



Published in final edited form as:

Alcohol. 2007 March ; 41(2): 95–132.

Functional gene expression differences between inbred alcohol-preferring and —non-preferring rats in five brain regions

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Abstract

The objective of this study was to determine if there are innate differences in gene expression in selected CNS regions between inbred alcohol-preferring (iP) and —non-preferring (iNP) rats. Gene expression was determined in the nucleus accumbens (ACB), amygdala (AMYG), frontal cortex (FC), caudate-putamen (CPU), and hippocampus (HIP) of alcohol-naïve adult male iP and iNP rats, using Affymetrix Rat Genome U34A microarrays ($n = 6/\text{strain}$). Using Linear Modeling for Microarray Analysis with a false discovery rate threshold of 0.1, there were 16 genes with differential expression in the ACB, 54 in the AMYG, 8 in the FC, 24 in the CPU, and 21 in the HIP. When examining the main effect of strain across regions, 296 genes were differentially expressed. Although the relatively small number of genes found significant within individual regions precluded a powerful analysis for over-represented Gene Ontology categories, the much larger list resulting from the main effect of strain analysis produced 17 over-represented categories ($P < .05$), including axon guidance, gliogenesis, negative regulation of programmed cell death, regulation of programmed cell death, regulation of synapse structure function, and transmission of nerve impulse. Co-citation analysis and graphing of significant genes revealed a network involved in the neuropeptide Y (NPY) transmitter system. Correlation of all significant genes with those located within previously established rat alcohol QTLs revealed that of the total of 313 significant genes, 71 are located within such QTLs. The many regional and overall gene expression differences between the iP and iNP rat lines may contribute to the divergent alcohol drinking phenotypes of these rats.

Keywords

Alcohol-preferring P rat; Alcohol—non-preferring NP rat; Microarrays; Gene expression; Nucleus accumbens; Amygdala; Frontal cortex; Hippocampus; Caudate-putamen

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1. Introduction

Alcoholism and alcohol abuse are complex disorders that result from a combination of genetic and environmental factors. Selective breeding strategies for ethanol preference have yielded divergent rat lines that possess different frequencies of genes that impact ethanol preference, whereas the frequency of trait-irrelevant genes remains randomly distributed (Lumeng et al., 1977). The alcohol-preferring (P) and alcohol—non-preferring (NP) rat lines were established from a randomly bred, closed colony of Wistar rats using free-choice access to 10% (vol/vol) ethanol and water (Lumeng et al., 1977). P rats meet the proposed criteria (Cicero, 1979) for an animal model of alcoholism (reviewed in McBride & Li, 1998;Murphy et al., 2002). In brief, the P line of rats (1) consumes in excess of 5 g ethanol/kg body weight/day, attaining blood alcohol concentrations in the range of 50-200 mg%; (2) works to obtain ethanol when food and water are freely available; (3) consumes ethanol for its pharmacological effects, and not solely for caloric value nor taste or odor properties; (4) develops functional and metabolic tolerance; (5) develops physical dependence; and (6) demonstrates robust relapse ethanol drinking after a period of abstinence. On the other hand, NP rats consume less than 1 g ethanol/kg/day and do not attain measurable blood alcohol concentrations under free-choice conditions. Compared to NP rats, P rats are more sensitive to the low-dose stimulating effects of ethanol (Rodd et al., 2004;Waller et al., 1986), less sensitive to the high-dose motor impairing effects of ethanol (Lumeng et al., 1982), and develop acute tolerance more rapidly (Waller et al., 1983).

Innate differences in neurotransmitter and receptor systems in several brain regions have been reported between the selectively bred P and NP rat lines (reviewed in McBride & Li, 1998;Murphy et al., 2002). P rats have reduced serotonin (5-HT) and dopamine (DA) innervations (Zhou et al., 1991,1994a,1994b,1995), as well as differences in 5-HT (McBride et al., 1993a,1994,1997;Wong et al., 1993), DA (McBride et al., 1993b), and opioid (McBride et al., 1998;Strother et al., 2001) receptors. Furthermore, neuropeptide Y (NPY) (Ehlers et al., 1998), corticotropin-releasing factor (Ehlers et al., 1992), neurotensin (Ehlers et al., 1999), substance P, and neurokinin levels (Slawecki et al., 2001) are all significantly lower in CNS regions of P compared to NP rats. Additionally, higher functional neuronal activity has been found in numerous brain regions of the P rat compared to the NP rat (Smith et al, 2001;Strother et al., 2005).

Witzmann et al. (2003) examined differences in protein levels in the hippocampus (HIPP) and nucleus accumbens (ACB) of alcohol-naïve inbred-P (iP) and inbred-NP (iNP) rats, and found that almost all of the proteins that differed were lower in the iP rats compared to the iNP rats. Those proteins that could be identified were involved in many key aspects of neuronal function such as metabolism, cell signaling, and protein transport, which may suggest that there are basic differences in synaptic transmission mechanisms between the two rat strains (Witzmann et al., 2003). Edenberg et al. (2005) compared gene expression differences in the HIPP of two different strains of iP and iNP rats, when microarray analyses were conducted several months apart. The results indicated excellent repeatability of the assay. Genes involved in cell growth and adhesion, cellular stress reduction and antioxidation, protein trafficking, cellular signaling pathways, and synaptic function were differentially expressed in the HIPP (Edenberg et al., 2005). Worst et al. (2005) reported on the transcriptome analysis in the anterior cerebral cortex of alcohol-naïve Alko, alcohol (AA) and Alko, nonalcohol (ANA) rats, and found differences in mRNA levels between the AA and ANA rats that could alter transmitter release (e.g., vesicle-associated membrane protein 2, syntaxin 1, syntaxin binding protein). Kerns et al. (2005) examined gene expression differences in response to acute ethanol in the ACB, prefrontal cortex, and ventral tegmental area of C57BL/6J and DBA/2J mice, which have high and low alcohol drinking characteristics, respectively. Ethanol-regulated genes were region specific and involved in glucocorticoid signaling, neurogenesis, myelination, neuropeptide signaling,

and retinoic acid signaling. Gene expression profiles were also reported for whole brain of inbred long-sleep and inbred short-sleep mice (Xu et al., 2001). A total of 41 genes or expressed sequence tags (ESTs) displayed significant differences between these inbred strains of mice. Expression of genes encoding tyrosine protein kinase and ubiquitin carboxyl terminal hydrolase was higher in the brain of inbred long-sleep compared to short-sleep mice. In a comprehensive transcriptome meta-analysis of different mice strains, Mulligan et al. (2006) identified several cis-regulated candidate genes for an alcohol preference quantitative trait loci (QTL) on chromosome 9.

Portions of the present data have been used for comparison analyses in two recently published studies, although none of the present data have been presented in duplicate form. In one study, the present HIPP data were used with other HIPP data to evaluate the reliability of the microarray analysis, when assays were conducted months apart (Edenberg et al., 2005). In the second study (Rodd et al., 2006), the data were used as part of a convergent functional genomics approach to identify common genes across different experimental approaches and between human and animal findings. In that study, however, the iP—iNP data were not analyzed using rigorous statistical criteria (for a gene to be considered significant, an false discovery rate (FDR)-uncorrected $P < .05$ was considered sufficient), and the results were presented only in a summarized format, which were then integrated with information from other studies. As the P and NP lines are well established animal models in the alcohol field, we believe it is important that the present findings, derived using rigorous region-by-region analyses, are presented because they yield a much more complete and statistically reliable picture of the genetic factors involved in the high and low alcohol drinking behavior in these rat lines.

The objective of the present study was to determine if there are innate differences between inbred P and NP rats in the expression of functionally relevant genes in selected brain regions. The current study focuses on five distinct brain regions: the ACB, caudate-putamen (CPU), amygdala (AMYG), HIPP, and frontal cortex (FC). These regions were selected based on their inclusion in the mesolimbic and mesocortical systems, both of which are critically important in the initiation and maintenance of goal directed and reward mediated behaviors (reviewed in Bonci et al., 2003; and Maldonado, 2003).

2. Materials and methods

2.1. Animals and RNA preparation

Inbred adult male rats, 90-100 days old, from the iP-5C and iNP-1 strains were used in these experiments. Inbreeding by brother—sister mating was initiated after the S30 generation of mass selection and was in the F37 generation at the start of these experiments. It should be noted that the iP and iNP rats have not been characterized to the extent to which the parent selected lines have been studied. However, preliminary studies indicate that alcohol intake (Bell et al., 2004), and differences in sweet preference, anxiety, spontaneous motor activity, and the development of rapid tolerance (Stewart et al., 2004) are similar to the parent lines.

Animals were received in our facilities 3 weeks prior to the experiment. Rats were double housed on a 12:12-h light dark cycle with lights on at 0700 h. Rats had water and rat chow ad libitum. Animals were habituated to handling and to the guillotine daily between 0900 and 1000 h for 10 days prior to sacrifice. The animals used in these experiments were maintained in facilities fully accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care. All research protocols were approved by the Institutional Animal Care and Use Committee and are in accordance with the guidelines of the Institutional Animal Care and Use Committee of the National Institute on Drug Abuse, NIH, and the *Guide for the Care and Use of Laboratory Animals* (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council 1996).

Animals were sacrificed by decapitation between 0900 and 1000 h over consecutive days, with equal numbers of animals from each strain sacrificed each day. This minimized differences in time of sacrifice and dissection, and maintained the experimental balance across the two strains. The head was immediately placed in a cold box maintained at -15°C , where the brain was rapidly removed and placed on a glass plate for dissection. All equipment used to obtain tissue was treated with RNase Zap (Ambion, Inc. Austin, TX) to prevent RNA degradation. The ACB, CPU, FC, AMYG, and HIPP were dissected according to the coordinates of Paxinos and Watson (1998). Briefly, the ACB, CPU, and FC were dissected from a 2 mm section generated by a coronal cut at 2 mm anterior to the optic chiasm (Bregma 1.70 mm) and a coronal cut at the optic chiasm (Bregma -0.26 mm). The AMYG was dissected by a cut at the lateral borders of the lateral hypothalamus (Bregma -2.12 mm) and ventral of the rhinal fissure, with cortical tissue then trimmed at the lateral edges of the dissected slice. The entire HIPP was dissected from the remaining brain by a midline incision between the hemispheres and gently rolling the HIPP out of the cerebral cortex. We have previously demonstrated the consistency of dissection of discrete brain regions in our laboratory (Liang et al., 2003; Witzmann et al., 2003). Dissected tissues were immediately homogenized in Trizol reagent (Invitrogen, Carlsbad, CA) and processed according to the manufacturer's protocol, but with twice the suggested ratio of Trizol to tissue. Ethanol precipitated RNA was further purified through RNeasy® columns (Qiagen, Valencia, CA) according to the manufacturer's protocol. The yield, concentration, and purity of the RNA were excellent, and were determined by running a spectrum from 210 to 350 nm and analyzing the ratio of large and small ribosomal bands using an Agilent Bioanalyzer.

2.2. Labeling and hybridization

RNA from each individual rat was labeled and analyzed separately on an Affymetrix Rat Genome U34A microarray. Starting with 10 μg of total RNA from each animal, first- and second-strand cDNA synthesis was carried out according to the standard protocol (Affymetrix: *GeneChip® Expression Analysis Technical Manual*. Santa Clara, CA: Affymetrix; 2001). Biotinylated cRNA was synthesized in vitro from the double-stranded cDNA using the ENZO Bio-Array High Yield RNA Transcript Labeling Kit (ENZO Diagnostics, Inc., Farmingdale, NY) according to the Affymetrix protocol. Fragmented, biotinylated cRNA (15 μg) was mixed into 300 μl of hybridization cocktail, of which 200 μl were used for each hybridization. Hybridization was for 17 h at 42°C . Washing, staining, and scanning were carried out according to the standard protocol.

To minimize potential systematic errors, all stages of the experiment were balanced across phenotypes. That is, equal numbers of iP and iNP animals were sacrificed each day, and equal numbers of RNA preparations from iP and iNP animals were processed through the labeling, hybridization, washing, and scanning protocols on each day, in different alternating orders. Whenever possible, common premixes of reagents were used to minimize effects due to differences in reagent preparation.

2.3. Data and neuroinformatic analyses

Each GeneChip® was scanned using an Affymetrix Model 3000 scanner and underwent image analysis using Affymetrix GCOS software. Microarray data are available from the National Center for Biotechnology Information's Gene Expression Omnibus, <http://www.ncbi.nlm.nih.gov/geo/>, (Barrett et al., 2005; Edgar et al., 2002) under series accession no. GSE4494 (GSM100999... GSM101057). Raw cell files were then imported into the statistical programming environment R (R Development Core Team, 2006) for further analysis with tools available from the Bioconductor Project (Gentleman et al., 2004), themselves further expanded by the authors using the R language. Expression data from 59 arrays were normalized and converted to \log_2 as a set using the Robust Multi-chip Average (RMA) method (Irizarry et al., 2003) implemented in the Bioconductor package RMA. As a standardization step to facilitate

later comparisons with other experiments, expression levels were scaled such that the mean expression of all arrays was $\log_2(1000)$. To increase power and decrease the FDR (see below), probe sets were subjected to further filtering steps. As we were primarily concerned with identifying genes that could be subjected to further bioinformatic analysis, all probe sets currently annotated by Affymetrix as “expressed sequence tags” or whose gene names contain the words “riken,” “predicted,” or “similar to” were filtered out. We next filtered out probe sets with a very low likelihood of actual expression in our samples, accomplished with the Bioconductor package “genefilter.” Probe sets that did not have at least 25% of samples with normalized, scaled expression greater than 64 were filtered out. Finally, we wished to filter out, in an unbiased manner, probe sets with very low variability across samples. This was accomplished by constructing a distribution of the interquartile range of all probe sets from all samples of both groups and then filtering out those probe sets that fell in the lowest 25% of this distribution using the Bioconductor package genefilter according to the method described by Scholtens and von Heydebreck (2005). Linear modeling to calculate gene-wise P values was performed using the package Linear Modeling for Microarray Analysis (LIMMA) (Smyth, 2004) P values were then corrected for FDR by the method of Benjamini & Hochberg (1995). Probe sets were considered to be differentially expressed if the FDR adjusted P value was $P < .10$ (FDR 10%). Using this method, the data were analyzed two ways. In the first analysis, each individual brain region was analyzed separately, using only strain as a factor in the linear model. In the second analysis, the five brain regions tested were combined in the linear model, using factors of region and strain, and the main effect of strain was examined. This analysis will be referred to as the “overall analysis.”

Testing for over-representation of Gene Ontology (GO) (Ashburner et al., 2000; Harris et al., 2004) biologic process categories was performed using the Bioconductor package GOstats (Gentleman, 2004). Briefly, for each gene set tested, a list of unique Entrez-Gene identifiers was constructed. This list was then compared to the list of all known Entrez-Gene identifiers that are represented on the Affymetrix chipset RGU34A. Identification of over-represented GO categories was then accomplished within GOstats using the hypergeometric distribution. To filter out uninteresting categories, those categories with less than 9 or greater than 300 genes represented on the chipset were excluded from the analysis, as were categories with less than five significant genes. Categories were called significant for $P < .05$.

Co-citation analysis was accomplished within R using a modification of the package “MedlineR” (Lin et al., 2004). Gene aliases were obtained from the Rat Genome Database, <http://rgd.mcw.edu/>. A list of all PubMed, <http://www.pubmedcentral.nih.gov/>, occurrences of genes and their aliases in abstracts and keywords was constructed for each gene, from which a co-citation matrix was constructed. The Bioconductor packages “graph” (Gentleman et al., 2004) and “Rgraphviz” (Gentry, 2006) were used to graphically display networks of co-cited genes.

2.4. Quantitative real-time PCR

Real-time (RT) polymerase chain reaction (PCR) was carried out using SybrGreen chemistry and the ABI Prism 7700 Sequence Detection System (Applied Biosystems). The amplification primers were designed using Vector NTI software. Total RNA, isolated for the microarray analyses, was used for these analyses. Following reverse transcription of the RNA (TaqMan Reverse Transcription Reagents, Applied Biosystems), an aliquot of each reverse transcription reaction was amplified in triplicate. This reaction was repeated to generate six values for each test group. Two control reactions were run for each RNA preparation: (1) a reverse transcription and PCR reaction with no added RNA to control for contamination of the reagents and (2) a PCR reaction without the reverse transcription reaction in the presence of RNA to detect DNA contamination of the RNA preparation. To correct for sample-to-sample variation, an

endogenous control, glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was amplified with the target and served as an internal reference to normalize the data. The average GAPDH C_t values for iP and iNP were the same in each brain region tested, making this an appropriate control gene to normalize the expression of the candidate genes of interest. Relative quantification of data from the ABI Prism 7700 Sequence Detection System was performed using the standard curve method (Applied Biosystems, User Bulletin #2; <http://www.appliedbiosystems.com>). Quantitative real-time polymerase-chain-reaction (qRT-PCR) measurements were conducted on genes to verify differences observed with microarray hybridization. Genes were selected on the basis of significant differential expression in at least one brain region and reasonable fold changes. When this list was compiled, initial analysis had been completed using MAS5 background correction; after the RMA algorithm had been substituted for MAS5, mRNA samples were no longer of sufficient quality to select a new list.

3. Results

Principal component analysis, using all probe sets that passed through the filters described in Methods, indicated that regional differences in gene expression were greater than strain differences, as illustrated by a biplot of the first and second principal components (Fig. 1). The clusters representing arrays from the ACB, CPU, and FC are tightly grouped, with the exception of one outlier in each region. Those from the HIPPO give a fairly good grouping, but not as tight as the other three regions; the AMYG gives the least grouping of data, with one outlier that groups with the HIPPO cluster. As can be seen from the figure, there is no clear pattern of separation of the iP and iNP lines within brain region. Visualization of the third and fourth principal components (not shown) also did not resolve line differences within regions.

We used LIMMA (Smyth, 2004) on RMA preprocessed (Irizarry et al., 2003), \log_2 transformed, filtered data (see Methods for details), to determine differences between the inbred strains. The FDR, as calculated by the method of Benjamini and Hochberg (1995), was set at ≤ 0.10 . In an analysis of individual brain regions ($n = 6$ iNP, 6 iP in all regions except the FC, in which data were missing from one iP animal), significant differential gene expression was found in the five brain regions (Tables 1 and 2). The number of differences between the two inbred lines in each of the five individual regions ranged from 8 to 63, with the order of number of differences being AMYG > CPU > HIPPO > ACB > FC (Table 1). Across regions, the total number of genes that demonstrated differential expression ranged from 8 to 54; the number of genes that were located within established alcohol QTLs (Bice et al., 1998; Carr et al., 1998, 2003; Foroud et al., 2002, 2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003) ranged from 1 to 16. Table 2 lists the significant genes that were different within each region along with individual fold changes and gene symbols. Table 3 contains detailed expression levels and standard deviations for all the regionally significant probe sets.

Over-represented GO biologic process categories ($P < .05$) were statistically sought using the Bioconductor package GOstats (Gentleman et al., 2004). Briefly, GO categories of significant genes were tested for over-representation using the hypergeometric distribution. An analysis of each of the five individual brain regions did not reveal any over-represented GO biologic process categories, perhaps because there were too few differentially expressed genes in each region.

An overall analysis of all brain regions, which used a linear model with strain and brain region as factors, demonstrated significant differential expression of 296 genes (351 probe sets) (FDR ≤ 0.10). Of these, 173 genes (198 probe sets) demonstrated higher and 123 genes (153 probe sets) lower expression levels in the iP rats than in the iNP rats (Table 4). Although almost all of the genes identified as being differentially expressed within the individual regions were also identified in the overall analysis, the latter method detected many that fell below the threshold

of statistical detection for individual regions, most likely because of the increased power gained by including a much larger number of arrays in the linear model (Table 5). There were 53 genes (71 probe sets) found significant in at least one individual region and in the overall analysis; 241 genes (280 probe sets) were found significant only in the overall analysis. Additionally, there were 15 genes (17 probe sets) found significant in the AMYG that were not significant in the overall analysis, one of which was also significant in the ACB.

Analysis for over-represented GO categories in the set of significant genes found with the overall analysis indicated that 17 GO categories were over-represented ($P < .05$). Six of the most neurobiologically interesting categories are axon guidance, gliogenesis, negative regulation of programmed cell death, regulation of programmed cell death, regulation of synapse structure function, and transmission of nerve impulse (Table 6); the full list can be viewed in Table 7. More genes demonstrate increased expression in the iP versus iNP rat comparison in the categories of regulation of cell death, negative regulation of cell death, regulation of synapse structure and function, and gliogenesis; whereas, more genes demonstrate decreased expression in the iP versus iNP in the category of axon guidance. Equal numbers of genes with increased and decreased expression in the iP versus iNP are present in the category of transmission of nerve impulse.

For the purposes of further discussion, the authors found it desirable to use a gene classification schema that would include genes found significant in individual regions and that would include functional neuroinformatic categories such as neuroplasticity. Such customized, neuroinformatic classifications of genes found significant in any of the individual regions, or in the combined analysis, were obtained by first assigning all genes to their appropriate GO biologic process categories, regardless of statistical significance of the category. Of the categories obtained, further selection was made based on the number of genes within category and degree of neuroinformatic interest. The resultant GO categories were synaptic transmission, regulation of action potential, positive regulation of transport, potassium ion transport, chloride transport, metal ion homeostasis (collapsed to form “neurotransmission,” Table 8); apoptosis, axon guidance, axonogenesis, cell migration, central nervous system development, cytoskeleton organization and biogenesis, gliogenesis, myelination, negative regulation of apoptosis, neuron differentiation, positive regulation of apoptosis, regulation of apoptosis, regulation of axonogenesis, regulation of neurogenesis, regulation of programmed cell death, and regulation of synapse structure and function (collapsed to form “neuroplasticity,” Table 9); and small GTPase mediated signal transduction, negative regulation of protein kinase activity, negative regulation of enzyme activity, transmembrane receptor protein tyrosine kinase signaling pathway (collapsed to form “intracellular messaging,” Table 10). Finally, the lists of genes thus classified were supplemented with manual curation based on a search of the literature. One last category was obtained by classifying genes as transcription factors based on results obtained with Genomatix Suite (Genomatix, Munich, Germany; Table 11).

3.1. qRT-PCR confirmation

qRT-PCR measurements were conducted on genes to verify differences observed with microarray hybridization. Genes were selected on the basis of significant differential expression in at least one brain region and reasonable fold changes (Table 12). *GSTa4* and *Scn1a* are not differentially expressed using the RMA analysis presented here, but were with an earlier analysis using MAS5 (unpublished observation). The direction of the expression differences using qRT-PCR was the same as in the microarray data for all genes and regions tested. For the *Akap11* gene, the magnitude of the change of the qRT-PCR data for all five regions was far greater than that observed in the microarray data (fold change in CPU was 785, and in HIPP 1,900), which probably reflects technical differences between the two assays.

