

## Effects of inhibitors of SLC9A-type sodium-proton exchangers on *Survival Motor Neuron 2* (*SMN2*) mRNA splicing and expression

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## **ABBREVIATIONS**

ACTB,  $\beta$ -actin; ASIC1A, acid-sensing ionic channel 1A; ATXN1, ataxin-1; BLA,  $\beta$ -lactamase; COL3A, collagen IIIA; DHCR7, 7-dehydrocholesterol reductase; DMA, 5-(N,N-dimethyl)amiloride; EIPA, 5-(N-ethyl-N-isopropyl)amiloride; FABP3, fatty acid binding protein 3; FOXM1, forkhead box protein M1; GAPD, glyceraldehyde 3-phosphate dehydrogenase; HMA, 5-(N,N-hexamethylene)amiloride; hnRNPA1, heterogeneous nuclear ribonucleoprotein A1; NHE, sodium/proton exchanger; IPA, Ingenuity Pathways Analysis; PCA, principal component analysis; PRKAR2B, protein kinase cAMP-dependent type II regulatory subunit beta; RPLP0, large ribosomal protein P0; SaM68, Src-associated in mitosis 68 kDa; SF2/ASF, splicing factor 2 homolog/alternative-splicing factor; SI, splicing factor; SMA, spinal muscular atrophy; SMN1, survival motor neuron 1; SMN2, survival motor neuron 2; SRp20, serine/arginine-rich splicing factor 20 kDa; STRN3, striatin 3; TIA1, T cell-restricted intracellular antigen 1; Tra2 $\beta$ 1, transformer 2 beta homolog; TRPP3, transient receptor potential cation channel subfamily P member 3; TRPV4, transient receptor potential cation channel subfamily V member 4; URA, upstream regulator analysis

## ABSTRACT

Spinal muscular atrophy (SMA) is an autosomal recessive, pediatric-onset disorder caused by the loss of spinal motor neurons thereby leading to muscle atrophy. SMA is caused by the loss of or mutations in the *survival motor neuron 1* (*SMN1*) gene. *SMN1* is duplicated in humans to give rise to the paralogous *SMN2* gene. This paralog is nearly identical except for a cytosine to thymine (C-to-T) transition within an exonic splicing enhancer (ESE) element within exon 7. As a result, the majority of *SMN2* transcripts lack exon 7 (*SMN $\Delta$ 7*) which produces a truncated and unstable SMN protein. Since *SMN2* copy number is inversely related to disease severity, it is a well-established target for SMA therapeutics development. 5-(N-ethyl-N-isopropyl)amiloride (EIPA), an inhibitor of sodium/proton exchangers (NHEs), has previously been shown to increase exon 7 inclusion and SMN protein levels in SMA cells. In this study, NHE inhibitors were evaluated for their ability to modulate *SMN2* expression. EIPA as well as 5-(N,N-hexamethylene)amiloride (HMA) increase exon 7 inclusion in *SMN2* splicing reporter lines as well as in SMA fibroblasts. The EIPA-induced exon 7 inclusion occurs via a unique mechanism that does not involve previously identified splicing factors. Transcriptome analysis identified novel targets, including *TIA1* and *FABP3*, for further characterization. EIPA and HMA are more selective at inhibiting the NHE5 isoform, which is expressed in fibroblasts as well as in neuronal cells. These results show that NHE5 inhibition increases *SMN2* expression and may be a novel target for therapeutics development.

## SIGNIFICANCE STATEMENT

This study demonstrates a molecular mechanism by which inhibitors of the sodium-protein exchanger increase the alternative splicing of *SMN2* in spinal muscular atrophy cells. NHE5 selective inhibitors increase the inclusion of full-length *SMN2* mRNAs by targeting *TIA1* and *FABP3* expression, which is distinct from other small molecule regulators of *SMN2* alternative splicing. This study provides a novel means to increase full-length *SMN2* expression and a novel target for therapeutics development.

