.83 | 28298 | Rpl32 | NM_013226 |
| 10878910 | 10.00 | 11.11 | 1.11 | 2.16 | 27139 | Rps26 | NM_013224 |
| 10878954 | 8.19 | 9.04 | 0.85 | 1.80 | 65136 | Rps8 | NM_031706 |
| 10880710 | 3.96 | 5.00 | 1.04 | 2.06 | 313633 | Ephb2 | NM_001127319 |
| 10881596 | 4.05 | 4.98 | 0.93 | 1.90 | 313705 | Ptchd2 | NM_001107992 |
| 10882221 | 5.23 | 6.10 | 0.86 | 1.82 | 680723 | Tmem88b | NM_001109426 |
| 10886036 | 5.18 | 6.03 | 0.86 | 1.81 | 116674 | Jdp2 | NM_053894 |
| 10891400 | 5.47 | 6.44 | 0.98 | 1.97 | 64629 | Porf1 | ENSRNOT00000005162 |
| 10891679 | 3.84 | 4.84 | 1.00 | 2.00 | 314386 | Gpr68 | NM_001108049 |
| 10892702 | 9.55 | 10.45 | 0.90 | 1.87 | 28298 | Rpl32 | NM_013226 |
| 10892937 | 5.93 | 6.90 | 0.97 | 1.95 | 29287 | Rps19 | NM_001037346 |
| 10894055 | 4.90 | 5.87 | 0.97 | 1.96 | 314612 | Shc2 | NM_001108065 |
| 10894681 | 3.46 | 4.72 | 1.25 | 2.39 | 24616 | Pah | NM_012619 |
| 10894810 | 6.69 | 7.96 | 1.27 | 2.41 | 314721 | Anks1b | ENSRNOT00000064242 |
| 10894812 | 9.54 | 10.68 | 1.13 | 2.19 | 314721 | Anks1b | ENSRNOT00000064242 |
| 10894814 | 8.48 | 9.80 | 1.32 | 2.49 | 314721 | Anks1b | ENSRNOT00000064242 |
| 10897450 | 4.97 | 5.85 | 0.88 | 1.84 | 300317 | Kctd17 | NM_001134529 |
| 10899465 | 4.89 | 6.07 | 1.18 | 2.26 | 25641 | Igfbp6 | NM_013104 |
| 10899824 | 8.93 | 9.93 | 1.00 | 2.00 | 124440 | Rpl41 | NM_139083 |
| 10899868 | 9.28 | 10.32 | 1.04 | 2.05 | 27139 | Rps26 | NM_013224 |
| 10900533 | 7.47 | 8.59 | 1.12 | 2.17 | 29285 | Rps15 | NM_017151 |
| 10900618 | 7.94 | 8.86 | 0.92 | 1.89 | 29328 | Gpx4 | NM_017165 |
| 10901178 | 8.62 | 9.60 | 0.98 | 1.97 | 691531 | Rps28 | NM_001105730 |
| 10902047 | 2.67 | 4.50 | 1.83 | 3.56 | 299757 | Nts | NM_001102381 |
| 10903583 | 6.68 | 7.68 | 1.01 | 2.01 | 81763 | Rpl5 | NM_031099 |
| 10904227 | 5.88 | 6.86 | 0.98 | 1.98 | 29287 | Rps19 | NM_001037346 |
| 10905277 | 6.56 | 7.47 | 0.91 | 1.88 | 25269 | Pvalb | NM_022499 |
| 10905558 | 6.83 | 7.82 | 0.99 | 1.98 | 287417 | Rpl26 | NM_001105788 |
| 10907297 | 3.76 | 4.65 | 0.89 | 1.85 | 300236 | Smagp | NM_182817 |
| 10907324 | 4.08 | 4.95 | 0.87 | 1.83 | 683264 | Galnt6 | NM_001172063 |
| 10908347 | 4.44 | 5.68 | 1.24 | 2.36 | 25638 | Pde4a | NM_013101 |
| 10909002 | 3.39 | 4.80 | 1.41 | 2.67 | 619560 | Rup2 | NM_001034950 |
| 10909009 | 2.12 | 3.94 | 1.83 | 3.55 | 619560 | Rup2 | AF368860 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10909758 | 8.33 | 9.51 | 1.19 | 2.28 | 81775 | Rps21 | NM_031111 |
| 10909892 | 6.43 | 7.39 | 0.96 | 1.95 | 25420 | Cryab | NM_012935 |
| 10910458 | 9.55 | 10.49 | 0.94 | 1.92 | 689284 | Rpl38 | NM_001077592 |
| 10914308 | 9.02 | 10.12 | 1.10 | 2.14 | 29236 | Rpsa | NM_017138 |
| 10915345 | 5.30 | 6.22 | 0.93 | 1.90 | 313783 | Olfm2 | NM_001015017 |
| 10918055 | 3.75 | 4.67 | 0.91 | 1.88 | 315741 | Paqr5 | NM_001014092 |
| 10918776 | 7.03 | 7.90 | 0.87 | 1.82 | 681849 | LOC681849 | ENSRNOT00000067627 |
| 10920967 | 2.90 | 3.76 | 0.86 | 1.81 | 363165 | Csrnp1 | NM_001108786 |
| 10921036 | 3.59 | 5.10 | 1.50 | 2.83 | 363168 | Lyzl4 | ENSRNOT00000026173 |
| 10921274 | 7.90 | 8.82 | 0.92 | 1.89 | 316164 | Satb1 | NM_001012129 |
| 10922268 | 4.54 | 5.66 | 1.12 | 2.18 | 170843 | Khdrbs2 | NM_133318 |
| 10924217 | 9.88 | 10.80 | 0.91 | 1.89 | 363248 | Rpl37a | NM_001108801 |
| 10926386 | 4.45 | 5.39 | 0.94 | 1.93 | 681367 | LOC681367 | XM_001061427 |
| 10926683 | 5.93 | 6.98 | 1.05 | 2.07 | 301265 | Pla2g7 | NM_001009353 |
| 10927281 | 6.87 | 7.73 | 0.86 | 1.81 | 29284 | Rps14 | NM_022672 |
| 10927372 | 3.86 | 4.98 | 1.12 | 2.17 | 367251 | Ankrd39 | NM_001135014 |
| 10930091 | 6.64 | 7.55 | 0.91 | 1.88 | 316643 | Chchd2 | NM_001015019 |
| 10930762 | 1.98 | 3.22 | 1.24 | 2.36 | 171521 | Cyp2c13 | NM_138514 |
| 10933957 | 9.74 | 10.61 | 0.87 | 1.82 | 28298 | Rpl32 | NM_013226 |
| 10934500 | 9.55 | 10.53 | 0.99 | 1.98 | 27139 | Rps26 | NM_013224 |
| 10937356 | 9.22 | 10.26 | 1.05 | 2.07 | 27139 | Rps26 | NM_013224 |
| 10938962 | 8.59 | 9.64 | 1.04 | 2.06 | 81775 | Rps21 | NM_031111 |
| 10940358 | 3.97 | 5.10 | 1.13 | 2.19 | 293862 | Fam50a | NM_001170573 |