Expression levels of Akap11 in iNP were near back-ground levels in the array experiment; qRT-PCR assays allow one to measure much lower levels of RNA with more accuracy in that range (background is much lower), which allows one to better estimate the fold change.

4. Discussion

The major findings of this study were that (1) there was a greater degree of between-region differential expression than within-region, between-strain differential expression (Fig. 1); (2) there was within-region, between-strain differential expression in all five regions examined, with many of these genes classifiable as being related to neurotransmission (Table 8), neuroplasticity (Table 9), intracellular messaging (Table 10), and regulation of transcription (Table 11), with the AMYG as the region demonstrating the greatest number of genes differentially expressed; (3) considerable statistical power could be obtained by minimizing the effect of variance by examining the main effect of strain in a linear model that contained all five brain regions and that with this approach over 300 genes demonstrated differential expression; and (4) in this main effect of strain model, the significant genes represented 17 over-represented GO categories, for example, axon guidance, gliogenesis, negative regulation of programmed cell death, regulation of programmed cell death, regulation of synapse structure function, and transmission of nerve impulse (Table 6).

Inbred P and NP rats were used in the present study in an attempt to reduce the biological variability in the gene expression data. However, there are two potential weaknesses with this approach, in that the particular inbred strains used in the present study may not necessarily have the same characteristics as the parent foundation lines of selectively bred P and NP rats; and, in that inbreeding randomly fixes genes that are not relevant to the phenotype of alcohol preference, which can result in some irrelevant differences in gene expression levels. Although preliminary findings indicate that similar differences are found for the inbred strains and parent lines in sweet preference, anxiety, spontaneous motor activity, and the development of rapid tolerance (Stewart et al., 2004), as well as alcohol drinking (Bell et al., 2004), extrapolating the results to the selectively bred lines should be done cautiously.

4.1. Within-region analysis

Principal components analysis (Fig. 1) revealed that the first two principal components resolve the differences between arrays based on brain region, but not on strain, indicating that most of the differences in gene expression between arrays in the present experiment are accounted for by brain region and not by strain. This finding is in agreement with observations made by others that regional differences in gene expression in the adult mouse brain are greatly influenced by embryological origins (Zapala et al., 2005) and that, across a range of behavioral phenotypes, the number of between-brain region differences of expression can be greater than within-region differences (Nadler et al., 2006; Pavlidis & Noble, 2001).

The AMYG had the greatest number of differences in gene expression between the iP and iNP strains (Tables 1 and 2), which may be a result of the multiple nuclei within this region that mediate different behavioral functions. Of the 54 differentially expressed genes in this region, the biologic process most represented is neuroplasticity, in which 8 genes have been implicated (Table 9). Co-citation analysis indicated a relationship between two pairs of these genes. *Fgfr1* and *Pak2* both show lower expression in the iP rat than iNP rat, and are involved in the Ras/ERK/PAK2 pathway that governs neuronal differentiation (Shin et al., 2002). Neuritin and attractin, both of which show higher expression in the iP than iNP rat, have been identified as part of a cluster of genes that are up-regulated during the recovery phase of spinal cord injury (Di Giovanni et al., 2004). A 36% reduction in expression of *Phgdh* in the AMYG of the iP rat compared to the iNP rat has the potential to alter cell survival, neuritogenesis, and voltage propagation (Furuya et al., 2000) in this region. The expression of sodium channel, voltage-

gated, type III, alpha polypeptide (*Scn3a*) was significantly lower in the AMYG of the iP than iNP line, and was generally lower in the other regions of the iP rats. Widespread differences in the expression of *Scn3a* between the iP and iNP lines could contribute to differences in the overall neuronal excitability in these animals (Hains et al., 2003) and potentially alter responses of the two lines to alcohol.

Thirteen of the 54 differentially expressed genes in the AMYG were located within established alcohol QTLs (Bice et al., 1998; Carr et al., 1998,2003; Foroud et al., 2002,2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003) (Table 5). The pathway involving caspase 3 (lower expression in iP rats) and interleukin-1 receptor-associated kinase 2 (higher expression in iP rats) is involved in the age-related decline in function of hippocampal cells (Lynch & Lynch, 2002). Amphoretin-induced gene and ORF (Amigo), higher in the AMYG of the iP than iNP rat, is a transmembrane protein that modulates neurite out-growth (Kuja-Panula et al., 2003), and thus has the potential to mediate neuroplastic responses to alcohol.

The CPU demonstrated the second highest number of differentially expressed genes (Table 1). Src homology 2 domain-containing transforming protein C3 (*Shc3*) had lower expression in the iP than in the iNP. Although classified by GO as having a function in neurotransmission (Table 6), *Shc3* is perhaps more appropriately thought of as playing a role in the regulation of neuronal development and synaptic function (Liu & Meakin, 2002). In the CPU, 8 of the 24 differentially expressed genes were located within established alcohol QTLs (Bice et al., 1998; Carr et al., 1998,2003; Foroud et al., 2002,2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003) (Table 5). Among these 8 genes, several are involved in protein formation, that is, ribosomal protein S2 heat shock protein 2, and zinc finger protein 386 (Kruppel-like). Some of the differences in the CPU between the iP and iNP rats may reflect differences in response to the low-dose stimulating (Rodd et al., 2004; Waller et al., 1986) and high-dose motor impairing (Lumeng et al., 1982) effects of alcohol exhibited by the parent lines.

The HIPP demonstrated significant differential expression of 21 genes (Table 1). Slit homolog 1 (Drosophila), higher in the iP line, has been implicated in processes related to neuroplasticity (Table 9), specifically in axon guidance (Chang et al., 2006; Long et al., 2004; Thompson et al., 2006). One of the 21 differentially expressed genes in the HIPP, ribosomal protein S2, was located within established alcohol QTLs (Bice et al., 1998; Carr et al., 1998,2003; Foroud et al., 2002,2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003) (Table 5). Some of these differences in the HIPP between iP and iNP rats may be associated with the differences in the development and/or persistence of tolerance to the motor impairing effects of alcohol observed for the parent lines (Bell et al., 2001; Gatto et al., 1987a,1987b; Waller et al., 1983).

In a previous study that jointly analyzed the HIPP data here and data from different inbred iP and iNP strains, many more differences were observed in the HIPP between iP and iNP rats, most likely due to the higher power of that study (a total of 10 arrays used for each group) (Edenberg et al., 2005). Nine of the 21 genes reported here (indicated in Table 2 with footnote "b") were found in the previous study; the absence of a greater overlap is likely due to differences in the study design discussed above, differences in the preprocessing of data (MAS5 was used in the previous study, whereas RMA was used in the present study), and the unavoidable fact that the true FDR of the two studies, while estimated to be low, was almost certainly not zero.

The ACB demonstrated significant differential expression of 16 genes (Table 1). Catalase, expressed higher in the iP line, is the major enzyme metabolizing ethanol to acetaldehyde in the CNS (Aragon et al., 1991,1992; Cohen et al., 1980; Zimatkin and Lindros, 1996). Gill et al. (1996) have also reported higher catalase activity in the CNS of P rats compared to NP rats. Two of the 15 differentially expressed genes in the ACB were located within established

alcohol QTLs (Bice et al., 1998; Carr et al., 1998,2003; Foroud et al., 2002,2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003), that is, ribosomal protein S2 and proteasome (prosome, macropain) subunit, alpha type 5 (Table 5). Some of the differences in the ACB could be related to the disparate alcohol drinking characteristics of the iP and iNP strains.

The FC demonstrated significant differential expression of eight genes (Table 1). The one gene that is differentially expressed in the FC but in no other region is glial fibrillary acidic protein (*Gfap*). This gene is abundantly expressed in glial cells of the central nervous system and can be used as a marker for glial cell density and health. It is decreased in the FC of human adult alcoholics and more so in alcoholics with depressive symptoms (Miguel-Hidalgo et al., 2002). Humans with a history of chronic alcoholism have been found to have substantial glial pathology in the FC irrespective of current alcohol use or liver pathology (Cullen & Halliday, 1994). It is possible that higher *Gfap* expression in the FC of the iP line confers protective benefits. The FC has only two significant genes that map to established alcohol QTLs (Bice et al., 1998; Carr et al., 1998,2003; Foroud et al., 2002,2003; Radcliffe et al., 2004; Terenina-Rigaldie et al., 2003) (Table 5), ribosomal protein S2 and proteasome (prosome, macropain) subunit, alpha type 5.

4.2. Overall strain differences

Within the 296 genes found significant in the overall analysis (Table 4), 17 GO categories were over-represented ($P < .05$, Table 7). Six categories associated with neuronal function included axon guidance, gliogenesis, negative regulation of programmed cell death, regulation of programmed cell death, regulation of synapse structure function, and transmission of nerve impulse (Table 6).

To guide determination of relationships between and within genes of the significant GO categories listed in Tables 8-11, a co-citation network graph was constructed. Of the 63 genes present in the combined lists (Tables 8-11), 24 genes are present in a co-citation graph with a threshold for inclusion of four co-citations per link (Fig. 2). The expression of *Cdkn1a* and *Bcl2l1* was lower in the iP than iNP strain; both are involved in regulation of apoptosis, suggesting the reduced expression of these genes may have a positive impact on neuronal function. *Ntf3* and *Ntf5* code for proteins classified as neurotrophic factors, that is, they function to promote both neuroplasticity and neuro-protection (Filus & Rybakowski, 2005). There is evidence that these two neurotrophic factors might be involved in maintaining functional tolerance to ethanol (Szabo & Hoffman, 1995).

Cntf codes for a neurotrophic factor; however, unlike the Ntfs, this factor has been shown to play a positive role in myelinogenesis (Stankoff et al., 2002). *Cntf* and *Ntf3* have both been shown to play a positive role in psychostimulant-induced behavioral sensitization via their participation in DA-mediated neuronal plasticity (Pierce & Bari, 2001). The higher expression of both of these factors in the iP than iNP strain could be a factor contributing to the reinforcing properties of ethanol observed for the P but not NP line (Gatto et al., 1994). The differences in expression of *Ntf* and *Cntf* between iP and iNP rats might indicate that the neuronal system in general might be more geared toward undergoing positive neuronal changes in response to environmental manipulations.

The lower expression of *Npy* in the iP than iNP strain may be the result of the combined effects of higher expression of *Cnft* and lower expression of *Ntf5* in the iP rats. *Cnft* has been shown to decrease the expression of *Npy* (Rao et al., 1992) and the *Cnft* analogue CNTF (A \times 15) has been shown to exert a delayed effect in suppressing the expression of *Npy* in calorie restricted, diet-induced, obese rats (Bluher et al., 2004). *Ntf5*, but not *Ntf3* has been shown to stimulate the expression of *Npy* in the rat neocortex (Wirth et al., 1998). The findings indicating lower expression of *Npy* in the iP than iNP rats are in general agreement with reports on tissue levels

of NPY reported for the selectively bred P and NP lines (Ehlers et al., 1998;Hwang et al., 2004). A brief survey of other genes connected to *Npy* reveals that the products of *Reln* and *Npy5r* also interact with *Npy*. *Reln*, secreted by GABAergic interneurons, is involved in the control of neuronal migration and *Npy* immunopositive cells have *Reln* receptors (Pesold et al., 1999). A decrease in the expression of *Reln* in the iP line is consistent with the decreased expression of *Npy* in this line. The higher expression of *Npy5r* in the iP than iNP strain may reflect a compensatory response of having lower expression levels of *Npy*. The *Npy5r* antagonist L-152,804 has recently been shown to reduce ethanol self-administration and reinforcement in the iP rat (Schroeder et al., 2003,2005). The higher expression of *Npy5r* may be a factor contributing to the high alcohol drinking behavior of the iP rats.

A review of Table 8 indicates that the metabotropic glutamate, glycine, and GABA receptors may also have roles in contributing to the disparate alcohol drinking behaviors of the iP and iNP rats. Table 9 lists many genes that may mediate differences in neuronal development and neuroplasticity between the iP and iNP strains, for example, neurexin 3 is an axonal receptor of neuroligin and this complex can control excitatory and inhibitory synapse formation (Dean et al., 2003;Hussain & Sheng, 2005). Table 10 lists many genes that are different between the strains and may play pivotal roles in intracellular messaging, for example, the expression of *Prkce* (protein kinase C, epsilon) is almost 30% lower in the iP than iNP strain. This relationship between alcohol drinking and *Prkce* levels is opposite to that found in *Prkce* knockout mice, which demonstrated decreased preference for ethanol and increased sensitivity to the behavioral effects of ethanol (Choi et al., 2002;Hodge et al., 1999). These apparently contradictory findings between the inbred rat strains and the mutant mice may be due to species differences and/or to compensatory changes in the knockout mouse. Finally, Table 11 lists transcription factors that were different between the iP and iNP line in the overall analysis. Too little is known about the role of transcription factors in the development of specific neural structures and cell types to speculate on the effects of these differences.

Among the top 20 or so candidates identified in the convergent functional genomics analysis of Rodd et al. (2006), there were seven genes (*Fnl1*, *Syn2*, *Agt*, *Lyz*, *Nrn1*, *Aldh1a1*, and *Prkce*) that were also identified in the overall analysis in the present study as being significantly different between iP and iNP rats (Table 4). These genes should be considered as potential candidates contributing to high alcohol drinking behavior.

In summary, through careful analysis of differential expression of the genome of the iP and iNP rat strains, we have seen that the biggest difference is not between lines, but between regions. We have also seen that, at least in the alcohol-naïve state, the AMYG demonstrates the greatest number of differences in gene expression of the five regions examined, although all five regions demonstrate at least some genes with significant differential expression (FDR < 0.10). Taken together, the individual region and combined region analyses indicate that the expressions of genes involved in biologic networks of neurotransmitters, intracellular messengers, neuroplastins, neurotrophins, and transcription factors may all contribute to behavioral and neurobiological differences between the iP and iNP rats and their parent stocks. A network involving *Npy* and related genes has the most supporting evidence from both the data of this experiment and a co-citation bioinformatic analysis.

Acknowledgments

This study was supported in part by AA07611, AA07462, AA13521 [INIA], and AA16652 [INIA]. Microarrays were analyzed using the facilities of the Center for Medical Genomics at Indiana University School of Medicine, which is supported in part by the Indiana Genomics Initiative (INGEN®) of Indiana University. INGEN is supported in part by the Lilly Endowment Inc.

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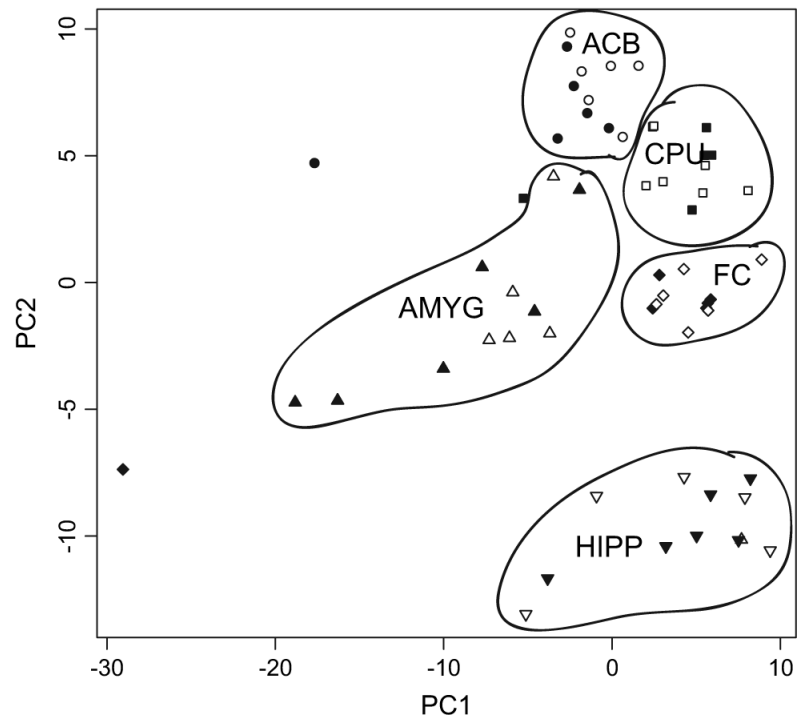


Fig 1. Principal components plot of all 59 arrays. Only processed, filtered data were used (see Methods for details) in the computation. Principal component 1 is plotted on the horizontal axis and principal component 2 is plotted on the vertical axis. Clusters of arrays corresponding to specific brain regions are as outlined. Open symbols represent arrays for inbred alcohol-preferring rats; closed symbols are for arrays from inbred alcohol —non-preferring rats.

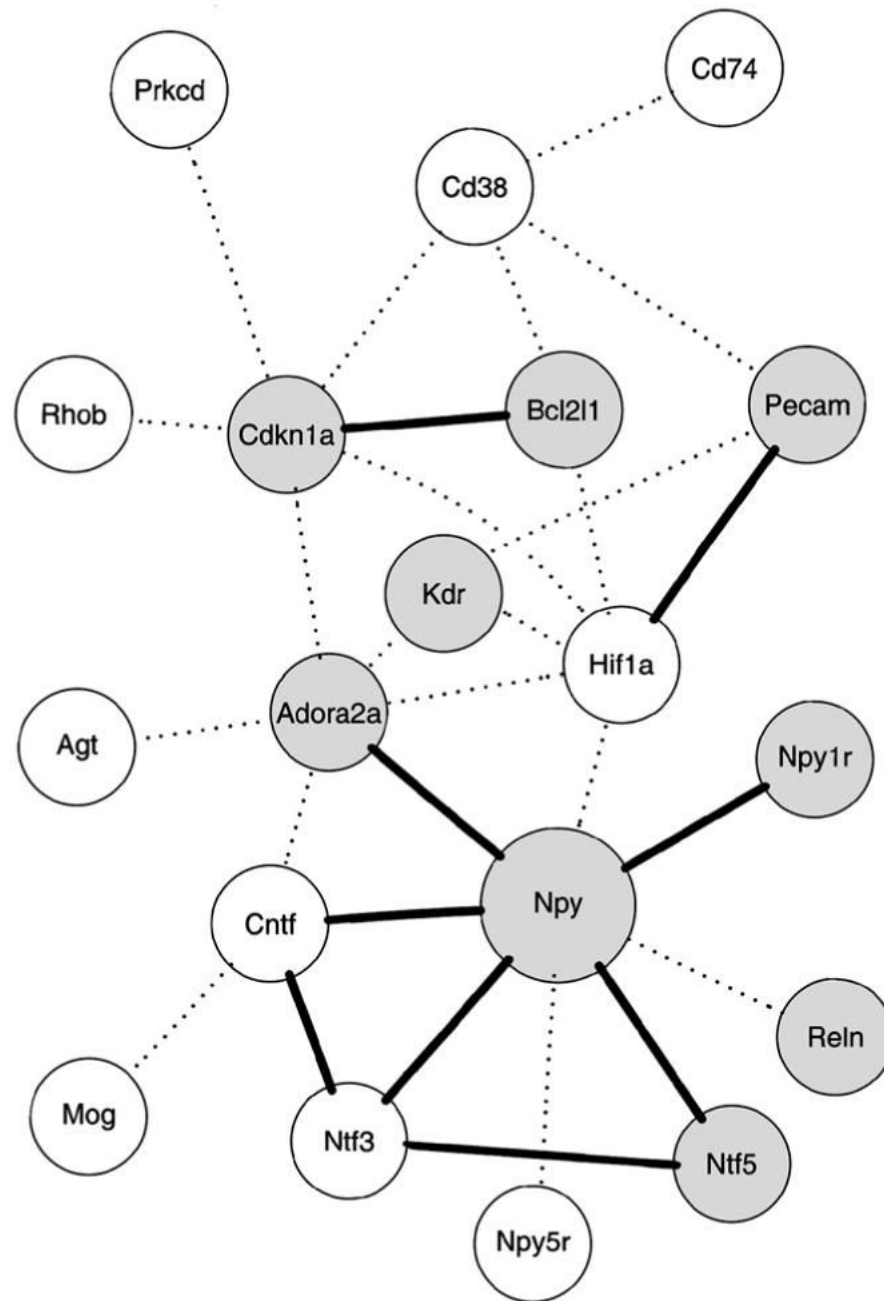


Fig 2.

Co-citation network graph constructed with modified BioConductor software and manual curation (see Methods for details). Grey filled circles denote genes that have decreased expression in the inbred alcohol-preferring rat, unfilled circles denote genes that have increased expression. Those links supported by 16 or greater co-citations are depicted with bold solid lines, whereas those with less than 16 are depicted with dotted lines. The circle for *Npy* has been enlarged for emphasis. Genes *Slit1*, *Slit3*, *C1s*, *B2m*, and *Il18* also met the minimum criteria but were only peripherally related or not related to the interactions shown in the figure. Therefore, for the sake of clarity, these genes were not included.

Summary of biostatistical and bioinformatic analyses for individual regions and for the combined regions examining the main effect of strain^a

Table 1

	Accumbens	Amygdala	Frontal cortex	Hippocampus	Caudate-putamen	Combined regions
Total significant genes (FDR < 0.10)	16	54	8	21	24	351
iP>iNP	7	32	3	7	10	198
iNP>iP	9	22	5	14	14	153
Minimum significant fold difference (abs ^b)	1.37	1.18	1.39	1.21	1.19	
Minimum significant fold difference (abs ^b)	2.11	2.08	2.08	2.28	2.24	
Significant genes in alcohol QTLs	2	16	2	1	8	70
Significant GO categories ($P < .05$)	0	0	0	0	0	12
Significant gene—gene co-citations	0	0	0	0	0	121

FDR = false discovery rate; iP = inbred alcohol—preferring rat; iNP = inbred alcohol/non-preferring rat; GO = Gene Ontology.

^a See Methods for details of each analysis.

^b Absolute value.

