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

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Short title:

REM sleep deprivation of rats for 9-days 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 inessential physiological processes, such as protein synthesis and neuronal metabolism etc. are affected differently in the brain and liver tissue of rats after9-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 that9-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 more particularly on rapid eye movement (REM) sleep. 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 changes on 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 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 an 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 large platform control, (hence after, control) 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 where it significantly affected the acute phase response, apoptotic cell death and oxidative stress in the liver [40,52,53]. 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 [54,55].

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[56]. 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. Several 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 -80^0C 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 analysis of 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 based on 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. 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 [57,58].

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 [59,60]. A recent research shows the dementia-related functions of ***Tmem 106b***, regulated by microRNAs[61].

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 [62,63]. 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[64]. 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 to understand its consequences.

REM sleep loss also affected several genes such as ***prostaglandin-endoperoxide synthase*** (***Ptgs2***), ***B-cell lymphoma2*** (***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 [65–71]. However, some emerging evidence also suggests that sleep loss / insomnia prior to the onset of cancer is independently associated with cancer risk [66,70,72,73]. ***Ptgs2***, an enzyme, plays a key role in various pathological processes by catalyzing conversion of arachidonic acid to prostaglandins[74]. 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[75]. Similarly, ***Bcl-2, Kit, K-Ras***, and ***Fos*** genes have been found associated with cancer[76–79]. These genes play an important role in the sleep-wake cycle regulation and are shown to be correlated with sleep [36,37,80–82].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 [83–85]. The ***PLa2g***is further found positively associated with sleep loss and psoriasis in humans [86,87] Similarly, ***Gpd2***gene is found associated with intellectual disability in humans [88] and positively affected due to circadian desynchrony in mouse [89]. The chronic sleep deprivation in rats affected the protein profile of ***Gpd2*** in hypothalamic Astrocytes[90]. 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 [51,91,92] while others have shown decreased locomotor activity [93]. 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[94,95].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 [96–101]. We also found conflicting reports on the sensory perception of pain that were negatively affected in our studies relative to others [102,103]. There are few studies indicating that it is only total sleep deprivation that raises the intensity to pain rather than REM sleep deprivation [104,105]. Nonetheless, selective REM sleep deprivation is correlated with enhanced placebo analgesia effects[106].

Furthermore, there are some report describing individual variations in REM sleep loss and its association with the perception of pain [107]. 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.[108].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 [109]. Several studies are suggesting that there is a strong correlation between sleep loss and an increased risk of obesity and diabetes [110–112].

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 [116–119].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 to explain 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.

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7. Conflict of Interests

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

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Figure 1: Relative expression of six candidate brain and liver tissue genes 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 $2^{-\Delta\Delta CT}$ 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 moment of sleep deprivation in the eye. 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 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 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 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 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.

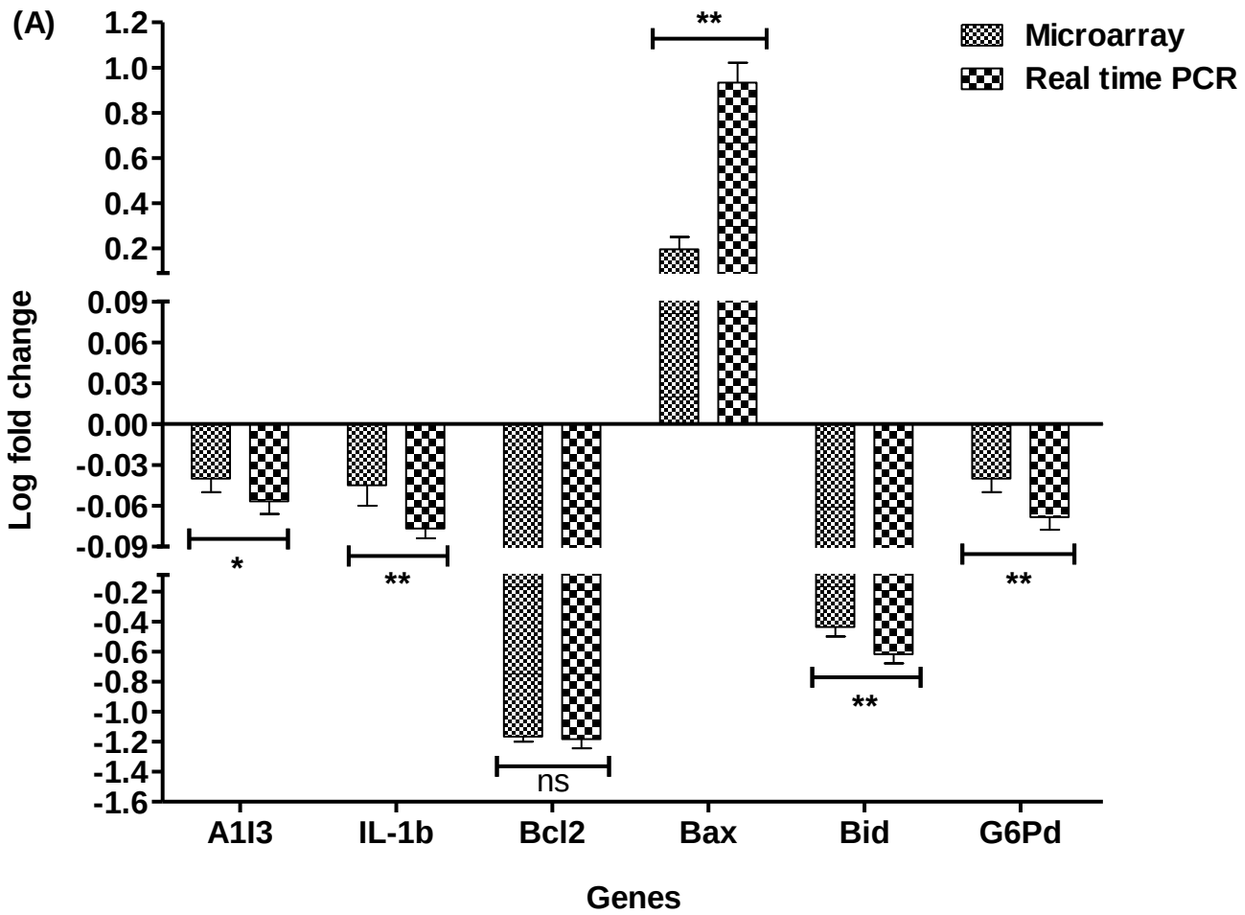
Figure 7: KEGG pathways affected by rapid eye movement sleep deprivation in rats in the liver. (A) Up-regulated, (B) Down-regulated. The x-axis is the number of nodes affected. The y-axis is the p-value ($p<0.05$). Color coding reflects the total number of nodes evaluated in the database.