**Supplementary table (ST-3B): List of genes downregulated in brain**

| Probe Set ID | Control Brain | Sleep Deprived Brain | Log Fold Change | Fold Change | Entrez ID | Gene Symbol | Accession |
|---|---|---|---|---|---|---|---|
| 10702201 | 5.59 | 4.73 | -0.86 | 0.55 | 361458 | Akap7 | NM_001001801 |
| 10702626 | 6.12 | 4.91 | -1.21 | 0.43 | 361472 | Mthfd1l | NM_001108462 |
| 10702991 | 4.68 | 3.67 | -1.02 | 0.49 | 25153 | Mas1 | NM_012757 |
| 10705825 | 5.51 | 4.65 | -0.86 | 0.55 | 246264 | Zfp382 | NM_144749 |
| 10708616 | 7.21 | 6.08 | -1.13 | 0.46 | 293112 | Crebzf | NM_001106279 |
| 10709020 | 9.84 | 8.79 | -1.05 | 0.48 | 685076 | Pgm2l1 | NM_001109454 |
| 10709844 | 5.46 | 4.42 | -1.04 | 0.49 | 308937 | Wee1 | NM_001012742 |
| 10715149 | 4.35 | 3.30 | -1.05 | 0.48 | 294072 | Tmem20 | ENSRNOT00000044895 |
| 10715519 | 5.67 | 4.80 | -0.87 | 0.55 | 293939 | Erlin1 | NM_001106353 |
| 10716026 | 6.12 | 5.05 | -1.07 | 0.48 | 294043 | Sorcs3 | NM_001106367 |
| 10717053 | 3.43 | 2.38 | -1.05 | 0.48 | 308717 | Slc35d3 | NM_001107522 |
| 10717069 | 6.29 | 5.25 | -1.04 | 0.49 | 140929 | Pde7b | NM_080894 |
| 10717325 | 4.44 | 3.51 | -0.94 | 0.52 | 308028 | Slc2a12 | NM_001107451 |
| 10719134 | 4.63 | 3.58 | -1.05 | 0.48 | 499083 | Zscan18 | ENSRNOT00000036880 |
| 10720126 | 3.49 | 2.62 | -0.87 | 0.55 | 687333 | LOC687333 | ENSRNOT00000025586 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10722218 | 4.11 | 3.23 | -0.88 | 0.54 | 404658 | Mrgprb4 | ENSRNOT00000045792 |
| 10722532 | 5.36 | 4.09 | -1.27 | 0.41 | 25302 | Chrna7 | NM_012832 |
| 10723351 | 4.35 | 3.48 | -0.87 | 0.55 | 116996 | Il16 | NM_001105749 |
| 10724785 | 6.69 | 5.64 | -1.05 | 0.48 | 361625 | Nrip3 | NM_001108498 |
| 10725778 | 5.06 | 4.18 | -0.88 | 0.54 | 113900 | Nupr1 | NM_053611 |
| 10726999 | 4.57 | 3.28 | -1.29 | 0.41 | 24483 | Igf2 | NM_031511 |
| 10727717 | 6.79 | 5.68 | -1.11 | 0.46 | 266734 | Npas4 | NM_153626 |
| 10729314 | 9.46 | 8.61 | -0.85 | 0.55 | 83585 | Gda | NM_031776 |
| 10730206 | 7.14 | 6.28 | -0.85 | 0.55 | 65047 | Slit1 | NM_022953 |
| 10734045 | 6.24 | 5.08 | -1.16 | 0.45 | 287371 | Lrrc48 | NM_001013857 |
| 10734422 | 5.23 | 4.36 | -0.88 | 0.54 | 117251 | Dnah9 | ENSRNOT00000005583 |
| 10739351 | 4.86 | 2.66 | -2.20 | 0.22 | 29719 | Kcnj16 | NM_053314 |
| 10739984 | 4.91 | 4.02 | -0.89 | 0.54 | 303735 | Rnf213 | ENSRNOT00000004904 |
| 10741907 | 6.97 | 6.01 | -0.97 | 0.51 | 25498 | Npm1 | NM_012992 |
| 10743715 | 4.80 | 3.18 | -1.62 | 0.32 | 497926 | Shisa6 | ENSRNOT00000057509 |
| 10744081 | 5.82 | 4.33 | -1.49 | 0.36 | 360546 | Efnb3 | NM_001100980 |
| 10748498 | 5.07 | 3.95 | -1.12 | 0.46 | 29481 | Rgs9 | NM_019224 |
| 10750551 | 7.40 | 6.53 | -0.88 | 0.54 | 29202 | Epha6 | ENSRNOT00000047310 |
| 10750928 | 7.54 | 6.59 | -0.95 | 0.52 | 303963 | Dzip3 | ENSRNOT00000002678 |
| 10751237 | 4.51 | 3.29 | -1.22 | 0.43 | 498085 | RGD1563835 | ENSRNOT00000042756 |
| 10751700 | 7.89 | 7.00 | -0.89 | 0.54 | 192361 | Ppp1r2 | NM_138823 |
| 10752576 | 5.49 | 4.49 | -0.99 | 0.50 | 287925 | Pkp2 | NM_001100499 |
| 10752738 | 7.18 | 6.32 | -0.87 | 0.55 | 29734 | Hspa13 | NM_019271 |
| 10753269 | 6.49 | 5.45 | -1.03 | 0.49 | 25743 | Kcnj6 | NM_013192 |
| 10758020 | 7.30 | 6.33 | -0.98 | 0.51 | 288620 | Cct6a | NM_001033684 |
| 10762426 | 5.93 | 4.74 | -1.20 | 0.44 | 117271 | Hrk | NM_057130 |
| 10763421 | 3.92 | 2.91 | -1.00 | 0.50 | 297865 | Dsel | ENSRNOT00000043890 |
| 10763933 | 7.54 | 6.32 | -1.22 | 0.43 | 289020 | Lrrn2 | NM_001177368 |
| 10764139 | 6.93 | 6.05 | -0.88 | 0.54 | 304807 | Rabif | NM_001007678 |
| 10764460 | 6.98 | 5.95 | -1.04 | 0.49 | 304827 | Kcnt2 | NM_198762 |
| 10764551 | 5.85 | 4.97 | -0.87 | 0.55 | 29527 | Ptgs2 | NM_017232 |
| 10764837 | 7.03 | 6.07 | -0.97 | 0.51 | 304881 | Tor1aip2 | NM_001165896 |
| 10765044 | 4.73 | 3.84 | -0.88 | 0.54 | 289150 | Cenpl | NM_001033061 |
| 10765413 | 5.21 | 4.24 | -0.97 | 0.51 | 83574 | Rxrg | NM_031765 |
| 10766953 | 5.16 | 4.03 | -1.13 | 0.46 | 24224 | Bcl2 | NM_016993 |
| 10768269 | 6.55 | 5.35 | -1.20 | 0.44 | 155012 | Cfh | NM_130409 |
| 10768357 | 4.45 | 2.88 | -1.57 | 0.34 | 289076 | Rgs18 | NM_001047084 |
| 10769177 | 5.66 | 4.34 | -1.31 | 0.40 | 684623 | LOC684623 | ENSRNOT00000003659 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10770161 | 5.12 | 4.08 | -1.03 | 0.49 | 289270 | Pld5 | ENSRNOT00000005332 |
| 10772534 | 8.47 | 7.28 | -1.20 | 0.44 | 289606 | Gabra2 | NM_001135779 |
| 10774267 | 7.13 | 5.93 | -1.20 | 0.44 | 689106 | Vstm2a | ENSRNOT00000006897 |
| 10774432 | 4.50 | 3.42 | -1.09 | 0.47 | 690096 | LOC690096 | ENSRNOT00000012255 |
| 10775283 | 4.45 | 3.15 | -1.31 | 0.40 | 360910 | Abcg3l2 | NM_001014133 |
| 10776437 | 5.81 | 4.92 | -0.89 | 0.54 | 64030 | Kit | NM_022264 |
| 10777011 | 6.24 | 5.09 | -1.15 | 0.45 | 289657 | Tbc1d19 | NM_001106008 |
| 10777137 | 5.84 | 4.39 | -1.45 | 0.37 | 360272 | Slit2 | NM_022632 |
| 10778179 | 5.00 | 3.71 | -1.29 | 0.41 | 114107 | Kremen1 | NM_053649 |
| 10781467 | 6.53 | 4.79 | -1.73 | 0.30 | 29595 | Htr2a | NM_017254 |
| 10781496 | 6.25 | 5.32 | -0.94 | 0.52 | 306071 | Lcp1 | NM_001012044 |
| 10781745 | 6.67 | 5.81 | -0.86 | 0.55 | 306055 | Pcdh17 | NM_001107279 |
| 10781787 | 9.58 | 8.69 | -0.88 | 0.54 | 29150 | Matr3 | NM_019149 |
| 10782187 | 4.94 | 3.22 | -1.72 | 0.30 | 498564 | Itgbl1 | NM_001017505 |
| 10782590 | 8.34 | 7.36 | -0.98 | 0.51 | 66030 | Synpr | NM_023974 |
| 10785724 | 8.09 | 7.04 | -1.05 | 0.48 | 50672 | Ednrb | NM_017333 |
| 10788542 | 3.41 | 2.12 | -1.29 | 0.41 | 306511 | RGD1561928 | ENSRNOT00000042609 |
| 10788889 | 4.27 | 3.20 | -1.07 | 0.48 | 306564 | Htra4 | NM_001107321 |
| 10791000 | 5.71 | 4.14 | -1.56 | 0.34 | 290655 | Crlf1 | NM_001106074 |
| 10791250 | 5.42 | 3.71 | -1.71 | 0.31 | 24539 | Lpl | NM_012598 |
| 10791950 | 6.61 | 5.76 | -0.85 | 0.55 | 364601 | Efha2 | ENSRNOT00000017025 |
| 10793429 | 4.53 | 3.42 | -1.11 | 0.46 | 290952 | RGD1563615 | ENSRNOT00000046525 |
| 10793433 | 3.75 | 2.74 | -1.01 | 0.50 | 290952 | RGD1563615 | ENSRNOT00000046525 |
| 10793446 | 4.99 | 3.56 | -1.44 | 0.37 | 290952 | RGD1563615 | ENSRNOT00000046525 |
| 10794195 | 5.51 | 3.70 | -1.81 | 0.28 | 24316 | Drd1a | NM_012546 |
| 10796507 | 5.20 | 4.10 | -1.10 | 0.47 | 291328 | Slc39a12 | NM_001106124 |
| 10796751 | 7.76 | 6.39 | -1.37 | 0.39 | 24380 | Gad2 | NM_012563 |
| 10797648 | 6.68 | 5.41 | -1.27 | 0.41 | 291015 | Ogn | NM_001106103 |
| 10797657 | 3.29 | 2.36 | -0.93 | 0.52 | 83717 | Omd | NM_031817 |
| 10798119 | 4.41 | 3.26 | -1.15 | 0.45 | 291084 | Nqo2 | NM_001004214 |
| 10798390 | 6.64 | 5.69 | -0.94 | 0.52 | 306934 | Fam65b | NM_001014009 |
| 10798479 | 3.67 | 2.59 | -1.08 | 0.47 | 306966 | Znf184 | NM_001100573 |
| 10798856 | 6.86 | 5.93 | -0.93 | 0.52 | 361258 | Cul2 | NM_001108417 |
| 10799733 | 7.92 | 6.65 | -1.27 | 0.41 | 680404 | C1ql3 | NM_001109403 |
| 10800140 | 7.94 | 5.06 | -2.88 | 0.14 | 291794 | Snrpd1 | NM_001106163 |
| 10801174 | 4.59 | 3.57 | -1.02 | 0.49 | 291654 | Pcdhb5 | NM_001114602 |
| 10802391 | 5.47 | 3.56 | -1.90 | 0.27 | 24611 | Gnal | ENSRNOT00000025172 |
| 10803037 | 8.88 | 8.01 | -0.87 | 0.55 | 307206 | Neto1 | NM_001107371 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10803394 | 8.19 | 7.23 | -0.96 | 0.51 | 65196 | B4galt6 | NM_031740 |
| 10803474 | 6.68 | 5.83 | -0.85 | 0.55 | 307553 | Nol4 | NM_001107401 |
| 10804714 | 5.87 | 4.63 | -1.24 | 0.42 | 307396 | Pcyox1l | NM_001134542 |
| 10805591 | 3.35 | 2.35 | -1.00 | 0.50 | 498895 | RGD1559751 | ENSRNOT00000058177 |
| 10806492 | 6.78 | 5.85 | -0.93 | 0.53 | 25479 | Vps35 | ENSRNOT00000024020 |
| 10806864 | 7.13 | 6.15 | -0.98 | 0.51 | 364981 | Scoc | NM_001013235 |
| 10807632 | 7.40 | 6.41 | -0.99 | 0.50 | 80773 | Cyb5b | NM_030586 |
| 10808603 | 6.78 | 5.78 | -1.00 | 0.50 | 361433 | Cpne7 | NM_001108454 |
| 10810736 | 5.74 | 4.63 | -1.11 | 0.46 | 24530 | Lcat | NM_017024 |
| 10810964 | 4.23 | 3.14 | -1.10 | 0.47 | 117059 | Calb2 | NM_053988 |
| 10812879 | 6.16 | 4.36 | -1.80 | 0.29 | 24473 | Htr1a | NM_012585 |
| 10813249 | 7.21 | 5.41 | -1.81 | 0.29 | 310358 | RGD1308448 | NM_001107671 |
| 10813563 | 4.73 | 3.80 | -0.93 | 0.52 | 294789 | Ranbp3l | ENSRNOT00000050942 |
| 10813817 | 4.59 | 3.27 | -1.32 | 0.40 | 29163 | Cdh9 | NM_001168630 |
| 10813872 | 6.57 | 5.69 | -0.88 | 0.54 | 310174 | Cdh18 | NM_001107656 |
| 10814396 | 5.37 | 3.50 | -1.87 | 0.27 | 365748 | Bhlhe22 | NM_001108940 |
| 10815655 | 4.41 | 2.97 | -1.44 | 0.37 | 66024 | Npy2r | NM_023968 |
| 10815679 | 3.90 | 3.01 | -0.88 | 0.54 | 24590 | Mme | NM_012608 |
| 10817419 | 5.45 | 4.46 | -0.98 | 0.51 | 29175 | Ctsk | NM_031560 |
| 10820300 | 4.77 | 3.74 | -1.03 | 0.49 | 309995 | Xrcc4 | NM_001006999 |
| 10820586 | 5.24 | 4.29 | -0.95 | 0.52 | 25439 | F2r | NM_012950 |
| 10820613 | 5.31 | 3.72 | -1.59 | 0.33 | 29643 | Sv2c | NM_031593 |
| 10820693 | 8.21 | 7.30 | -0.90 | 0.53 | 294673 | Hexb | NM_001011946 |
| 10822107 | 4.90 | 3.99 | -0.91 | 0.53 | 310190 | Fam105a | BC107649 |
| 10822386 | 7.64 | 6.64 | -1.00 | 0.50 | 114906 | Pkia | NM_053772 |
| 10823303 | 9.93 | 8.96 | -0.97 | 0.51 | 81531 | Pfn2 | NM_030873 |
| 10823412 | 3.45 | 2.46 | -0.99 | 0.50 | 192251 | Gpr149 | NM_138891 |
| 10823937 | 4.41 | 2.97 | -1.44 | 0.37 | 66024 | Npy2r | NM_023968 |
| 10824041 | 6.17 | 5.32 | -0.85 | 0.55 | 60382 | Arfip1 | NM_021763 |
| 10824422 | 5.29 | 4.42 | -0.87 | 0.55 | 310641 | Trim46 | NM_001107691 |
| 10825495 | 5.36 | 4.46 | -0.89 | 0.54 | 310732 | Slc22a15 | NM_001107707 |
| 10825915 | 3.67 | 2.74 | -0.93 | 0.52 | 24424 | Gstm2 | NM_177426 |