## KEYWORDS

spinal muscular atrophy; *SMN2*; alternative splicing; drug discovery; EIPA; HMA; sodium-proton exchanger



## INTRODUCTION

Proximal spinal muscular atrophy (SMA) is an early-onset neurodegenerative disease characterized by the loss of  $\alpha$ -motor neurons in the anterior horn of the spinal cord which leads to muscle weakness and atrophy (Crawford and Pardo, 1996; Tisdale and Pellizzoni, 2015). SMA is an autosomal recessive disease with an incidence of 1 in 6,000-10,000 births (Cuscó et al., 2002; Pearn, 1978). SMA results from the loss or mutation of *SMN1* (*survival motor neuron 1*) on chromosome 5q13 (Lefebvre et al., 1995). Uniquely in humans, a large tandem chromosomal duplication has led to a second copy of this gene known as *SMN2* (Lorson et al., 1999; Monani et al., 1999). *SMN2* is functionally distinguishable from *SMN1* by a single nucleotide difference (*SMN2* c.850C>T) in exon 7 that disrupts an exonic splice enhancer. As a result, about 80-90% of *SMN2* mRNAs lack exon 7 (*SMN $\Delta$ 7*) and produce a protein that is both unstable and not fully functional (Burnett et al., 2009; Cho and Dreyfuss, 2010; Lorson and Androphy, 2000). Because 10-20% of the *SMN2* gene product is fully functional (Lorson et al., 1999; Monani et al., 1999), increased genomic copies of *SMN2* inversely correlate with disease severity among individuals with SMA (Butchbach, 2016). Studies using transgenic mouse models for SMA have shown that increased *SMN2* copy number lessens the phenotypic severity of disease (Hsieh-Li et al., 2000; Michaud et al., 2010; Monani et al., 2000).

As *SMN2* is a major genetic modifier of SMA phenotype, it has become the primary target for the development of small molecule therapies for SMA (Cherry et al., 2014). *SMN2* gene expression can be regulated by increasing promoter activation, increasing inclusion of exon 7 in *SMN2* mRNA transcripts and including translational read-through of *SMN $\Delta$ 7* mRNAs (Calder et al., 2016). Although there is currently no cure for SMA, a splice modifying oligonucleotide that increases *SMN2* exon 7 inclusion (nusinersen, Spinraza) recently received FDA approval for SMA patients (Finkel et al., 2017; Mercuri et al., 2018). Splice modifying oligonucleotides, however, have suboptimal properties including not being able to cross the blood-brain barrier, not being orally bioavailable, potentially being toxic at high doses and being expensive to manufacture (Sumner and Crawford, 2018). Despite these

exciting advances, other therapies are needed, particularly if they are complementary to these current therapeutic options.

Small molecule inducers of *SMN2* exon 7 inclusion have been identified. NVS-SM1 (branaplam) is a small molecule *SMN2* exon 7 splicing modulator that is orally bioavailable and CNS penetrant (Palacino et al., 2015). The pyridopyrimidinone class of small molecule modulators of *SMN2* exon 7, including RG7800 and RG7916 (risdiplam), have also shown efficacy in cell culture as well as in animal models for SMA (Feng et al., 2016; Naryshkin et al., 2014; Ratni et al., 2018; Ratni et al., 2016; Sivaramakrishnan et al., 2017; Wang et al., 2018; Woll et al., 2016). Risdiplam (Evrysdi; Genetech and Roche) was recently approved by the FDA for treating SMA patients (Baranello et al., 2021). Other classes of small molecules have been identified as modulators of *SMN2* exon 7 splicing. EIPA (5-(N-ethyl-N-isopropyl)-amiloride), an inhibitor of Na<sup>+</sup>/H<sup>+</sup> exchangers (NHEs, also known as SLC9A family), upregulates *SMN2* expression in SMA lymphoblastoid cells by increasing the inclusion of exon 7 in *SMN2* transcripts (Yuo et al., 2008). In this study, we examine the effects of other NHE inhibitors—both structurally related to EIPA as well as other classes of inhibitors—on *SMN2* alternative splicing at exon 7 and *SMN* expression in SMA cells. The modulatory effects of EIPA and its analogues are also compared against RG7800, a well-characterized *SMN2* exon 7 splicing modulator.

## MATERIALS AND METHODS

### Test Compounds

Amiloride, cariporide, 5-(N-ethyl-N-isopropyl)amiloride (EIPA), 5-(N,N dimethyl)amiloride (DMA), and zoniporide were obtained from Cayman Chemicals (Ann Arbor, MI) while 5-(N, N-hexamethylene)amiloride (HMA) was purchased from Sigma-Aldrich (St. Louis, MO). The structures of the amiloride test compounds are shown in **Figure 1**. RG7800 was obtained from MedKoo Biosciences, Inc (Morrisville, NC). All stock solutions were made by dissolving the compound in DMSO (Sigma-Aldrich).