Supplementary Figure 1: Effect 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.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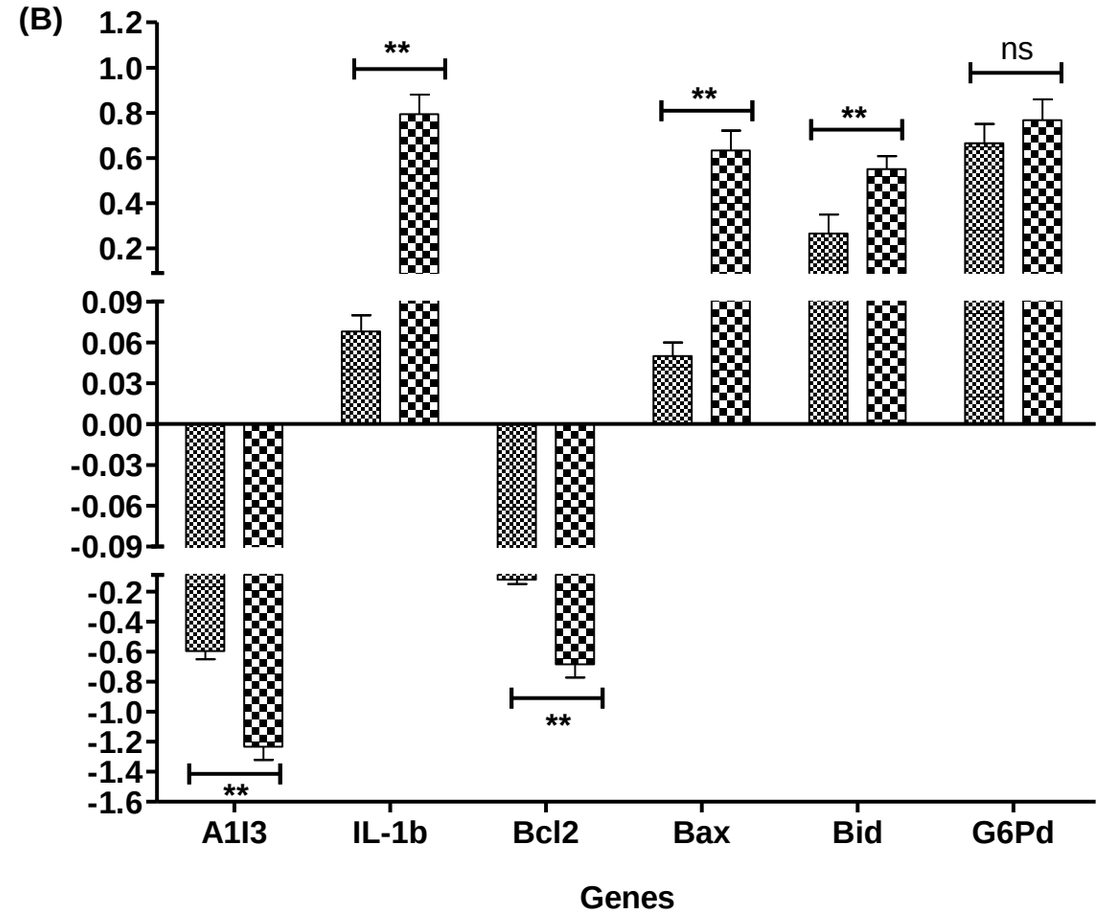