| 10826148 | 5.97 | 4.92 | -1.05 | 0.48 | 295382 | Ntng1 | NM_001106465 |
| 10826261 | 7.18 | 5.74 | -1.44 | 0.37 | 64443 | Gpr88 | NM_031696 |
| 10826392 | 8.58 | 7.35 | -1.24 | 0.42 | 295401 | Lppr4 | NM_001001508 |
| 10827231 | 5.97 | 4.85 | -1.12 | 0.46 | 83476 | Cyr61 | NM_031327 |
| 10828344 | 5.32 | 3.47 | -1.85 | 0.28 | 294269 | RT1-Da | NM_001008847 |
| 10832577 | 6.25 | 4.52 | -1.73 | 0.30 | 25369 | Adora2a | NM_053294 |
| 10836638 | 7.55 | 6.68 | -0.87 | 0.55 | 311114 | Klhl23 | NM_001134504 |
| 10838039 | 7.57 | 6.37 | -1.20 | 0.44 | 295934 | Chst1 | NM_001011955 |
| 10838255 | 3.59 | 2.70 | -0.89 | 0.54 | 691083 | LOC691083 | NM_001144862 |
| 10838326 | 6.20 | 5.21 | -0.99 | 0.50 | 25469 | Kcna4 | NM_012971 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10839726 | 5.00 | 4.03 | -0.97 | 0.51 | 64300 | Mthfd1 | NM_022508 |
| 10842677 | 4.91 | 4.01 | -0.91 | 0.53 | 100328908 | RGD1565819 | NM_001171096 |
| 10844082 | 5.63 | 4.62 | -1.01 | 0.50 | 311836 | Ntng2 | NM_001107825 |
| 10844275 | 4.36 | 3.20 | -1.16 | 0.45 | 311861 | Fibcd1 | NM_001107829 |
| 10844801 | 6.59 | 5.72 | -0.86 | 0.55 | 366029 | Zbtb6 | NM_001108953 |
| 10844949 | 5.19 | 4.15 | -1.04 | 0.49 | 311926 | Lrp1b | NM_001107843 |
| 10844960 | 6.15 | 5.29 | -0.87 | 0.55 | 311926 | Lrp1b | NM_001107843 |
| 10844962 | 5.43 | 4.30 | -1.13 | 0.46 | 311926 | Lrp1b | NM_001107843 |
| 10844968 | 4.90 | 3.89 | -1.01 | 0.50 | 311926 | Lrp1b | NM_001107843 |
| 10845416 | 5.96 | 4.84 | -1.12 | 0.46 | 245921 | Acvr1c | NM_139090 |
| 10845809 | 5.94 | 5.07 | -0.87 | 0.55 | 497770 | Scn3a | NM_013119 |
| 10846685 | 5.19 | 4.26 | -0.94 | 0.52 | 29458 | Neurod1 | NM_019218 |
| 10847758 | 6.20 | 5.22 | -0.99 | 0.51 | 366140 | Fjx1 | NM_001108955 |
| 10849857 | 4.89 | 3.79 | -1.10 | 0.47 | 29190 | Pdyn | NM_019374 |
| 10850543 | 8.11 | 7.00 | -1.11 | 0.46 | 499903 | Napb | ENSRNOT00000006329 |
| 10850929 | 7.15 | 6.27 | -0.88 | 0.54 | 363469 | Sms | NM_001033899 |
| 10852953 | 5.77 | 4.70 | -1.06 | 0.48 | 499975 | Fam126a | ENSRNOT00000014023 |
| 10853683 | 3.73 | 2.81 | -0.92 | 0.53 | 24806 | Tac1 | NM_012666 |
| 10853842 | 8.47 | 7.59 | -0.88 | 0.54 | 493810 | Capza2 | NM_001009180 |
| 10855549 | 6.05 | 3.66 | -2.39 | 0.19 | 297096 | Snx10 | NM_001013085 |
| 10856472 | 8.08 | 7.16 | -0.92 | 0.53 | 679668 | LRRTM1 | NM_001109374 |
| 10858165 | 7.87 | 6.97 | -0.89 | 0.54 | 24772 | Cxcl12 | NM_001033883 |
| 10858707 | 3.03 | 1.99 | -1.04 | 0.49 | 297594 | Cdca3 | NM_001007648 |
| 10859342 | 5.85 | 4.42 | -1.42 | 0.37 | 50677 | Ptpro | NM_017336 |
| 10860481 | 6.06 | 5.20 | -0.86 | 0.55 | 29751 | Sema3a | NM_017310 |
| 10860535 | 7.03 | 6.18 | -0.85 | 0.56 | 688590 | Rundc3b | NM_001047116 |
| 10860623 | 5.42 | 4.54 | -0.89 | 0.54 | 85261 | Mterf | NM_053499 |
| 10861038 | 6.66 | 5.72 | -0.94 | 0.52 | 500032 | Thsd7a | ENSRNOT00000052063 |
| 10861066 | 7.76 | 6.87 | -0.88 | 0.54 | 312132 | Tmem106b | NM_001004267 |
| 10862527 | 5.66 | 4.79 | -0.87 | 0.55 | 155183 | Skap2 | NM_130413 |
| 10863615 | 7.24 | 6.38 | -0.85 | 0.55 | 500233 | Exoc6b | NM_001109246 |
| 10863688 | 3.64 | 2.68 | -0.96 | 0.51 | 500237 | Cml2 | NM_001173449 |
| 10866576 | 9.42 | 8.49 | -0.93 | 0.52 | 497798 | RGD1561357 | ENSRNOT00000010623 |
| 10866850 | 7.44 | 6.51 | -0.93 | 0.53 | 24525 | Kras | NM_031515 |
| 10867060 | 4.81 | 3.91 | -0.90 | 0.54 | 500377 | Tuba8 | NM_001024339 |
| 10867497 | 7.68 | 6.66 | -1.01 | 0.50 | 500400 | Fam110b | BC091289 |
| 10867731 | 6.97 | 5.82 | -1.15 | 0.45 | 83839 | Calb1 | NM_031984 |
| 10868186 | 7.18 | 6.16 | -1.01 | 0.50 | 25248 | Cnr1 | NM_012784 |
| 10868289 | 8.60 | 7.66 | -0.94 | 0.52 | 65028 | Dnaja1 | NM_022934 |
| 10869010 | 6.40 | 5.11 | -1.29 | 0.41 | 313219 | Zfp189 | NM_001107930 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10869094 | 5.75 | 4.90 | -0.86 | 0.55 | 313211 | Nipsnap3b | NM_001009422 |
| 10869253 | 7.81 | 6.88 | -0.93 | 0.52 | 83626 | Ugcg | NM_031795 |
| 10870733 | 5.04 | 4.15 | -0.89 | 0.54 | 298385 | Magoh | NM_001100536 |
| 10874193 | 7.78 | 6.83 | -0.95 | 0.52 | 313729 | Errfi1 | NM_001014071 |
| 10875256 | 7.13 | 6.01 | -1.12 | 0.46 | 312946 | Tmem68 | NM_001107903 |
| 10875300 | 6.07 | 4.18 | -1.89 | 0.27 | 29237 | Penk | NM_017139 |
| 10875532 | 6.43 | 5.55 | -0.87 | 0.55 | 54705 | Pdp1 | NM_019372 |
| 10883801 | 7.18 | 5.38 | -1.80 | 0.29 | 50871 | Hpcal1 | NM_017356 |
| 10884215 | 3.32 | 2.38 | -0.94 | 0.52 | 85489 | Twist1 | NM_053530 |
| 10884309 | 8.50 | 7.34 | -1.16 | 0.45 | 54248 | Dgkb | NM_019304 |
| 10884811 | 6.93 | 5.74 | -1.19 | 0.44 | 314164 | Lrfn5 | NM_001108024 |
| 10886031 | 5.13 | 4.18 | -0.96 | 0.52 | 314322 | Fos | NM_022197 |
| 10889575 | 6.65 | 5.37 | -1.28 | 0.41 | 298944 | Gpr22 | NM_001106722 |
| 10890229 | 5.12 | 4.22 | -0.90 | 0.54 | 85261 | Mterf | NM_053499 |
| 10891402 | 4.94 | 3.37 | -1.57 | 0.34 | 65162 | Dio2 | NM_031720 |
| 10893661 | 8.32 | 7.00 | -1.32 | 0.40 | 58979 | Gng7 | NM_024138 |
| 10895152 | 6.37 | 5.29 | -1.08 | 0.47 | 60427 | Kitlg | NM_021843 |
| 10895241 | 3.96 | 2.79 | -1.17 | 0.45 | 299756 | Mgat4c | NM_001135814 |
| 10895499 | 4.22 | 2.85 | -1.37 | 0.39 | 171048 | Tspan8 | NM_133526 |
| 10895508 | 5.30 | 4.14 | -1.16 | 0.45 | 94202 | Ptprr | NM_053594 |
| 10896541 | 9.05 | 8.18 | -0.87 | 0.55 | 81526 | Nov | NM_030868 |
| 10899552 | 5.39 | 4.30 | -1.09 | 0.47 | 24790 | Sp1 | NM_012655 |
| 10899676 | 9.08 | 8.20 | -0.88 | 0.54 | 29691 | Pde1b | NM_022710 |
| 10901409 | 6.98 | 6.13 | -0.85 | 0.55 | 314694 | Chst11 | NM_001108079 |
| 10902080 | 4.56 | 3.70 | -0.86 | 0.55 | 299762 | Tmtc2 | XM_001080732 |
| 10902843 | 6.50 | 5.65 | -0.85 | 0.56 | 171329 | Usp15 | NM_145184 |
| 10903501 | 6.45 | 5.15 | -1.30 | 0.41 | 314941 | Lrp12 | NM_001134883 |
| 10903651 | 4.58 | 2.92 | -1.66 | 0.32 | 314942 | LOC314942 | ENSRNOT00000057108 |
| 10903653 | 4.22 | 2.93 | -1.29 | 0.41 | 314942 | LOC314942 | ENSRNOT00000057108 |
| 10908990 | 4.79 | 3.89 | -0.90 | 0.54 | 315554 | Pus3 | NM_001108134 |
| 10909328 | 8.21 | 7.06 | -1.15 | 0.45 | 245956 | Scn3b | NM_139097 |
| 10909849 | 4.42 | 3.21 | -1.21 | 0.43 | 24318 | Drd2 | NM_012547 |
| 10911380 | 4.44 | 3.55 | -0.89 | 0.54 | 116676 | Aldh1a2 | NM_053896 |
| 10912054 | 4.04 | 2.94 | -1.09 | 0.47 | 363111 | Ripply2 | ENSRNOT00000013285 |
| 10912614 | 3.65 | 2.32 | -1.33 | 0.40 | 24546 | Slco2a1 | NM_022667 |
| 10912718 | 7.27 | 5.42 | -1.85 | 0.28 | 367160 | Cpne4 | NM_001109003 |
| 10914935 | 7.80 | 6.49 | -1.31 | 0.40 | 363015 | RGD1310444 | XM_002729871 |
| 10916379 | 4.01 | 2.91 | -1.10 | 0.47 | 300608 | RGD1311744 | ENSRNOT00000066669 |
| 10916697 | 5.45 | 4.25 | -1.20 | 0.44 | 315599 | Nlrx1 | NM_001025010 |
| 10918955 | 4.55 | 3.60 | -0.96 | 0.51 | 246776 | Filip1 | NM_145682 |
| 10918979 | 6.52 | 5.08 | -1.44 | 0.37 | 25075 | Htr1b | NM_022225 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10919694 | 5.49 | 4.62 | -0.87 | 0.55 | 300967 | Tmem108 | ENSRNOT00000014519 |
| 10921208 | 3.08 | 2.07 | -1.01 | 0.50 | 85426 | Slc5a7 | NM_053521 |
| 10922895 | 4.52 | 2.96 | -1.56 | 0.34 | 24785 | Slc9a4 | NM_173098 |
| 10922909 | 4.31 | 3.35 | -0.96 | 0.51 | 24783 | Slc9a2 | NM_012653 |
| 10923338 | 5.36 | 4.05 | -1.31 | 0.40 | 301416 | Coq10b | NM_001009671 |
| 10923782 | 9.44 | 8.34 | -1.10 | 0.47 | 286928 | Abi2 | NM_173143 |
| 10923866 | 6.30 | 5.35 | -0.95 | 0.52 | 501153 | Zdbf2 | ENSRNOT00000016038 |
| 10926740 | 6.98 | 5.83 | -1.15 | 0.45 | 316256 | Tnfrsf21 | NM_001108207 |
| 10927903 | 6.89 | 5.83 | -1.07 | 0.48 | 363228 | Tmeff2 | NM_001108795 |
| 10928056 | 8.26 | 7.29 | -0.97 | 0.51 | 316400 | Pgap1 | NM_201990 |
| 10928522 | 7.81 | 6.92 | -0.89 | 0.54 | 316444 | Mdh1b | ENSRNOT00000017207 |
| 10928837 | 6.77 | 5.43 | -1.34 | 0.40 | 25285 | Igfbp5 | NM_012817 |
| 10929263 | 7.98 | 6.41 | -1.57 | 0.34 | 24765 | Scg2 | NM_022669 |
| 10929482 | 8.47 | 6.87 | -1.60 | 0.33 | 316573 | Dner | BC086329 |
| 10929536 | 4.82 | 3.62 | -1.21 | 0.43 | 316578 | Slc16a14 | NM_001108229 |
| 10931669 | 4.80 | 3.93 | -0.87 | 0.55 | 288979 | C1ql2 | NM_001105949 |
| 10932066 | 7.51 | 6.54 | -0.97 | 0.51 | 313445 | Klhl13 | ENSRNOT00000067114 |
| 10932646 | 7.61 | 6.75 | -0.86 | 0.55 | 360785 | Ap1s1 | BC168682 |
| 10932795 | 7.72 | 6.72 | -1.00 | 0.50 | 113976 | Acsl4 | NM_053623 |
| 10933393 | 4.16 | 2.48 | -1.68 | 0.31 | 24397 | Glra2 | NM_012568 |
| 10934270 | 4.56 | 3.59 | -0.97 | 0.51 | 302421 | Gdpd2 | NM_001106944 |
| 10935038 | 4.09 | 3.17 | -0.92 | 0.53 | 501624 | Bex4 | NM_001037554 |
| 10935418 | 3.16 | 1.96 | -1.20 | 0.44 | 317589 | Mst4 | ENSRNOT00000010596 |
| 10935882 | 3.50 | 2.44 | -1.07 | 0.48 | 293849 | Zfp275 | NM_001106343 |
| 10936360 | 6.95 | 5.55 | -1.40 | 0.38 | 313436 | Zcchc12 | NM_001014065 |
| 10936742 | 5.07 | 4.21 | -0.86 | 0.55 | 554353 | Gpr34 | NM_001024925 |
| 10937302 | 6.64 | 5.29 | -1.35 | 0.39 | 25187 | Htr2c | NM_012765 |
| 10937362 | 7.96 | 7.06 | -0.91 | 0.53 | 29433 | Pak3 | NM_019210 |
| 10937479 | 7.81 | 6.90 | -0.91 | 0.53 | 117043 | RragB | NM_053972 |
| 10937660 | 6.97 | 6.03 | -0.93 | 0.52 | 501550 | Trappc2 | NM_001024965 |
| 10937769 | 5.22 | 4.15 | -1.07 | 0.48 | 302671 | Ap1s2 | NM_001127531 |
| 10938897 | 7.98 | 7.02 | -0.96 | 0.51 | 246284 | Atrx | NM_001105757 |
| 10939002 | 6.31 | 5.02 | -1.29 | 0.41 | 363487 | RGD1566265 | NM_001134589 |
| 10939226 | 6.47 | 5.11 | -1.35 | 0.39 | 317183 | Pcdh19 | NM_001169129 |
| 10939460 | 6.24 | 5.37 | -0.88 | 0.54 | 367915 | Rab9b | NM_001109018 |
| 10939764 | 4.76 | 3.07 | -1.69 | 0.31 | 25236 | Gpc3 | NM_012774 |
| 10939837 | 7.92 | 6.97 | -0.95 | 0.52 | 302864 | Mmgt1 | NM_001106970 |