Table 2

Regionally significant genes (FDR < 0.10)

Symbol	Gene description	iP vs. iNP fold change
Accumbens		
Ahi1	Abelson helper integration site 1	-1.54
Gsta4	glutathione <i>S</i> -transferase, alpha 4	-1.52
Lin7c	lin-7 homolog C (C. elegans)	-1.51
Rps2	ribosomal protein S2	-1.48
RT1-Aw2 ^a	RT1 class Ib, locus Aw2	-1.37
Sephs2	selenophosphate synthetase 2	-1.61
Stk38	serine/threonine kinase 38	-1.37
Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.38
Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.40
Akap11	A kinase (PRKA) anchor protein 11	1.50
Ampd3	adenosine monophosphate deaminase 3	1.37
Cat	Catalase	1.42
Lyz	Lysozyme	2.11
Pgk1	Phosphoglycerate kinase 1	2.05
Pma5	proteasome (prosome, macropain) subunit, alpha type 5	1.44
RT1-Bb	RT1 class II, locus Bb	1.46
Amygdala		
Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	-1.28
Phgdh ^a	3-phosphoglycerate dehydrogenase	-1.36
Ahi1	Abelson helper integration site 1	-1.35
Csnk1d	casein kinase 1, delta	-1.18
Casp3	caspase 3, apoptosis related cysteine protease	-1.21
Ddr2	discoidin domain receptor family, member 2	-1.18
Fgfr1	Fibroblast growth factor receptor 1	-1.21
Fn1 ^a	fibronectin 1	-1.32
Gsta4 ^a	glutathione <i>S</i> -transferase, alpha 4	-1.78
Nyw1	ischemia related factor NYW-1	-1.38
Kdr	kinase insert domain protein receptor	-1.50
Lin7c	lin-7 homolog C (C. elegans)	-1.27
Lox	lysyl oxidase	-1.22
Pak2	p21 (CDKN1A)-activated kinase 2	-1.20
Rps2 ^a	ribosomal protein S2	-1.63
RT1-Aw2 ^a	RT1 class Ib, locus Aw2	-1.41
Sephs2	selenophosphate synthetase 2	-1.39
Scn3a ^a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.44
Slc28a2	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	-1.25
Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.77
Shc3	src homology 2 domain-containing transforming protein C3	-1.29
Tagln	Transgelin	-1.22
	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP	
Atic	cyclohydrolase	1.32
Acs11	acyl-CoA synthetase long-chain family member 1	1.27
Amigo	amphoretin-induced gene and ORF	1.22
Argbp2 ^a	Arg/Abl-interacting protein ArgBP2	1.22
Asns	asparagine synthetase	1.25
Atrn	Attractin	1.33
Btg2	B-cell translocation gene 2, antiproliferative	1.19
Celsr2	cadherin EGF LAG seven-pass G-type receptor 2	1.25
Cd24 ^a	CD24 antigen	1.32
Chgb	chromogranin B	1.25
Eif2b1 ^a	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.29
Fth1	ferritin, heavy polypeptide 1	1.29
Gfm	G elongation factor	1.30
Irak2	interleukin-1 receptor-associated kinase 2	1.22
Ldhb	lactate dehydrogenase B	1.23
Lcp2	lymphocyte cytosolic protein 2	1.18
Lyz	Lysozyme	1.81
Nrn1	Neuritin	1.19
Nptx1	neuronal pentraxin 1	1.32
Pdlim3	PDZ and LIM domain 3	1.28
Pmpcb	peptidase (mitochondrial processing) beta	1.26
Pcm1	pericentriolar material 1	1.52
Pgk1	phosphoglycerate kinase 1	2.08
Prps1	phosphoribosyl pyrophosphate synthetase 1	1.19
Pbef1	pre-B-cell colony enhancing factor 1	1.25
Pma5	proteasome (prosome, macropain) subunit, alpha type 5	1.57
RT1-N3	RT1 class Ib gene, H2-TL-like, grc region (N3)	1.26
RT1-Bb	RT1 class II, locus Bb	1.39
Sh3gl3	SH3 domain protein 2 C1	1.18

Symbol	Gene description	iP vs. iNP fold change
Spats1	spermatogenesis associated, serine-rich 1	1.29
Scp2	sterol carrier protein 2	1.25
Thrsp	thyroid hormone responsive protein	1.30
Frontal cortex		
Phgdh	3-phosphoglycerate dehydrogenase	-1.42
Gsta4	glutathione S-transferase, alpha 4	-1.75
Rps2	ribosomal protein S2	-1.76
Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.39
Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.44
Gfap	glial fibrillary acidic protein	1.44
Pgk1	phosphoglycerate kinase 1	2.08
Pma5	proteasome (prosome, macropain) subunit, alpha type 5	1.78
Hippocampus		
Phgdh, ^{ab}	3-phosphoglycerate dehydrogenase	-1.39
Azi2	5-azacytidine induced gene 2	-1.28
Ahi1	Abelson helper integration site 1	-1.48
B2m	beta-2 microglobulin	-1.31
Fn1	fibronectin 1	-1.55
Gsta4 ^a	glutathione S-transferase, alpha 4	-2.07
Lxn	Latexin	-1.34
Rab5a ^b	RAB5A, member RAS oncogene family	-1.29
Rps2	ribosomal protein S2	-1.53
RT1-Aw2 ^b	RT1 class Ib, locus Aw2	-1.41
Sephs2 ^b	selenophosphate synthetase 2	-1.47
Stk38	serine/threonine kinase 38	-1.21
Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.47
Tagln	Transgelin	-1.23
Akap11 ^b	A kinase (PRKA) anchor protein 11	1.32
Dcn ^b	Decorin	1.29
Grb14 ^b	growth factor receptor bound protein 14	1.32
Iag2 ^b	implantation-associated protein	1.31
Pgk1 ^b	phosphoglycerate kinase 1	2.28
RT1-N3	RT1 class Ib gene, H2-TL-like, grc region (N3)	1.35
Slit1	slit homolog 1 (Drosophila)	1.32
Caudate-putamen		
Phgdh ^a	3-phosphoglycerate dehydrogenase	-1.33
Ahi1	Abelson helper integration site 1	-1.46
Apobec1	apolipoprotein B editing complex 1	-1.23
Fn1	fibronectin 1	-1.35
Gsta4 ^a	glutathione S-transferase, alpha 4	-2.00
Lin7c	lin-7 homolog C (C. elegans)	-1.31
Prkag1	protein kinase, AMP-activated, gamma 1 noncatalytic subunit	-1.19
Rpl6	ribosomal protein L6	-1.21
Rps2	ribosomal protein S2	-1.64
RT1-Aw2 ^a	RT1 class Ib, locus Aw2	-1.39
Sephs2	selenophosphate synthetase 2	-1.45
Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.46
Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.41
Shc3	src homology 2 domain-containing transforming protein C3	-1.39
Akap5	A kinase (PRKA) anchor protein 5	1.39
Akr1b4	aldo-keto reductase family 1, member B4 (aldose reductase)	1.21
Agt	Angiotensinogen	1.30
Asns	asparagine synthetase	1.20
Cryab	crystallin, alpha B	1.35
Hspa2	heat shock protein 2	1.24
Nefh	neurofilament, heavy polypeptide	1.44
Pgk1	phosphoglycerate kinase 1	2.24
Pma5	proteasome (prosome, macropain) subunit, alpha type 5	1.63
Znf386	zinc finger protein 386 (Kruppel-like)	1.22

FDR = false discovery rate; iP = inbred alcohol-preferring rat; iNP = inbred alcohol non-preferring rat.

^a Genes represented by significant differential expression (FDR < 0.10) of more than one probe set. The largest absolute fold change for the gene among significant probe sets is listed. In all cases, the significant probe sets expressed differential expression in the same direction.

^b Gene also significant in Edenberg et al. (2005)

Table 3

Detailed expression levels and S.D.s for all regionally significant probe sets

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
Accumbens										
rc_AI639111_at	Rn. 93081	308923	Ahl1	Abelson helper integration site 1	-1.54	0.00	810	107	527	60
X62660mRNA_g_at	Rn. 57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.52	0.00	1092	184	719	125
AF090136_at	Rn. 44269	60442	Lin7c	lin-7 homolog C (C. elegans)	-1.51	0.00	160	14	106	11
L81138exon_i_at	Rn. 2115	83789	Rps2	ribosomal protein S2	-1.48	0.00	438	30	299	53
M10094_g_at	Rn. 40130	24737	RT1-	RT1 class Ib, locus Aw2	-1.36	0.00	392	19	288	25
M11071_f_at	Rn. 40130	24737	RT1-	RT1 class Ib, locus Aw2	-1.37	0.00	2623	290	1915	148
Y00766_at	Rn. 87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.38	0.00	643	82	464	50
rc_AA799700_at	Rn. 100471	308993	Seps2	selenophosphate synthetase 2	-1.61	0.00	354	62	221	43
AJ001290cnds_at	Rn. 79242	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.40	0.00	784	43	566	85
rc_AA800712_g_at	Rn. 13142	361813	Stk38	serine/threonine kinase 38	-1.37	0.00	855	44	632	105
U48288_at	Rn. 10557	25228	Akap1	A kinase (PRKA) anchor protein 11	1.50	0.00	312	54	464	46
U90888_at	Rn. 11106	25095	Ampd3	adenosine monophosphate deaminase 3	1.37	0.00	102	12	139	19
rc_AA926149_g_at	Rn. 3001	24248	Cat	catalase	1.42	0.00	197	33	278	34
rc_AA892775_at	Rn. 2283	25211	Lyz	lysozyme	2.11	0.00	1185	159	2524	501
rc_AA892797_at	Rn. 108127	24644	Pgk1	phosphoglycerate kinase 1	2.05	0.00	2189	729	4392	1061
rc_AA891383_i_at	Rn. 1276	29672	Psm5	proteasome (prosome, macropain) subunit, alpha type 5	1.44	0.00	123	17	176	16
U65217_i_at	Rn. 33311	309622	RT1-	RT1 class II, locus Bb	1.46	0.00	48	5	69	7
Amygdala										
rc_AI639111_at	Rn. 93081	308923	Ahl1	Abelson helper integration site 1	-1.35	0.00	818	118	602	60
U84410_s_at	Rn. 10562	25402	Casp3	caspase 3, apoptosis related	-1.21	0.00	200	12	166	15
rc_AI013513_at	Rn. 8046	64462	Csnk1d	casein kinase 1, delta	-1.18	0.00	730	23	621	24
AF016247_at	Rn. 92730	83573	Ddr2	discoidin domain receptor family, member 2	-1.18	0.00	142	7	120	5
D12498_s_at	Rn. 9797	79114	Fgfr1	Fibroblast growth factor receptor 1	-1.21	0.00	671	45	556	27
U82612cnds_g_at	Rn. 1604	25661	Fn1	fibronectin 1	-1.25	0.00	445	57	354	22
X05834_at	Rn. 1604	25661	Fn1	fibronectin 1	-1.32	0.00	1070	95	812	109
X62660mRNA_at	Rn. 57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.32	0.00	714	35	545	72
X62660mRNA_g_at	Rn. 57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.78	0.00	1182	55	679	163
X55286_g_at	Rn. 9437	25675	Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	-1.28	0.00	363	32	283	16
U93306_at	Rn. 88869	25589	Kdr	kinase insert domain protein receptor	-1.50	0.00	121	18	82	15
AF090136_at	Rn. 44269	60442	Lin7c	lin-7 homolog C (C. elegans)	-1.27	0.00	139	11	109	6

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
S66184_s_at	Rn.11372	24914	Lox	lysyl oxidase	-1.22	0.00	204	16	167	9
rc_A1176253_at	Rn.133954	59319	Nyw1	ischemia related factor NYW-1	-1.38	0.00	122	15	89	13
U35345_s_at	Rn.3840	29432	Pak2	p21 (CDKN1A)-activated kinase 2	-1.20	0.00	145	9	121	7
X97772_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.36	0.00	1710	150	1261	142
X97772_g_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.28	0.00	1466	111	1150	119
L81136cfs_f_at	Rn.2115	83789	Rps2	ribosomal protein S2	-1.20	0.00	1150	36	959	44
L81138exon_i_at	Rn.2115	83789	Rps2	ribosomal protein S2	-1.63	0.00	484	36	298	29
M11071_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.41	0.00	2488	163	1767	141
M31018_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.23	0.00	1191	70	971	86
Y00766_at	Rn.87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.44	0.00	527	99	363	33
Y00766_g_at	Rn.87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.41	0.00	1620	407	1130	112
rc_AA799700_at	Rn.100471	308993	Seps2	selenophosphate synthetase 2 src homology 2 domain-containing transforming protein C3	-1.39	0.00	332	31	239	23
AB001453_at	Rn.59227	114858	Shc3	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	-1.29	0.00	1166	154	903	87
U66723_s_at	Rn.10140	60423	Slc28a2	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	-1.25	0.00	350	35	280	19
AJ001290cnds_at	Rn.79242	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.77	0.00	839	48	479	85
M83107_at	Rn.34397	25123	Tagln	transgelin	-1.22	0.00	507	42	416	27
D90109_at	Rn.6215	25288	Acs11	acyl-CoA synthetase long-chain family member 1	1.27	0.00	444	30	563	49
rc_AA891631_at	Rn.116338	295365	Amigo	amphoretin-induced gene and ORF	1.22	0.00	559	47	680	50
AF026505_at	Rn.24612	114901	Argbp2	Arg/Abl-interacting protein ArgBP2	1.21	0.00	441	16	535	53
rc_AA891194_s_at	Rn.24612	114901	Argbp2	Arg/Abl-interacting protein ArgBP2	1.22	0.00	637	19	779	83
U07201_at	Rn.11172	25612	Asns	asparagine synthetase 5-aminimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	1.25	0.00	348	27	435	39
D89514_at	Rn.15114	81643	Atic	attractin	1.32	0.00	318	27	419	34
rc_AA859645_at	Rn.53846	83526	Attrn	attractin	1.33	0.00	477	44	635	59
M60921_g_at	Rn.27923	29619	Btg2	B-cell translocation gene 2, antiproliferative	1.19	0.00	254	12	302	20
U49062_at	Rn.6007	25145	Cd24	CD24 antigen	1.32	0.00	895	99	1185	122
U49062_g_at	Rn.6007	25145	Cd24	CD24 antigen	1.24	0.00	476	43	589	53
rc_AA875414_at	Rn.2912	83465	Ce1s2	cadherin EGF LAG seven-pass G-type receptor 2	1.25	0.00	957	103	1199	104
AF019974_at	Rn.11090	24259	Chgb	chromogranin B	1.25	0.00	3207	381	4004	293

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
rc_A1031019_at	Rn.9181	64514	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.17	0.00	346	21	406	12
rc_A1031019_g_at	Rn.9181	64514	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.29	0.00	254	13	328	26
rc_A1169802_at	54447 Rn.	25319	Fth1	ferritin, heavy polypeptide 1	1.29	0.00	4188	348	5445	782
L14684_at	10913 Rn.	114017	Gfm	G elongation factor	1.30	0.00	212	21	275	24
rc_AA799581_at	17123 Rn.	362418	Irak2	interleukin-1 receptor-associated kinase 2	1.22	0.00	583	58	710	37
rc_AA892316_at	Rn.1057	155918	Lcp2	lymphocyte cytosolic protein 2	1.18	0.00	131	7	154	9
U07181_g_at	Rn.1785	24534	Ldhh	lactate dehydrogenase B	1.23	0.00	4975	374	6116	291
rc_AA892775_at	Rn.2283 Rn.	25211	Lyz	lysozyme	1.81	0.00	1393	121	2562	518
rc_A1072943_at	54707 Rn.	266777	Npix1	neuronal pentraxin 1	1.32	0.00	429	40	566	66
U88958_at	Rn.3546	83834	Nm1	neurtin	1.19	0.00	4572	160	5426	249
rc_AA891220_at	Rn.7264 Rn.	297508	Pbef1	pre-B-cell colony enhancing factor 1	1.25	0.00	301	22	377	36
U95920_at	98622 Rn.	81740	Pcm1	pericentriolar material 1	1.52	0.00	488	47	737	49
AF002281_at	13361 Rn.	114108	Pdlim3	PDZ and LIM domain 3	1.28	0.00	125	10	160	16
rc_AA892797_at	108127 Rn.	24644	Pgk1	phosphoglycerate kinase 1	2.08	0.00	2158	476	4493	1110
D13907_g_at	Rn.841	64198	Pmpcb	peptidase (mitochondrial processing) beta	1.26	0.00	321	36	405	36
X16554_at	Rn.9761	29562	Ppps1	phosphoribosyl pyrophosphate synthetase 1	1.19	0.00	535	25	639	49
rc_AA891383_i_at	Rn.1276 Rn.	29672	Psmab5	proteasome (prosome, macropain) subunit, alpha type 5	1.57	0.00	123	14	196	38
U65217_i_at	33311 Rn.	309622	RT1-Bb	RT1 class II, locus Bb	1.39	0.00	51	4	72	8
L23128_g_at	107070 Rn.	24750	RT1-N3	RT1 class Ib gene, H2-TL-like, gic region (N3)	1.26	0.00	583	40	732	22
M62763complete_seq_at	31887 Rn.	25541	Scp2	sterol carrier protein 2	1.25	0.00	352	32	442	46
AF009604_at	Rn.5909 Rn.	81921	Sh3gl3	SH3 domain protein 2 C1	1.18	0.00	1346	80	1590	66
Re_A1639256_at	40672 Rn.	301255	Spats1	spermatogenesis associated, serine-rich 1	1.29	0.00	159	12	205	16
K01934mRNA#2_at	81140 Rn.	25357	Thrsp	thyroid hormone responsive protein	1.30	0.00	384	33	499	53
Frontal cortex										
X62660mRNA_g_at	Rn. 57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.75	0.00	1075	121	622	151
X97772_at	Rn.6872	58835	Phgdh	phosphoglycerate dehydrogenase	-1.42	0.00	1485	105	1052	130
L81138exon_i_at	Rn.2115 Rn.	83789	Rps2	ribosomal protein S2	-1.76	0.00	475	31	269	11
Y00766_at	87394 Rn.	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.39	0.00	493	22	355	26
AJ001290cnds_at	79242 Rn.	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.44	0.00	779	67	542	71
AF028784mRNA#1_s_at	Rn. 91512	24387	Gfap	glial fibrillary acidic protein	1.44	0.00	6593	636	9536	1118
rc_AA892797_at	Rn. 108127	24644	Pgk1	phosphoglycerate kinase 1	2.08	0.00	2464	483	5107	862

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
rc_AA891383_i_at Hippocampus	Rn.1276	29672	Psm5f	prosome, (prosome, macropain) subunit, alpha type 5	1.78	0.00	119	19	215	56
rc_AI639111_at	Rn.93081	308923	Ahl1	Abelson helper integration site 1	-1.48	0.00	705	89	476	45
rc_AA893602_at	Rn.14812	316051	Azi2	5-azacytidine induced gene 2	-1.28	0.00	642	51	501	21
rc_AI170268_at	Rn.1868	24223	B2m	beta-2 microglobulin	-1.31	0.00	2242	272	1704	162
X05834_at	Rn.1604	25661	Fn1	fibronectin 1	-1.55	0.00	694	62	448	31
X62660mRNA_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.36	0.00	718	76	526	38
X62660mRNA_g_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-2.07	0.00	1099	219	526	49
X76985_at	Rn.11404	59073	Lxn	latexin	-1.34	0.00	904	89	672	45
X97772_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.33	0.00	1704	167	1279	133
X97772_g_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.39	0.00	1522	166	1094	39
rc_AA800305_at	Rn.44477	64633	Rab5a	RAB5A, member RAS oncogene family	-1.29	0.00	463	31	362	42
L81138xon_i_at	Rn.2115	83789	Rps2	ribosomal protein S2	-1.53	0.00	469	27	307	16
M11071_f_at	Rn.40130	24737	Aw2	RT1 class Ib, locus Aw2	-1.41	0.00	2351	271	1660	100
rc_AA799700_at	Rn.100471	308993	Sephs2	selenophosphate synthetase 2	-1.47	0.00	382	33	260	17
AJ001290cnds_at	Rn.79242	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.47	0.00	846	81	583	117
rc_AA800712_g_at	Rn.13142	361813	Stk38	serine/threonine kinase 38	-1.21	0.00	836	43	691	36
M83107_at	Rn.34397	25123	Tagln	transgelin	-1.23	0.00	435	34	353	17
U48288_at	Rn.10557	25228	Akap11	A kinase (PRKA) anchor protein 11	1.32	0.00	309	30	408	29
Z12298cnds_s_at	Rn.106103	29139	Dcn	decorin	1.29	0.00	477	49	614	48
AF076619_at	Rn.30028	58844	Grb14	growth factor receptor bound protein 14	1.32	0.00	342	30	451	35
AF008554_at	Rn.43578	116967	Iag2	implantation-associated protein	1.31	0.00	173	17	228	27
rc_AA892797_at	Rn.108127	24644	Pgk1	phosphoglycerate kinase 1	2.28	0.00	2064	556	4664	923
L23128_g_at	Rn.107070	24750	RT1-N3	RT1 class Ib gene, H2-TL-like, gre region (N3)	1.35	0.00	581	46	781	34
AB011530_at Striatum	Rn.30002	65047	Slit1	slit homolog 1 (Drosophila)	1.32	0.00	640	42	846	42
rc_AI639111_at	Rn.93081	308923	Ahl1	Abelson helper integration site 1	-1.46	0.00	745	75	511	76
L07114_at	Rn.10002	25383	Apoec1	apolipoprotein B editing complex 1	-1.23	0.00	146	5	118	4
X05834_at	Rn.1604	25661	Fn1	fibronectin 1	-1.35	0.00	810	42	605	99
X62660mRNA_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.35	0.00	651	18	482	34
X62660mRNA_g_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-2.00	0.00	1047	109	523	34

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
AF090136_at	Rn.44269	60442	Lin7c	lin-7 homolog C (C. elegans)	-1.31	0.00	148	11	113	7
rc_A1008677_s_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.33	0.00	741	45	562	66
X97772_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.28	0.00	1600	95	1250	73
X97772_g_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.29	0.00	1369	90	1062	73
U42413_at	Rn.11089	25520	Pfkfb1	protein kinase, AMP-activated, gamma 1 noncatalytic subunit	-1.19	0.00	1211	33	1020	52
S71021_s_at	Rn.2660	117042	Rpl6	ribosomal protein L6	-1.21	0.00	5829	167	4808	255
L81138exon_i_at	Rn.2115	83789	Rps2	ribosomal protein S2	-1.64	0.00	427	35	260	16
M11071_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.39	0.00	2183	79	1574	93
M31018_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.26	0.00	1039	38	825	91
Y00766_at	Rn.87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.46	0.00	632	56	439	84
rc_AA799700_at	Rn.100471	308993	Sephs2	selenophosphate synthetase 2 src homology 2 domain-containing transforming protein C3	-1.45	0.00	328	44	225	23
AB001453_at	Rn.59227	114858	Shc3	containing transforming protein C3	-1.39	0.00	1361	103	985	125
AJ001290cds_at	Rn.79242	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.41	0.00	791	61	566	89
M12112mRNA#3_s_at	Rn.6319	24179	Agt	angiotensinogen	1.30	0.00	477	42	621	44
U67136_at	Rn.122003	171026	Akap5	A kinase (PRKA) anchor protein 5	1.39	0.00	163	12	229	35
M60322_g_at	Rn.107801	24192	Akr1b4	aldo-keto reductase family 1, member B4 (aldose reductase)	1.21	0.00	537	35	650	37
U07201_at	Rn.11172	25612	Asns	asparagine synthetase	1.20	0.00	334	15	402	22
M55534mRNA_s_at	Rn.98208	25420	Cryab	crystallin, alpha B	1.35	0.00	869	155	1161	83
X15705cds_at	Rn.112579	60460	Hspa2	heat shock protein 2	1.24	0.00	130	6	161	11
rc_AA818677_at	Rn.108194	24587	Nefh	neurofilament, heavy polypeptide	1.44	0.00	586	68	841	62
rc_AA892797_at	Rn.108127	24644	Pgk1	phosphoglycerate kinase 1	2.24	0.00	2151	294	4847	896
rc_AA891383_i_at	Rn.1276	29672	Psmas5	proteasome (prosome, macropain) subunit, alpha type 5	1.63	0.00	122	24	197	26
U67082_at	Rn.10663	25165	Znf386	zinc finger protein 386 (Kruppel-like)	1.22	0.00	194	11	236	13

S.D. = standard deviation; FDR = false discovery rate; iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat; RMA = Robust Multi-Chip Average.