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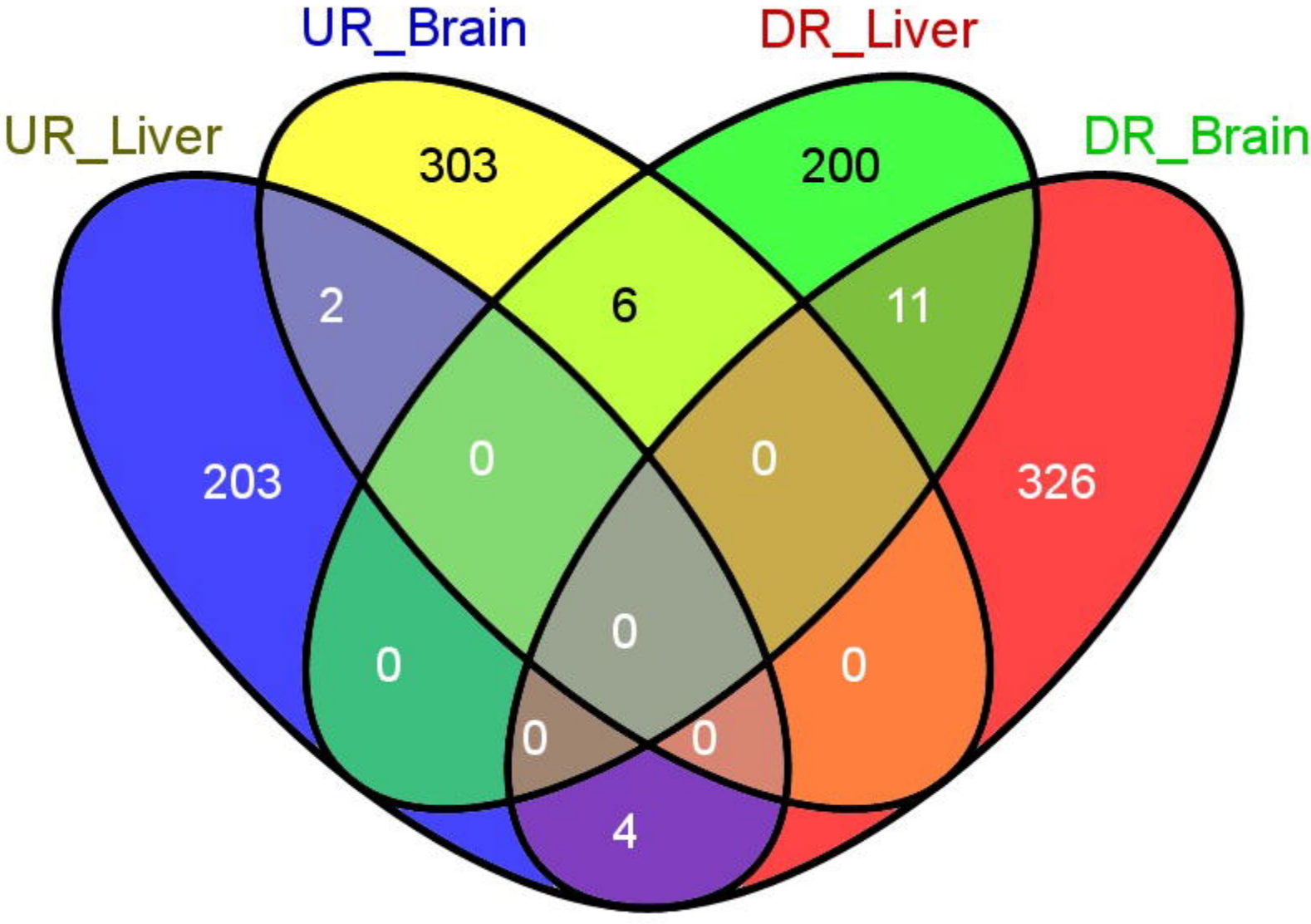
UR_Brain
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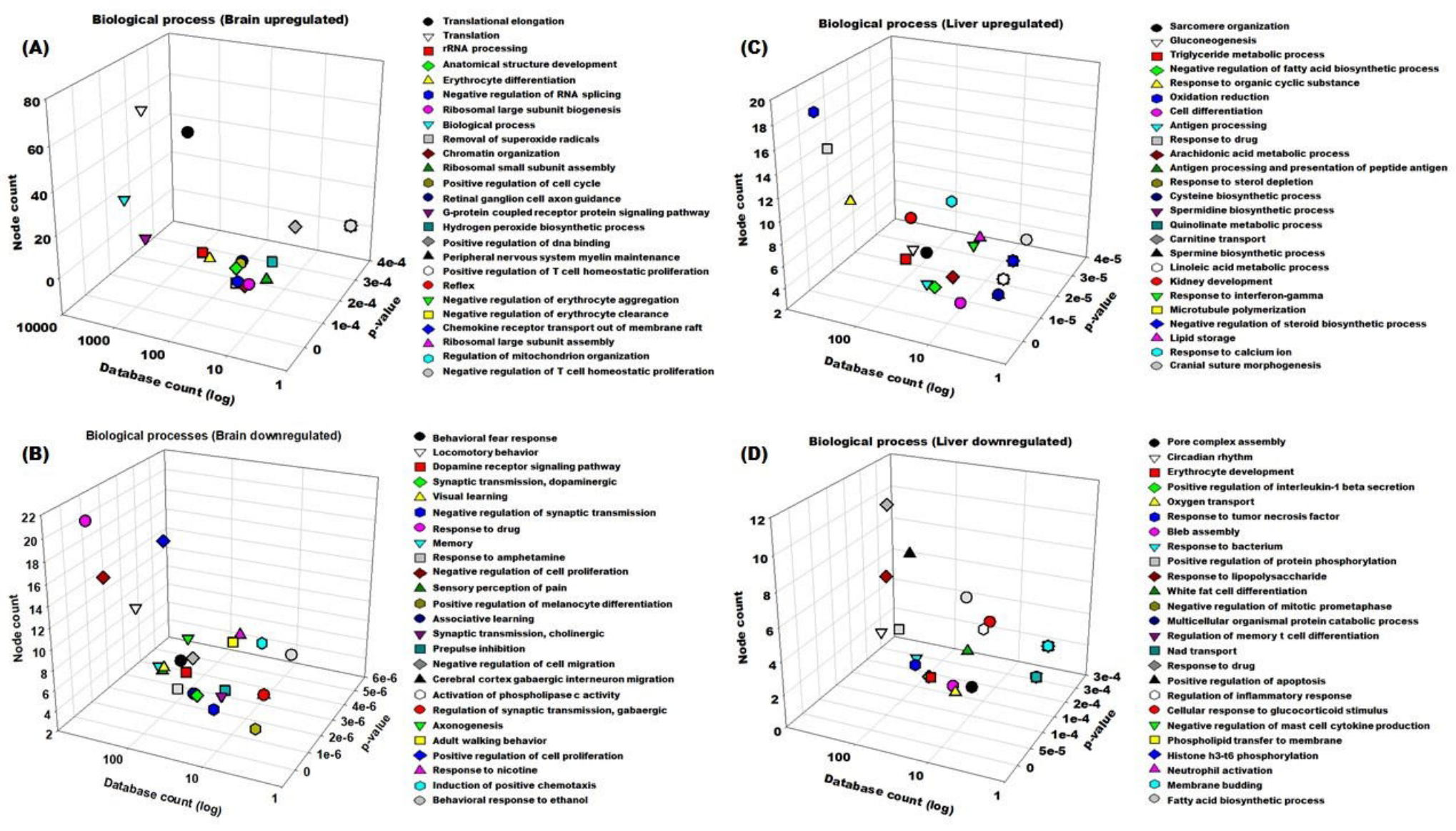