**Supplementary table (ST-3C): List of genes upregulated in liver**

| Probe Set ID | Control Liver | Sleep Deprived Liver | Log Fold Change | Fold Change | Gene Symbol | Accession |
|---|---|---|---|---|---|---|
| 10704284 | 9.50 | 10.74 | 1.24 | 2.36 | Slc27a5 | NM_024143 |
| 10707151 | 5.06 | 6.32 | 1.25 | 2.39 | Tmem86a | NM_001135016 |
| 10708665 | 4.24 | 5.34 | 1.10 | 2.15 | Rab30 | NM_001015012 |
| 10712657 | 8.66 | 9.95 | 1.28 | 2.44 | Cpt1a | NM_031559 |
| 10713974 | 4.99 | 5.86 | 0.88 | 1.83 | Slc15a3 | NM_139341 |
| 10714323 | 5.37 | 7.66 | 2.29 | 4.91 | Aldh1a1 | NM_022407 |
| 10714413 | 6.98 | 7.94 | 0.96 | 1.94 | Klf9 | NM_057211 |
| 10715364 | 9.40 | 10.92 | 1.51 | 2.86 | Got1 | NM_012571 |
| 10715416 | 4.57 | 6.75 | 2.18 | 4.54 | Loxl4 | NM_001107592 |
| 10717459 | 4.93 | 6.34 | 1.40 | 2.65 | Tppp | NM_001108461 |
| 10723728 | 6.21 | 7.14 | 0.93 | 1.91 | Aqp11 | NM_173105 |
| 10726604 | 4.07 | 5.01 | 0.94 | 1.91 | RGD1311186 | NM_001106310 |
| 10726824 | 8.05 | 9.02 | 0.98 | 1.97 | Slc25a22 | NM_001014027 |
| 10728466 | 5.16 | 6.89 | 1.73 | 3.32 | UST4r | NM_134379 |
| 10730031 | 3.13 | 5.51 | 2.39 | 5.23 | Cyp2c13 | ENSRNOT00000015801 |
| 10730599 | 4.87 | 7.61 | 2.74 | 6.70 | Cyp17a1 | NM_012753 |
| 10732068 | 7.27 | 8.13 | 0.86 | 1.82 | Dci | NM_017306 |
| 10736863 | 3.74 | 4.62 | 0.88 | 1.84 | Ccl4 | NM_053858 |
| 10738399 | 8.91 | 10.70 | 1.79 | 3.45 | G6pc | NM_013098 |
| 10738477 | 3.88 | 5.02 | 1.14 | 2.21 | Arl4d | NM_001107052 |
| 10738576 | 7.84 | 8.76 | 0.92 | 1.90 | Grn | NM_017113 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10742645 | 4.90 | 6.28 | 1.37 | 2.59 | Slc22a5 | NM_019269 |
| 10744233 | 2.97 | 4.05 | 1.08 | 2.12 | Tmem102 | ENSRNOT00000020578 |
| 10744245 | 2.86 | 3.80 | 0.95 | 1.93 | Nlgn2 | NM_053992 |
| 10744460 | 4.84 | 5.85 | 1.02 | 2.02 | Cxcl16 | NM_001017478 |
| 10745345 | 3.42 | 4.50 | 1.08 | 2.12 | Evi2a | ENSRNOT00000039261 |
| 10746139 | 7.90 | 8.90 | 1.00 | 2.00 | Scpep1 | NM_133383 |
| 10747262 | 3.15 | 4.12 | 0.97 | 1.96 | Krt19 | NM_199498 |
| 10749612 | 9.75 | 10.69 | 0.94 | 1.92 | Actg1 | NM_001127449 |
| 10750524 | 6.77 | 8.04 | 1.27 | 2.41 | Mx2 | NM_134350 |
| 10751295 | 4.15 | 5.52 | 1.38 | 2.60 | Pla1a | NM_138882 |
| 10751352 | 8.17 | 9.78 | 1.61 | 3.05 | Krt8 | NM_199370 |
| 10751896 | 3.49 | 5.92 | 2.43 | 5.39 | Cldn1 | NM_031699 |
| 10754058 | 3.31 | 4.21 | 0.90 | 1.87 | Ccdc52 | NM_001008285 |
| 10755088 | 3.49 | 4.39 | 0.90 | 1.86 | Rtp4 | NM_001108321 |
| 10757082 | 4.05 | 4.99 | 0.94 | 1.91 | Zfand2a | NM_001008363 |
| 10757632 | 4.16 | 5.44 | 1.28 | 2.43 | Ccl24 | NM_001013045 |
| 10757962 | 9.23 | 10.74 | 1.52 | 2.86 | Asl | NM_021577 |
| 10759018 | 6.45 | 7.39 | 0.94 | 1.92 | Mlec | NM_001013983 |
| 10762324 | 7.63 | 9.17 | 1.54 | 2.90 | Sds | NM_053962 |
| 10762740 | 4.06 | 5.27 | 1.21 | 2.31 | Oasl | NM_001009681 |
| 10765090 | 10.14 | 11.25 | 1.12 | 2.17 | Actg1 | NM_001127449 |
| 10766923 | 5.66 | 7.02 | 1.36 | 2.57 | Rnf152 | NM_001106305 |
| 10767175 | 7.69 | 9.22 | 1.53 | 2.89 | Insig2 | NM_178091 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10767290 | 6.12 | 7.58 | 1.46 | 2.75 | Acmsd | NM_134372 |
| 10768998 | 3.90 | 4.80 | 0.90 | 1.87 | Tor3a | NM_001009683 |
| 10769361 | 8.58 | 9.51 | 0.93 | 1.90 | Fmo1 | NM_012792 |
| 10769476 | 6.52 | 8.11 | 1.59 | 3.01 | Atp1b1 | NM_013113 |
| 10770710 | 3.53 | 4.74 | 1.21 | 2.31 | Atf3 | NM_012912 |
| 10771655 | 3.40 | 4.56 | 1.15 | 2.23 | Cxcl10 | NM_139089 |
| 10771660 | 4.50 | 6.57 | 2.06 | 4.17 | Cxcl9 | NM_145672 |
| 10771936 | 7.90 | 8.88 | 0.97 | 1.96 | Ugt2a3 | NM_001135869 |
| 10771998 | 6.48 | 7.47 | 0.99 | 1.99 | RGD1559459 | ENSRNOT00000065079 |
| 10772986 | 4.27 | 5.36 | 1.09 | 2.12 | Ppargc1a | NM_031347 |
| 10773221 | 7.64 | 8.70 | 1.05 | 2.08 | Slc2a9 | ENSRNOT00000042200 |
| 10773773 | 8.07 | 8.92 | 0.86 | 1.81 | Sec14l4 | NM_001109090 |
| 10776954 | 5.68 | 6.55 | 0.86 | 1.82 | Rell1 | NM_001113776 |
| 10777918 | 7.04 | 7.88 | 0.85 | 1.80 | Drg1 | NM_001009685 |
| 10778620 | 4.72 | 6.18 | 1.46 | 2.75 | Slc1a4 | NM_198763 |
| 10779673 | 4.79 | 5.68 | 0.89 | 1.85 | Lgals3 | NM_031832 |
| 10781321 | 3.79 | 5.63 | 1.84 | 3.58 | Tnfrsf10b | NM_001108873 |
| 10789857 | 5.38 | 6.28 | 0.90 | 1.87 | Il17rb | NM_001107290 |
| 10790670 | 4.61 | 5.71 | 1.10 | 2.14 | Klf2 | NM_001007684 |
| 10791233 | 7.28 | 8.30 | 1.02 | 2.02 | Atp6v1b2 | NM_057213 |
| 10791552 | 3.60 | 5.41 | 1.82 | 3.52 | Gpm6a | NM_178105 |
| 10794829 | 4.47 | 5.39 | 0.92 | 1.90 | Tubb2a | NM_001109119 |
| 10796016 | 5.55 | 6.43 | 0.87 | 1.83 | RGD1564865 | NM_001164396 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10796018 | 6.82 | 8.02 | 1.21 | 2.31 | RGD1564865 | NM_001164396 |
| 10796440 | 5.01 | 6.00 | 0.99 | 1.99 | Pter | NM_022224 |
| 10796445 | 6.41 | 7.40 | 0.98 | 1.98 | Vim | NM_031140 |
| 10797811 | 3.18 | 4.07 | 0.89 | 1.85 | Cd83 | NM_001108410 |
| 10800991 | 6.04 | 7.19 | 1.15 | 2.22 | Pura | ENSRNOT00000025756 |
| 10802013 | 7.54 | 8.94 | 1.40 | 2.63 | Cd74 | NM_013069 |
| 10803653 | 9.91 | 10.90 | 0.99 | 1.99 | Actg1 | NM_001127449 |
| 10805731 | 4.58 | 5.43 | 0.86 | 1.81 | Tk2 | NM_001106166 |
| 10807464 | 5.89 | 6.92 | 1.02 | 2.03 | Pla2g15 | NM_001004277 |
| 10813214 | 9.80 | 10.77 | 0.97 | 1.96 | Hmgcs1 | NM_017268 |
| 10813628 | 2.51 | 3.97 | 1.47 | 2.76 | Prlr | NM_012630 |
| 10813992 | 7.13 | 8.16 | 1.04 | 2.05 | LOC683212 | XR_086164 |
| 10815281 | 5.43 | 6.49 | 1.05 | 2.08 | Ccrn4l | NM_138526 |
| 10815503 | 10.49 | 11.53 | 1.04 | 2.05 | Tm4sf4 | NM_053785 |
| 10817686 | 7.70 | 8.81 | 1.11 | 2.16 | Fmo5 | NM_144739 |
| 10818090 | 7.53 | 8.51 | 0.98 | 1.97 | Slc16a1 | NM_012716 |
| 10819024 | 5.60 | 6.51 | 0.90 | 1.87 | Pla2g12a | NM_001108565 |
| 10819402 | 2.52 | 4.70 | 2.18 | 4.54 | Adh6 | NM_001012084 |
| 10819523 | 4.21 | 5.18 | 0.97 | 1.96 | Gbp2 | NM_133624 |
| 10819644 | 7.37 | 8.24 | 0.87 | 1.83 | Ddah1 | NM_022297 |
| 10819905 | 5.36 | 6.45 | 1.08 | 2.12 | Ptger3 | NM_012704 |
| 10820494 | 11.83 | 12.95 | 1.12 | 2.17 | Bhmt | NM_030850 |
| 10821851 | 2.77 | 4.11 | 1.34 | 2.53 | Il7r | NM_001106418 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10825244 | 5.76 | 6.88 | 1.13 | 2.18 | Chd1l | NM_001107704 |