Positive fold difference is iP/iNP; negative is iNP/iP.

Expression levels are those obtained after RMA background correction and scaling as indicated in Methods.

Table 4
Complete list of probe sets that were significantly different between iP and iNP rats in the overall analysis

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
M33648_at	Rn.29594	24450	Hmgcs2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-1.07	0.00	726	74	686	89
M33648_g_at	Rn.29594	24450	Hmgcs2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-1.15	0.00	410	105	366	117
rc_A1008677_s_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.27	0.00	718	78	570	77
X97772_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.33	0.00	1642	158	1244	159
X97772_g_at	Rn.6872	58835	Phgdh	3-phosphoglycerate dehydrogenase	-1.31	0.00	1426	156	1095	124
rc_AA893602_at	Rn.14812	316051	Azi2	5-azacytidine induced gene 2	-1.23	0.00	633	49	518	60
rc_A1639111_at	Rn.93081	308923	Ahi1	Abelson helper integration site 1	-1.46	0.00	736	121	510	89
D00512_at	Rn.4054	25014	Acat1	acetyl-coenzyme A acetyltransferase 1	-1.11	0.00	274	19	248	13
rc_A1170212_s_at	Rn.11007	140667	Ap3m2	adaptor-related protein complex 3, mu 2 subunit	-1.12	0.01	2016	190	1829	313
rc_AA891812_at	Rn.5788	24170	Add1	adducin 1 (alpha)	-1.09	0.00	3262	284	2993	279
X83715_at	Rn.5788	24170	Add1	adducin 1 (alpha)	-1.14	0.00	1377	148	1232	207
S47609_s_at	Rn.11180	25369	Adora2a	adenosine A2a receptor	-1.08	0.00	918	359	862	361
D17309_at	Rn.25716	192242	Akr1d1	aldo-keto reductase family 1, member D1	-1.09	0.00	214	24	197	28
D86297_at	Rn.32517	25748	Alas2	aminolevulinic acid synthase 2	-1.14	0.00	934	146	818	135
AF029107_at	Rn.62687	83610	Apba2	amyloid beta (A4) precursor protein-binding, family A, member 2	-1.13	0.01	1429	187	1291	266
L07114_at	Rn.10002	25383	Apobec1	apolipoprotein B editing complex 1	-1.15	0.00	146	15	127	12
J04024_at	Rn.2305	29693	Atp2a2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	-1.13	0.00	501	44	450	81
U34963_s_at	Rn.10323	24888	Bcl2l1	Bcl2-like 1	-1.11	0.00	324	36	295	45
U72350_at	Rn.10323	24888	Bcl2l1	Bcl2-like 1	-1.07	0.00	749	76	700	73
AF065431_s_at	Rn.82709	64547	Bcl2l1	BCL2-like 1 (apoptosis facilitator)	-1.08	0.01	95	10	88	9
Re_A1170268_at	Rn.1868	24223	B2m	beta-2 microglobulin	-1.18	0.00	2407	338	2059	373
D63860_s_at	Rn.53974	25667	Bmp3	bone morphogenetic protein 3	-1.06	0.01	141	13	133	10
D83349_at	Rn.108785	29182	Cdh22	cadherin 22	-1.43	0.00	1807	436	1380	565
J02844_s_at	Rn.4896	83842	Crot	carnitine O-octanoyltransferase	-1.12	0.00	187	23	166	15
U26033_at	Rn.4896	83842	Crot	carnitine O-octanoyltransferase	-1.15	0.00	96	11	83	12
Re_A1013513_at	Rn.8046	64462	Csnk1d	casein kinase 1, delta	-1.10	0.00	765	72	696	76
Re_A1639196_at	Rn.33757	66013	Arhgef9	Cdc42 guanine nucleotide exchange factor (GEF) 9	-1.22	0.01	742	78	644	181
U07619_at	Rn.9980	25584	F3	coagulation factor III	-1.19	0.00	150	18	126	21
L41275cds_s_at	Rn.10089	114851	Cdkn1a	cyclin-dependent kinase inhibitor 1A	-1.11	0.00	357	36	321	34
L33894_at	Rn.10058	79127	Dck	deoxycytidine kinase	-1.12	0.00	86	10	77	9
Z46882cds_at	Rn.2889	25416	Dpysl2	dihydropyrimidinase-like 2	-1.10	0.00	381	30	349	52
D85035_g_at	Rn.133148	81656	Dpyd	dihydropyrimidine dehydrogenase	-1.11	0.00	97	17	87	12
Re_AA894273_at	Rn.7398	64157	Ddah1	dimethylarginine dimethylaminohydrolase 1	-1.19	0.00	212	18	179	22

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
AJ011607_at	Rn.11846	301323	Prim2	DNA primase, p58 subunit	-1.13	0.00	161	14	142	11
AF013144_at	Rn.10877	171109	Dusp5	dual specificity phosphatase 5	-1.07	0.00	423	45	396	49
X94185cds_s_at	Rn.4313	116663	Dusp6	dual specificity phosphatase 6	-1.28	0.01	1483	235	1238	411
Rc_AA893770_g_at	Rn.144669	245963	Egff7	EGF-like domain 7	-1.07	0.01	546	34	511	52
X02610_at	Rn.4236	24333	Eno1	enolase 1, alpha	-1.15	0.00	6777	494	5917	561
X02610_g_at	Rn.4236	24333	Eno1	enolase 1, alpha	-1.11	0.00	11825	997	10717	1427
X59290miRNA_at	Rn.62934	60589	Epha8	Eph receptor A8	-1.08	0.00	332	37	307	29
X78689cds_at	Rn.24569	79208	Epha5	EphA5	-1.11	0.01	160	24	145	22
D89730_at	Rn.8037	305604	Efemp1	epidermal growth factor-containing fibulin-like extracellular matrix protein 1	-1.15	0.00	535	196	456	146
D89730_g_at	Rn.8037	305604	Efemp1	epidermal growth factor-containing fibulin-like extracellular matrix protein 1	-1.13	0.00	64	17	56	12
D12498_s_at	Rn.9797	79114	Fgfr1	Fibroblast growth factor receptor 1	-1.11	0.00	813	248	753	278
M91599miRNA_at	Rn.24104	25114	Fgfr4	fibroblast growth factor receptor 4	-1.09	0.00	168	21	154	14
L00191cds#1_s_at	Rn.1604	25661	Fnl1	fibronectin 1	-1.27	0.00	410	118	318	72
M28259cds_at	Rn.1604	25661	Fnl1	fibronectin 1	-1.13	0.00	116	23	101	11
Rc_AA955600_at	Rn.1604	25661	Fnl1	fibronectin 1	-1.07	0.01	69	6	65	6
U82612cds_g_at	Rn.1604	25661	Fnl1	fibronectin 1	-1.15	0.00	439	52	381	47
X05834_at	Rn.1604	25661	Fnl1	fibronectin 1	-1.34	0.00	952	203	722	220
L27421_at	Rn.62653	65153	Freq	frequenin homolog (Drosophila)	-1.22	0.00	183	35	150	33
M92076_at	Rn.41715	24416	Grm3	glutamate receptor, metabotropic 3	-1.31	0.00	1399	384	1117	457
X96790_at	Rn.10409	81672	Grm7	glutamate receptor, metabotropic 7	-1.08	0.00	72	6	67	7
X62660miRNA_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.29	0.00	680	65	526	57
X62660miRNA_g_at	Rn.57528	300850	Gsta4	glutathione S-transferase, alpha 4	-1.81	0.00	1099	146	613	135
X55246_at	Rn.10109	25674	Gtra1	glycine receptor, alpha 1 subunit	-1.11	0.00	983	132	883	104
L02896_at	Rn.7044	58920	Gpc1	glypican 1	-1.12	0.00	369	51	332	48
L06986_at	Rn.10935	24388	Gfi1	growth factor independent 1	-1.09	0.00	103	9	95	8
Rc_AA859837_at	Rn.24783	83585	Gda	guanine deaminase	-1.28	0.00	3722	794	3130	1013
Rc_AA859837_g_at	Rn.24783	83585	Gda	guanine deaminase	-1.21	0.00	9381	1873	8042	2310
M17526_g_at	Rn.90161	50664	Gnao	guanine nucleotide binding protein, alpha o	-1.26	0.01	5794	1240	4845	1689
D13417_g_at	Rn.19727	29577	Hes1	hairy and enhancer of split 1 (Drosophila)	-1.08	0.00	404	32	376	37
X56325miRNA_s_at	Rn.107334	25632	Hba-a1	hemoglobin alpha, adult chain 1	-1.19	0.00	25130	5747	21396	6048
M94918miRNA_f_at	Rn.36966	24440	Hbb	hemoglobin beta chain complex	-1.21	0.00	14307	4436	11865	4004
U89695_at	Rn.29981	84017	Hmg2	high mobility group AT-hook 2	-1.07	0.01	107	12	100	7
AB007689_g_at	Rn.30014	29547	Homer2	homer homolog 2 (Drosophila)	-1.09	0.00	140	18	128	13

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
Rc_AA893384_g_at	Rn.1499	292892	Irf3	interferon regulatory factor 3	-1.06	0.00	1298	106	1223	114
Rc_AI639313_at	Rn.87882	84009	Kalm	kalirin, RhoGEF kinase	-1.09	0.01	260	23	240	31
U93306_at	Rn.88869	25589	Kdr	kinase insert domain protein receptor	-1.28	0.00	95	19	74	14
K02814_at	Rn.128333	24903	Kng1	kininogen 1	-1.09	0.00	758	66	695	61
AF071204_at	Rn.44216	60427	Kitl	kit ligand	-1.07	0.01	79	7	74	7
AF071204_g_at	Rn.44216	60427	Kitl	kit ligand	-1.09	0.00	93	10	86	12
X76985_at	Rn.11404	59073	Lxn	latexin	-1.19	0.00	881	304	750	277
AF090134_at	Rn.31766	85327	Lin7a	lin-7 homolog a (C. elegans)	-1.16	0.00	633	96	549	105
AF090136_at	Rn.44269	60442	Lin7c	lin-7 homolog C (C. elegans)	-1.35	0.00	152	20	112	8
M64795_f_at_d	—	24735	RT1@	Major histocompatibility locus	-1.14	0.00	918	56	808	76
M15944_at	Rn.33598	24590	Mme	membrane metallo endopeptidase	-1.05	0.01	70	6	66	5
AF095741_at	Rn.11802	171451	Mg87	Mg87 protein	-1.11	0.00	950	91	856	69
Rc_AI227608_s_at	Rn.2455	29477	Maqt	microtubule-associated protein tau	-1.29	0.00	6120	525	5022	1247
Rc_AA892864_at	Rn.40396	29254	Mgll	monoglyceride lipase	-1.11	0.01	1353	202	1228	260
X06564_at	Rn.11283	24586	Ncam1	neural cell adhesion molecule 1	-1.20	0.01	1023	142	892	241
L14851_at	Rn.10926	116508	Nrxn3	neurexin 3	-1.11	0.00	1187	216	1081	218
M82826_i_at	Rn.10686	24592	Nf1	neurofibromatosis 1	-1.16	0.00	1786	191	1556	255
V01543mRNA_at	Rn.1878	25247	Nsg1	neuron specific gene family member 1	-1.07	0.00	1376	126	1292	107
M15880_at	Rn.9714	24604	Npy	neuropeptide Y	-1.14	0.00	2120	345	1857	327
U16845_at	Rn.10075	50864	Hnt	neurotrimin	-1.43	0.00	855	178	676	289
M86742cds_s_at	Rn.44225	25730	Ntf5	neurotrophin 5	-1.06	0.01	378	28	358	22
D63673_at	Rn.10675	117265	Pex6	peroxisomal biogenesis factor 6	-1.08	0.01	854	103	786	67
M98826mRNA_g_at	Rn.10399	29353	Phkg1	phosphorylase kinase gamma 1	-1.08	0.00	226	20	209	14
U77697_at	Rn.1878	29583	Pecam	platelet/endothelial cell adhesion molecule	-1.14	0.00	215	23	188	17
J02776_s_at	Rn.9346	29240	Polb	polymerase (DNA directed), beta	-1.08	0.00	176	25	162	16
L14003UTR#1_f_at	Rn.54456	25046	Pigr	polymeric immunoglobulin receptor	-1.07	0.00	273	25	255	20
AJ007627_at	Rn.144567	27150	Kcnh3	potassium voltage-gated channel, subfamily H (eag-related), member 3	-1.09	0.01	2628	383	2392	276
rc_AA799421_at	Rn.34966	29340	Prkce	protein kinase C, epsilon	-1.29	0.00	1503	262	1264	437
U42413_at	Rn.11089	25520	Prkag1	protein kinase, AMP-activated, gamma 1 noncatalytic subunit	-1.13	0.00	1181	72	1042	68
U47031_at	Rn.7176	29659	P2rx4	purinergic receptor P2X, ligand-gated ion channel 4	-1.08	0.00	373	31	343	29
rc_AA894207_g_at	Rn.28921	246324	Rab31	RAB31, member RAS oncogene family	-1.18	0.01	5493	959	4781	1121

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
AF072935_at	Rn.44477	64633	Rab5a	RAB5A, member RAS oncogene family	-1.10	0.00	644	65	586	49
rc_AA800305_at	Rn.44477	64633	Rab5a	RAB5A, member RAS oncogene family	-1.15	0.00	446	73	390	63
rc_AA900900_s_at	Rn.7107	84014	Ralbpl	ralbA binding protein 1	-1.11	0.01	369	41	335	60
rc_AA893471_s_at	Rn.98353	24718	Reln	reelin	-1.14	0.00	1103	160	975	178
AF035151_s_at	Rn.9796	54292	Rgs12	regulator of G-protein signaling 12	-1.07	0.01	771	114	723	94
AB015191_at	Rn.1943	60414	Rhcd	Rhesus blood group CE and D	-1.09	0.01	458	51	420	46
AB015191_g_at	Rn.1943	60414	Rhcd	Rhesus blood group CE and D	-1.08	0.00	292	33	268	22
rc_AA799672_s_at	Rn.2660	117042	Rpl6	ribosomal protein L6	-1.15	0.00	9605	697	8390	658
S71021_s_at	Rn.2115	117042	Rpl6	ribosomal protein L6	-1.14	0.00	5383	511	4715	479
L81136cds_f_at	Rn.2115	83789	Rps2	ribosomal protein S2	-1.15	0.00	1095	77	957	56
L81138exon_i_at	Rn.2115	83789	RT1-	ribosomal protein S2	-1.60	0.00	459	37	287	34
M24026_f_at	Rn.145396	309600	CE12	RT1 class I, CE12	-1.17	0.00	2027	223	1734	202
AF074609mRNA_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.14	0.00	791	126	691	88
M110094_g_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.20	0.00	370	32	307	30
M11071_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.38	0.00	2376	260	1724	160
M24324_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.09	0.00	2890	191	2660	224
M31018_f_at	Rn.40130	24737	RT1-Aw2	RT1 class Ib, locus Aw2	-1.22	0.00	1141	126	936	121
AF025308_f_at	Rn.160576	24977	RT1-C1	RT1 class Ib, locus C1	-1.12	0.00	823	70	733	57
AF029240_g_at	Rn.143874	294228	RT1-S3	RT1 class Ib, locus S3	-1.06	0.00	406	26	382	36
rc_AI235890_s_at	Rn.143874	294228	RT1-S3	RT1 class Ib, locus S3	-1.21	0.00	236	33	195	24
X56596_at	Rn.33311	309622	RT1-Bb	RT1 class II, locus Bb	-1.16	0.00	240	21	206	18
rc_AA799700_at	Rn.100471	308993	Sepsb2	selenophosphate synthetase 2	-1.45	0.00	341	47	234	28
Y07534cds_s_at	Rn.91257	24794	Spin2b	Serine protease inhibitor	-1.07	0.00	995	84	930	71
rc_AA800712_g_at	Rn.13142	361813	Stk38	serine/threonine kinase 38	-1.17	0.00	810	62	695	82
U90261UTR#1_g_at	Rn.107226	84357	Sh3kbp1	SH3-domain kinase binding protein 1	-1.10	0.00	2509	473	2303	500
AB011531_at	Rn.12298	83467	Slit3	slit homolog 3 (Drosophila)	-1.08	0.00	579	59	534	53
Y00766_at	Rn.87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.36	0.00	536	116	393	69
Y00766_g_at	Rn.87394	25657	Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.38	0.00	1529	337	1117	235
U66723_s_at	Rn.10140	60423	Slc28a2	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	-1.15	0.00	341	47	294	19
AF004017_at	Rn.11114	84484	Slc4a4	solute carrier family 4, member 4	-1.24	0.00	1156	249	950	248
AJ001290cds_at	Rn.79242	114507	Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.49	0.00	808	64	548	93
M96601_at	Rn.9968	29464	Slc6a6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	-1.37	0.00	339	85	259	97

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AB001453_at	Rn. 59227	114858	Shc3	src homology 2 domain-containing transforming protein C3	-1.28	0.00	1213	183	941	110
rc_AA875411_s_at	Rn. 37542	65041	Skd3	suppressor of K+ transport defect 3	-1.06	0.00	696	55	654	48
rc_AA891445_at	Rn. 37542	65041	Skd3	suppressor of K+ transport defect 3	-1.11	0.00	591	71	532	75
AF053938_s_at	Rn.9908	192117	Syngap1	synaptic Ras GTPase activating protein 1 homolog (rat)	-1.15	0.00	496	36	429	27
U20105_at	Rn. 48074	60565	Sy6	synaptotagmin 6	-1.09	0.00	138	21	127	19
U20106_at	Rn. 91884	59267	Sy7	synaptotagmin 7	-1.13	0.00	138	13	122	15
U85113_at	Rn. 74259	60567	Syt10	synaptotagmin X	-1.07	0.01	100	11	93	7
D12519_s_at	Rn.9943	116470	Six1a	syntaxin 1A (brain)	-1.10	0.01	3399	943	3090	954
U88630_at	Rn.2398	81813	Tieg	TGF β inducible early growth response	-1.07	0.00	146	13	136	11
D30041_at	Rn. 87066	25233	Akt2	thymoma viral proto-oncogene 2	-1.11	0.01	304	45	274	46
rc_AA818982_at	Rn.3364	25359	Tmpo	Thymopoietin	-1.16	0.01	161	29	141	32
rc_AA89854_at	Rn. 90996	360243	Top2a	topoisomerase (DNA) 2 alpha	-1.09	0.01	276	32	254	34
rc_AA893702_s_at	Rn.1829	64365	Tcn2	transcobalamin 2	-1.07	0.00	1309	122	1224	125
rc_Al639517_at	Rn. 23354	84382	Tcf4	transcription factor 4	-1.20	0.00	136	18	114	23
U09228_at	Rn. 23354	84382	Tcf4	transcription factor 4	-1.18	0.01	421	55	371	102
rc_AA874857_at	Rn. 114933	498407	pur-beta	transcription factor Pur-beta	-1.16	0.00	111	20	97	20
M83107_at	Rn. 34397	25123	Tagln	Transgelin	-1.17	0.00	482	101	408	81
rc_Al639532_at	Rn. 43529	296369	Tnnc2	troponin C2, fast	-1.15	0.00	412	210	349	183
rc_Al169370_at	Rn. 99661	64158	Tubal	tubulin, alpha 1	-1.09	0.00	16608	1110	15260	1350
rc_Al230748_at	Rn. 36610	116646	Tpt1	tumor protein, translationally controlled 1	-1.11	0.00	6404	796	5832	817
rc_Al639378_at	Rn. 40168	362760	Galnt1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetyl-galactosaminyltransferase-like 1	-1.11	0.00	112	11	102	15
rc_Al1071435_at	Rn. 51354	25218	Vps52	vacuolar protein sorting 52 (yeast)	-1.22	0.00	852	79	701	72
M32167_at	Rn.1923	83785	Vegfa	vascular endothelial growth factor A	-1.09	0.00	1166	100	1074	89
M32167_g_at	Rn.1923	83785	Vegfa	vascular endothelial growth factor A 5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	-1.16	0.00	104	25	88	18
D89514_at	Rn. 15114	81643	Atic	ribonucleotide formyltransferase/IMP cyclohydrolase	1.25	0.00	344	47	431	51
U48288_at	Rn. 10557	25228	Akap1	A kinase (PRKA) anchor protein 11	1.24	0.00	345	51	429	59
U67136_at	Rn. 122003	171026	Akap5	A kinase (PRKA) anchor protein 5	1.23	0.00	139	21	175	46
J00692_at	Rn. 82732	29437	Acta1	actin, alpha 1, skeletal muscle	1.10	0.00	366	35	404	68
S56508_s_at	Rn. 33697	117243	Acs16	acyl-CoA synthetase long-chain family member 6	1.15	0.00	617	81	711	121
U90888_at	Rn. 11106	25095	Ampd3	adenosine monophosphate deaminase 3	1.27	0.00	96	14	123	26