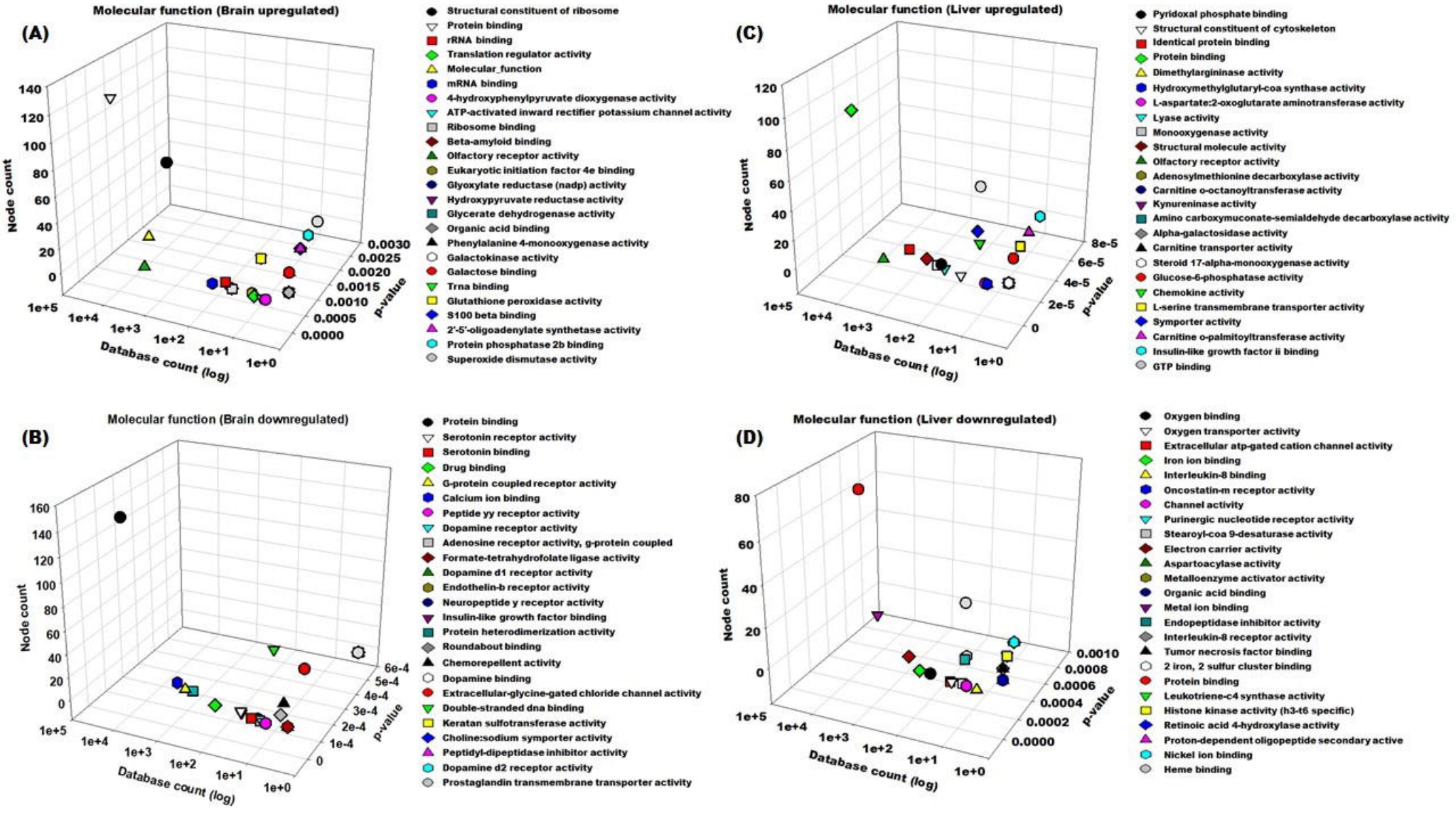
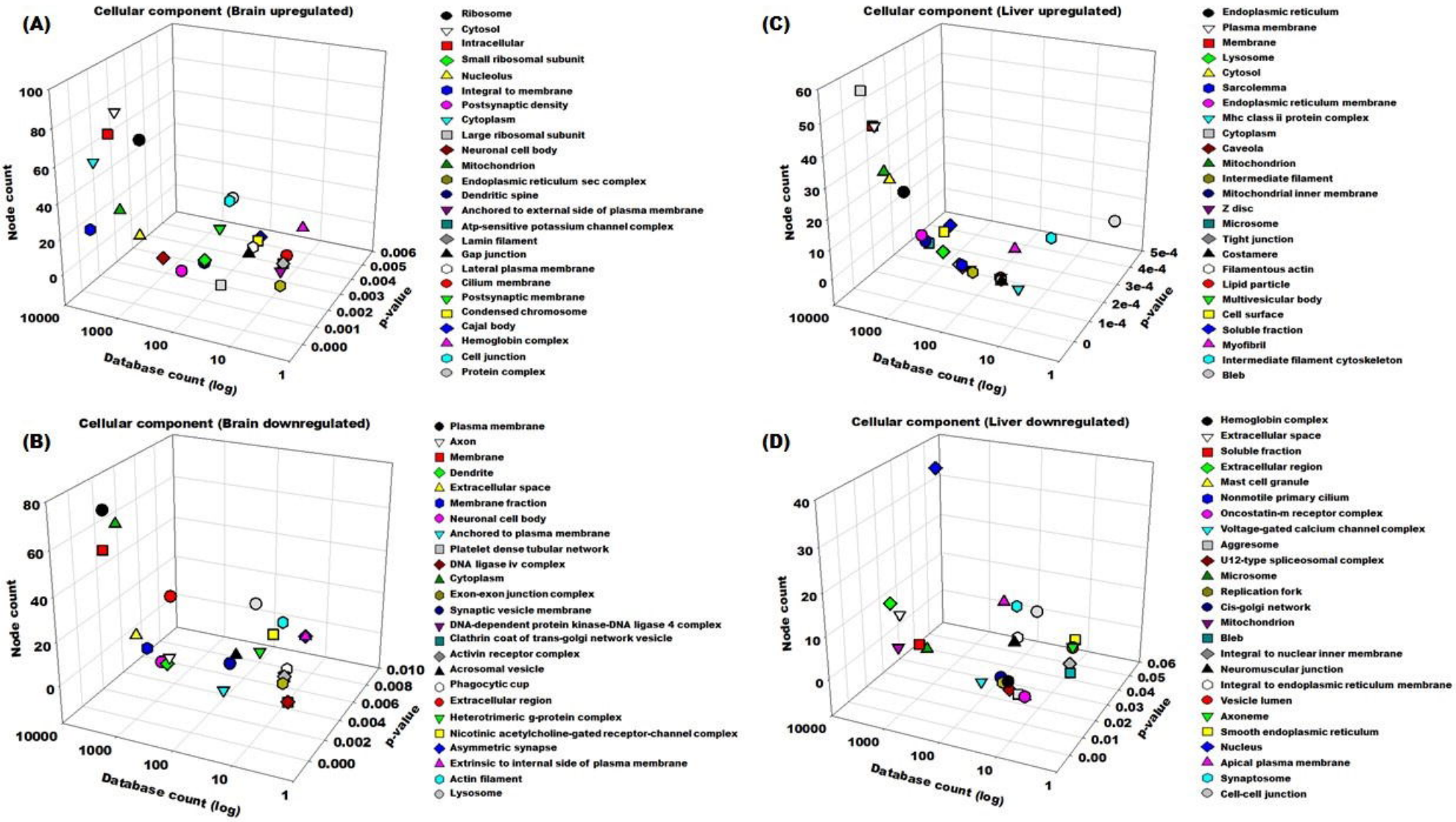
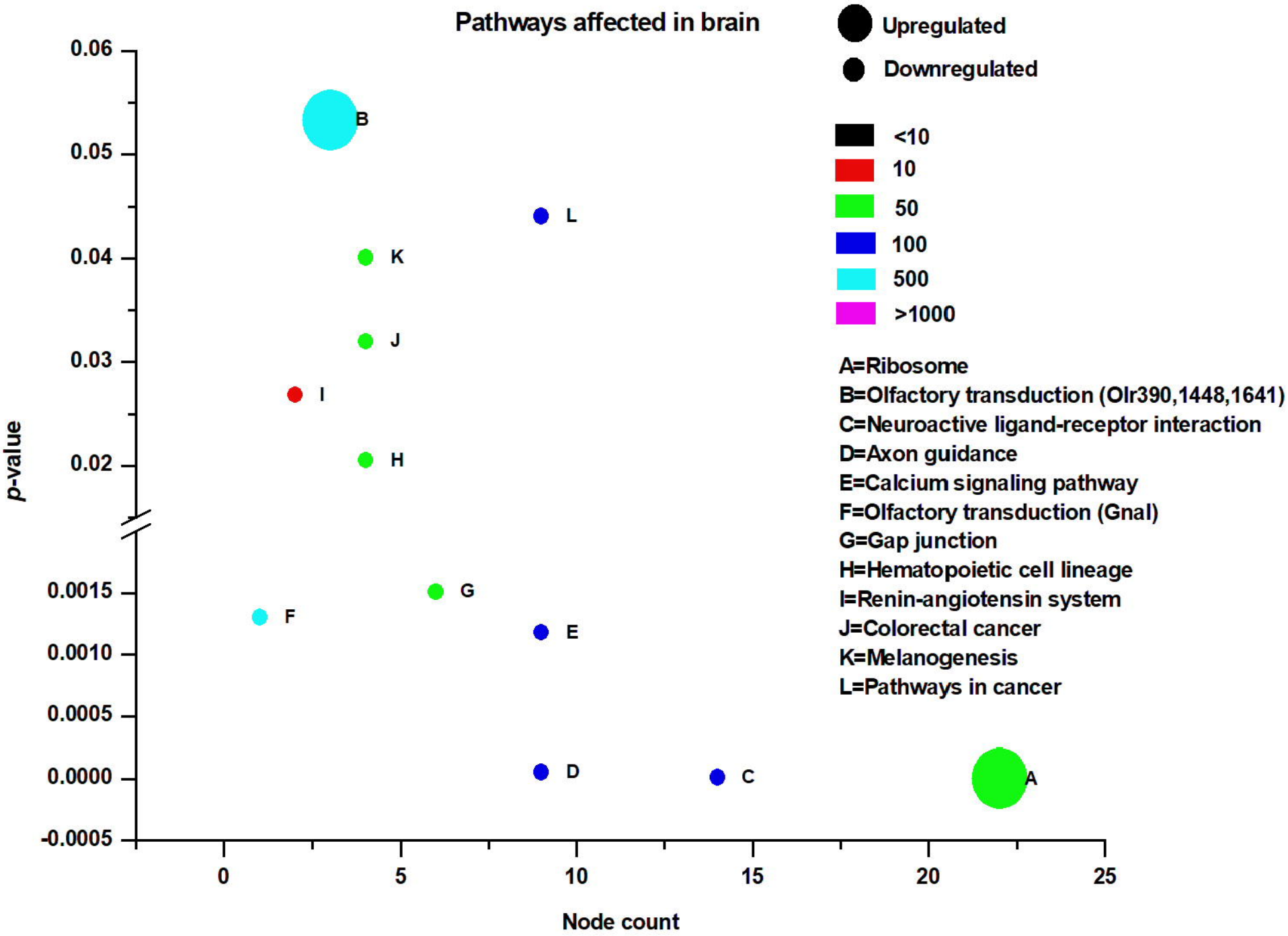
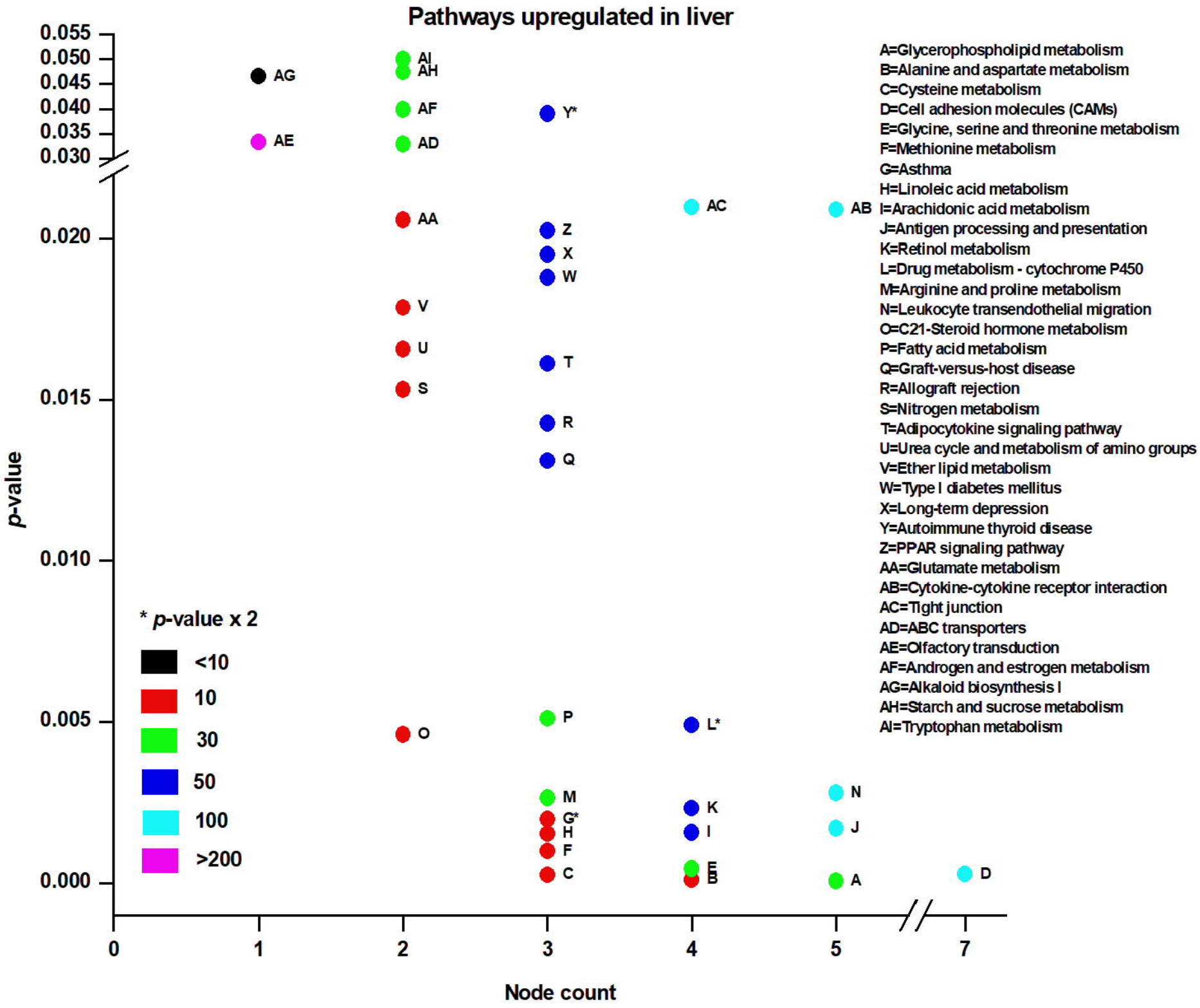
0
0
4