| 10826691 | 6.12 | 7.06 | 0.94 | 1.92 | Ap1ar | ENSRNOT00000055607 |
| 10827517 | 9.91 | 11.24 | 1.33 | 2.51 | Cth | NM_017074 |
| 10828154 | 5.24 | 6.18 | 0.94 | 1.92 | Hspa1b | NM_212504 |
| 10828344 | 7.29 | 8.92 | 1.63 | 3.10 | RT1-Da | NM_001008847 |
| 10828351 | 4.88 | 6.01 | 1.14 | 2.20 | RT1-Ba | NM_001008831 |
| 10829244 | 4.28 | 5.26 | 0.98 | 1.97 | Pwp2 | NM_001168653 |
| 10829346 | 3.57 | 4.46 | 0.89 | 1.85 | Lrrc3 | NM_145679 |
| 10830630 | 5.37 | 6.62 | 1.25 | 2.38 | Rtn4ip1 | NM_001107644 |
| 10831308 | 2.88 | 3.92 | 1.03 | 2.05 | Slc44a4 | NM_212541 |
| 10831567 | 5.17 | 6.46 | 1.29 | 2.45 | RT1-Bb | NM_001004084 |
| 10831747 | 5.06 | 6.22 | 1.15 | 2.22 | Wdr46 | NM_212491 |
| 10832563 | 6.63 | 7.51 | 0.88 | 1.84 | Gstt3 | NM_001137643 |
| 10833617 | 6.33 | 7.55 | 1.22 | 2.33 | RGD1561777 | ENSRNOT00000035047 |
| 10833659 | 6.48 | 7.40 | 0.93 | 1.90 | Amd1 | NM_031011 |
| 10835703 | 3.86 | 5.00 | 1.14 | 2.20 | RGD1564854 | NM_001109341 |
| 10836019 | 9.10 | 10.25 | 1.15 | 2.21 | Kynu | NM_053902 |
| 10836277 | 4.67 | 5.57 | 0.90 | 1.87 | Gpd2 | NM_012736 |
| 10837537 | 9.82 | 10.79 | 0.97 | 1.95 | Actg1 | NM_001127449 |
| 10838729 | 3.75 | 4.70 | 0.95 | 1.94 | Rpusd2 | NM_001135845 |
| 10839771 | 6.92 | 7.80 | 0.88 | 1.84 | Slc20a1 | NM_031148 |
| 10840085 | 6.82 | 7.71 | 0.90 | 1.86 | Cds2 | NM_053643 |
| 10841240 | 3.71 | 5.20 | 1.49 | 2.82 | LOC690521 | ENSRNOT00000042148 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10844183 | 4.61 | 6.41 | 1.79 | 3.47 | Crat | NM_001004085 |
| 10844801 | 5.23 | 6.17 | 0.94 | 1.92 | Zbtb6 | NM_001108953 |
| 10846604 | 4.28 | 5.20 | 0.91 | 1.88 | LOC311134 | ENSRNOT00000037015 |
| 10846781 | 3.94 | 4.86 | 0.93 | 1.90 | Tfpi | NM_001177321 |
| 10849275 | 7.28 | 9.30 | 2.02 | 4.05 | Slc28a2 | NM_031664 |
| 10849279 | 6.12 | 7.06 | 0.94 | 1.92 | Slc28a2 | NM_031664 |
| 10850631 | 7.22 | 8.24 | 1.02 | 2.03 | RGD1308874 | NM_001034003 |
| 10850775 | 4.57 | 5.43 | 0.87 | 1.82 | Trib3 | NM_144755 |
| 10853229 | 4.81 | 5.94 | 1.13 | 2.18 | Gnai1 | NM_013145 |
| 10853300 | 5.46 | 6.66 | 1.21 | 2.31 | Abcb1a | NM_133401 |
| 10853816 | 4.05 | 4.98 | 0.92 | 1.89 | Cav1 | NM_031556 |
| 10854548 | 11.18 | 12.13 | 0.95 | 1.93 | Akr1d1 | NM_138884 |
| 10855449 | 5.42 | 6.88 | 1.46 | 2.75 | Gpnmb | NM_133298 |
| 10857314 | 4.72 | 5.89 | 1.17 | 2.24 | Slc6a6 | NM_017206 |
| 10858374 | 9.06 | 9.97 | 0.91 | 1.88 | Slc6a13 | NM_133623 |
| 10860076 | 4.59 | 5.44 | 0.86 | 1.81 | Nos3 | NM_021838 |
| 10860548 | 5.73 | 6.91 | 1.18 | 2.26 | Crot | NM_031987 |
| 10861066 | 7.30 | 8.23 | 0.93 | 1.90 | Tmem106b | NM_001004267 |
| 10861986 | 9.65 | 10.58 | 0.93 | 1.90 | Insig1 | NM_022392 |
| 10867329 | 2.75 | 4.05 | 1.30 | 2.46 | Mybl1 | NM_001106632 |
| 10870773 | 4.88 | 5.91 | 1.03 | 2.04 | RGD1305274 | NM_001106674 |
| 10873688 | 4.42 | 5.35 | 0.93 | 1.91 | Arhgef19 | NM_001108692 |
| 10875119 | 2.84 | 3.73 | 0.89 | 1.86 | RGD1561849 | NM_001109260 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10877907 | 6.87 | 8.03 | 1.16 | 2.23 | Adfp | NM_001007144 |
| 10878157 | 6.82 | 8.22 | 1.40 | 2.64 | Cyp2j4 | NM_023025 |
| 10878780 | 9.69 | 11.14 | 1.45 | 2.72 | Cyp4a2 | NM_001044770 |
| 10878787 | 9.61 | 10.94 | 1.33 | 2.52 | Cyp4a3 | NM_175760 |
| 10878938 | 4.91 | 6.33 | 1.41 | 2.66 | Plk3 | NM_022187 |
| 10879380 | 5.99 | 6.88 | 0.89 | 1.86 | Ppcs | NM_001039010 |
| 10879516 | 8.47 | 9.96 | 1.48 | 2.80 | Mfsd2 | NM_001106683 |
| 10885851 | 5.03 | 6.36 | 1.33 | 2.52 | Acot2 | NM_138907 |
| 10886786 | 8.86 | 10.17 | 1.31 | 2.48 | Hdmcp | NM_001001509 |
| 10887622 | 5.02 | 5.93 | 0.92 | 1.89 | Crip | NM_001134933 |
| 10888196 | 5.82 | 6.74 | 0.92 | 1.90 | Abcg5 | NM_053754 |
| 10889728 | 4.60 | 5.53 | 0.92 | 1.90 | Arl4a | NM_019186 |
| 10890206 | 6.12 | 7.25 | 1.13 | 2.18 | Rpl10l | ENSRNOT00000047597 |
| 10893035 | 3.38 | 4.24 | 0.86 | 1.82 | Timeless | NM_031340 |
| 10894100 | 6.59 | 7.60 | 1.01 | 2.01 | Ppap2c | NM_139252 |
| 10894167 | 5.04 | 6.03 | 0.99 | 1.99 | Cyp4f39 | ENSRNOT00000007548 |
| 10897304 | 4.22 | 5.14 | 0.92 | 1.89 | Gpr172b | NM_001109670 |
| 10897360 | 7.99 | 8.93 | 0.95 | 1.93 | Gpt | NM_031039 |
| 10899713 | 9.07 | 10.03 | 0.96 | 1.95 | Hsd17b6 | NM_173305 |
| 10899764 | 3.43 | 4.46 | 1.03 | 2.04 | Slc39a5 | NM_001108728 |
| 10900905 | 2.69 | 3.56 | 0.87 | 1.83 | Olr1088 | ENSRNOT00000012907 |
| 10901910 | 7.09 | 7.97 | 0.89 | 1.85 | Amdhd1 | ENSRNOT00000007331 |
| 10907524 | 8.28 | 9.87 | 1.59 | 3.01 | Krt8 | NM_199370 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10908108 | 3.81 | 4.75 | 0.93 | 1.91 | RGD1309410 | NM_001134584 |
| 10909072 | 4.68 | 5.53 | 0.86 | 1.81 | Esam | NM_001004245 |
| 10911145 | 2.94 | 5.64 | 2.70 | 6.51 | Car12 | NM_001080756 |
| 10911287 | 5.88 | 7.02 | 1.14 | 2.20 | Anxa2 | NM_019905 |
| 10913487 | 6.80 | 7.68 | 0.89 | 1.85 | Shisa5 | NM_001006989 |
| 10914411 | 7.53 | 9.59 | 2.06 | 4.16 | Cyp8b1 | NM_031241 |
| 10915018 | 3.66 | 4.66 | 1.00 | 2.00 | Panx1 | NM_199397 |
| 10917727 | 4.59 | 5.47 | 0.87 | 1.83 | Neil1 | NM_001025754 |
| 10918288 | 4.81 | 5.70 | 0.89 | 1.85 | Plekho2 | ENSRNOT00000042633 |
| 10918364 | 4.58 | 5.71 | 1.12 | 2.18 | LOC691658 | ENSRNOT00000057704 |
| 10918848 | 5.85 | 7.04 | 1.20 | 2.29 | Slc17a5 | NM_001009713 |
| 10919712 | 6.15 | 7.43 | 1.28 | 2.43 | Ccrl1 | ENSRNOT00000015265 |
| 10921687 | 8.77 | 10.55 | 1.78 | 3.44 | Gnmt | NM_017084 |
| 10922151 | 2.57 | 3.84 | 1.28 | 2.42 | Gsta5 | NM_001009920 |
| 10924223 | 3.91 | 5.73 | 1.82 | 3.52 | Igfbp2 | NM_013122 |
| 10928902 | 3.98 | 4.96 | 0.97 | 1.97 | Tmbim1 | NM_001007713 |
| 10930738 | 6.37 | 7.39 | 1.02 | 2.03 | Oit3 | NM_001001507 |
| 10931017 | 3.49 | 4.51 | 1.02 | 2.02 | Sema6b | NM_053471 |
| 10933366 | 5.47 | 7.36 | 1.88 | 3.69 | Rab9a | NM_053458 |
| 10933809 | 7.28 | 8.61 | 1.32 | 2.50 | Tmem47 | NM_001109317 |
| 10935177 | 7.17 | 8.06 | 0.89 | 1.85 | Cldn2 | NM_001106846 |
| 10937254 | 7.41 | 8.28 | 0.87 | 1.83 | Pls3 | NM_031084 |
| 10937570 | 7.11 | 7.96 | 0.85 | 1.80 | LOC685431 | XR_086366 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10939310 | 6.42 | 7.45 | 1.03 | 2.04 | Gla | NM_001108820 |