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
rc_AA945321_at	Rn.34353	24186	Alb	Albumin	1.06	0.00	427	33	454	49
AF001898_at	Rn.6132	24188	Aldh1a1	aldehyde dehydrogenase family 1, member A1	1.20	0.00	944	179	1129	178
M60322_g_at	Rn.107801	24192	Akr1b4	aldo-keto reductase family 1, member B4 (aldose reductase)	1.19	0.00	520	59	620	95
rc_AA891631_at	Rn.116338	295365	Amigo	amphoretin-induced gene and ORF	1.11	0.00	572	53	638	103
M12112mRNA#3_s_at	Rn.6319	24179	Agt	Angiotensinogen	1.20	0.00	745	259	884	260
rc_AA943892_at	Rn.6319	24179	Agt	Angiotensinogen	1.16	0.00	1780	577	2057	600
D42137exon_s_at	Rn.3318	25673	Anxa5	annexin A5	1.10	0.00	1157	173	1277	258
X55572_at	Rn.11339	25239	Apod	apolipoprotein D	1.25	0.00	2018	598	2492	665
U07201_at	Rn.11172	25612	Asns	asparagine synthetase	1.19	0.00	356	41	425	61
rc_AA859645_at	Rn.53846	83526	Attrn	Attractin	1.26	0.00	493	50	622	96
M60921_g_at	Rn.27923	29619	Btg2	B-cell translocation gene 2, antiproliferative BH3 interacting (with BCL2 family) domain, apoptosis agonist	1.13	0.00	247	21	279	30
rc_AA925846_s_at	Rn.89639	117271	Bid3	Bisphosphate 30-nucleotidase 1	1.09	0.00	673	79	747	151
AJ000347_g_at	Rn.8453	64473	Bpnt1	brain and kidney protein	1.13	0.00	680	65	772	115
U30831_at	Rn.31973	192189	Bk	brain glycogen phosphorylase	1.10	0.00	2315	350	2559	519
rc_AA800190_at	Rn.1518	25739	Pygb	Ca2+-dependent secretion activator	1.10	0.01	1522	220	1672	209
U16802_at	Rn.88197	26989	Cadps	cadherin EGF LAG seven-pass G-type receptor 2	1.08	0.01	1803	221	1935	261
rc_AA875414_at	Rn.2912	83465	Celsr2	calbindin 1	1.14	0.00	963	149	1095	204
M31178_g_at	Rn.3908	83839	Calb1	calcium/calmodulin-dependent protein kinase kinase 1, alpha	1.16	0.00	1252	317	1475	502
S83194_s_at	Rn.4851	60341	Camkk1	calmodulin 1	1.12	0.00	2788	905	3100	1056
X13933_s_at	Rn.4166	24242	Calm1	calponin 3, acidic	1.07	0.01	6373	726	6809	851
rc_AA944422_at	Rn.57635	54321	Cnn3	cAMP responsive element modulator	1.16	0.00	804	140	932	155
S66024_at	Rn.10251	25620	Crem	carbonic anhydrase 6	1.07	0.00	146	14	157	17
rc_AL638943_at	Rn.43383	298657	Car6	Catalase	1.09	0.00	162	13	178	22
M11670_at	Rn.3001	24248	Cat	Catalase	1.18	0.00	111	14	132	20
rc_AA926149_g_at	Rn.3001	24248	Cat	Catalase	1.32	0.00	185	45	242	60
U49062_at	Rn.6007	25145	Cd24	CD24 antigen	1.18	0.00	1045	236	1227	274
U49062_g_at	Rn.6007	25145	Cd24	CD24 antigen	1.09	0.00	591	145	634	116
X53517_at	Rn.2357	29185	Cd37	CD37 antigen	1.08	0.00	351	20	381	29
D29646_at	Rn.11414	25668	Cd38	CD38 antigen	1.13	0.00	94	11	106	14
X13016_at	Rn.3705	245962	Cd48	CD48 antigen	1.18	0.00	88	16	105	29
rc_AA818025_g_at	Rn.1231	25407	Cd59	CD59 antigen	1.10	0.01	1730	220	1909	327
X13044_at	Rn.33804	25599	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.21	0.00	349	126	432	178
X13044_g_at	Rn.33804	25599	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.18	0.00	453	105	547	177

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X14254cds_g_at	Rn.33804	25599	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.12	0.00	451	77	509	106
AB009999_g_at	Rn.18983	81925	Cds1	CDP-diacylglycerol synthase 1	1.09	0.01	1216	182	1333	305
rc_A1176308_at	Rn.60067	64465	Cdc42	cell division cycle 42 homolog (S. cerevisiae)	1.12	0.01	1827	265	2043	345
AF000578_at	Rn.54977	85434	Cdc51	cell division cycle 5-like (S. pombe)	1.10	0.00	228	18	252	31
M95768_at	Rn.11199	81652	Ctbs	chitinase, di-N-acetyl-	1.08	0.00	369	34	401	46
rc_A1169005_at	Rn.4089	65160	Ctbs1a	chloride channel, nucleotide-sensitive, 1A	1.14	0.00	830	67	950	138
rc_AA892559_at	Rn.6067	25707	Ctbf	ciliary neurotrophic factor	1.11	0.00	234	25	260	38
X92097_at	Rn.1022	65165	Rnp24	coated vesicle membrane protein	1.10	0.00	421	49	462	49
L20427_at	Rn.3824	29309	Coq3	coenzyme Q3 homolog, methyltransferase (yeast)	1.07	0.01	664	56	709	82
rc_A1178135_at	Rn.2765	29681	Clqbp	complement component 1, q subcomponent binding protein	1.09	0.00	944	94	1032	157
X71127_at	Rn.6702	29687	Clqb	complement component 1, q subcomponent, beta polypeptide	1.08	0.01	1066	108	1155	180
D88250_at	Rn.4037	192262	ClS	complement component 1, s subcomponent	1.07	0.00	118	11	128	15
M29866_s_at	Rn.11378	24232	C3	complement component 3	1.19	0.00	147	19	176	27
X52477_at	Rn.11378	24232	C3	complement component 3	1.12	0.00	280	26	316	40
D87248_at	Rn.10644	27256	Cntn6	contactin 6	1.09	0.00	178	24	195	32
X59737mRNA_g_at	Rn.155589	29593	Ckmt1	creatine kinase, mitochondrial 1, ubiquitous	1.10	0.01	3684	630	4035	780
M55534mRNA_s_at	Rn.98208	25420	Cryab	crystallin, alpha B	1.32	0.00	827	170	1092	245
X60351cds_s_at	Rn.98208	25420	Cryab	crystallin, alpha B	1.29	0.00	1307	264	1677	347
rc_AA893699_s_at	Rn.4157	362201	Ccndbp1	cyclin D-type binding-protein 1	1.11	0.00	976	92	1089	136
rc_AA866477_at	Rn.2026	303393	Cox7b	cytochrome c oxidase subunit VIIb	1.09	0.01	2623	300	2848	379
U40004_s_at	Rn.91314	313375	Cyp2j9	cytochrome P450, family 2, subfamily j, polypeptide 9	1.08	0.00	267	29	289	30
U36992_at	Rn.53969	25429	Cyp7b1	cytochrome P450, family 7, subfamily b, polypeptide 1	1.12	0.00	493	88	560	125
X59859_i_at	Rn.106103	29139	Den	Decorin	1.12	0.00	736	184	817	162
Z12298cds_s_at	Rn.106103	29139	Den	Decorin	1.17	0.00	536	112	625	132
D86041_at	Rn.7398	64157	Ddah1	Dimethylarginine dimethylaminohydrolase 1	1.21	0.00	997	148	1221	243
rc_A1058941_s_at	Rn.7398	64157	Ddah1	Dimethylarginine dimethylaminohydrolase 1	1.10	0.00	206	22	229	37
AJ011607_g_at	Rn.11846	301323	Prim2	DNA primase, p58 subunit	1.06	0.00	433	36	459	34
rc_A1170685_at	Rn.3904	84026	Dnaj2	Dnaj (Hsp40) homolog, subfamily A, member 2	1.11	0.01	1919	256	2131	322
rc_AA799570_at	Rn.27927	300721	Dnaj4a	Dnaj (Hsp40) homolog, subfamily A, member 4	1.10	0.00	1282	170	1418	239
U15138_at	Rn.31981	81655	Dncl2	dynein, cytoplasmic, light intermediate polypeptide 2	1.09	0.01	4691	641	5078	587

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U08976_at	Rn.6148	64526	Ech1	enoyl coenzyme A hydratase 1, peroxisomal	1.12	0.00	455	52	511	71
M26125_at	Rn.3603	25315	Ephx1	epoxide hydrolase 1, microsomal	1.09	0.01	552	76	606	92
rc_AI031019_at	Rn.9181	64514	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.19	0.00	352	25	417	44
rc_AI031019_g_at	Rn.9181	64514	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.23	0.00	258	15	319	44
rc_AI230914_at	Rn.8873	64511	Fntb	farnesyltransferase, CAAX box, beta	1.17	0.00	779	60	912	86
X73371_at	33323	289211	Fcgr2b	Fc receptor, IgG, low affinity IIb	1.11	0.00	83	6	93	13
rc_AI169802_at	Rn.54447	25319	Fth1	ferritin, heavy polypeptide 1	1.26	0.00	4521	639	5668	729
AJ007291_g_at	30105	117287	ParK7	fertility protein SP22	1.15	0.00	2290	213	2642	331
M84719_at	Rn.867	25256	Fmo1	flavin containing monooxygenase 1	1.13	0.01	278	77	325	123
M59861_at	Rn.2328	64392	Fthfd	Formyltetrahydrofolate dehydrogenase	1.07	0.01	746	111	803	152
L14684_at	Rn.10913	114017	Gfm	G elongation factor	1.18	0.00	234	28	275	40
AF058795_at	Rn.118960	83633	Gpr51	G protein-coupled receptor 51	1.12	0.00	2365	558	2636	680
X15466cnds_at	Rn.114781	25450	Gabbr1	gamma-aminobutyric acid receptor, subunit beta 1	1.21	0.00	1653	291	2002	376
AF028784mRNA#1_s_at	Rn.91512	24387	Gfap	glial fibrillary acidic protein	1.23	0.00	10243	2952	12547	3161
AB008807_at	Rn.25166	114846	Gsto1	glutathione S-transferase omega 1	1.20	0.00	1386	171	1669	222
X04229cnds_s_at	Rn.93760	24423	Gstm1	glutathione S-transferase, mu 1	1.11	0.01	3563	725	3951	672
E01415cnds_s_at	Rn.6036	81869	Gstm3	glutathione S-transferase, mu type 3	1.15	0.00	2997	371	3469	448
L10326_at	Rn.31	24896	Gnas	GNAS complex locus	1.10	0.00	2300	259	2538	434
AF076619_at	Rn.30028	58844	Grb14	growth factor receptor bound protein 14	1.21	0.00	299	38	366	71
X15705cnds_at	Rn.112579	60460	Hspa2	heat shock protein 2	1.27	0.00	159	47	208	81
D17711cnds_s_at	Rn.11854	117282	Hnrpk	heterogenous nuclear ribonucleoprotein K	1.07	0.00	1766	194	1895	200
U09551_at	Rn.89226	27080	Hbp1	high mobility group box transcription factor 1	1.07	0.01	179	15	191	18
rc_AA892014_r_at	Rn.3516	114612	Bat1a	HLA-B-associated transcript 1A	1.06	0.01	212	13	224	18
AF009656mRNA_s_at	Rn.47	24465	Hprt	hypoxanthine guanine phosphoribosyl transferase	1.15	0.00	1046	181	1188	158
Y09507_at	Rn.10852	29560	Hif1a	hypoxia inducible factor 1, alpha subunit	1.10	0.00	471	48	517	57
X96437mRNA_g_at	Rn.23638	294235	Ler3	immediate early response 3	1.11	0.00	240	28	267	42
AF008554_at	Rn.43578	116967	Iag2	Implantation-associated protein	1.18	0.00	189	21	225	42
X56917_at	Rn.9877	81677	Ipkka	inositol 1,4,5-trisphosphate 3-kinase A	1.08	0.00	2083	307	2247	403
X83231_at	Rn.89576	50693	Ith3	inter-alpha trypsin inhibitor, heavy chain 3	1.16	0.00	1528	280	1778	379
AJ222813_s_at	Rn.11118	29197	Il18	interleukin 18	1.15	0.00	203	32	233	34
U77777_s_at	Rn.11118	29197	Il18	interleukin 18	1.17	0.00	91	17	107	27
M58587_at	Rn.1716	24499	Il6r	interleukin 6 receptor	1.11	0.01	309	55	343	59
rc_AA799581_at	Rn.17123	362418	Irak2	interleukin-1 receptor-associated kinase 2	1.08	0.00	632	57	679	67

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
U20181_at	Rn.10132	64831	Ireb2	iron responsive element binding protein 2	1.06	0.01	361	29	383	38
rc_A1231213_g_at	Rn.3022	83628	Kai1	kangai 1	1.11	0.00	909	128	1007	117
rc_A1639470_g_at	Rn.125065	450225	Krt10	keratin 10	1.07	0.01	105	8	113	12
D25224_at	Rn.999	29236	Lamr1	laminin receptor 1 (ribosomal protein SA)	1.08	0.00	3716	323	4049	487
rc_A1232268_at	Rn.10293	116565	Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.15	0.00	779	109	913	197
Z11995cds_at	Rn.10293	116565	Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.08	0.00	223	23	242	25
Z11995cds_g_at	Rn.10293	116565	Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.13	0.00	499	51	567	69
rc_AA892775_at	Rn.2283	25211	Lyz	Lysozyme	1.54	0.00	1177	182	1910	700
rc_A1639359_at	Rn.98599	58808	Mpp4	membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4)	1.08	0.00	78	8	83	8
AF102854_at	Rn.42893	59322	Cnksr2	membrane-associated guanylate kinase-interacting protein	1.08	0.00	696	87	752	104
U05784_s_at	Rn.41412	64862	Map1lc3b	Microtubule-associated proteins 1A/1B light chain 3	1.07	0.00	3095	215	3323	353
M64301_g_at	Rn.88457	58840	Mapk6	mitogen-activated protein kinase 6	1.08	0.01	1053	118	1130	179
rc_A111401_s_at	Rn.27882	29688	Mimp1	multiple inositol polyphosphate histidine phosphatase 1	1.08	0.00	357	32	384	41
L21995_s_at	Rn.9687	24558	Mog	Myelin oligodendrocyte glycoprotein	1.08	0.00	2345	453	2532	471
M99485_at	Rn.9687	24558	Mog	Myelin oligodendrocyte glycoprotein	1.11	0.01	1041	317	1145	300
D14688_s_at	Rn.103179	50685	Mhcb	myosin light chain, regulatory B	1.10	0.00	4342	372	4767	479
U88958_at	Rn.3546	83834	Nrn1	Neuritin	1.10	0.00	4094	1045	4477	1119
rc_AA943331_s_at	Rn.11271	24605	Nras	neuroblastoma ras oncogene	1.07	0.00	370	30	398	34
Z12152_at	Rn.10971	24588	Nef3	neurofilament 3, medium	1.16	0.00	1021	285	1163	300
rc_AA818677_at	Rn.108194	24587	Nefh	neurofilament, heavy polypeptide	1.18	0.00	809	258	931	271
X13804cds_at	Rn.108194	24587	Nefh	neurofilament, heavy polypeptide	1.11	0.00	514	98	561	91
AF031880_at	Rn.18568	83613	Nfl	neurofilament, light polypeptide	1.08	0.01	4871	681	5219	747
D82074_at	Rn.44289	29458	Neurod1	Neurogenic differentiation 1	1.14	0.00	124	23	143	36
rc_A1072943_at	Rn.54707	266777	Nptx1	neuronal pentraxin 1	1.14	0.00	489	147	552	164
Z11504cds_at	Rn.11642	29358	Npy1r	neuropeptide Y receptor Y1	1.08	0.00	296	35	319	44
U66274_at	Rn.10532	25340	Npy5r	neuropeptide Y receptor Y5	1.11	0.00	72	10	79	8
X97121_at	Rn.127792	64636	Ntsr2	neurotensin receptor 2	1.08	0.00	3808	326	4138	492
E03082cds_s_at	Rn.9715	81737	Ntf3	neurotrophin 3	1.07	0.00	121	15	130	23
U31203_at	Rn.10154	25495	Nog	Noggin	1.09	0.00	307	61	333	70
U93197_at	Rn.9783	171116	Opa1	optic atrophy 1 homolog (human)	1.12	0.00	296	33	333	51
M93297cds_at	Rn.1430	64313	Oat	Ornithine aminotransferase	1.11	0.00	899	132	994	143
X07944exon#1-12_s_at	Rn.874	24609	Odc1	Ornithine decarboxylase 1	1.06	0.01	817	91	865	72
rc_A1175539_at	Rn.2005	25269	Pvalb	Parvalbumin	1.16	0.00	1271	527	1451	606

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
AF002281_at	Rn.13361	114108	Pdlim3	PDZ and LIM domain 3	1.15	0.00	129	18	148	17
M57728_g_at	Rn.11175	296588	Pmpca	Peptidase (mitochondrial processing) alpha	1.09	0.00	392	34	427	46
D13907_at	Rn.841	64198	Pmpcb	Peptidase (mitochondrial processing) beta	1.10	0.00	466	48	515	67
D13907_g_at	Rn.841	64198	Pmpcb	Peptidase (mitochondrial processing) beta	1.12	0.00	375	51	421	65
U95920_at	Rn.98622	81740	Pcm1	pericentriolar material 1	1.30	0.00	534	83	693	105
E03344cds_s_at	Rn.4065	29534	Pxmp3	Peroxisomal membrane protein 3	1.08	0.01	135	13	145	17
rc_AA892797_at	Rn.108127	24644	Pgk1	Phosphoglycerate kinase 1	2.14	0.00	2205	508	4687	941
U16655_at	Rn.37434	140693	Pgcd4	phospholipase C, delta 4	1.12	0.00	377	37	425	56
D45920_at	Rn.10684	84587	Picll	phospholipase C-like 1	1.14	0.00	524	106	595	134
rc_AI232379_at	Rn.55127	25267	Pdgfra	platelet derived growth factor receptor, alpha polypeptide	1.13	0.00	230	43	265	76
rc_AA899935_at	Rn.24751	64189	Patfah1b	platelet-activating factor acetylhydrolase, isoform 1b, alpha2 subunit	1.07	0.01	601	70	644	57
AF022819_at	Rn.15693	59324	Kcnk1	potassium channel, subfamily K, member 1	1.08	0.00	1056	184	1135	258
X62840mRNA_s_at	Rn.33095	25327	Kcnc1	potassium voltage-gated channel, Shaw-related subfamily, member 1	1.17	0.00	586	141	679	189
AF033027_at	Rn.6525	64351	Ykt6	prenylated SNARE protein	1.11	0.00	493	52	546	64
D50093_s_at	Rn.3936	24686	Prnp	prion protein	1.10	0.01	4160	504	4561	570
D90265_s_at	Rn.2668	29668	Psmal	proteasome (prosome, macropain) subunit, alpha type 1	1.09	0.00	868	92	951	121
rc_AA891383_i_at	Rn.1276	29672	Psma5	proteasome (prosome, macropain) subunit, alpha type 5	1.55	0.00	127	26	196	33
M86870_at	Rn.39305	116598	Pdia4	protein disulfide isomerase associated 4	1.13	0.00	377	34	425	39
M18330_at	Rn.98279	170538	Ptkcd	protein kinase C, delta	1.14	0.00	247	34	284	54
M13707_at	Rn.9747	24681	Ptkcc	protein kinase C, gamma	1.11	0.00	3374	846	3768	950
AF062740_at	Rn.31799	54705	Ppm2c	protein phosphatase 2C, magnesium dependent, catalytic subunit	1.13	0.00	376	141	429	193
AF062740_g_at	Rn.31799	54705	Ppm2c	protein phosphatase 2C, magnesium dependent, catalytic subunit	1.10	0.01	869	268	968	361
L27843_s_at	Rn.9459	29463	Ptp4a1	protein tyrosine phosphatase 4a1	1.10	0.00	2226	208	2447	287
U40790_at	Rn.10278	29645	Ptpnj	protein tyrosine phosphatase, receptor type, J	1.28	0.00	925	106	1216	294
rc_AI072770_s_at	Rn.4550	24943	Ptp	proteolipid protein	1.14	0.00	6459	1959	7244	1900
D10729_s_at	Rn.29244	24968	Psmb8	proteasome (prosome, macropain) subunit, beta type 8	1.08	0.00	339	36	367	45
J03481mRNA_at	Rn.241	64192	Qdpr	quinoid dihydropteridine reductase	1.18	0.00	830	177	1001	285
J03481mRNA_g_at	Rn.241	64192	Qdpr	quinoid dihydropteridine reductase	1.18	0.00	1944	383	2288	470
M75153_at	Rn.1016	81830	Rab11a	RAB11a, member RAS oncogene family	1.12	0.00	821	101	925	185
rc_AI169372_at	Rn.105901	304268	Ras11a	RAS-like family 11 member A	1.13	0.00	309	49	349	58
AF036548_at	Rn.3504	117183	Rgc32	response gene to complement 32	1.09	0.00	408	47	450	65
AF036548_g_at	Rn.3504	117183	Rgc32	response gene to complement 32	1.14	0.00	1515	210	1730	273
X52817cds_s_at	Rn.55126	116644	Rtn1	reticulon 1	1.14	0.00	6407	742	7327	749
rc_AA900505_at	Rn.2042	64373	Rhob	rhoB gene	1.10	0.01	2569	427	2832	449
X93352_at	Rn.2262	81729	Rpl10a	ribosomal protein L10A	1.12	0.00	3857	408	4323	651
X13549_s_at	Rn.3359	81773	Rps10	ribosomal protein S10	1.10	0.00	4665	461	5131	681

Probe set	Unigene	Entrez gene	Symbol	Gene description	Fold difference	FDR	Mean iP	S.D. iP	Mean iNP	S.D. iNP
L23128_g_at	Rn.107070	24750	RT1-N3	RT1 class Ib gene, H2-TL-like, grc region (N3)	1.22	0.00	564	52	693	83
M15562_at	Rn.103146	294269	RT1-Da	RT1 class II, locus Da	1.17	0.00	308	47	368	96
M15562_g_at	Rn.103146	294269	RT1-Da	RT1 class II, locus Da	1.20	0.00	324	106	405	175
U75928UTR#1_s_at	Rn.98989	24791	Sparc	secreted acidic cysteine rich glycoprotein	1.19	0.00	2761	915	3269	935
M63901_at	Rn.6173	25719	Sgne1	secretory granule neuroendocrine protein 1	1.10	0.00	1081	110	1185	121
M63901_g_at	Rn.6173	25719	Sgne1	secretory granule neuroendocrine protein 1	1.09	0.00	4179	457	4561	570
AB011530_at	Rn.30002	65047	Slit1	slit homolog 1 (Drosophila)	1.17	0.00	616	65	728	106
rc_AI145680_s_at	Rn.6085	25027	Slc16a1	solute carrier family 16 (monocarboxylic acid transporters), member 1	1.09	0.00	884	72	963	115
Y16774_at	Rn.90036	64469	Slc30a4	solute carrier family 30 (zinc transporter), member 4	1.09	0.00	296	43	322	56
rc_AI639256_at	Rn.40672	301255	Spats1	spermatogenesis associated, serine-rich 1	1.28	0.00	160	19	204	29
U83883_at	Rn.36148	64635	Snd1	staphylococcal nuclease domain containing 1	1.13	0.00	973	123	1105	129
M15114_g_at	Rn.83595	83792	Scd2	stearyl-Coenzyme A desaturase 2	1.08	0.00	6769	655	7301	851
X99337cds_s_at	Rn.37476	56064	Sdfr1	stromal cell derived factor receptor 1	1.10	0.00	1369	160	1507	212
X99338cds_i_at	Rn.37476	56064	Sdfr1	stromal cell derived factor receptor 1	1.09	0.00	2601	296	2832	346
M27925_at	Rn.506	29179	Syn2	synapsin II	1.17	0.00	860	150	1014	211
L10362_at	Rn.58137	117556	Sv2b	synaptic vesicle glycoprotein 2b	1.11	0.01	1702	358	1888	396
rc_AI639484_at	Rn.58137	117556	Sv2b	synaptic vesicle glycoprotein 2b	1.09	0.00	3424	586	3738	811
U40188_at	Rn.11270	171152	Taf9l	TAF9-like RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31kDa	1.14	0.00	110	11	126	17
rc_AA893860_at	Rn.22757	294810	Tars	threonyl-tRNA synthetase	1.08	0.00	655	73	710	87
K01934mrRNA#2_at	Rn.81140	25357	Thrsp	thyroid hormone responsive protein	1.09	0.00	362	66	394	75
U09256_at	Rn.5950	64524	Tkt	transketolase	1.11	0.00	1117	94	1240	136
L04760_at	Rn.6763	81002	Trim23	tripartite motif protein 23	1.07	0.01	415	40	446	57
AB011679_at	Rn.2458	29214	Tubb5	tubulin, beta 5	1.16	0.00	336	57	387	43
rc_AI103911_at	Rn.2603	291103	Uqerf1	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	1.08	0.00	1213	97	1313	165
U14746_at	Rn.11059	24874	Vhl	von Hippel-Lindau syndrome homolog	1.10	0.00	585	62	646	109
rc_AA946044_s_at	Rn.4338	81515	Lyn	Yamaguchi sarcoma viral (v-yes-1) oncogene homolog	1.10	0.00	85	7	93	7
U67082_at	Rn.10663	25165	Znf386	zinc finger protein 386 (Kruppel-like)	1.15	0.00	201	22	232	31

S.D. = standard deviation; FDR = false discovery rate; iP = inbred alcohol-prefering rat; iNP = inbred alcohol-non-prefering rat; RMA = Robust multi-chip average.