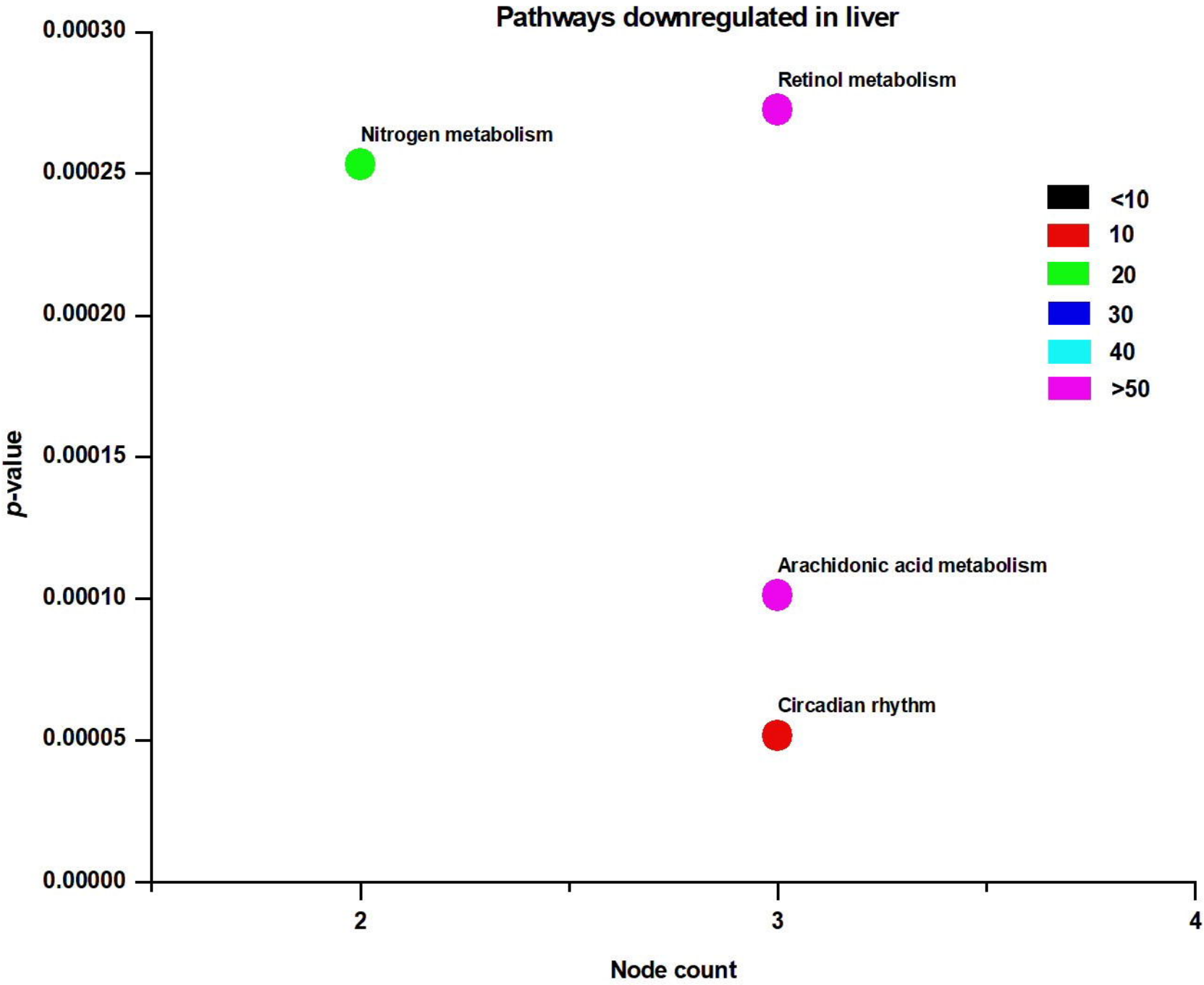

(A)
Biological process (Brain upregulated)
Node count
Database count (log)
p-value
Translational elongation
Translation
rRNA processing
Anatomical structure development
Erythrocyte differentiation
Negative regulation of RNA splicing
Ribosomal large subunit biogenesis
Biological process
Removal of superoxide radicals
Chromatin organization
Ribosomal small subunit assembly
Positive regulation of cell cycle
Retinal ganglion cell axon guidance
G-protein coupled receptor protein signaling pathway
Hydrogen peroxide biosynthetic process
Positive regulation of dna binding
Peripheral nervous system myelin maintenance
Positive regulation of T cell homeostatic proliferation
Reflex
Negative regulation of erythrocyte aggregation
Negative regulation of erythrocyte clearance
Chemokine receptor transport out of membrane raft
Ribosomal large subunit assembly
Regulation of mitochondrion organization
Negative regulation of T cell homeostatic proliferation
(B)
Biological processes (Brain downregulated)
Node count
Database count (log)
p-value
Behavioral fear response
Locomotory behavior
Dopamine receptor signaling pathway
Synaptic transmission, dopaminergic
Visual learning
Negative regulation of synaptic transmission
Response to drug
Memory
Response to amphetamine
Negative regulation of cell proliferation
Sensory perception of pain
Positive regulation of melanocyte differentiation
Associative learning
Synaptic transmission, cholinergic
Prepulse inhibition
Negative regulation of cell migration
Cerebral cortex gabaergic interneuron migration
Activation of phospholipase c activity
Regulation of synaptic transmission, gabaergic
Axonogenesis
Adult walking behavior
Positive regulation of cell proliferation
Response to nicotine
Induction of positive chemotaxis
Behavioral response to ethanol
(C)
Biological process (Liver upregulated)
Node count
Database count (log)
p-value
Sarcomere organization
Gluconeogenesis
Triglyceride metabolic process
Negative regulation of fatty acid biosynthetic process
Response to organic cyclic substance
Oxidation reduction
Cell differentiation
Antigen processing
Response to drug
Arachidonic acid metabolic process
Antigen processing and presentation of peptide antigen
Response to sterol depletion
Cysteine biosynthetic process
Spermidine biosynthetic process
Quinolinate metabolic process
Carnitine transport
Spermine biosynthetic process
Linoleic acid metabolic process
Kidney development
Response to interferon-gamma
Microtubule polymerization
Negative regulation of steroid biosynthetic process
Lipid storage
Response to calcium ion
Cranial suture morphogenesis
(D)
Biological process (Liver downregulated)
Node count
Database count (log)
p-value
Pore complex assembly
Circadian rhythm
Erythrocyte development
Positive regulation of interleukin-1 beta secretion
Oxygen transport
Response to tumor necrosis factor
Bleb assembly
Response to bacterium
Positive regulation of protein phosphorylation
Response to lipopolysaccharide
White fat cell differentiation
Negative regulation of mitotic prometaphase
Multicellular organismal protein catabolic process
Regulation of memory t cell differentiation
Nad transport
Response to drug
Positive regulation of apoptosis
Regulation of inflammatory response
Cellular response to glucocorticoid stimulus
Negative regulation of mast cell cytokine production
Phospholipid transfer to membrane
Histone h3-t6 phosphorylation
Neutrophil activation
Membrane budding
Fatty acid biosynthetic process