**Supplementary table (ST-3D): List of genes downregulated in liver**

| Probe Set ID | Control Liver | Sleep Deprived Liver | Log Fold Change | Fold Change | Entrez ID | Gene Symbol | Accession |
|---|---|---|---|---|---|---|---|
| 10703272 | 4.73 | 3.83 | -0.90 | 0.53 | 365122 | RGD1561706 | ENSRNOT00000059957 |
| 10705230 | 8.49 | 6.01 | -2.48 | 0.18 | 361523 | Cyp2b2 | ENSRNOT00000028196 |
| 10708687 | 4.26 | 3.21 | -1.05 | 0.48 | 499205 | Fam181b | BC158703 |
| 10709844 | 4.60 | 3.54 | -1.06 | 0.48 | 308937 | Wee1 | NM_001012742 |
| 10710647 | 5.18 | 4.30 | -0.88 | 0.54 | 25023 | Prkcb | NM_012713 |
| 10714254 | 4.64 | 3.51 | -1.12 | 0.46 | 499330 | LOC499330 | NM_001024292 |
| 10717325 | 4.59 | 3.51 | -1.08 | 0.47 | 308028 | Slc2a12 | NM_001107451 |
| 10720555 | 7.09 | 6.18 | -0.91 | 0.53 | 688574 | LOC688574 | ENSRNOT00000043132 |
| 10721880 | 3.44 | 2.53 | -0.91 | 0.53 | 308586 | Sec1 | NM_001135584 |
| 10724311 | 7.95 | 6.97 | -0.98 | 0.51 | 24440 | Hbb | NM_033234 |
| 10724319 | 7.21 | 6.06 | -1.14 | 0.45 | 361619 | MGC72973 | NM_198776 |
| 10730310 | 9.14 | 7.44 | -1.70 | 0.31 | 309375 | Marveld1 | NM_001107590 |
| 10730349 | 10.89 | 8.35 | -2.54 | 0.17 | 246074 | Scd1 | NM_139192 |
| 10730830 | 5.16 | 4.15 | -1.01 | 0.50 | 308760 | Rccd1 | ENSRNOT00000029471 |
| 10732652 | 9.55 | 8.54 | -1.00 | 0.50 | 114856 | Dusp1 | NM_053769 |
| 10736875 | 10.19 | 8.75 | -1.44 | 0.37 | 360228 | LOC360228 | NM_001003706 |
| 10741268 | 6.07 | 5.22 | -0.85 | 0.55 | 302983 | Mapk8ip3 | NM_001100673 |
| 10741756 | 11.56 | 10.70 | -0.85 | 0.55 | 25632 | Hba-a2 | NM_013096 |
| 10741778 | 11.16 | 10.29 | -0.87 | 0.55 | 25632 | Hba-a2 | NM_013096 |
| 10742402 | 5.82 | 4.55 | -1.27 | 0.41 | 114097 | Ltc4s | NM_053639 |
| 10744766 | 5.02 | 4.08 | -0.94 | 0.52 | 79251 | Aspa | NM_024399 |
| 10745224 | 6.04 | 4.17 | -1.87 | 0.27 | 65202 | Slc13a2 | NM_031746 |
| 10746209 | 6.84 | 5.70 | -1.15 | 0.45 | 363667 | Hlf | ENSRNOT00000055664 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10749372 | 6.19 | 4.81 | -1.38 | 0.38 | 89829 | Socs3 | NM_053565 |
| 10751931 | 7.55 | 6.03 | -1.53 | 0.35 | 303836 | Bcl6 | NM_001107084 |
| 10753214 | 10.17 | 9.12 | -1.06 | 0.48 | 266766 | Rcan1 | NM_153724 |
| 10756075 | 3.63 | 2.77 | -0.87 | 0.55 | 501794 | Vom2r60 | ENSRNOT00000041244 |
| 10757442 | 4.32 | 3.43 | -0.89 | 0.54 | 288585 | Rabl5 | NM_001011902 |
| 10759604 | 3.15 | 2.29 | -0.86 | 0.55 | 498128 | RGD1565374 | NM_001134602 |
| 10760877 | 5.71 | 4.55 | -1.16 | 0.45 | 288545 | RGD1305455 | NM_001024969 |
| 10761992 | 6.78 | 5.54 | -1.25 | 0.42 | 29665 | P2rx7 | NM_019256 |
| 10762426 | 3.88 | 3.00 | -0.88 | 0.54 | 117271 | Hrk | NM_057130 |
| 10766835 | 8.30 | 7.35 | -0.96 | 0.51 | 289392 | Plxna2 | NM_001105988 |
| 10767518 | 6.91 | 6.05 | -0.87 | 0.55 | 363984 | Ikbke | NM_001108854 |
| 10767539 | 6.35 | 5.27 | -1.07 | 0.47 | 360840 | Srgap2 | NM_001134958 |
| 10768412 | 8.79 | 7.57 | -1.22 | 0.43 | 289104 | Prg4 | NM_001105962 |
| 10772212 | 5.73 | 4.85 | -0.88 | 0.54 | 364136 | Aasdh | ENSRNOT00000002907 |
| 10775243 | 4.50 | 3.61 | -0.89 | 0.54 | 363337 | LOC363337 | BC082068 |
| 10775260 | 4.56 | 3.26 | -1.30 | 0.41 | 363337 | LOC363337 | BC082068 |
| 10775647 | 4.08 | 3.01 | -1.07 | 0.48 | 289486 | Fras1 | ENSRNOT00000002814 |
| 10775731 | 4.31 | 3.28 | -1.03 | 0.49 | 498335 | Cxcl13 | NM_001017496 |
| 10775900 | 8.58 | 6.83 | -1.75 | 0.30 | 81503 | Cxcl1 | NM_030845 |
| 10776873 | 4.61 | 3.62 | -0.99 | 0.50 | 305350 | RGD1565119 | ENSRNOT00000048106 |
| 10779093 | 6.24 | 5.36 | -0.89 | 0.54 | 408223 | Usp54 | NM_001008863 |
| 10781273 | 5.02 | 3.13 | -1.89 | 0.27 | 81801 | Stc1 | NM_031123 |
| 10781525 | 5.51 | 4.30 | -1.20 | 0.43 | 113936 | Cpb2 | BC107447 |
| 10784980 | 7.32 | 6.11 | -1.20 | 0.43 | 282843 | Sorbs3 | NM_001005762 |
| 10789442 | 9.65 | 8.50 | -1.16 | 0.45 | 58935 | Gas6 | NM_057100 |
| 10789869 | 6.13 | 5.10 | -1.03 | 0.49 | 29716 | Cacna1d | NM_017298 |
| 10796831 | 4.16 | 3.28 | -0.88 | 0.54 | 291345 | RGD1561231 | ENSRNOT00000047232 |
| 10797527 | 7.79 | 6.44 | -1.35 | 0.39 | 291005 | Gadd45g | NM_001077640 |
| 10797929 | 6.23 | 5.08 | -1.15 | 0.45 | 306860 | Gcnt2 | NM_001001511 |
| 10798438 | 6.98 | 6.07 | -0.91 | 0.53 | 24828 | Hist1h2aa | ENSRNOT00000050526 |
| 10798943 | 5.58 | 4.61 | -0.97 | 0.51 | 113938 | Snurf | NM_130738 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10798964 | 8.08 | 7.09 | -0.99 | 0.50 | 85419 | Lyst | NM_053518 |
| 10799888 | 5.28 | 4.15 | -1.12 | 0.46 | 291367 | RGD1564552 | ENSRNOT00000050803 |
| 10800024 | 4.75 | 3.61 | -1.13 | 0.46 | 291345 | RGD1561231 | ENSRNOT00000047232 |
| 10800919 | 6.57 | 5.45 | -1.13 | 0.46 | 24330 | Egr1 | NM_012551 |
| 10801260 | 4.11 | 2.90 | -1.21 | 0.43 | 680470 | Pcdhgb6 | ENSRNOT00000060466 |
| 10803194 | 5.52 | 4.65 | -0.87 | 0.55 | 680014 | Esco1 | NM_001126299 |
| 10803692 | 7.16 | 5.96 | -1.20 | 0.44 | 338475 | Nrep | NM_178096 |
| 10804127 | 4.46 | 3.49 | -0.97 | 0.51 | 25317 | Fgf1 | NM_012846 |
| 10804281 | 4.97 | 3.78 | -1.19 | 0.44 | 24833 | Spink3 | NM_012674 |
| 10806191 | 4.74 | 3.79 | -0.95 | 0.52 | 679726 | LOC679726 | ENSRNOT00000040473 |
| 10812734 | 5.61 | 4.76 | -0.85 | 0.55 | 502503 | Serf1 | ENSRNOT00000024291 |
| 10813949 | 5.29 | 4.13 | -1.16 | 0.45 | 619558 | Fam134b | ENSRNOT00000014423 |
| 10814184 | 3.82 | 2.68 | -1.14 | 0.45 | 310218 | Car1 | NM_001107660 |
| 10817142 | 4.31 | 3.43 | -0.87 | 0.55 | 310586 | RGD1566121 | ENSRNOT00000035763 |
| 10817222 | 7.94 | 7.05 | -0.89 | 0.54 | 499668 | Lingo4 | NM_001109189 |
| 10821698 | 5.01 | 4.10 | -0.91 | 0.53 | 310132 | Osmr | NM_001005384 |
| 10822242 | 11.78 | 10.22 | -1.56 | 0.34 | 54232 | Car3 | NM_019292 |
| 10826216 | 6.60 | 5.68 | -0.92 | 0.53 | 691538 | Rnpc3 | NM_001100810 |
| 10826723 | 8.96 | 7.91 | -1.05 | 0.48 | 64017 | Enpep | NM_022251 |
| 10826967 | 4.12 | 3.00 | -1.11 | 0.46 | 365948 | Bank1 | XM_345295 |
| 10830223 | 9.15 | 8.29 | -0.85 | 0.55 | 80841 | Fabp7 | NM_030832 |
| 10830270 | 5.06 | 3.41 | -1.64 | 0.32 | 499453 | RGD1565550 | ENSRNOT00000044322 |
| 10830279 | 7.05 | 5.99 | -1.07 | 0.48 | 499454 | RGD1560095 | ENSRNOT00000040584 |
| 10830854 | 7.92 | 6.70 | -1.22 | 0.43 | 29168 | Ubd | NM_053299 |
| 10832487 | 4.55 | 3.21 | -1.34 | 0.39 | 690315 | Derl3 | NM_001109577 |
| 10832772 | 7.40 | 5.83 | -1.58 | 0.34 | 309722 | Rhobtb1 | NM_001107622 |
| 10834335 | 3.76 | 2.76 | -1.00 | 0.50 | 414138 | Lcn6 | NM_001001519 |
| 10834670 | 4.76 | 3.70 | -1.07 | 0.48 | 311827 | Adamtsl2 | ENSRNOT00000036995 |
| 10838443 | 2.88 | 1.99 | -0.88 | 0.54 | 405231 | Olr786 | NM_001000916 |
| 10844331 | 10.33 | 5.05 | -5.28 | 0.03 | 170496 | Lcn2 | NM_130741 |
| 10846652 | 5.59 | 4.71 | -0.88 | 0.54 | 311137 | Zfp385b | NM_001107736 |
| 10847957 | 6.36 | 4.55 | -1.80 | 0.29 | 499847 | Prrg4 | NM_001109203 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10857130 | 7.91 | 7.06 | -0.86 | 0.55 | 29254 | Mgll | NM_138502 |
| 10858408 | 6.78 | 4.64 | -2.14 | 0.23 | 24153 | A2m | NM_012488 |
| 10859671 | 4.66 | 3.81 | -0.85 | 0.56 | 362464 | LOC362464 | ENSRNOT00000055473 |
| 10860314 | 3.51 | 2.59 | -0.92 | 0.53 | 286924 | Gnat3 | NM_173139 |
| 10861793 | 7.82 | 6.60 | -1.21 | 0.43 | 503568 | Slc13a4 | NM_001012621 |
| 10863608 | 3.90 | 2.79 | -1.11 | 0.46 | 312495 | Cyp26b1 | NM_181087 |
| 10863686 | 6.71 | 5.01 | -1.70 | 0.31 | 64570 | Nat8 | NM_022635 |
| 10867497 | 4.65 | 3.55 | -1.10 | 0.47 | 500400 | Fam110b | BC091289 |
| 10867667 | 7.52 | 6.51 | -1.01 | 0.50 | 117048 | Cdh17 | NM_053977 |
| 10869476 | 11.86 | 10.50 | -1.36 | 0.39 | 24614 | Orm1 | NM_053288 |
| 10875567 | 5.33 | 4.35 | -0.98 | 0.51 | 297903 | Fam92a1 | ENSRNOT00000022249 |
| 10877372 | 7.29 | 5.84 | -1.45 | 0.37 | 298107 | Mup5 | AB039828 |
| 10877755 | 8.66 | 7.71 | -0.96 | 0.51 | 29227 | Nfib | NM_031566 |
| 10881861 | 7.79 | 6.39 | -1.40 | 0.38 | 78962 | Per3 | NM_023978 |
| 10887486 | 5.85 | 4.98 | -0.86 | 0.55 | 362790 | RGD1308350 | ENSRNOT00000018225 |
| 10887492 | 5.87 | 4.70 | -1.17 | 0.44 | 362790 | RGD1308350 | ENSRNOT00000018225 |
| 10887939 | 4.89 | 4.03 | -0.85 | 0.55 | 313838 | Cdc42ep3 | NM_001048044 |
| 10890547 | 10.65 | 9.16 | -1.48 | 0.36 | 299131 | Dhrs7 | NM_001013098 |
| 10894414 | 3.61 | 2.70 | -0.91 | 0.53 | 300308 | LOC300308 | NM_001013952 |
| 10894525 | 5.94 | 5.07 | -0.87 | 0.55 | 299691 | Cry1 | NM_198750 |
| 10895888 | 6.80 | 5.91 | -0.89 | 0.54 | 362894 | R3hdm2 | NM_001130557 |
| 10895915 | 7.67 | 5.34 | -2.33 | 0.20 | 362895 | Stac3 | NM_001130558 |
| 10903573 | 6.94 | 4.77 | -2.17 | 0.22 | 500865 | Golsyn | ENSRNOT00000005584 |
| 10905312 | 5.60 | 4.17 | -1.43 | 0.37 | 171044 | Sstr3 | NM_133522 |
| 10906296 | 5.24 | 4.31 | -0.92 | 0.53 | 500917 | Odf3b | ENSRNOT00000055805 |
| 10909105 | 3.63 | 2.35 | -1.28 | 0.41 | 406021 | Olr1197 | NM_001001120 |
| 10912076 | 4.87 | 3.87 | -1.00 | 0.50 | 502642 | RGD1563348 | NM_001114939 |
| 10912908 | 7.43 | 6.46 | -0.97 | 0.51 | 83681 | Cish | NM_031804 |
| 10913043 | 4.46 | 3.54 | -0.92 | 0.53 | 300999 | Mst1r | NM_001106855 |
| 10917518 | 7.06 | 6.08 | -0.98 | 0.51 | 315676 | Dmxl2 | ENSRNOT00000066197 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 10917617 | 6.35 | 4.53 | -1.82 | 0.28 | 690919 | Nrg4 | ENSRNOT00000020332 |
| 10919010 | 4.85 | 3.93 | -0.93 | 0.53 | 113990 | Hmgn3 | NM_001007020 |
| 10919262 | 5.53 | 4.56 | -0.96 | 0.51 | 300888 | Tmed3 | NM_001004249 |
| 10920002 | 5.62 | 4.63 | -0.99 | 0.50 | 315992 | Dock3 | NM_001108184 |
| 10920498 | 4.91 | 3.95 | -0.96 | 0.51 | 316014 | Nbeal2 | ENSRNOT00000056130 |
| 10921141 | 7.34 | 6.47 | -0.87 | 0.55 | 301085 | Fyco1 | NM_001106870 |
| 10922260 | 4.20 | 3.31 | -0.89 | 0.54 | 316304 | Lgsn | NM_181383 |
| 10922499 | 4.42 | 3.28 | -1.14 | 0.45 | 679806 | Fer1l5 | ENSRNOT00000059806 |
| 10923432 | 10.86 | 9.46 | -1.39 | 0.38 | 493909 | Aox3 | NM_001008527 |
| 10923474 | 7.39 | 6.11 | -1.28 | 0.41 | 316424 | Aox4 | ENSRNOT00000033068 |
| 10923476 | 11.44 | 10.02 | -1.43 | 0.37 | 316424 | Aox4 | ENSRNOT00000033068 |
| 10924245 | 3.36 | 2.31 | -1.04 | 0.49 | 29385 | Il8rb | NM_017183 |
| 10926651 | 7.75 | 6.32 | -1.43 | 0.37 | 316249 | Enpp5 | NM_001012744 |
| 10926851 | 6.05 | 4.57 | -1.48 | 0.36 | 301287 | Pkhd1 | ENSRNOT00000060760 |
| 10928191 | 4.39 | 3.33 | -1.06 | 0.48 | 501145 | Satb2 | NM_001109306 |
| 10928452 | 7.58 | 6.68 | -0.91 | 0.53 | 363239 | Raph1 | NM_001108798 |
| 10929842 | 6.68 | 5.75 | -0.93 | 0.53 | 63840 | Per2 | NM_031678 |
| 10930766 | 9.51 | 7.07 | -2.44 | 0.18 | 25011 | Cyp2c12 | NM_031572 |
| 10932037 | 4.24 | 3.25 | -0.99 | 0.50 | 313434 | RGD1566363 | ENSRNOT00000039809 |
| 10932139 | 5.06 | 4.04 | -1.02 | 0.49 | 317170 | Slc9a7 | NM_001108242 |
| 10933772 | 3.74 | 2.81 | -0.93 | 0.52 | 192267 | Obp1f | NM_138903 |
| 10938524 | 6.71 | 5.08 | -1.63 | 0.32 | 312102 | Vsig4 | NM_001025004 |

## Supplementary table (ST4): List of common genes affected in brain and liver

### (A) Common genes "down-regulated" in the brain and liver:

| Gene Symbol | Accession No. | GO term molecular/biological functions |
|---|---|---|
| Wee1 | NM_001012742 | Protein tyrosine kinase activity |
| Slc2a12 | NM_001107451 | Carbohydrate transmembrane transporter activity |
| Hrk | NM_057130 | Apoptosis regulation, Bleb assembly |
| Fam110b | NM_001024341.1 | ---N.A.--- |

(B) **Common genes "up-regulated" in the brain and "down-regulated" in the liver:**

| Gene Symbol | Accession | GO term molecular/biological functions |
|---|---|---|
| Hba-a1 | NM_013096.2 | Heme binding, Oxidoreductase activity, Drug transport |
| Hba-a2 | NM_013096 | Heme binding, Oxidoreductase activity, Drug transport |
| Mup5 | NM_203325.1 | Fatty acid biosynthetic process, Catalytic activity |

(C) **Common genes "up-regulated" in the liver and "down-regulated" in the brain:**

| Gene Symbol | Accession | GO term molecular/biological functions |
|---|---|---|
| RT1-Da | NM_001008847 | Response to stimulus |
| Zbtb6 | NM_001108953 | --N.A.-- |
| Tmem106b | NM_001004267 | --N.A.-- |

## 8. References


[1] Hendricks JC, Finn SM, Panckeri KA, Chavkin J, Williams JA, Sehgal A, et al. Rest in Drosophila is a sleep-like state. Neuron 2000;25:129–38. doi:10.1016/S0896-6273(00)80877-6.