Positive fold difference is iP/iNP; negative is iNP/iP.

Expression levels are those obtained after RMA background correction and scaling as indicated in Methods.

Table 5

Significant fold differences in combined region analysis and in individual region analyses

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
D00512_at	Rn.4054	25014	8	-57,063,521		Acat1	acetyl-coenzyme A acetyltransferase 1	-1.11				
D90109_at	Rn.6215	25288	16	-49,036,966	Alc7 & 11	Acs11	acyl-CoA synthetase long-chain family member 6		1.27			
S56508_s_at	Rn.33697	117243	10	39,743,427		Acs16	acyl-CoA synthetase long-chain family member 6					
I00692_at	Rn.82732	29437	19	-54,086,370		Acta1	actin, alpha 1, skeletal muscle	1.15				
Re_AA891812_at	Rn.5788	24170	14	-81,752,822		Add1	adducin 1 (alpha)	1.10				
X83715_at	Rn.5788	24170	14	-81,752,822		Add1	adducin 1 (alpha)	-1.09				
S47609_s_at	Rn.11180	25369	20	-13,815,945		Adora2a	adenosine A2a receptor	-1.14				
M12112mRNA#3_s_at	Rn.6319	24179	19	-54,743,436		Agt	angiotensinogen	-1.08				
Re_AA943892_at	Rn.6319	24179	19	-54,743,436		Agt	angiotensinogen	1.20				
Re_A1639111_at	Rn.93081	308923	1	16,332,862		Abi1	Abelson helper integration site 1	1.16				
U48288_at	Rn.10557	25228	2	0		Akap11	A kinase (PRKA) anchor protein 11	-1.46	-1.54	-1.35		-1.48
U67136_at	Rn.122003	171026	6	98,926,570	Alc17	Akap5	A kinase (PRKA) anchor protein 5	1.24	1.50			1.32
M60322_g_at	Rn.107801	24192	4	-61,921,567	Alc14 & 16	Akr1b4	aldo-keto reductase family 1, member B4 (aldose reductase)	1.23				
D17309_at	Rn.25716	192242	4	65,249,037	Alc14 & 16	Akr1d1	aldo-keto reductase family 1, member D1	1.19				
D30041_at	Rn.87066	25233	1	82,764,343		Akt2	thymoma viral proto-oncogene 2	-1.09				
D86297_at	Rn.32517	25748	X	39,853,992		Alas2	aminolevulinic acid synthase 2	-1.11				
Re_AA945321_at	Rn.34353	24186	14	-19,126,964		Alb	albumin	-1.14				
AF001898_at	Rn.6132	24188	1	223,895,697		Aldh1a1	aldehyde dehydrogenase family 1, member A1	1.06				
Re_AA891631_at	Rn.116338	295365	2	203,715,385	Alc15	Amigo	amphoretin-induced gene and ORF	1.20				
U90888_at	Rn.11106	25095	1	168,644,154		Ampo3	adenosine monophosphate deaminase 3	1.11		1.22		
D42137exon_s_at	Rn.3318	25673	2	-122,894,171		Anxa5	annexin A5	1.27	1.37			
Re_A1170212_s_at	Rn.11007	140667	16	73,688,647		Ap3m2	adaptor-related protein complex 3, mu 2 subunit	1.10				
AF029107_at	Rn.62687	83610	1	119,049,224		Apha2	amyloid beta (A4) precursor protein-binding, family A, member 2	-1.12				
L07114_at	Rn.10002	25383	4	-159,278,107	Alc18	Apobec1	apolipoprotein B editing complex 1	-1.13				
X55572_at	Rn.11339	25239	11	882,464		Apod	apolipoprotein D	-1.15				
AF026505_at	Rn.24612	114901	16	-49,722,613	Alc7 & 11	Argbp2	Arg/Abl-interacting protein ArgBP2	1.25		1.21		
Re_AA891194_s_at	Rn.24612	114901	16	-49,722,613	Alc7 & 11	Argbp2	Arg/Abl-interacting protein ArgBP2	1.22		1.22		
Re_A1639196_at	Rn.33757	66013	X	-82,667,647		Arhgef9	Cdc42 guanine nucleotide exchange factor (GEF) 9	-1.22				
U07201_at	Rn.11172	25612	4	-32,877,146		Asns	asparagine synthetase	1.19		1.25		
D89514_at	Rn.15114	81643	9	70,823,725		Atic	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	1.25			1.32	
J04024_at	Rn.2305	29693	12	35,129,987	Alc6 & 10	Aip2a2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	1.25				
Re_AA859645_at	Rn.53846	83526	3	118,444,840		Airn	attractin	-1.13				
Re_AA893602_at	Rn.14812	316051	8	122,981,038		Azi2	5-azacytidine induced gene 2	1.26		1.33		-1.28
Re_A1170268_at	Rn.1868	24223	3	108,833,491		B2m	beta-2 microglobulin	-1.23				
Re_AA892014_r_at	Rn.3516	114612	20	-3,611,355		Bat1a	HLA-B-associated transcript 1A	-1.18				
U72350_at	Rn.10323	24888	3	-143,034,710		Bcl2l1	Bcl2-like 1	1.06				
U34963_s_at	Rn.10323	24888	3	-143,034,710		Bcl2l1	Bcl2-like 1	-1.07				
AF065431_s_at	Rn.82709	64547	3	115,597,895		Bcl2l11	BCL2-like 11 (apoptosis facilitator)	-1.11				
Re_AA925846_s_at	Rn.89639	117271	12	-39,383,652	Alc10	Bid3	BH3 interacting (with BCL2 family) domain, apoptosis agonist	-1.08				
U30831_at	Rn.31973	192189	1	-176,738,853		Bkl	brain and kidney protein	1.09				
D63860_s_at	Rn.53974	25667	14	-12,065,634		Bmp3	bone morphogenetic protein 3	1.10				
AJ000347_g_at	Rn.8453	64473	13	101,540,167		Bpnt1	bisphosphate 3 -nucleotidase 1	1.06				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
M60921_g_at	Rn.27923	29619	13	-47,041,028		Big2	B-cell translocation gene 2, antiproliferative complement component 1, q subcomponent, beta polypeptide	1.13		1.19		
X71127_at	Rn.6702	29687	5	-155,657,561	Alc4	Clqb	complement component 1, q subcomponent binding protein	1.08				
Rc_A1178135_at	Rn.2765	29681	10	-57,895,408		Clqbp	complement component 1, q subcomponent binding protein	1.09				
D88250_at	Rn.4037	192262	4	-160,981,068	Alc18	Clis	complement component 1, s subcomponent	1.07				
M29866_s_at	Rn.11378	24232	9	-64,513,131		C3	complement component 3	1.19				
X52477_at	Rn.11378	24232	9	-64,513,131		C3	complement component 3	1.12				
U16802_at	Rn.88197	26989	15	13,859,285		Cadps	Ca ²⁺ -dependent secretion activator	1.08				
M31178_g_at	Rn.3908	83839	5	-198,836,347	Alc4	Calb1	calbindin 1	1.16				
X13933_s_at	Rn.4166	24242	6	124,481,414	Alc17	Calml1	calmodulin 1	1.07				
S83194_s_at	Rn.4851	60341	10	59,922,371		Camkk1	calcium/calmodulin-dependent protein kinase kinase 1, alpha	1.12				
rc_A1638943_at	Rn.43383	298657	5	0	Alc4	Car6	carboxic anhydrase 6	1.09				
U84410_s_at	Rn.10562	25402	16	-48,944,301	Alc7 & 11	Casp3	caspase 3, apoptosis related cysteine protease	1.21				
rc_AA926149_g_at	Rn.3001	24248	3	88,550,504		Cat	catalase	1.32	1.42			
M11670_at	Rn.3001	24248	3	88,550,504		Cat	catalase	1.18				
rc_AA893699_s_at	Rn.4157	362201	3	107,683,801		Cendbp1	cyclin D-type binding-protein 1	1.11				
U49062_at	Rn.6007	25145	20	47,531,055	Cd24	Cd24	CD24 antigen	1.18				
U49062_g_at	Rn.6007	25145	20	47,531,055	Cd24	Cd24	CD24 antigen	1.09				
X53517_at	Rn.2357	29185	1	-95,788,071		Cd37	CD37 antigen	1.08		1.32		
D29646_at	Rn.11414	25668	14	-72,322,869		Cd38	CD38 antigen	1.13		1.24		
X13016_at	Rn.3705	245962	13	87,873,428		Cd48	CD48 antigen	1.18				
rc_AA818025_g_at	Rn.1231	25407	3	89,140,026		Cd59	CD59 antigen	1.10				
X13044_at	Rn.33804	25599	18	56,828,742		Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.21				
X13044_g_at	Rn.33804	25599	18	56,828,742		Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.18				
X14254cdis_g_at	Rn.33804	25599	18	56,828,742		Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.12				
rc_A1176308_at	Rn.60067	64465	5	156,116,164	Alc4	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)	1.12				
AF000578_at	Rn.54977	85434	9	11,162,952		Cdc51	cell division cycle 42 homolog (S. cerevisiae)	1.10				
D83349_at	Rn.	29182	6	-156,062,114	Alc17	Cdh22	cadherin 22	1.43				
L41275cdis_s_at	Rn.10089	114851	20	7,376,551		Cdkn1a	cyclin-dependent kinase inhibitor 1A	-1.11				
AB009999_g_at	Rn.18983	81925	14	-9,072,988		Cds1	CADP-diacylglycerol synthase 1	1.09				
rc_AA875414_at	Rn.2912	83465	2	0		Celsr2	cadherin EGF LAG seven-pass G-type receptor 2	1.14		1.25		
AF019974_at	Rn.11090	24259	3	120,477,308		Chgb	chromogranin B	1.14		1.25		
X59737mRNA_g_at	Rn.	155589	3	108,058,997		Ckmt1	creatine kinase, mitochondrial 1, ubiquitous	1.10				
rc_A1169005_at	Rn.4089	65160	1	155,025,118		Clns1a	chloride channel, nucleotide-sensitive, 1A	1.14				
AF102854_at	Rn.42893	59322	X	58,251,535		Cnksr2	membrane-associated guanylate kinase-interacting protein	1.08				
rc_AA944422_at	Rn.57635	54321	2	218,007,864	Alc15	Cnm3	calponin 3, acidic	1.16				
rc_AA892559_at	Rn.6067	25707	1	-216,001,097		Cntf	ciliary neurotrophic factor	1.11				
D87248_at	Rn.10644	27256	4	140,322,847	Alc14 & 16	Cntn6	contactin 6	1.09				
L20427_at	Rn.3824	29309	5	36,640,896	Alc4	Coq3	coenzyme Q3 homolog, methyltransferase (yeast)	1.07				
rc_AA866477_at	Rn.2026	303393	X	94,211,488		Cox7b	cytochrome c oxidase subunit VIIb	1.09				
S66024_at	Rn.10251	25620	17	62,793,252		Crem	cAMP responsive element modulator	1.07				
J02844_s_at	Rn.4896	83842	4	-22,023,912		Crot	carnitine O-octanoyltransferase	-1.12				
U26033_at	Rn.4896	83842	4	-22,023,912		Crot	carnitine O-octanoyltransferase	-1.15				
M55534mRNA_s_at	Rn.98208	25420	8	54,126,302		Cryab	crystallin, alpha B	1.32				
X60351cdis_s_at	Rn.98208	25420	8	54,126,302		Cryab	crystallin, alpha B	1.29				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
rc_AI013513_at	Rn.8046	64462	10	-110,177,115		Csnk1d	casein kinase 1, delta	-1.10				
M95768_at	Rn.11199	81652	2	244,635,104		Ctbs	chitinase, di-N-acetyl-	1.08		-1.18		
U40004_s_at	Rn.91314	313375	5	-116,749,562	Alc4	Cyp2j9	cytochrome P450, family 2, subfamily j, polypeptide 9	1.08				
U36992_at	Rn.53969	25429	2	0		Cyp7b1	cytochrome P450, family 7, subfamily b, polypeptide 1	1.12				
L33894_at	Rn.10058	79127	14	-20,886,695		Dck	deoxycytidine kinase	-1.12				
Z12298cds_s_at	Rn.106103	29139	7	35,024,504		Den	decorin	1.17				1.29
X59859_i_at	Rn.106103	29139	7	35,024,504		Den	decorin	1.12				
D86041_at	Rn.7398	64157	2	243,918,960		Ddah1	dimethylarginine dimethylaminohydrolase 1	1.21				
rc_AI058941_s_at	Rn.7398	64157	2	243,918,960		Ddah1	dimethylarginine dimethylaminohydrolase 1	1.10				
rc_AA894273_at	Rn.7398	64157	2	243,918,960		Ddah1	dimethylarginine dimethylaminohydrolase 1	-1.19				
AF016247_at	Rn.92730	83573	13	0		Ddr2	discoidin domain receptor family, member 2			-1.18		
rc_AI170685_at	Rn.3904	84026	19	22,858,527		Dnaj2	DnaJ (Hsp40) homolog, subfamily A, member 2	1.11				
rc_AA799570_at	Rn.27927	300721	8	58,269,846		Dnaj4	DnaJ (Hsp40) homolog, subfamily A, member 4	1.10				
U15138_at	Rn.31981	81655	19	469,162		Dncl2	dynen, cytoplasmic, light intermediate polypeptide 2	1.09				
D85035_g_at	Rn.133148	81656	2	214,894,962	Alc15	Dpyd	dihydropyrimidine dehydrogenase	-1.11				
Z46882cds_at	Rn.2889	25416	15	0		Dpysl2	dihydropyrimidine-like 2	-1.10				
AF013144_at	Rn.10877	171109	1	259,965,278		Dusp5	dual specificity phosphatase 5	-1.07				
X94185cds_s_at	Rn.4313	116663	7	36,913,534		Dusp6	dual specificity phosphatase 6	-1.28				
U08976_at	Rn.6148	64526	1	84,010,830		Ech1	enoyl coenzyme A hydratase 1, peroxisomal	1.12				
D89730_g_at	Rn.8037	305604	14	109,759,971		Efemp1	epidermal growth factor-containing fibulin-like extracellular matrix protein 1	-1.13				
D89730_at	Rn.8037	305604	14	109,759,971		Efemp1	epidermal growth factor-containing fibulin-like extracellular matrix protein 1	-1.15				
rc_AA893770_g_at	Rn.144669	245963	3	4,760,573		Egfr7	EGF-like domain 7	-1.07				
rc_AI031019_g_at	Rn.9181	64514	12	33,001,710	Alc6 & 10	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.23		1.29		
rc_AI031019_at	Rn.9181	64514	12	33,001,710	Alc6 & 10	Eif2b1	eukaryotic translation initiation factor 2B, subunit 1 alpha	1.19		1.17		
X02610_g_at	Rn.4236	24333	5	167,404,823	Alc4	Eno1	enolase 1, alpha	-1.11				
X02610_at	Rn.4236	24333	5	167,404,823	Alc4	Eno1	enolase 1, alpha	-1.15				
X78689cds_at	Rn.24569	79208	14	0		Epha5	EphA5	-1.11				
X59290mRNA_at	Rn.62934	60589	5	0	Alc4	Epha8	Eph receptor A8	-1.08				
M26125_at	Rn.3603	25315	13	-96,911,908		Ephx1	epoxide hydrolase 1, microsomal	1.09				
U07619_at	Rn.9980	25584	2	218,334,111		F3	coagulation factor III	-1.19				
X73371_at	Rn.33323	289211	13	-86,823,198	Alc15	Fcgr2b	Fc receptor, IgG, low affinity IIb	1.11		-1.21		
D12498_s_at	Rn.9797	79114	16	-70,870,238		Fgf1	Fibroblast growth factor receptor 1	-1.11				
M91599mRNA_at	Rn.24104	25114	17	0		Fgf4	fibroblast growth factor receptor 4	-1.09				
M84719_at	Rn.867	25256	13	-78,517,957		Fmo1	flavin containing monooxygenase 1	1.13				
X05834_at	Rn.1604	25661	9	-70,849,162		Fnl	fibronectin 1	-1.34		-1.32		-1.55
U82612cds_g_at	Rn.1604	25661	9	-70,849,162		Fnl	fibronectin 1	1.15		1.25		
rc_AA955600_at	Rn.1604	25661	9	-70,849,162		Fnl	fibronectin 1	-1.07				
M28259cds_at	Rn.1604	25661	9	-70,849,162		Fnl	fibronectin 1	1.13				
L00191cds#1_s_at	Rn.1604	25661	9	-70,849,162		Fnl	fibronectin 1	-1.27				
rc_AI230914_at	Rn.8873	64511	6	99,431,422	Alc17	Fntb	farnesyltransferase, CAAX box, beta	1.17				
L27421_at	Rn.62653	65153	3	10,200,569		Freq	frequency homolog (Drosophila)	-1.22				
rc_AI169802_at	Rn.54447	25319	1	212,588,882		Fth1	ferritin, heavy polypeptide 1	1.26		1.29		
M59861_at	Rn.2528	64392	0	0		Fthfd	formyltetrahydrofolate dehydrogenase	1.07				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
X15466cds_at	Rn.114781	25450	14	-38,532,649		Gabbr1	gamma-aminobutyric acid receptor, subunit beta 1	1.21				
rc_AI639378_at	Rn.40168	362760	6	0	Alc17	Galnt11	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase-like 1	-1.11				
rc_AA859837_g_at	Rn.24783	83585	1	-224,743,773		Gda	guanine deaminase	-1.21				
rc_AA859837_at	Rn.24783	83585	1	-224,743,773		Gda	guanine deaminase	-1.28				
AF028784mRNA#1_s_at	Rn.91512	24387	10	-92,074,249		Gfap	glial fibrillary acidic protein	1.23			1.44	
L06986_at	Rn.10935	24388	14	2,597,302		Gfi1	growth factor independent 1	-1.09				
L14684_at	Rn.10913	114017	2	157,233,008		Gfm	G elongation factor	1.18		1.30		
X55246_at	Rn.10109	25674	10	-40,936,489		Gfml	glycine receptor, alpha 1 subunit	-1.11				
M17526_g_at	Rn.90161	50664	19	-11,476,908		Gnao	guanine nucleotide binding protein, alpha o	-1.26				
L10326_at	Rn.31	24896	3	0		Gnas	GNAS complex locus	1.10				
L02896_at	Rn.7044	58920	0	0		Gpc1	glypican 1	-1.12				
AF058795_at	Rn.118960	83633	5	-63,241,575	Alc4	Gpr51	G protein-coupled receptor 51	1.12				1.32
AF076619_at	Rn.30028	58844	3	-46,728,757		Grb14	growth factor receptor bound protein 14	1.21				
M92076_at	Rn.41715	24416	4	0		Grm3	glutamate receptor, metabotropic 3	-1.31				
X96790_at	Rn.10409	81672	4	146,577,418	Alc14 & 16	Grm7	glutamate receptor, metabotropic 7	-1.08			-1.7	
X62660mRNA_g_at	Rn.57528	300850	8	0		Gsta4	glutathione S-transferase, alpha 4	-1.81	-1.52	-1.78	5	-2.07
X62660mRNA_at	Rn.57528	300850	8	0		Gsta4	glutathione S-transferase, alpha 4	-1.29		-1.32		-1.36
X04229cds_s_at	Rn.93760	24423	2	-203,538,197	Alc15	Gstm1	glutathione S-transferase, mu 1	1.11				
E01415cds_s_at	Rn.6036	81869	2	-203,454,119	Alc15	Gstm3	glutathione S-transferase, mu type 3	1.15				
AB008807_at	Rn.25166	114846	1	253,493,290		Gsto1	glutathione S-transferase omega 1	1.20				
X56325mRNA_s_at	Rn.107334	25632	10	-15,585,407	Alc5 & 9	Hba-a1	hemoglobin alpha, adult chain 1	-1.19				
M94918mRNA_f_at	Rn.36966	24440	1	-161,666,147		Hbb	hemoglobin beta chain complex	-1.21				
U09551_at	Rn.89226	27080	6	-50,204,414	Alc17	Hbp1	high mobility group box transcription factor 1	1.07				
D13417_g_at	Rn.19727	29577	11	-72,661,439		Hes1	hairy and enhancer of split 1 (Drosophila)	-1.08				
Y09507_at	Rn.10852	29560	6	96,422,479	Alc17	Hif1a	hypoxia inducible factor 1, alpha subunit	1.10				
U89695_at	Rn.29981	84017	7	-59,659,284		Hmg2	high mobility group AT-hook 2	-1.07				
X55286_g_at	Rn.9437	25675	2	-27,047,872		Hmgcr	3-hydroxy-3-methylglutaryl-Coenzyme A reductase		-1.28			
M33648_at	Rn.29594	24450	2	193,091,489		Hmgcs2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-1.07				
M33648_g_at	Rn.29594	24450	2	193,091,489		Hmgcs2	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2	-1.15				1.31
D17711cds_s_at	Rn.11854	117282	17	12,196,629		Hnrpk	heterogenous nuclear ribonucleoprotein K	1.07				
U16845_at	Rn.10075	50864	8	-28,587,115		Hnt	neurotrophin	-1.43				
AB007689_g_at	Rn.30014	29547	1	-137,905,533		Homer2	homer homolog 2 (Drosophila)	-1.09				
AF009656mRNA_s_at	Rn.47	24465	X	140,003,079		Hprt	hypoxanthine guanine phosphoribosyl transferase	1.15				
X15705cds_at	Rn.112579	60460	6	99,003,760	Alc17	Hspa2	heat shock protein 2	1.27				
AF008554_at	Rn.43578	116967	X	-94,168,934		Lag2	implantation-associated protein	1.18				
U77777_s_at	Rn.11118	29197	8	53,955,637		Il18	interleukin 18	1.17				
AJ222813_s_at	Rn.11118	29197	8	53,955,637		Il18	interleukin 18	1.15				
M58587_at	Rn.1716	24499	2	-182,028,156		Il6r	interleukin 6 receptor	1.11				
rc_AA799581_at	Rn.17123	362418	4	149,787,869	Alc14 & 16	Irak2	interleukin-1 receptor-associated kinase 2	1.08		1.22		
U20181_at	Rn.10132	64831	8	58,452,371		Ireb2	iron responsive element binding protein 2	1.06				