(A)
Molecular function (Brain upregulated)
Node count
Database count (log)
p-value
Structural constituent of ribosome
Protein binding
rRNA binding
Translation regulator activity
Molecular_function
mRNA binding
4-hydroxyphenylpyruvate dioxygenase activity
ATP-activated inward rectifier potassium channel activity
Ribosome binding
Beta-amyloid binding
Olfactory receptor activity
Eukaryotic initiation factor 4e binding
Glyoxylate reductase (nadp) activity
Hydroxypyruvate reductase activity
Glycerate dehydrogenase activity
Organic acid binding
Phenylalanine 4-monooxygenase activity
Galactokinase activity
Galactose binding
Trna binding
Glutathione peroxidase activity
S100 beta binding
2'-5'-oligoadenylate synthetase activity
Protein phosphatase 2b binding
Superoxide dismutase activity
(B)
Molecular function (Brain downregulated)
Node count
Database count (log)
p-value
Protein binding
Serotonin receptor activity
Serotonin binding
Drug binding
G-protein coupled receptor activity
Calcium ion binding
Peptide yy receptor activity
Dopamine receptor activity
Adenosine receptor activity, g-protein coupled
Formate-tetrahydrofolate ligase activity
Dopamine d1 receptor activity
Endothelin-b receptor activity
Neuropeptide y receptor activity
Insulin-like growth factor binding
Protein heterodimerization activity
Roundabout binding
Chemorepellent activity
Dopamine binding
Extracellular-glycine-gated chloride channel activity
Double-stranded dna binding
Keratan sulfotransferase activity
Choline:sodium symporter activity
Peptidyl-dipeptidase inhibitor activity
Dopamine d2 receptor activity
Prostaglandin transmembrane transporter activity
(C)
Molecular function (Liver upregulated)
Node count
Database count (log)
p-value
Pyridoxal phosphate binding
Structural constituent of cytoskeleton
Identical protein binding
Protein binding
Dimethylargininase activity
Hydroxymethylglutaryl-coa synthase activity
L-aspartate:2-oxoglutarate aminotransferase activity
Lyase activity
Monooxygenase activity
Structural molecule activity
Olfactory receptor activity
Adenosylmethionine decarboxylase activity
Carnitine o-octanoyltransferase activity
Kynureninase activity
Amino carboxymuconate-semialdehyde decarboxylase activity
Alpha-galactosidase activity
Carnitine transporter activity
Steroid 17-alpha-monooxygenase activity
Glucose-6-phosphatase activity
Chemokine activity
L-serine transmembrane transporter activity
Symporter activity
Carnitine o-palmitoyltransferase activity
Insulin-like growth factor ii binding
GTP binding
(D)
Molecular function (Liver downregulated)
Node count
Database count (log)
p-value
Oxygen binding
Oxygen transporter activity
Extracellular atp-gated cation channel activity
Iron ion binding
Interleukin-8 binding
Oncostatin-m receptor activity
Channel activity
Purinergic nucleotide receptor activity
Stearoyl-coa 9-desaturase activity
Electron carrier activity
Aspartoacylase activity
Metalloenzyme activator activity
Organic acid binding
Metal ion binding
Endopeptidase inhibitor activity
Interleukin-8 receptor activity
Tumor necrosis factor binding
2 iron, 2 sulfur cluster binding
Protein binding
Leukotriene-c4 synthase activity
Histone kinase activity (h3-t6 specific)
Retinoic acid 4-hydroxylase activity
Proton-dependent oligopeptide secondary active
Nickel ion binding
Heme binding

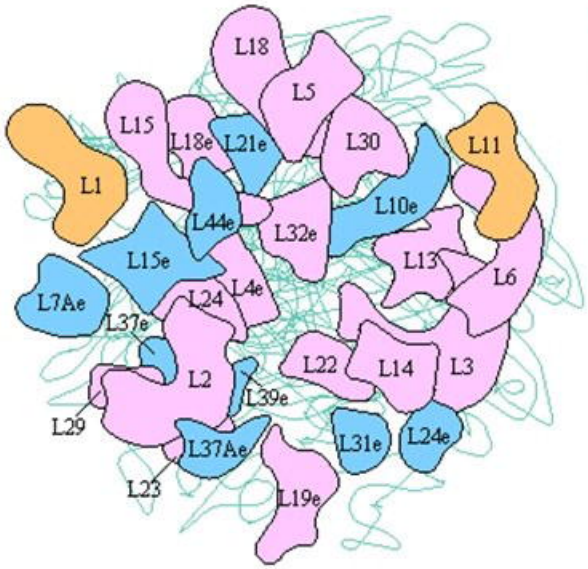

(A)
Cellular component (Brain upregulated)
Node count
Database count (log)
p-value
Ribosome
Cytosol
Intracellular
Small ribosomal subunit
Nucleolus
Integral to membrane
Postsynaptic density
Cytoplasm
Large ribosomal subunit
Neuronal cell body
Mitochondrion
Endoplasmic reticulum sec complex
Dendritic spine
Anchored to external side of plasma membrane
Atp-sensitive potassium channel complex
Lamin filament
Gap junction
Lateral plasma membrane
Cilium membrane
Postsynaptic membrane
Condensed chromosome
Cajal body
Hemoglobin complex
Cell junction
Protein complex
(B)
Cellular component (Brain downregulated)
Node count
Database count (log)
p-value
Plasma membrane
Axon
Membrane
Dendrite
Extracellular space
Membrane fraction
Neuronal cell body
Anchored to plasma membrane
Platelet dense tubular network
DNA ligase iv complex
Cytoplasm
Exon-exon junction complex
Synaptic vesicle membrane
DNA-dependent protein kinase-DNA ligase 4 complex
Clathrin coat of trans-golgi network vesicle
Activin receptor complex
Acrosomal vesicle
Phagocytic cup
Extracellular region
Heterotrimeric g-protein complex
Nicotinic acetylcholine-gated receptor-channel complex
Asymmetric synapse
Extrinsic to internal side of plasma membrane
Actin filament
Lysosome
(C)
Cellular component (Liver upregulated)
Node count
Database count (log)
p-value
Endoplasmic reticulum
Plasma membrane
Membrane
Lysosome
Cytosol
Sarcolemma
Endoplasmic reticulum membrane
Mhc class ii protein complex
Cytoplasm
Caveola
Mitochondrion
Intermediate filament
Mitochondrial inner membrane
Z disc
Microsome
Tight junction
Costamere
Filamentous actin
Lipid particle
Multivesicular body
Cell surface
Soluble fraction
Myofibril
Intermediate filament cytoskeleton
Bleb
(D)
Cellular component (Liver downregulated)
Node count
Database count (log)
p-value
Hemoglobin complex
Extracellular space
Soluble fraction
Extracellular region
Mast cell granule
Nonmotile primary cilium
Oncostatin-m receptor complex
Voltage-gated calcium channel complex
Aggresome
U12-type spliceosomal complex
Microsome
Replication fork
Cis-golgi network
Mitochondrion
Bleb
Integral to nuclear inner membrane
Neuromuscular junction
Integral to endoplasmic reticulum membrane
Vesicle lumen
Axoneme
Smooth endoplasmic reticulum
Nucleus
Apical plasma membrane
Synaptosome
Cell-cell junction


Pathways affected in brain
Upregulated
Downregulated
<10
10
50
100
500
>1000
A=Ribosome
B=Olfactory transduction (Olr390,1448,1641)
C=Neuroactive ligand-receptor interaction
D=Axon guidance
E=Calcium signaling pathway
F=Olfactory transduction (Gnal)
G=Gap junction
H=Hematopoietic cell lineage
I=Renin-angiotensin system
J=Colorectal cancer
K=Melanogenesis
L=Pathways in cancer
p-value
0.06
0.05
0.04
0.03
0.02
0.0015
0.0010
0.0005
0.0000
-0.0005
0
5
10
15
20
25
Node count