## Cell Culture

Fibroblast cells derived from type II SMA patients (GM03813, GM22592, and AIDHC-SP22) have a homozygous deletion of *SMN1* and 3 copies of *SMN2* (Stabley et al., 2015; Stabley et al., 2017). GM03814 fibroblasts (Scudiero et al., 1986) were derived from the carrier mother of GM03813 with 1 copy of *SMN1* and 5 copies of *SMN2* (Stabley et al., 2015). GM03813, GM22592 and GM03814 fibroblasts were obtained from Coriell Cell Repositories (Camden, NJ) while the other fibroblast lines were generated at Nemours Children's Hospital Delaware (Stabley et al., 2017). All fibroblast lines were authenticated using short tandem repeat profiling and digital PCR (Stabley et al., 2017). The *SMN2* exon 7 splicing reporter cell line NSC-34:SMN2:Mg2:bla5.3 (Andreassi et al., 2001) was obtained from Vertex Pharmaceuticals (Boston, MA).

Fibroblast lines as well as NSC-34:SMN2:Mg2:bla5.3 cells were maintained in Dulbecco's modified essential medium (DMEM; Life Technologies, Grand Island, NY) containing 10% Equafetal (Atlas Biologicals; Fort Collins, CO), 2 mM L-glutamine (Life Technologies) and 1% penicillin- streptomycin (Life Technologies). All cell lines were maintained in a humidified chamber at 37°C with 5% CO<sub>2</sub>.

## SMN2 Exon 7 Splicing Reporter Assay

NSC-34:SMN2:Mg2:bla5.3 cells (Andreassi et al., 2001) were seeded onto a black-walled, clear bottom 96-well tissue culture plates (Santa Cruz Biotechnology, Dallas, TX) at a density of  $5 \times 10^4$  cells/cm<sup>2</sup>. Drug compounds (n = 4/dose) were added to serum-free medium at a dilution of 1:500. 100  $\mu$ L of drug-containing medium was then added to maintenance medium over the seeded NSC-34 cells. After incubation for 19 hours, media containing drug compounds was aspirated and 100  $\mu$ L of fresh maintenance medium was added to each well. 20  $\mu$ L of 6X CCF2-AM Loading solution (GeneBlazer In Vivo Detection Kit, Life Technologies; containing 6  $\mu$ M CCF2-AM and 12 mM probenecid) were added to each of the assay wells and plates were incubated at room temperature

for 2 hours before the plates were read on a Victor X4 (Perkin Elmer, Waltham, MA) fluorescence plate reader ( $\lambda_{\text{ex}} = 405 \text{ nm}$ ,  $\lambda_{\text{em}} = 530 \text{ nm}$  and  $\lambda_{\text{em}} = 460 \text{ nm}$ ). The 460 nm:530 nm fluorescence ratios were then calculated for each sample.

## Drug Treatment of Cells

Fibroblasts were seeded 24 hours prior to drug treatment at a density of  $3.2 \times 10^4$  cells/well in a 6-well plate for RNA analysis and of  $4.0 \times 10^5$  cells/dish in a 10-cm dish for protein analysis. Test compounds were added to each sample at a 1:1000 dilution and compound-containing medium was replaced every 24 hours during the five-day treatment period. Cells were then harvested 24 hours after last drug compound treatment.

## RNA Isolation

Total RNA was extracted from cell pellets using the RNeasy Mini kit (QIAGEN; Germantown, MD) per the manufacturer's instructions. RNA quality was assessed using a 2100 Bioanalyzer (Applied Biosystems).

## SMN Exon 7 Inclusion Assay

First-strand cDNA was synthesized from total RNA (500 ng) using the iScript™ cDNA Synthesis Kit (Bio-Rad, Hercules, CA, USA) as described previously (Gentillon et al., 2017). PCRs were run for sample cDNAs using GoTaq Green Polymerase Mix (Promega; Madison, WI) with the following primer sets (Integrated DNA Technologies; Coralville, IA): *SMN*, SMNex6 (F) 5'-cccatatgtccagattctcttgat-3'; SMNex8(R) 5'-ctacaacacccttctcacag-3'; *human collagen-III* (*COL3A*), *COL3A* (F) 5'-gctctgctcatccactatt-3' and *COL3A*(R) 5'-ggaataccagggtcaccattt-3'. PCR products were resolved through a 2% agarose gels via electrophoresis. Images were captured with an Alphamager gel documentation station (ProteinSimple, San Jose, CA) and band intensities were quantified using Image J 1.45s (National Institutes of Health, Bethesda, MD).