[2] Shaw PJ, Cirelli C, Greensoan RJ, Tononi G. Correlates of sleep and waking in Drosophila melanogaster. Science (80- ) 2000;287:1834–7. doi:10.1126/science.287.5459.1834.

[3] Zimmerman JE, Naidoo N, Raizen DM, Pack AI. Conservation of sleep: insights from non-mammalian model systems. Trends Neurosci 2008;31:371–6. doi:10.1016/j.tins.2008.05.001.

[4] Yokogawa T, Marin W, Faraco J, Pézeron G, Appelbaum L, Zhang J, et al. Characterization of sleep in zebrafish and insomnia in hypocretin receptor mutants. PLoS Biol 2007;5:2379–97. doi:10.1371/journal.pbio.0050277.

[5] Prober DA, Rihel J, Onah AA, Sung R-J, Schier AF. Hypocretin/Orexin

Overexpression Induces An Insomnia-Like Phenotype in Zebrafish. J Neurosci 2006;26:13400–10. doi:10.1523/JNEUROSCI.4332-06.2006.

[6] Zhdanova I V., Wang SY, Leclair OU, Danilova NP. Melatonin promotes sleep-like state in zebrafish. Brain Res 2001;903:263–8. doi:10.1016/S0006-8993(01)02444-1.

[7] Raizen DM, Zimmerman JE, Maycock MH, Ta UD, You YJ, Sundaram M V., et al. Lethargus is a Caenorhabditis elegans sleep-like state. Nature 2008;451:569–72. doi:10.1038/nature06535.

[8] Eban-Rothschild A, Bloch G. Circadian rhythms and sleep in honey bees. Honeybee Neurobiol. Behav., 2012, p. 31–45. doi:10.1007/978-94-007-2099-2.

[9] Eban-Rothschild AD, Bloch G. Differences in the sleep architecture of forager and young honeybees (Apis mellifera). J Exp Biol 2008;211:2408–16. doi:10.1242/jeb.016915.

[10] Klein BA, Seeley TD. Work or sleep? Honeybee foragers opportunistically nap during the day when forage is not available. Anim Behav 2011;82:77–83. doi:10.1016/j.anbehav.2011.03.026.

[11] Nagari M, Gera A, Jonsson S, Bloch G. Signals from the brood modulate the sleep of brood tending bumblebee workers. BioRxiv 2018. doi:10.1101/500744.

[12] Rechtschaffen A, Gilliland MA, Bergmann BM, Winter JB. Physiological correlates of prolonged sleep deprivation in rats. Science (80- ) 1983;221:182–4. doi:10.1126/science.6857280.

[13] Webb WB, Agnew HW. Sleep deprivation, age, and exhaustion time in the rat. Science (80- ) 1962;136:1122. doi:10.1126/science.136.3522.1122.

[14] Mirsky AF, Cardon P V. A comparison of the behavioral and physiological changes accompanying sleep deprivation and chlorpromazine administration in man. Electroencephalogr Clin Neurophysiol 1962. doi:10.1016/0013-4694(62)90002-0.

[15] Kayser MS, Mainwaring B, Yue Z, Sehgal A. Sleep deprivation suppresses aggression in Drosophila. Elife 2015. doi:10.7554/eLife.07643.

[16] Rial RV, Nicolau MC, Gamundí A, Akaârir M, Aparicio S, Garau C, et al. The trivial function of sleep. Sleep Med Rev 2007. doi:10.1016/j.smrv.2007.03.001.

[17] Rattenborg NC, Lesku JA, Martinez-Gonzalez D, Lima SL. The non-trivial functions of sleep. Sleep Med Rev 2007. doi:10.1016/j.smrv.2007.04.003.

[18] Cirelli C, Tononi G. Is sleep essential? PLoS Biol 2008;6:1605–11. doi:10.1371/journal.pbio.0060216.

[19] Opp MR, Baracchi F. Sleep and immune function. Curr. Adv. Sleep Biol., 2009. doi:10.1007/s00424-011-1044-0.

[20] Opp MR, Krueger JM. Sleep and immunity: A growing field with clinical impact. Brain Behav Immun 2015. doi:10.1016/j.bbi.2015.03.011.

[21] Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, Inflammatory, and Metabolic Consequences of Sleep Deprivation. Prog Cardiovasc Dis 2009. doi:10.1016/j.pcad.2008.10.003.

[22] Cirelli C. Cellular consequences of sleep deprivation in the brain. Sleep Med Rev 2006. doi:10.1016/j.smrv.2006.04.001.

[23] Geissmann Q, Beckwith EJ, Gilestro GF. Most sleep does not serve a vital function. Evidence from Drosophila melanogaster. BioRxiv 2018. doi:10.1101/361667.

[24] Nagari M, Gera A, Jonsson S, Bloch G. Bumble Bee Workers Give Up Sleep to Care for Offspring that Are Not Their Own. Curr Biol 2019;29:3488–93. doi:10.1016/j.cub.2019.07.091.

[25] Shein-Idelson M, Ondracek JM, Liaw HP, Reiter S, Laurent G. Slow waves, sharp waves, ripples, and REM in sleeping dragons. Science (80- ) 2016. doi:10.1126/science.aaf3621.

[26] Boyce R, Glasgow SD, Williams S, Adamantidis A. Sleep research: Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation. Science (80- ) 2016;352:812–6. doi:10.1126/science.aad5252.

[27] Graves L, Heller E, Pack A, Abel T. Sleep deprivation selectively impairs memory consolidation for contextual fear conditioning. Learn Mem 2003;10:168–176. doi:10.1101/lm.48803.LEARNING.

[28] Kumar T, Jha SK. Sleep Deprivation Impairs Consolidation of Cued Fear Memory in Rats. PLoS One 2012;7. doi:10.1371/journal.pone.0047042.

[29] Youngblood BD, Zhou J, Smagin GN, Ryan DH, Harris RBS. Sleep deprivation by the "flower pot" technique and spatial reference memory. Physiol Behav 1997;61:249–56. doi:10.1016/S0031-9384(96)00363-0.

[30] Chokroverty S. Physiological changes of sleep. Sleep Disord. Med. Basic Sci. Tech. Considerations Clin. Asp. Fourth Ed., 2017, p. 153–94. doi:10.1007/978-1-4939-6578-6_11.

[31] Mallick BN, Singh S, Pal D. Role of alpha and beta adrenoceptors in locus coeruleus stimulation-induced reduction in rapid eye movement sleep in freely moving rats. Behav Brain Res 2005;158:9–21. doi:10.1016/j.bbr.2004.08.004.

[32] Mônico-Neto M, Dáttilo M, Ribeiro DA, Lee KS, de Mello MT, Tufik S, et al. REM sleep deprivation impairs muscle regeneration in rats. Growth Factors 2017;0:000. doi:10.1080/08977194.2017.1314277.

[33] Van Der Helm E, Yao J, Dutt S, Rao V, Saletin JM, Walker MP. REM sleep depotentiates amygdala activity to previous emotional experiences. Curr Biol 2011;21:2029–32. doi:10.1016/j.cub.2011.10.052.

[34] Grosmark AD, Mizuseki K, Pastalkova E, Diba K, Buzsáki G. REM Sleep Reorganizes Hippocampal Excitability. Neuron 2012;75:1001–7.

doi:10.1016/j.neuron.2012.08.015.

[35] Li W, Ma L, Yang G, Gan WB. REM sleep selectively prunes and maintains new synapses in development and learning. Nat Neurosci 2017;20:427–37. doi:10.1038/nn.4479.

[36] Somarajan BI, Khanday MA, Mallick BN. Rapid eye movement sleep deprivation induces neuronal apoptosis by noradrenaline acting on alpha1 adrenoceptor and by triggering mitochondrial intrinsic pathway. Front Neurol 2016;7. doi:10.3389/fneur.2016.00025.

[37] Atul Pandey; Devesh Kumar; Gopesh Ray; Santosh Kar. Rapid eye movement sleep deprivation causes apoptotic cell-death of the hepatocytes in rat. Biorxiv 2018. doi:https://doi.org/10.1101/375717.

[38] Biswas S, Mishra P, Mallick BN. Increased apoptosis in rat brain after rapid eye movement sleep loss. Neuroscience 2006;142:315–31. doi:10.1016/j.neuroscience.2006.06.026.

[39] Pandey AKAK, Kar SKSK. REM sleep deprivation of rats induces acute phase response in liver. Biochem Biophys Res Commun 2011;410:242–6. doi:10.1016/j.bbrc.2011.05.123.

[40] Pandey A, Kar SK. Rapid Eye Movement sleep deprivation of rat generates ROS in the hepatocytes and makes them more susceptible to oxidative stress. Sleep Sci 2018. doi:10.5935/1984-0063.20180039.

[41] Mignot E. Why we sleep: The temporal organization of recovery. PLoS Biol 2008;6:661–9. doi:10.1371/journal.pbio.0060106.

[42] Cirelli C, Bushey D. Sleep and wakefulness in Drosophila melanogaster. Ann. N. Y. Acad. Sci., vol. 1129, 2008, p. 323–9. doi:10.1196/annals.1417.017.

[43] Cirelli C, Gutierrez CM, Tononi G. Extensive and Divergent Effects of Sleep and

Wakefulness on Brain Gene Expression. Neuron 2004;41:35–43. doi:10.1016/S0896-6273(03)00814-6.

[44] Cirelli C, LaVaute TM, Tononi G. Sleep and wakefulness modulate gene expression in Drosophila. J Neurochem 2005;94:1411–9. doi:10.1111/j.1471-4159.2005.03291.x.

[45] Cirelli C. Locus Ceruleus Control of State-Dependent Gene Expression. J Neurosci 2004;24:5410–9. doi:10.1523/JNEUROSCI.0949-04.2004.

[46] Jones S, Pfister-Genskow M, Benca RM, Cirelli C. Molecular correlates of sleep and wakefulness in the brain of the white-crowned sparrow. J Neurochem 2008;105:46–62. doi:10.1111/j.1471-4159.2007.05089.x.

[47] Mackiewicz M, Shockley KR, Romer MA, Galante RJ, Zimmerman JE, Naidoo N, et al. Macromolecule biosynthesis: a key function of sleep. Physiol Genomics 2007;31:441–57. doi:10.1152/physiolgenomics.00275.2006.

[48] Maret S, Dorsaz S, Gurcel L, Pradervand S, Petit B, Pfister C, et al. Homer1a is a core brain molecular correlate of sleep loss. Proc Natl Acad Sci 2007;104:20090–5. doi:10.1073/pnas.0710131104.

[49] Zimmerman JE, Rizzo W, Shockley KR, Raizen DM, Naidoo N, Mackiewicz M, et al. Multiple mechanisms limit the duration of wakefulness in *Drosophila* brain. Physiol Genomics 2006;27:337–50. doi:10.1152/physiolgenomics.00030.2006.

[50] Hicks RA, Okuda A, Thomsen D. Depriving rats of REM sleep: the identification of a methodological problem. Am J Psychol 1977;90:95–102. doi:10.2307/1421644.

[51] van Hulzen ZJM, Coenen AML. Paradoxical sleep deprivation and locomotor activity in rats. Physiol Behav 1981;27:741–4. doi:10.1016/0031-9384(81)90250-X.

[52] Pandey AK, Kar SK. REM sleep deprivation of rats induces acute phase response in liver. Biochem Biophys Res Commun 2011;410. doi:10.1016/j.bbrc.2011.05.123.

[53] Computing RA language and environment for statistcal. R development core team. R

Found Stat Comput 2013;55:275–86.

[54] R Foundation for Statistical Computing. R: A Language and Environment for Statistical Computing. R Found. Stat. Comput., vol. 1, 2016. doi:10.1007/978-3-540-74686-7.

[55] Ashburner M, Ball CA, Blake JA, Butler H, Cherry JM, Eppig JT, et al. Creating the Gene Ontology resource: Design and implementation. Genome Res 2001. doi:10.1101/gr.180801.

[56] Dyken ME, Yamada T, Glenn CL, Berger HA. Obstructive sleep apnea associated with cerebral hypoxemia and death. Neurology 2004. doi:10.1212/01.WNL.0000106952.84223.F3.

[57] Muller NL, Francis PW, Gurwitz D, Levison H, Bryan AC. Mechanism of hemoglobin desaturation during rapid-eye-movement sleep in normal subjects and in patients with cystic fibrosis. Am Rev Respir Dis 1980. doi:10.1164/arrd.1980.121.3.463.

[58] Gaudet P, Livstone MS, Lewis SE, Thomas PD. Phylogenetic-based propagation of functional annotations within the Gene Ontology consortium. Brief Bioinform 2011. doi:10.1093/bib/bbr042.

[59] Schwenk BM, Lang CM, Hogl S, Tahirovic S, Orozco D, Rentzsch K, et al. The FTLD risk factor TMEM106B and MAP6 control dendritic trafficking of lysosomes. EMBO J 2014. doi:10.1002/embj.201385857.

[60] Chen-Plotkin AS, Unger TL, Gallagher MD, Bill E, Kwong LK, Volpicelli-Daley L, et al. TMEM106B, the Risk Gene for Frontotemporal Dementia, Is Regulated by the microRNA-132/212 Cluster and Affects Progranulin Pathways. J Neurosci 2012. doi:10.1523/JNEUROSCI.0521-12.2012.