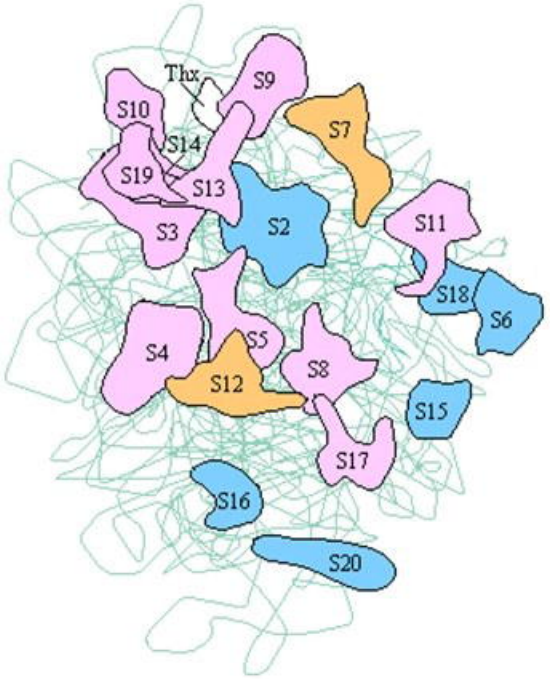

Pathways upregulated in liver
p-value
Node count
0.055
0.050
0.045
0.040
0.035
0.030
0.020
0.015
0.010
0.005
0.000
0
1
2
3
4
5
7
AG
AE
AI
AH
AF
AD
AA
V
U
S
O
Y*
Z
X
W
T
R
Q
P
M
G*
H
F
C
AC
L*
K
I
E
B
AB
N
J
A
D
* p-value x 2
<10
10
30
50
100
>200
A=Glycerophospholipid metabolism
B=Alanine and aspartate metabolism
C=Cysteine metabolism
D=Cell adhesion molecules (CAMs)
E=Glycine, serine and threonine metabolism
F=Methionine metabolism
G=Asthma
H=Linoleic acid metabolism
I=Arachidonic acid metabolism
J=Antigen processing and presentation
K=Retinol metabolism
L=Drug metabolism - cytochrome P450
M=Arginine and proline metabolism
N=Leukocyte transendothelial migration
O=C21-Steroid hormone metabolism
P=Fatty acid metabolism
Q=Graft-versus-host disease
R=Allograft rejection
S=Nitrogen metabolism
T=Adipocytokine signaling pathway
U=Urea cycle and metabolism of amino groups
V=Ether lipid metabolism
W=Type I diabetes mellitus
X=Long-term depression
Y=Autoimmune thyroid disease
Z=PPAR signaling pathway
AA=Glutamate metabolism
AB=Cytokine-cytokine receptor interaction
AC=Tight junction
AD=ABC transporters
AE=Olfactory transduction
AF=Androgen and estrogen metabolism
AG=Alkaloid biosynthesis I
AH=Starch and sucrose metabolism
AI=Tryptophan metabolism


Pathways downregulated in liver
Retinol metabolism
Nitrogen metabolism
Arachidonic acid metabolism
Circadian rhythm
<10
10
20
30
40
>50
0.00030
0.00025
0.00020
0.00015
0.00010
0.00005
0.00000
p-value
2
3
4
Node count

RIBOSOME



Large subunit (Haloarcula marismortui)



Small subunit (Thermus aquaticus)

Ribosomal RNAs

Bacteria / Archaea	23S	5S		16S
Eukaryotes	25S	5S	5.8S	18S

Ribosomal proteins

EF-Tu: S10, L3, L4, L23, L2, S19, L22, S3, RP-L16, L29
S20e, L3e, L4e, L23Ae, L8e, S15e, L17e, S3e, L35e

L7/L12 stalk

S17, L14, L24, L5, S14, S8, L6, L18, S5, L30, L15 — SecY
S11e, L23e, L26e, S4e, L11e, S29e, S15Ae, L9e, L32e, L19e, L5e, S2e, L7e, L27Ae

IF1: L36, S13, S11, S4 — RpoA: L17, L13, S9
L34e, L14e, S18e, S14e, S9e, L18e, L13Ae, S16e

EF-Tu,G: S7, S12, L7A — RpoC,B: L7/L12, L12, L10, L1, L11
S5e, S23e, L30e, L7Ae, LP1,LP2, LP0, L10Ae, L12e

S2, SAe — EF-Ts — IF2: S15, S13e — IF3: L35, L20, L34 — RF1: L31, L32, L9, S18, S6

L28, L33, L21, L27, FtsY,Ffh, S16, L19, S1, S20, S21, L25

L10e, L13e, L15e, L21e, L24e, L31e, L35Ae, L37e, L37Ae, L39e, L40e, L41e, L44e

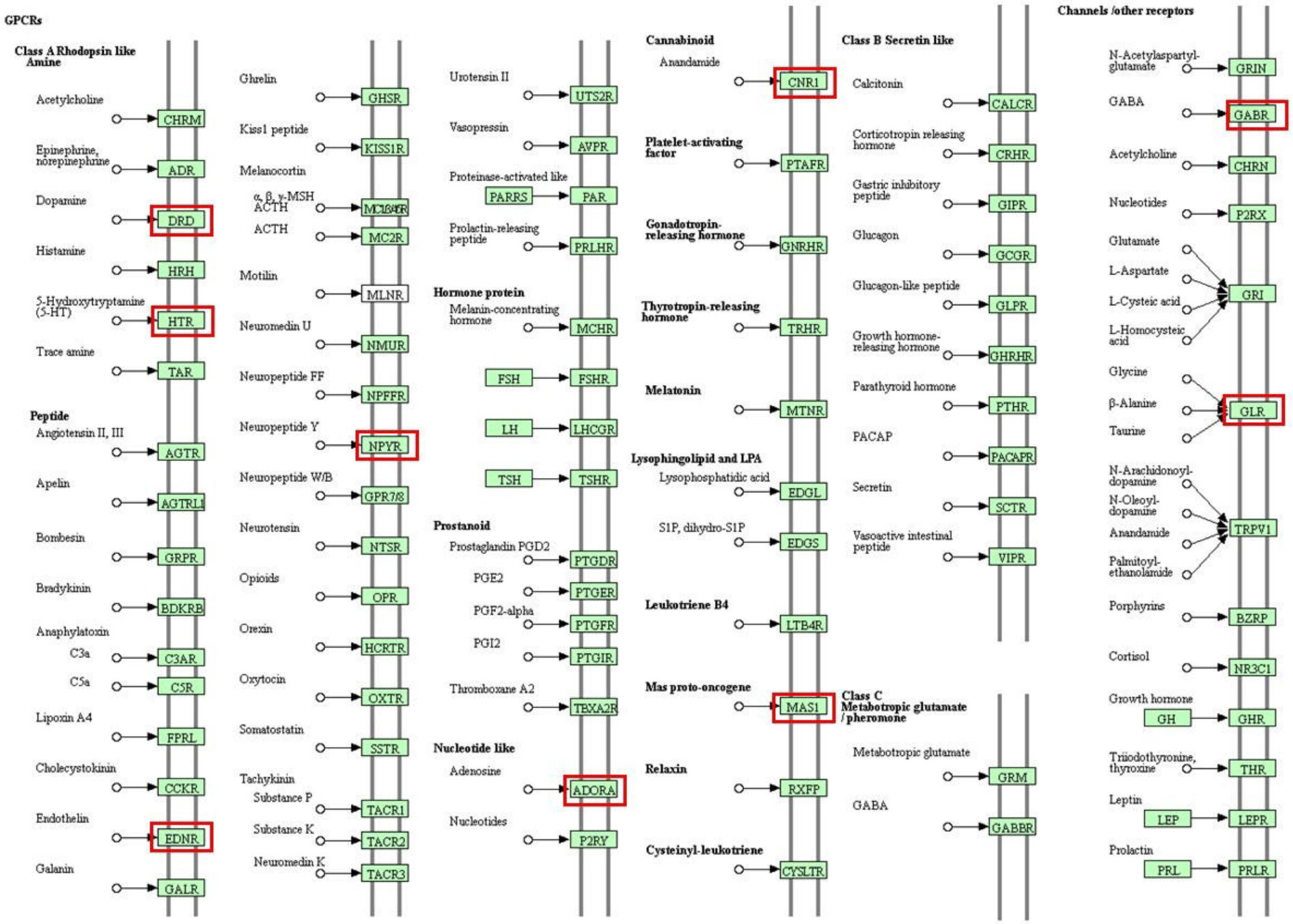
S3Ae, S6e, S8e, S17e, S19e, S24e, S25e, S26e, S27e, S27Ae, S28e, S30e, LX