rc_AA893384_g_at	Rn.1499	292892	1	95,548,394		Irf3	interferon regulatory factor 3	1.06				
X83231_at	Rn.89576	50693	16	6,341,044	Alc7, 11, & 13	Irfh3	inter-alpha trypsin inhibitor, heavy chain 3	1.16				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
X56917_at	Rn.9877	81677	3	106,153,909		Ipkka	inositol 1,4,5-trisphosphate 3-kinase A	1.08				
rc_AI231213_g_at	Rn.3022	83628	3	-77,728,200		Kai1	kangai 1	1.11				
rc_AI639313_at	Rn.87882	84009	11	68,205,034		Kalm	kalirin, RhoGEF kinase	1.09				
X62840mRNA_s_at	Rn.33095	25327	1	97,006,385		Kenc1	potassium voltage-gated channel, Shaw-related subfamily, member 1	1.17				
AJ007627_at	Rn.144567	27150	7	138,061,054		Kcnh3	potassium voltage-gated channel, subfamily H (eag-related), member 3	-1.09				
AF022819_at	Rn.15693	59324	19	56,221,480		Kcnk1	potassium channel, subfamily K, member 1	1.08				
U93306_at	Rn.88869	25589	14	0		Kdr	kinase insert domain protein receptor	1.28	1.50			
AF071204_at	Rn.44216	60427	7	37,734,427		Kitl	kit ligand	1.07				
AF071204_g_at	Rn.44216	60427	7	37,734,427		Kitl	kit ligand	-1.09				
K02814_at	Rn.128333	24903	11	80,167,087		King1	kininogen 1	1.09				
rc_AI639470_g_at	Rn.125065	450225	10	-88,302,989		Krt10	keratin 10	1.07				
D25224_at	Rn.999	29236	8	125,119,975		Lamr1	laminin receptor 1 (ribosomal protein SA)	1.08				
rc_AA892316_at	Rn.1057	155918	10	19,021,026	Alc9 & 12	Lcp2	lymphocyte cytosolic protein 2			1.18		
U07181_g_at	Rn.1785	24534	4	180,306,690	Alc18	Ldhb	lactate dehydrogenase B	1.11		1.23		
X96437mRNA_g_at	Rn.23638	294235	20	-3,076,800		Ler3	immediate early response 3	-1.16				
AF090134_at	Rn.31766	85327	7	45,990,892		Lin7a	lin-7 homolog a (C. elegans)	-1.35				
AF090136_at	Rn.44269	60442	3	95,224,369		Lin7c	lin-7 homolog C (C. elegans)		-1.51	-1.27		
S66184_s_at	Rn.11372	24914	18	-47,931,499		Lox	lysyl oxidase			1.22		
rc_AI232268_at	Rn.10293	116565	14	0		Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.15				
Z11995cds_g_at	Rn.10293	116565	14	0		Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.13				
Z11995cds_at	Rn.10293	116565	14	0		Lrpap1	low density lipoprotein receptor-related protein associated protein 1	1.08				1.34
X76985_at	Rn.11404	59073	2	-157,259,999		Lxn	lathexin	-1.19				
rc_AA946044_s_at	Rn.4338	81515	5	16,933,105	Alc4	Lyn	Yamaguchi sarcoma viral (v-yes-1) oncogene homolog	1.10				
rc_AA892775_at	Rn.2283	25211	7	-56,628,438		Lyz	lysozyme	1.54	2.11	1.81		
U05784_s_at	Rn.41412	64862	19	51,852,067		Map1lc3b	microtubule-associated proteins 1A/1B light chain 3	1.07				
M64301_g_at	Rn.88457	58840	8	-80,231,782		Mapk6	mitogen-activated protein kinase 6	1.08				
rc_AI227608_s_at	Rn.2455	29477	10	93,425,375		Mapt	microtubule-associated protein tau	-1.29				
AF095741_at	Rn.11802	171451	13	-100,998,349		Mg87	Mg87 protein	-1.11				
rc_AA892864_at	Rn.40396	29254	4	123,066,973	Alc14 & 16	Mgl1	monoglyceride lipase	-1.11				
rc_AI111401_s_at	Rn.27882	29688	1	0		Mimpp1	multiple inositol polyphosphate histidine phosphatase 1	1.08				
M15944_at	Rn.33598	24590	2	152,981,686		Mime	membrane metallo endopeptidase	-1.05				
M99485_at	Rn.9687	24558	20	1,601,730		Mog	myelin oligodendrocyte glycoprotein	1.11				
L21995_s_at	Rn.9687	24558	20	1,601,730	Mog	Mog	myelin oligodendrocyte glycoprotein	1.08				
rc_AI639359_at	Rn.98599	58808	9	-57,843,928		Mpp4	membrane protein, palmitoylated 4 (MAGUK p55 subfamily member 4)	1.08				
D14688_s_at	Rn.103179	50685	9	-110,380,900		Mrlcb	myosin light chain, regulatory B	1.10				
X06564_at	Rn.11283	24586	8	-52,841,403		Ncam1	neural cell adhesion molecule 1	-1.20				
Z12152_at	Rn.10971	24588	15	-47,714,153		Nef3	neurofilament 3, medium	1.16				
rc_AA818677_at	Rn.108194	24587	14	-85,614,415		Nefh	neurofilament, heavy polypeptide	1.18				
X13804cds_at	Rn.108194	24587	14	-85,614,415		Nefh	neurofilament, heavy polypeptide	1.11				
D82074_at	Rn.44289	29458	3	-62,121,015		Neurod1	neurogenic differentiation 1	1.14				
M82826_i_at	Rn.10686	24592	10	65,545,464		Nf1	neurofibromatosis 1	-1.16				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
AF031880_at	Rn.18568	83613	15	47,652,082		Nfi	neurofilament, light polypeptide	1.08				
U31203_at	Rn.10154	25495	10	0		Nog	noggin	1.09				
rc_AI072943_at	Rn.54707	266777	10	-108,933,164		Npx1	neuronal pentraxin 1	1.14		1.32		
M15880_at	Rn.9714	24604	4	78,314,142	Alc14 & 16	Npy	neuropeptide Y	-1.14				
Z11504cds_at	Rn.11642	29358	16	-24,747,181	Alc7 & 11	Npy1r	neuropeptide Y receptor Y1	1.08				
U66274_at	Rn.10532	25340	16	24,765,172	Alc7 & 11	Npy5r	neuropeptide Y receptor Y5	1.11				
rc_AA943331_s_at	Rn.11271	24605	2	198,255,369		Nras	neuroblastoma ras oncogene	1.07				
U88958_at	Rn.3546	83834	0	0		Nrn1	neurtin	1.10		1.19		
L14851_at	Rn.10926	116508	6	112,277,485	Alc17	Nrxn3	neurexin 3	-1.11				
V01543mRNA_at	Rn.2865	25247	14	77,934,337		Nsg1	neuron specific gene family member 1	-1.07				
E03082cds_s_at	Rn.9715	81737	4	-162,680,717	Alc18	Nuf3	neurotrophin 3	1.07				
M86742cds_s_at	Rn.44225	25730	1	95,963,687		Nuf5	neurotrophin 5	-1.06				
X97121_at	127792	64636	0	0		Ntsr2	neurotensin receptor 2	1.08				
rc_AI176253_at	Rn.133954	59319	3	0		Nyw1	ischemia related factor NYW-1		-1.38			
M93297cds_at	Rn.1430	64313	1	-192,176,503		Oat	ornithine aminotransferase	1.11				
X07944exon#1-12_s_at	Rn.874	24609	6	41,312,265	Alc17	Odc1	ornithine decarboxylase 1	1.06				
U93197_at	Rn.9783	171116	11	-73,063,058		Opal1	optic atrophy 1 homolog (human)	1.12				
U47031_at	Rn.7176	29659	12	-34,807,290	Alc6 & 10	P2rx4	purinergic receptor P2X, ligand-gated ion channel 4	-1.08				
rc_AA899935_at	Rn.24751	64189	8	-48,947,322		Pafah1b2	platelet-activating factor acetylhydrolase, isoform 1b, alpha2 subunit	1.07				
U55345_s_at	Rn.3840	29432	11	70,587,549		Pak2	p21 (CDKN1A)-activated kinase 2	-1.20				
AJ007291_g_at	Rn.30105	117287	5	-168,060,336	Alc4	Park7	fertility protein SP22	1.15				
rc_AA891220_at	Rn.7264	297508	6	51,132,285	Alc17	Pbef1	pre-B-cell colony enhancing factor 1	1.25				
U95920_at	Rn.98622	81740	16	0		Pcm1	pericentriolar material 1	1.30		1.52		
rc_AI232379_at	Rn.55127	25267	14	0		Pdgfra	platelet derived growth factor receptor, alpha polypeptide	1.13				
M86870_at	Rn.39305	116598	4	-76,205,527	Alc14 & 16	Pdia4	protein disulfide isomerase associated 4	1.13				
AF002281_at	Rn.13361	114108	16	-49,637,142	Alc7 & 11	Pdlim3	PDZ and LIM domain 3	1.15		1.28		
U77697_at	Rn.1878	29583	0	-96,070,590		Pecam	platelet/endothelial cell adhesion molecule	-1.14				
D63673_at	Rn.10675	117265	9	10,081,699		Pex6	peroxisomal biogenesis factor 6	-1.08				
rc_AA892797_at	108127	24644	X	94,397,574		Pgk1	phosphoglycerate kinase 1	2.14	2.05	2.08	2.08	2.28
X97772_at	Rn.6872	58835	2	-193,110,696		Phgdh	3-phosphoglycerate dehydrogenase	-1.33				
X97772_g_at	Rn.6872	58835	2	-193,110,696		Phgdh	3-phosphoglycerate dehydrogenase	-1.31			-1.4	
rc_AI008677_s_at	Rn.6872	58835	2	-193,110,696		Phgdh	3-phosphoglycerate dehydrogenase	-1.27			2	
M98826mRNA_g_at	Rn.10399	29353	12	-27,893,003	Alc10	Phkg1	phosphorylase kinase gamma 1	-1.08				
L14003UTR#1_f_at	Rn.54456	25046	13	43,799,887		Ptgr	polymeric immunoglobulin receptor	-1.07				
U16655_at	Rn.37434	140693	9	74,025,487		Ptcd4	phospholipase C, delta 4	1.12				
D45920_at	Rn.10684	84587	9	54,335,647		Ptcl1	phospholipase C-like 1	1.14				
rc_AI072770_s_at	Rn.4550	24943	X	124,562,059		Ptlf	proteolipid protein	1.14				
M57728_g_at	Rn.11175	296588	3	4,560,960		Pmpca	peptidase (mitochondrial processing) alpha	1.09				
D13907_g_at	Rn.841	64198	4	-8,746,903		Pmpcb	peptidase (mitochondrial processing) beta	1.12				
D13907_at	Rn.841	64198	4	-8,746,903		Pmpcb	peptidase (mitochondrial processing) beta	1.10				
J02776_s_at	Rn.9346	29240	16	73,864,971		Polb	polymrase (DNA directed), beta	-1.08		1.26		
AF062740_at	Rn.31799	54705	5	-26,234,515	Alc4	Ppm2c	catalytic subunit	1.13				
AF062740_g_at	Rn.31799	54705	5	-26,234,515	Alc4	Ppm2c	protein phosphatase 2C, magnesium dependent, catalytic subunit	1.10				
A1011607_g_at	Rn.11846	301323	9	-32,207,688		Prim2	DNA primase, p58 subunit	1.06				
A1011607_at	Rn.11846	301323	9	-32,207,688		Prim2	DNA primase, p58 subunit	-1.13				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
U42413_at	Rn.11089	25520	7	-137,658,778		Prkag1	protein kinase, AMP-activated, gamma 1	-1.13				
M13707_at	Rn.9747	24681	1	-64,223,859	Alc7, 11, &	Prkcc	noncatalytic subunit protein kinase C, gamma	1.11				
M18330_at	Rn.98279	170538	16	-5,954,214	13	Prkcd	protein kinase C, delta	1.14				
rc_AA799421_at	Rn.34966	29340	6	9,631,241	Alc17	Prkce	protein kinase C, epsilon	-1.29				
D50093_s_at	Rn.3936	24686	3	119,581,709		Prnp	prion protein	1.10		1.19		
X16554_at	Rn.9761	29562	X	128,323,278		Prps1	phosphoribosyl pyrophosphate synthetase 1					
D90265_s_at	Rn.2668	29668	1	-172,373,871		Psmal1	proteasome (prosome, macropain) subunit, alpha type 1	1.09				
rc_AA891383_i_at	Rn.1276	29672	2	203,787,813	Alc15	Psmal5	proteasome (prosome, macropain) subunit, alpha type 5	1.55	1.44	1.57	1.78	
D10729_s_at	Rn.29244	24968	20	-4,786,490		Psmb8	proteasome (prosome, macropain) subunit, beta type 8	1.08				
L27843_s_at	Rn.9459	29463	9	-29,618,696		Ptp4a1	protein tyrosine phosphatase 4a1	1.10				
U40790_at	Rn.10278	29645	3	-74,693,135		Ptptrj	protein tyrosine phosphatase, receptor type, j	1.28				
rc_AA874857_at	Rn.114933	498407	14	-87,249,491		pur-beta	transcription factor Pur-beta	-1.16				
rc_AI175539_at	Rn.2005	25269	7	-116,148,899		Pvalb	parvalbumin	1.16				
E03344cds_s_at	Rn.4065	29534	2	98,306,852		Pxmp3	peroxisomal membrane protein 3	1.08				
rc_AA800190_at	Rn.1518	25739	3	0		Pygb	brain glycogen phosphorylase	1.10				
J03481mrna_at	Rn.241	64192	14	70,744,388		Qdpr	quinoid dihydropteridine reductase	1.18				
J03481mrna_g_at	Rn.241	64192	14	70,744,388		Qdpr	quinoid dihydropteridine reductase	1.18				
M75153_at	Rn.1016	81830	8	-68,950,978		Rab11a	RAB11a, member RAS oncogene family	1.12				
rc_AA894207_g_at	Rn.28921	246324	9	-104,618,026		Rab31	RAB31, member RAS oncogene family	-1.18				
rc_AA800305_at	Rn.44477	64633	9	-1,492,865		Rab5a	RAB5A, member RAS oncogene family	-1.15				-1.29
AF072935_at	Rn.44477	64633	9	-1,492,865		Rab5a	RAB5A, member RAS oncogene family	-1.10				
rc_AA900900_s_at	Rn.7107	84014	9	-104,826,889		Ralbp1	ralA binding protein 1	-1.11				
rc_AI169372_at	Rn.105901	304268	12	-8,735,920		Ras11a	RAS-like family 11 member A	1.13				
rc_AA893471_s_at	Rn.98353	24718	4	8,150,872		Reln	reelin	-1.14				
AF036548_g_at	Rn.3504	117183	15	0		Rgc32	response gene to complement 32	1.14				
AF036548_at	Rn.3504	117183	15	0		Rgc32	response gene to complement 32	1.09				
AF035151_s_at	Rn.9796	54292	14	-81,365,932		Rgs12	regulator of G-protein signaling 12	-1.07				
AB015191_g_at	Rn.1943	60414	5	153,648,680	Alc4	Rhced	Rhesus blood group CE and D	-1.08				
AB015191_at	Rn.1943	60414	5	153,648,680	Alc4	Rhced	Rhesus blood group CE and D	-1.09				
rc_AA900505_at	Rn.2042	64373	6	-32,055,314	Alc17	Rhob	RhoB gene	1.10				
X92097_at	Rn.1022	65165	12	-33,028,678	Alc6 & 10	Rup24	coated vesicle membrane protein	1.10				
X93352_at	Rn.2262	81729	20	6,569,309		Rpl10a	ribosomal protein L10A	1.12				
S71021_s_at	Rn.2660	117042	12	-36,347,261	Alc6 & 10	Rpl6	ribosomal protein L6	1.14				
rc_AA799672_s_at	Rn.2660	117042	12	-36,347,261	Alc6 & 10	Rpl6	ribosomal protein L6	1.15				
X13549_s_at	Rn.3359	81773	20	-5,849,544		Rps10	ribosomal protein S10	1.10				
L81138exon_i_at	Rn.2115	83789	10	13,975,349	Alc5 & 9	Rps2	ribosomal protein S2	-1.60	-1.48	-1.63	-1.7	-1.53
L81136cds_f_at	Rn.2115	83789	10	13,975,349	Alc5 & 9	Rps2	ribosomal protein S2	-1.15	1.20		6	
M64795_f_at	-	24735	20	0		RT1@	Major histocompatibility locus	-1.14				
M11071_f_at	Rn.40130	24737	20	3,412,286		RT1-Aw2	RT1 class Ib, locus Aw2	-1.38	-1.37	-1.41		-1.41
M10094_g_at	Rn.40130	24737	20	3,412,286		RT1-Aw2	RT1 class Ib, locus Aw2	-1.20	-1.36			
M31018_f_at	Rn.40130	24737	20	3,412,286		RT1-Aw2	RT1 class Ib, locus Aw2	-1.22		-1.23		
M24324_f_at	Rn.40130	24737	20	3,412,286		RT1-Aw2	RT1 class Ib, locus Aw2	-1.09				
AF074609mrna_f_at	Rn.40130	24737	20	3,412,286		RT1-Aw2	RT1 class Ib, locus Aw2	-1.14				
U65217_i_at	Rn.33311	309622	20	-4,730,786		RT1-Bb	RT1 class II, locus Bb	-1.14	1.46	1.39		
X56596_at	Rn.33311	309622	20	-4,730,786		RT1-Bb	RT1 class II, locus Bb	-1.16				
M24026_f_at	Rn.145396	309600	20	147,139		RT1-CE12	RT1 class I, CE12	1.17				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
AF025308_f_at	Rn.160576	24977	20	3,552,628		RT1-CI	RT1 class Ib, locus CI	-1.12				
M15562_g_at	Rn.103146	294269	20	4,636,585		RT1-Da	RT1 class II, locus Da	1.20				
M15562_at	Rn.103146	294269	20	4,636,585		RT1-Da	RT1 class II, locus Da	1.17				
L23128_g_at	Rn.107070	24750	20	2,807,067		RT1-N3	RT1 class Ib gene, H2-TL-like, grc region (N3)	1.22		1.26		1.35
AF029240_g_at	Rn.143874	294228	20	0		RT1-S3	RT1 class Ib, locus S3	-1.06				
rc_AI235890_s_at	Rn.143874	294228	20	0		RT1-S3	RT1 class Ib, locus S3	-1.21				
X52817cds_s_at	Rn.55126	116644	6	-94,400,519	Alc17	Rin1	reticulon 1	1.14				
M15114_g_at	Rn.83595	83792	1	249,616,941		Scd2	stearoyl-Coenzyme A desaturase 2	1.08				
Y00766_at	Rn.87394	25657	3	-47,398,275		Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.36	-1.38	-1.44	-1.3	9
Y00766_g_at	Rn.87394	25657	3	-47,398,275		Scn3a	sodium channel, voltage-gated, type III, alpha polypeptide	-1.38		1.41		
M62763complete_seq_at	Rn.31887	25541	5	-129,158,061	Alc4	Scp2	sterol carrier protein 2			1.25		
X99337cds_s_at	Rn.37476	56064	8	62,408,946		Sdfrl	stromal cell derived factor receptor 1	1.10				
X99338cds_i_at	Rn.37476	56064	8	62,408,946		Sdfrl	stromal cell derived factor receptor 1	1.09				
rc_AA799700_at	Rn.100471	308993	1	0		Sephs2	selenophosphate synthetase 2	-1.45	-1.61	-1.39		-1.47
M63901_at	Rn.6173	25719	3	-99,525,619		Sgne1	secretory granule neuroendocrine protein 1	1.10				
M63901_g_at	Rn.6173	25719	3	-99,525,619		Sgne1	secretory granule neuroendocrine protein 1	1.09				
AF009604_at	Rn.5909	81921	1	138,476,741		Sh3g3	SH3 domain protein 2 C1			1.18		
U90261UTR#1_g_at	Rn.107226	84357	X	-56,129,005		Sh3kbp1	SH3-domain kinase binding protein 1	1.10				
AB001453_at	Rn.59227	114858	17	0		Shc3	src homology 2 domain-containing transforming protein C3	-1.28		-1.29		
rc_AA875411_s_at	Rn.37542	65041	1	159,205,528		Skd3	suppressor of K+ transport defect 3	1.06				
rc_AA891445_at	Rn.37542	65041	1	159,205,528		Skd3	suppressor of K+ transport defect 3	1.11				
rc_AI145680_s_at	Rn.6085	25027	2	199,823,090		Slc16a1	solute carrier family 16 (monocarboxylic acid transporters), member 1	1.09				
U66723_s_at	Rn.10140	60423	3	-109,256,103		Slc28a2	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	-1.15		-1.25		
Y16774_at	Rn.90036	64469	3	-109,549,289		Slc30a4	solute carrier family 30 (zinc transporter), member 4	1.09				
AF004017_at	Rn.11114	84484	14	-20,381,544		Slc4a4	solute carrier family 4, member 4	-1.24			-1.4	4
AI001290cds_at	Rn.79242	114507	11	32,119,517		Slc5a3	solute carrier family 5 (inositol transporters), member 3	-1.49	-1.40	-1.77		-1.47
M96601_at	Rn.9968	29464	4	126,120,297		Slc6a6	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	-1.37				
AB011530_at	Rn.30002	65047	1	-246,928,385	Alc14 & 16	Slit1	slit homolog 1 (Drosophila)	1.17				1.32
AB011531_at	Rn.12298	83467	10	20,098,220		Slit3	slit homolog 3 (Drosophila)	-1.08				
U83883_at	Rn.36148	64635	4	55,601,577		Snd1	staphylococcal nuclease domain containing 1	1.13				
U75928UTR#1_s_at	Rn.98989	24791	10	-40,823,352		Sparc	secreted acidic cysteine rich glycoprotein	1.19				
rc_AI639256_at	Rn.40672	301255	9	11,125,212		Spats1	spermatogenesis associated, serine-rich 1	1.28		1.29		
Y07534cds_s_at	Rn.91257	24794	6	-128,383,141		Spin2b	Serine protease inhibitor	-1.07				
rc_AA800712_g_at	Rn.13142	361813	20	-7,257,777	Alc17	Stk38	serine/threonine kinase 38	-1.17	-1.37			-1.21
DI2519_s_at	Rn.9943	116470	12	-690,406		Stx1a	syntaxin 1A (brain)	-1.10				
L10362_at	Rn.58137	117556	1	-130,761,497		Sv2b	synaptic vesicle glycoprotein 2b	1.11				
rc_AI639484_at	Rn.58137	117556	1	-130,761,497		Sv2b	synaptic vesicle glycoprotein 2b	1.09				
M27925_at	Rn.506	29179	4	151,500,081	Alc14 & 16	Syn2	synapsin II	1.17				