[61] Cirelli C, Faraguna U, Tononi G. Changes in brain gene expression after long-term sleep deprivation. J Neurochem 2006. doi:10.1111/j.1471-4159.2006.04058.x.

[62] Cirelli C, Tononi G. Gene expression in the brain across the sleep-waking cycle. Brain Res 2000. doi:10.1016/S0006-8993(00)03008-0.

[63] Grønli J, Soulé J, Bramham CR. Sleep and protein synthesis-dependent synaptic plasticity: impacts of sleep loss and stress. Front Behav Neurosci 2014. doi:10.3389/fnbeh.2013.00224.

[64] Fiorentino L, Ancoli-Israel S. Sleep dysfunction in patients with cancer. Curr Treat Options Neurol 2007. doi:10.1007/s11940-007-0019-0.

[65] Fang HF, Miao NF, Chen CD, Sithole T, Chung MH. Risk of cancer in patients with insomnia, parasomnia, and obstructive sleep apnea: A nationwide nested case-control study. J Cancer 2015. doi:10.7150/jca.12490.

[66] Sateia MJ, Lang BJ. Sleep and cancer: Recent developments. Curr Oncol Rep 2008. doi:10.1007/s11912-008-0049-0.

[67] Shi T, Min M, Sun C, Zhang Y, Liang M, Sun Y. Does insomnia predict a high risk of cancer? A systematic review and meta-analysis of cohort studies. J Sleep Res 2020. doi:10.1111/jsr.12876.

[68] Martínez-Garćia MÁ, Martorell-Calatayud A, Nagore E, Valero I, Selma MJ, Chiner E, et al. Association between sleep disordered breathing and aggressiveness markers of malignant cutaneous melanoma. Eur Respir J 2014. doi:10.1183/09031936.00115413.

[69] Lin CL, Liu TC, Wang YN, Chung CH, Chien WC. The association between sleep disorders and the risk of colorectal cancer in patients: A Population-based Nested Case–Control Study. In Vivo (Brooklyn) 2019. doi:10.21873/invivo.11513.

[70] Sillah A, Watson NF, Schwartz SM, Gozal D, Phipps AI. Sleep apnea and subsequent cancer incidence. Cancer Causes Control 2018. doi:10.1007/s10552-018-1073-5.

[71] Chiu HY, Huang CJ, Fan YC, Tsai PS. Insomnia but Not Hypnotics Use Associates with the Risk of Breast Cancer: A Population-Based Matched Cohort Study. J

Women's Heal 2018. doi:10.1089/jwh.2017.6626.

[72] Sturgeon SR, Luisi N, Balasubramanian R, Reeves KW. Sleep duration and endometrial cancer risk. Cancer Causes Control 2012. doi:10.1007/s10552-012-9912-2.

[73] Liu R, Xu KP, Tan GS. Cyclooxygenase-2 inhibitors in lung cancer treatment: Bench to bed. Eur J Pharmacol 2015. doi:10.1016/j.ejphar.2015.11.007.

[74] Lin XM, Luo W, Wang H, Li RZ, Huang YS, Chen LK, et al. The role of prostaglandin-endoperoxide synthase-2 in chemoresistance of non-small cell lung cancer. Front Pharmacol 2019. doi:10.3389/fphar.2019.00836.

[75] Mueller S, Engleitner T, Maresch R, Zukowska M, Lange S, Kaltenbacher T, et al. Evolutionary routes and KRAS dosage define pancreatic cancer phenotypes. Nature 2018. doi:10.1038/nature25459.

[76] LoRusso PM, Herbst RS, Rischin D, Ranson M, Calvert H, Raymond E, et al. Improvements in quality of life and disease-related symptoms in phase I trials of the selective oral epidermal growth factor receptor tyrosine kinase inhibitor ZD1839 in non-small cell lung cancer and other solid tumors. Clin Cancer Res 2003.

[77] Thomadaki H, Scorilas A. BCL2 family of apoptosis-related genes: Functions and clinical implications in cancer. Crit Rev Clin Lab Sci 2006. doi:10.1080/10408360500295626.

[78] Cruse G, Metcalfe DD, Olivera A. Functional deregulation of KIT: Link to mast cell proliferative diseases and other neoplasms. Immunol Allergy Clin North Am 2014. doi:10.1016/j.iac.2014.01.002.

[79] Redline S, Tishler P V. The genetics of sleep apnea. Sleep Med Rev 2000. doi:10.1053/smrv.2000.0120.

[80] Cirelli C, Tononi G. On the Functional Significance of c-fos Induction During the

Sleep-waking Cycle. Sleep 2000. doi:10.1093/sleep/23.4.9.

[81] Cirelli C, Pompeiano M, Tononi G. Sleep deprivation and c-fos expression in the rat brain. J Sleep Res 1995. doi:10.1111/j.1365-2869.1995.tb00157.x.

[82] Gregory A, Kurian MA, Maher ER, Hogarth P, Hayflick SJ. PLA2G6-Associated Neurodegeneration. 1993.

[83] Gregory A, Westaway SK, Holm IE, Kotzbauer PT, Hogarth P, Sonek S, et al. Neurodegeneration associated with genetic defects in phospholipase A2. Neurology 2008. doi:10.1212/01.wnl.0000327094.67726.28.

[84] Kinghorn KJ, Castillo-Quan JI, Bartolome F, Angelova PR, Li L, Pope S, et al. Loss of PLA2G6 leads to elevated mitochondrial lipid peroxidation and mitochondrial dysfunction. Brain 2015. doi:10.1093/brain/awv132.

[85] Ollila H. Genetics of sleep, Sleep and Comorbidities: Connection at the Genetic Level. National Institute for Health and Welfare, Helsinki, 2013.

[86] Gao Y, Yi X, Ding Y. Combined transcriptomic analysis revealed AKR1B10 played an important role in psoriasis through the dysregulated lipid pathway and overproliferation of keratinocyte. Biomed Res Int 2017. doi:10.1155/2017/8717369.

[87] Barge-Schaapveld DQCM, Ofman R, Knegt AC, Alders M, Höhne W, Kemp S, et al. Intellectual Disability and Hemizygous GPD2 Mutation. Am J Med Genet Part A 2013. doi:10.1002/ajmg.a.35873.

[88] Barclay JL, Husse J, Bode B, Naujokat N, Meyer-Kovac J, Schmid SM, et al. Circadian desynchrony promotes metabolic disruption in a mouse model of shiftwork. PLoS One 2012. doi:10.1371/journal.pone.0037150.

[89] Kim JH, Kim JH, Cho YE, Baek MC, Jung JY, Lee MG, et al. Chronic sleep deprivation-induced proteome changes in astrocytes of the rat hypothalamus. J Proteome Res 2014. doi:10.1021/pr500431j.

[90] Arriaga F, Dugovic C, Wauquier A. Effects of lithium on dopamine behavioural supersensitivity induced by rapid eye movement sleep deprivation. Neuropsychobiology 1988. doi:10.1159/000118468.

[91] Albert I, Cicala GA, Siegel J. The behavioral effects of REM sleep deprivation in rats. Psychophysiology 1970. doi:10.1111/j.1469-8986.1970.tb02244.x.

[92] Asakura W, Matsumoto K, Ohta H, Watanabe H. REM sleep deprivation decreases apomorphine-induced stimulation of locomotor activity but not stereotyped behavior in mice. Gen Pharmacol 1992. doi:10.1016/0306-3623(92)90092-X.

[93] Maquet P. Functional neuroimaging of normal human sleep by positron emission tomography. J Sleep Res 2000;9:207–31. doi:jsr214 [pii].

[94] Van Luutelaar ELJM, Coenen AML. Differential behavioural effects of two instrumental paradoxical sleep deprivation techniques in rats. Biol Psychol 1982. doi:10.1016/0301-0511(82)90033-3.

[95] Drewes AM, Svendsen L, Taagholt SJ, Bjerregård K, Nielsen KD, Hansen B. Sleep in rheumatoid arthritis: A comparison with healthy subjects and studies of sleep/wake interactions. Br J Rheumatol 1998. doi:10.1093/rheumatology/37.1.71.

[96] Ağargün MY, Tekeoğlu I, Güneş A, Adak B, Kara H, Ercan M. Sleep quality and pain threshold in patients with fibromyalgia. Compr Psychiatry 1999. doi:10.1016/S0010-440X(99)90008-1.

[97] Raymond I, Nielsen TA, Lavigne G, Manzini C, Choinière M. Quality of sleep and its daily relationship to pain intensity in hospitalized adult burn patients. Pain 2001. doi:10.1016/S0304-3959(01)00282-2.

[98] Schrimpf M, Liegl G, Boeckle M, Leitner A, Geisler P, Pieh C. The effect of sleep deprivation on pain perception in healthy subjects: A meta-analysis. Sleep Med 2015. doi:10.1016/j.sleep.2015.07.022.

[99] Stroemel-Scheder C, Kundermann B, Lautenbacher S. The effects of recovery sleep on pain perception: A systematic review. Neurosci Biobehav Rev 2020. doi:10.1016/j.neubiorev.2020.03.028.

[100] Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T. Sleep loss and REM sleep loss are hyperalgesic. Sleep 2006. doi:10.1093/sleep/29.2.145.

[101] Staffe AT, Bech MW, Clemmensen SLK, Nielsen HT, Larsen DB, Petersen KK. Total sleep deprivation increases pain sensitivity, impairs conditioned pain modulation and facilitates temporal summation of pain in healthy participants. PLoS One 2019. doi:10.1371/journal.pone.0225849.

[102] Kim SH, Park JY, Shin HE, Lee SB, Ryu DW, Kim TW, et al. The influence of rapid eye movement sleep deprivation on nociceptive transmission and the duration of facial allodynia in rats: A behavioral and Fos immunohistochemical study. J Headache Pain 2019. doi:10.1186/s10194-019-0977-0.

[103] Azevedo E, Manzano GM, Silva A, Martins R, Andersen ML, Tufik S. The effects of total and REM sleep deprivation on laser-evoked potential threshold and pain perception. Pain 2011. doi:10.1016/j.pain.2011.04.032.

[104] Onen SH, Alloui A, Gross A, Eschallier A, Dubray C. The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. J Sleep Res 2001. doi:10.1046/j.1365-2869.2001.00240.x.

[105] Chouchou F, Chauny JM, Rainville P, Lavigne GJ. Selective REM sleep deprivation improves expectation-related placebo analgesia. PLoS One 2015. doi:10.1371/journal.pone.0144992.

[106] Smith MT, Edwards RR, Stonerock GL, McCann UD. Individual variation in rapid eye movement sleep is associated with pain perception in healthy women: Preliminary

data. Sleep 2005. doi:10.1093/sleep/28.7.809.

[107] Onen SH, Alloui A, Jourdan D, Eschalier A, Dubray C. Effects of rapid eye movement (REM) sleep deprivation on pain sensitivity in the rat. Brain Res 2001. doi:10.1016/S0006-8993(01)02320-4.

[108] Koban M, Swinson KL. Chronic REM-sleep deprivation of rats elevates metabolic rate and increases UCP1 gene expression in brown adipose tissue. Am J Physiol - Endocrinol Metab 2005. doi:10.1152/ajpendo.00543.2004.

[109] Knutson KL, Spiegel K, Penev P, Van Cauter E. The metabolic consequences of sleep deprivation. Sleep Med Rev 2007. doi:10.1016/j.smrv.2007.01.002.

[110] Knutson KL, Van Cauter E. Associations between sleep loss and increased risk of obesity and diabetes. Ann. N. Y. Acad. Sci., 2008. doi:10.1196/annals.1417.033.

[111] Martyn-Nemeth P, Phillips SA, Mihailescu D, Farabi SS, Park C, Lipton R, et al. Poor sleep quality is associated with nocturnal glycaemic variability and fear of hypoglycaemia in adults with type 1 diabetes. J Adv Nurs 2018. doi:10.1111/jan.13765.

[112] Gaudet P, Dessimoz C. Gene ontology: Pitfalls, biases, and remedies. Methods Mol. Biol., 2017. doi:10.1007/978-1-4939-3743-1_14.

[113] Tomczak A, Mortensen JM, Winnenburg R, Liu C, Alessi DT, Swamy V, et al. Interpretation of biological experiments changes with evolution of the Gene Ontology and its annotations. Sci Rep 2018. doi:10.1038/s41598-018-23395-2.

[114] Carbon S, Douglass E, Dunn N, Good B, Harris NL, Lewis SE, et al. The Gene Ontology Resource: 20 years and still GOing strong. Nucleic Acids Res 2019. doi:10.1093/nar/gky1055.

[115] Du J, Li M, Yuan Z, Guo M, Song J, Xie X, et al. A decision analysis model for KEGG pathway analysis. BMC Bioinformatics 2016. doi:10.1186/s12859-016-1285-1.

[116] Du J, Yuan Z, Ma Z, Song J, Xie X, Chen Y. KEGG-PATH: Kyoto encyclopedia of genes and genomes-based pathway analysis using a path analysis model. Mol Biosyst 2014. doi:10.1039/c4mb00287c.

[117] Bauer-Mehren A, Furlong LI, Sanz F. Pathway databases and tools for their exploitation: Benefits, current limitations and challenges. Mol Syst Biol 2009. doi:10.1038/msb.2009.47.

[118] Khatri P, Sirota M, Butte AJ. Ten years of pathway analysis: Current approaches and outstanding challenges. PLoS Comput Biol 2012. doi:10.1371/journal.pcbi.1002375.