L6e, L18Ae, L22e, L27e, L28e, L29e, L36e, L38e

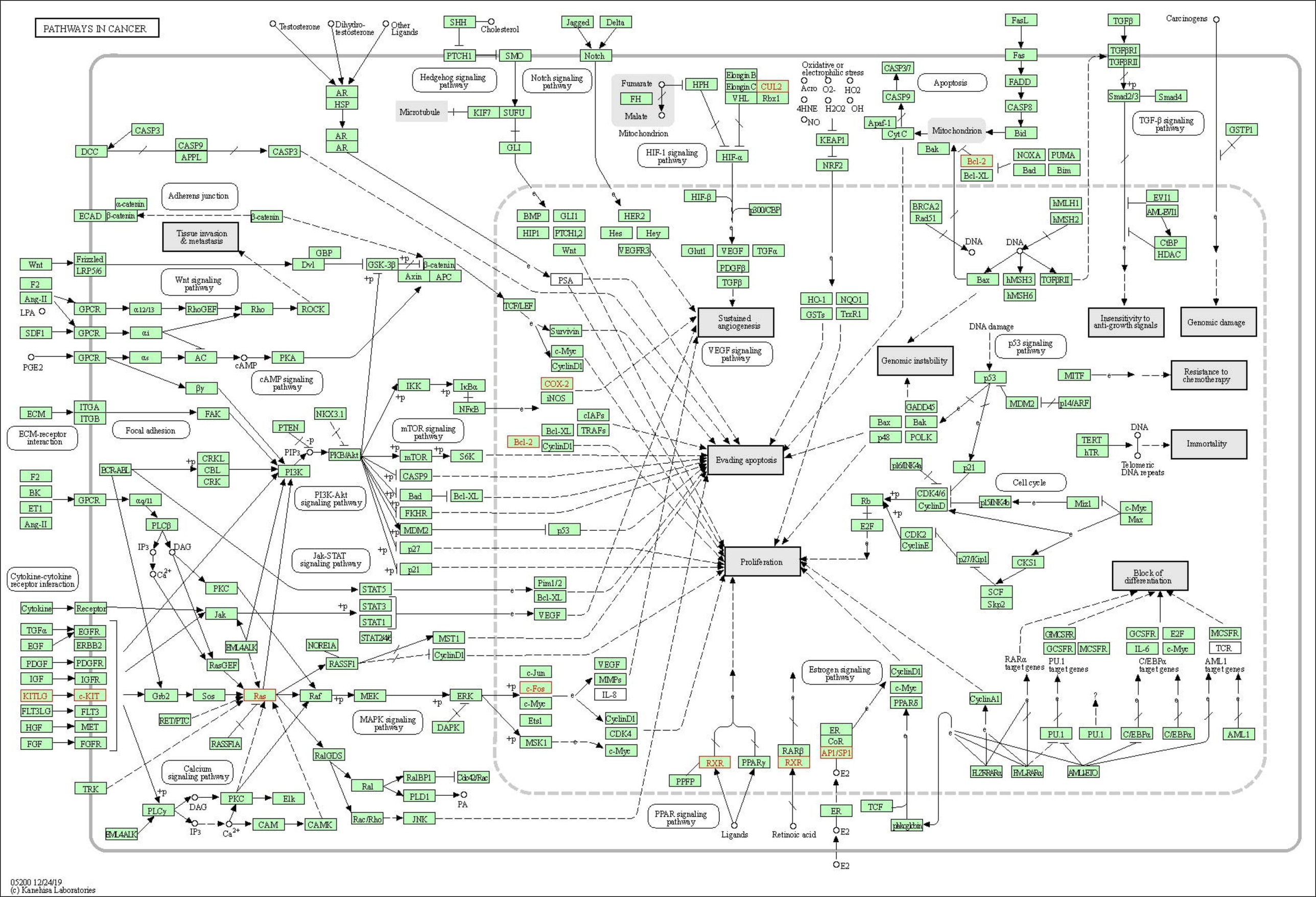
S7e, S10e, S12e, S21e

03010 4/6/17
(c) Kanehisa Laboratories

NEUROACTIVE LIGAND-RECEPTOR INTERACTION



04080 7/10/13
(c) Kanehisa Laboratories



05200 12/24/19
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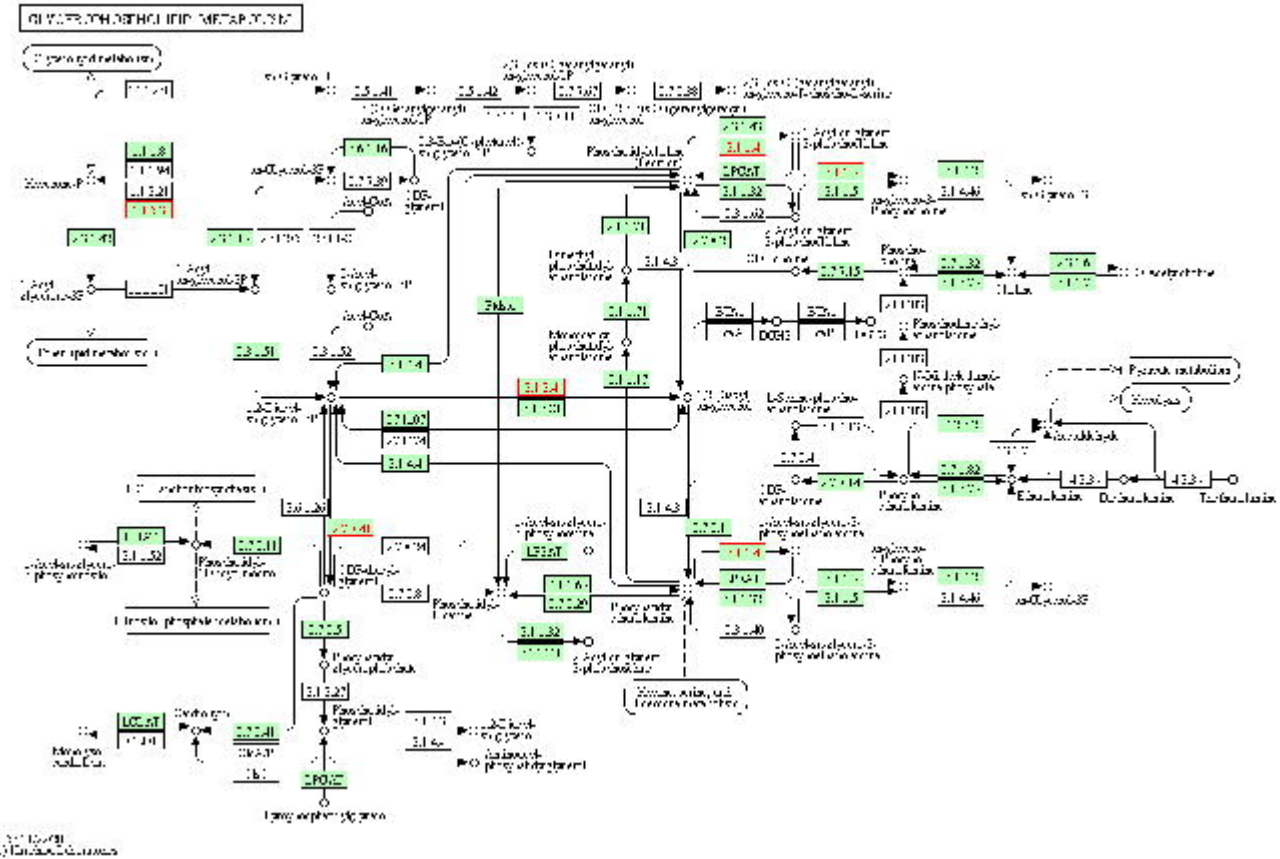

Supplementary materials:

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	ENSRNOT00000

							045792
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	100328	RGD15	NM_001171096

					908	65819	
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	ENSRNOT00000 016038
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	ENSRNOT00000 017207
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	Slc16a1 4	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	ENSRNOT00000 067114
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	ENSRNOT00000 010596
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	RGD15 66265	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		ENSRNOT000000

						RGD1561231	47232
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	ENSRNOT000000

							56130
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.--