Probe set	Unigene	Entrez gene	Chr.	Base pair location	QTL	Gene symbol	Gene name	Comb. regions	ACB	AMYG	FC	HIPP
AF053938_s_at	Rn.9908	192117	20	-32,816,659		Syngap1	synaptic Ras GTPase activating protein 1 homolog (rat)	-1.15				
U85513_at	Rn.74259	60567	7	-128,149,672		Syt10	synaptotagmin X	-1.07				
U20105_at	Rn.48074	60565	2	198,770,093		Syt6	synaptotagmin 6	-1.09				
U20106_at	Rn.91884	59267	1	213,035,104		Syt7	synaptotagmin 7	-1.13				
U40188_at	Rn.11270	171152	X	-94,415,515		Taf9l	TAF9-like RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31kDa	1.14				
M83107_at	Rn.34397	25123	8	-48,910,973		Tagln	transgelin	-1.17		-1.22		-1.23
rc_AA893860_at	Rn.22757	294810	2	-60,694,140		Tars	threonyl-tRNA synthetase	1.08				
U09228_at	Rn.23354	84382	18	66,209,063		Tcf4	transcription factor 4	-1.18				
rc_AI639517_at	Rn.23354	84382	18	66,209,063		Tcf4	transcription factor 4	-1.20				
rc_AA893702_s_at	Rn.1829	64365	14	-84,598,335		Ten2	transcobalamin 2	-1.07				
K01934mrRNA#2_at	Rn.81140	25357	1	-154,725,746		Thrsp	thyroid hormone responsive protein	1.09		1.30		
U88630_at	Rn.2398	81813	7	-73,842,010		Tieg	TGFB inducible early growth response	-1.07				
U09256_at	Rn.5950	64524	16	5,908,756	Alc7, 11, & 13	Tkt	transketolase	1.11				
rc_AA818982_at	Rn.3364	25359	7	-28,106,846		Tmpo	thymopoietin	-1.16				
rc_AI639532_at	Rn.43529	296369	3	-155,713,170		Tnnc2	troponin C2, fast	-1.15				
rc_AA899854_at	Rn.90996	360243	10	-87,785,706		Top2a	topoisomerase (DNA) 2 alpha	-1.09				
rc_AI230748_at	Rn.36610	116646	15	56,768,246		Tpt1	tumor protein, translationally controlled 1	-1.11				
L04760_at	Rn.6763	81002	2	0		Trim23	tripartite motif protein 23	1.07				
rc_AI1169370_at	Rn.99661	64158	7	-137,805,841		Tubal	tubulin, alpha 1	-1.09				
AB011679_at	Rn.2458	29214	20	3,060,491		Tubb5	tubulin, beta 5	1.16				
rc_AI103911_at	Rn.2603	291103	17	40,432,646		Uqcrfsl	ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1	1.08				
M32167_at	Rn.1923	83785	9	10,519,065		Vegfa	vascular endothelial growth factor A	-1.09				
M32167_g_at	Rn.1923	83785	9	10,519,065		Vegfa	vascular endothelial growth factor A	-1.16				
U14746_at	Rn.11059	24874	4	149,774,236	Alc14 & 16	Vhl	von Hippel-Lindau syndrome homolog	1.10				
rc_AI071435_at	Rn.51354	25218	20	-5,074,730		Vps52	vacuolar protein sorting 52 (yeast)	-1.22				
AF033027_at	Rn.6525	64351	14	86,638,972		Ykt6	prenylated SNARE protein	1.11				
U67082_at	Rn.10663	25165	6	143,317,934	Alc17	Znf386	zinc finger protein 386 (Kruppel-like)	1.15				

Comb. regions = combined regions; Acb. = accumbens; Amyg. = amygdala; Fr. Ctx. = frontal cortex; Hipp. = hippocampus; CPU = caudate-putamen.

Positive fold differences are I/INP; negative are iNP/iP.

Biologically interesting, nonredundant, significantly over-represented GO biologic process categories^a

Table 6

GO term	Fischer exact <i>P</i> value	Number of significant genes	Number of significant genes (iPO>NP)	Number of significant genes (iP<INP)
Transmission of nerve impulse	.047	26	13	13
Regulation of programmed cell death	.014	24	14	10
Negative regulation of programmed cell death	.014	13	7	6
Axon guidance	.017	7	2	5
Regulation of synapse structure and function	.037	6	4	3
Glutogenesis	.002	5	3	2

GO = Gene Ontology; iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat; FDR = false discovery rate.

^a As determined by Fisher's Exact test using the hypergeometric distribution ($P < .05$) on genes significant in the combined regions analysis (FDR < 0.10). Categories with >300 or <10 total genes in the chipset and those with <5 significant genes in a category were excluded. For the complete list of significant categories ($P < .05$), see Table 7.

Table 7

All significant Gene Ontology (GO) biologic process categories

GO ID	GO term	Fischer exact <i>P</i>	Sig genes	Total genes in chipset
GO:0008219	Cell death	0.033	28	288
GO:0016265	Death	0.037	28	291
GO:0019226	Transmission of nerve impulse	0.047	26	272
GO:0007268	Synaptic transmission	0.041	25	256
GO:0043067	Regulation of programmed cell death	0.014	24	221
GO:0042981	Regulation of apoptosis	0.023	23	219
GO:0043066	Negative regulation of apoptosis	0.014	13	97
GO:0043069	Negative regulation of programmed cell death	0.014	13	97
GO:0001568	Blood vessel development	0.038	10	78
GO:0042060	Wound healing	0.028	9	64
GO:0006959	Humoral immune response	0.028	9	64
GO:0007411	Axon guidance	0.017	7	40
GO:0019882	Antigen presentation	0.001	6	17
GO:0046651	Lymphocyte proliferation	0.037	6	37
GO:0050803	Regulation of synapse structure and function	0.037	6	37
GO:0030333	Antigen processing	0.001	5	13
GO:0042063	Glutogenesis	0.002	5	14

Table 8

Neurotransmission-related significant genes^a

Entrez gene	Gene symbol	Gene name	QTL	Combined regions fold (iP vs. INP)	Individual region ^b significant in (fold)
Decreased expression					
140667	Ap3m2	adaptor-related protein complex 3, mu 2 subunit		-1.12	
25369	Adora2a	adenosine A2a receptor		-1.08	
83610	Apba2	amyloid beta (A4) precursor protein-binding, family A, member 2		-1.13	
65153	Freq	frequency homolog (Drosophila)		-1.22	
24416	Grm3	glutamate receptor, metabotropic 3		-1.31	
81672	Grm7	glutamate receptor, metabotropic 7	Alc14 & 16	-1.08	
25674	Gtra1	glycine receptor, alpha 1 subunit		-1.11	
50664	Gnao	guanine nucleotide binding protein, alpha o		-1.26	
29547	Homer2	homer homolog 2 (Drosophila)		-1.09	
84009	Kalrn	kalirin, RhoGEF-kinase		-1.09	
24903	Kng1	kininogen 1		-1.09	
116508	Nrxn3	neurexin 3	Alc17	-1.11	
24604	Npy	neuropeptide Y	Alc14 & 16	-1.14	
25730	Ntf5	neurotrophin 5		-1.06	
27150	Kcnh3	potassium voltage-gated channel, subfamily H (age-related), member 3		-1.09	
29659	P2rx4	purinergic receptor P2X, ligand-gated ion channel 4	Alc6 & 10	-1.08	
114858	Shc3	src homology 2 domain-containing transforming protein C3		-1.28	AMYG (e1.29), CPU (e1.39)
60567	Syt10	synaptotagmin X		-1.07	
116470	Six1a	syntaxin 1A (brain)		-1.10	
Increased expression					
295365	Amigo	amphoretin-induced gene and ORF	Alc15	1.11	AMYG (1.22)
26989	Cadps	Ca2+-dependent secretion activator		1.08	
65160	Chn1a	chloride channel, nucleotide-sensitive, 1A		1.14	
24259	Chgb	chromogranin B		1.11	AMYG (1.25)
25707	Cntf	ciliary neurotrophic factor		1.11	
24232	C3	complement component 3		1.19	
289211	Fcgr2b	Fc receptor, IgG, low affinity IIb		1.11	
25319	Fth1	ferritin, heavy polypeptide 1		1.26	
83633	Gpr51	G protein-coupled receptor 51	Alc4	1.12	AMYG (1.29)
25450	Gabbr1	gamma-aminobutyric acid receptor, subunit beta 1		1.21	
64831	Ireb2	iron responsive element binding protein 2		1.06	
24558	Mog	myelin oligodendrocyte glycoprotein		1.08	
25340	Npy5r	neuropeptide Y receptor Y5	Alc7 & 11	1.11	
81737	Ntf3	neurotrophin 3	Alc18	1.07	
59324	Kcnk1	potassium channel, subfamily K, member 1		1.08	
25327	Kcnc1	potassium voltage-gated channel, Shaw-related subfamily, member 1		1.17	
24686	Pmp	piron protein		1.10	
24681	Prkcc	protein kinase C, gamma		1.11	
116644	Rtn1	reticulon 1	Alc17	1.14	
29179	Syn2	synapsin II	Alc14 & 16	1.17	
117556	Sv2b	synaptic vesicle glycoprotein 2b		1.11	

iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat.

^a Defined as categorized by a Gene Ontology category (synaptic transmission, regulation of action potential, positive regulation of transport, potassium ion transport, chloride transport, metal ion homeostasis) or found through manual curation to have neurotransmission-related function (Ap3m2, Chn1a, Chgb, Grm7, Gtra1, Gnao, Homer2, Kalrn, Kng1, Kcnh3, P2rx4, Rtn1, Six1a).

^bACB = nucleus accumbens, AMYG = amygdala, FC = frontal cortex, HIPP = hippocampus, CPU = caudate-putamen.

Table 9

Neuroplasticity-related significant genes^a

Entrez gene	Gene symbol	Gene name	QTL	Combined regions fold (iP vs. iNP)	Individual region ^b significant in (fold)
Decreased expression					
58835	Phgdh	3-phosphoglycerate dehydrogenase		-1.27	CPU (e1.33)
25369	Adora2a	adenosine A2a receptor		-1.08	
24888	Bcl2l1	Bcl2-like 1		-1.11	
64547	Bcl2l1l	BCL2-like 1l (apoptosis facilitator)	Alc17	-1.08	
29182	Cdh22	cadherin 22	Alc7 & 11	-1.43	ACB (e1.21)
25402	Casp3	caspase 3, apoptosis related cysteine protease			
114851	Cdkn1a	cyclin-dependent kinase inhibitor 1A		-1.11	
79208	Epha5	Epha5		-1.11	
79114	Fgfr1	Fibroblast growth factor receptor 1		-1.11	AMYG (e1.21)
25661	Fnl1	fibronectin 1		-1.27	
65153	Freq	frequency homolog (Drosophila)		-1.22	
24416	Grm3	glutamate receptor, metabotropic 3		-1.31	
25589	Kdr	kinase insert domain protein receptor		-1.28	AMYG (e1.50)
116508	Nrxn3	neuroligin 3	Alc17	-1.11	
25730	Ntf5	neurotrophin 5		-1.06	
29432	Pak2	p21 (CDKN1A)-activated kinase 2		NS	AMYG (e1.20)
29583	Pecam	platelet/endothelial cell adhesion molecule		-1.14	
29240	Polb	polymerase (DNA directed), beta		-1.08	
24718	Reln	reelin		-1.14	
84357	Sh3kbp1	SH3-domain kinase binding protein 1		-1.1	
83467	Slit3	slit homolog 3 (Drosophila)		-1.08	
60567	Sytl0	synaptotagmin X		-1.07	
116646	Tpt1	tumor protein, translationally controlled 1		-1.11	
83785	Vegfa	vascular endothelial growth factor A ^c		-1.16	
Increased expression					
29437	Acta1	actin, alpha 1, skeletal muscle		1.1	
24188	Aldh1a1	aldehyde dehydrogenase family 1, member A1		1.2	
295365	Amigo	amphoretin-induced gene and ORF	Alc15	1.11	AMYG (1.22)
24179	Agt	angiotensinogen		1.2	CPU (1.30)
83526	Atm	atactin		1.26	AMYG (1.33)
117271	Bid3	BH3 interacting (with BCL2 family) domain, apoptosis agonist	Alc10	1.09	
25668	Cd38	CD38 antigen		1.13	
25599	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility class II antigen-associated)		1.21	
64465	Cdc42	cell division cycle 42 homolog (S. cerevisiae)	Alc4	1.12	
25707	Cntf	ciliary neurotrophic factor		1.11	
192262	C1s	complement component 1, s subcomponent	Alc18	1.07	
27256	Cntn6	contactin 6	Alc14 & 16	1.09	
29139	Den	decorin ^c		1.17	HIPP (1.29)
29560	Hif1a	hypoxia inducible factor 1, alpha subunit	Alc17	1.1	
294235	Ler3	immediate early response 3		1.11	
29197	Il18	interleukin 18		1.15	
362418	Irak2	interleukin-1 receptor-associated kinase 2	Alc14 & 16	1.08	AMYG (1.22)
24558	Mog	myelin oligodendrocyte glycoprotein		1.08	
83834	Nrn1	neuritin		1.1	AMYG (1.19)
24588	Nef3	neurofilament 3, medium		1.16	
24587	Nefh	neurofilament, heavy polypeptide		1.18	
83613	Nfl	neurofilament, light polypeptide		1.08	CPU (1.44)
81737	Ntf3	neurotrophin 3	Alc18	1.07	

Entrez gene	Gene symbol	Gene name	QTL	Combined regions fold (iP vs. iNP)	Individual region ^b significant in (fold)
171116	Opal1	optic atrophy 1 homolog (human)		1.12	
114108	Pdlim3	PDZ and LIM domain 3	Alc7 & 11	1.15	AMYG (1.28)
29534	Pxmp3	peroxisomal membrane protein 3		1.08	
170538	Prkcd	protein kinase C, delta	Alc7, 11, & 13	1.14	
64373	Rhob	rhoB gene	Alc17	1.1	
81921	Sh3gl3	SH3 domain protein 2 C1		NS	AMYG (1.18)
65047	Slit1	slit homolog 1 (Drosophila)		1.17	HIPP (1.32)
29214	Tubb5	tubulin, beta 5		1.16	

iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat.

^aDefined as categorized by a Gene Ontology category (apoptosis, regulation of apoptosis, negative regulation of apoptosis, regulation of programmed cell death, positive regulation of apoptosis, central nervous system development, gliogenesis, myelination, axon guidance, axonogenesis, cell migration, regulation of axonogenesis, regulation of neurogenesis, regulation of synapse structure and function, cytoskeleton organization and biogenesis, neuron differentiation) or found through manual curation to have neuroplasticity-related function (Cdh22, Cdc42, Fgfr1, Vegfa, Vegfb, Den, Ephra5, Nrn1, Bid3, Casp3, Ler3, Pak2, Sh3kbp1).

^bACB = nucleus accumbens, AMYG = amygdala, FC = frontal cortex, HIPP = hippocampus, CPU = caudate-putamen.

^cGene represented by more than one significant probe set. Largest of the multiple fold changes is reported in column 5.

Table 10

Intracellular messaging-related significant genes^a

Entrez gene	Gene symbol	Gene name	QTL	Combined regions fold (iP vs. iNP)	Individual region ^b significant in (fold)
Decreased expression (iP vs. iNP)					
66013	Arhgef9	Cdc42 guanine nucleotide exchange factor (GEF) 9		-1.22	
114851	Cdkn1a	cyclin-dependent kinase inhibitor 1A		-1.11	
171109	Dusp5	dual specificity phosphatase 5		-1.07	
116663	Dusp6	dual specificity phosphatase 6		-1.28	
25114	Fgfr4	fibroblast growth factor receptor 4		-1.09	
25661	Fn1	fibronectin 1		-1.27	
24416	Grm3	glutamate receptor, metabotropic 3		-1.31	
25589	Kdr	kinase insert domain protein receptor		-1.28	
24592	Nf1	neurofibromatosis 1		-1.16	
29353	Phkg1	phosphorylase kinase gamma 1	Alc10	-1.08	AMYG (-1.50)
29583	Pecam	platelet/endothelial cell adhesion molecule		-1.14	
29340	Prkce	protein kinase C, epsilon	Alc17	-1.29	
84014	Ralbp1	ralA binding protein 1		-1.11	
24718	Reln	reelin		-1.14	
24794	Spin2b	Serine protease inhibitor	Alc17	-1.07	
361813	Stk38	serine/threonine kinase 38		-1.17	ACB (e1.37), CPU (e1.21)
192117	Syngap1	synaptic Ras GTPase activating protein 1 homolog (rat)		-1.15	
Increased expression (iP vs. iNP)					
25673	Anxa5	annexin A5		1.10	
83839	Calb1	calbindin 1	Alc4	1.16	
24242	Calm1	calmodulin 1	Alc17	1.07	
25420	Cryab	crystallin, alpha B		1.32	CPU (1.35)
83633	Gpr51	G protein-coupled receptor 51	Alc4	1.12	
155918	LCPU2	lymphocyte cytosolic protein 2	Alc9 & 12		AMYG (1.18)
59322	Cnksr2	membrane-associated guanylate kinase-interacting protein		1.08	
58840	Mapk6	mitogen-activated protein kinase 6		1.08	
24605	Nras	neuroblastoma ras oncogene		1.07	
84587	Plcl1	phospholipase C-like 1		1.14	
54705	Ppm2c	protein phosphatase 2C, magnesium dependent, catalytic subunit ^c	Alc4	1.13	
29645	Ptpnj	protein tyrosine phosphatase, receptor type, J		1.28	
64373	Rhob	rhoB gene	Alc17	1.10	

iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat.

^a Defined as categorized by a Gene Ontology category (small GTPase mediated signal transduction, negative regulation of protein kinase activity, negative regulation of enzyme activity, transmembrane receptor protein tyrosine kinase signaling pathway) or were found through manual curation to have an intracellular messaging-related function (Anxa5, Calb1, Calm1, Dusp5, Dusp6, Cnksr2, Mapk6, Nf1, Plcl1, Phkg1, Prkce, Ppm2c, Ppm2c, Spin2b, Stk38, Syngap1).

^b ACB = nucleus accumbens, AMYG = amygdala, FC = frontal cortex, HIPP = hippocampus, CPU = caudate-putamen.

^c Gene represented by more than one significant probe set. Largest of the multiple fold changes is reported in column 5.

Transcription-related significant genes^a

Table 11

Entrez gene	Gene symbol	Gene name	QTL	Combined regions fold (iP vs. iNP)	Individual region ^b significant in (fold)
Decreased expression (iP vs. iNP)					
24388	Gfi1	growth factor independent 1		-1.09	
29577	Hes1	hairy and enhancer of split 1 (Drosophila)		-1.08	
84017	Hmga2	high mobility group AT-hook 2		-1.07	
292892	Irf3	interferon regulatory factor 3		-1.06	
246324	Rab31	RAB31, member RAS oncogene family		-1.18	
81813	Tieg	TGFB inducible early growth response		-1.07	
84382	Tcf4 ^c	transcription factor 4		-1.20	
498407	pur-beta	transcription factor Pur-beta		-1.16	
Increased expression (iP vs. iNP)					
25620	Crem	cAMP responsive element modulator		1.07	
362201	Cndbp1	cyclin D-type binding-protein 1		1.11	
300721	Dnaj4	DnaJ (Hsp40) homolog, subfamily A, member 4		1.10	
27080	Hbp1	high mobility group box transcription factor 1	Alc17	1.07	
29560	Hif1a	hypoxia inducible factor 1, alpha subunit	Alc17	1.1	
29458	Neurod1	neurogenic differentiation 1		1.14	
81830	Rab11a	RAB11a, member RAS oncogene family		1.12	
304268	Ras11a	RAS-like family 11 member A		1.13	
64635	Snd1	staphylococcal nuclease domain containing 1		1.13	
171152	Tat9l	TAF9-like RNA polymerase II, TATA box binding protein (TBP)-associated factor, 31kDa		1.14	
24874	Vhl	von Hippel-Lindau syndrome homolog	Alc14 & 16	1.10	
81515	Lyn	Yamaguchi sarcoma viral (v-yes-1) oncogene homolog	Alc4	1.10	
25165	Znf586	zinc finger protein 386 (Kruppel-like)	Alc17	1.15	CPU (1.22)

iP = inbred alcohol-preferring rat; iNP = inbred alcohol-non-preferring rat.

^aDefined as transcription factors by Genomatix Suite (Crem, Gfi1, Hbp1, Hif1a, Irf3, Klf10, Neurod1, Tat9l, Tcf4) or found through manual curation to have functions or putative functions related to the regulation of transcription.

^bACB = nucleus accumbens, AMYG = amygdala, FC = frontal cortex, HIPP = hippocampus, CPU = caudate-putamen.

^cGene represented by more than one significant probe set. Largest of the multiple fold changes is reported in column 5.

Table 12

Quantitative RT-PCR confirmation of microarray fold change (iP vs. iNP) data

Gene name	Frontal cortex		Caudate-putamen		Nucleus accumbens	
	Microarray	qRT-PCR	Microarray	qRT-PCR	Microarray	qRT-PCR
Akap11	1.04	1.05 ^a	1.23	786 ^a	1.5 ^b	386 ^a
Sen1a	1.03	1.19	1.23	1.54	1.07	1.16
Fth1	1.30	1.12	1.22	1.20 ^d	1.27	1.14
GSTa4	-1.75 ^b	-1.99 ^a	-2.00 ^b	-2.13 ^a	-1.52 ^b	-2.94 ^a
Scn3a	-1.39 ^b	-1.62 ^a	-1.46 ^b	-1.47	-1.38 ^b	-1.04

iP = inbred alcohol-preferring rat; iNP = inbred alcoholnon-preferring rat; qRT-PCR = real-time PCR; FDR = false discovery rate.

^a Statistically significant ($P < 0.05$).^b Statistically significant (FDR < 0.10).