## Quantitative Reverse Transcriptase-Polymerase Chain Reaction (qPCR)

qPCR was completed for each treated sample using the iScript™ cDNA Synthesis Kit and the Bullseye EvaGreen qPCR MasterMix (Midsci, Valley Park, MO) as described previously (Gentillon et al., 2017). Each sample was assayed in triplicate. The following primer sets were used: *full-length SMN (FL-SMN)* (SMNex6F) 5'-ccatatgtccagattctcttgatga-3', (SMNex78R) 5'-atgccagcatttctccttaattta-3'; *SMNΔ7* (SMNex6F), (SMNex68R) 5'-atgccagcatttccatataatagc-3'; *full-length striatin-3 (FL-STRN3)* (STRN3F) 5'-ggaagaaaggggtgaagagg-3', (STRN3R) 5'-tgattcctgaagggtatgtg-3'; *STRN3 lacking exons 8 and 9 (STRN3Δ89)* (STRN3D89F) 5'-cagaatgggctgaaccaataa-3', (STRN3D89R) 5'-accgtcaagtctgcaagggtc-3'; *forkhead box protein M1A (FOXM1A)* (FOXM1AF) 5'-gaacatgaccatcaaaaccgaactc-3', (FOXM1AR) 5'-aaattaaacaagctggtgatgggtg-3'; (FOXM1B) (FOXM1BF) 5'-ggaccaggtgttaagcagcag-3', (FOXM1BR) 5'-caatgcggactcgcttgctat-3'; (FOXM1C) (FOXM1CF) 5'-tgcccgagcagttggaatca-3', (FOXM1CR) 5'-tcctcagctagcagcaccttg-3'; *heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1)* (hnRNPA1-F) 5'-agggcgaaggtaggctggca-3', (hnRNPA1-R) 5'-gcttcctcagctcttcgggct-3'; *transformer 2 beta homolog (hTra2β1)* (hTRA2bF) 5'-cacatcgaccggcgacagca-3' (hTRA2bR) 5'-ccccgatccgtgagcacttcc-3'; *splicing factor-2 homolog/alternative-splicing factor (SF2/ASF)* (hSF2ASF-F) 5'-cagagtgggtgtctctg-3', (hSF2ASF-R) 5'-ctccacgacaccagtgcc-3'; *Src-associated in mitosis 68 kDa (SaM68)* (hSAM68F) 5'-atctctgtaattgggaaagggc-3', (hSAM68R) 5'-agagcataagcctcacatgg-3'; *serine/arginine-rich splicing factor 20 kDa (SRp20)* (hSRp20F) 5'-atgcatcgtgattcctg-3', (hSRp20R) 5'-ctgcgacgaggtggagg-3'; *T-cell-restricted intracellular antigen-1 (TIA1)* (TIA1-F) 5'-cagcgttcacaagatcatttcc-3', (TIA1-R) 5'-tcccttagacttctctgttgc-3'; *fatty acid binding protein 3 (FABP3)* (FABP3-F) 5'-aaatgggacgggcaagag-3', (FABP3-R) 5'-tgcctctttctcataagtgcg-3'; *7-dehydrocholesterol reductase (DHCR7)* (DHCR7-F) 5'-gcaacccaacattcccaaag-3', (DHCR7-R) 5'-agtgaaaaccagtccacctc-3'; *transient receptor potential cation channel subfamily V member 4 (TRPV4)* (TRPV4-F) 5'-accttttccgattcctgctc-3', (TRPV4-R) 5'-tcctcattgcacaccttcattg-3'; *ataxin-1 (ATXN1)* (ATXN1-F) 5'-catccagagtgcagagataagc-3', (ATXN1-R) 5'-

ctctacaaaaacttcaacgctg-3' and *protein kinase cAMP-dependent type II regulatory subunit beta*

(*PRKAR2B*) (*PRKAR2B-F*) 5'-tgatcaagggtgacgatggtg-3', (*PRKAR2B-R*) 5'-tgtacattaaggccagttcgc-3'.

Primers for the human reference transcripts *β-actin* (*ACTB*), *large ribosomal protein P0* (*RPLP0*) and *glyceraldehyde 3-phosphate dehydrogenase* (*GAPD*) were purchased from Real Time Primers LLC (Elkins Park, PA).

The relative transcript levels were calculated using the efficiency-adjusted  $2^{-\Delta\Delta C_t}$  method (Schmittgen and Livak, 2008; Yuan et al., 2008). The PCR efficiency (E) for each primer set was calculated from the slope of a  $C_t$  vs.  $\log_{10}$ (cDNA serial dilution) curve ( $E = 10^{[-1/\text{slope}]}$ ) (Pfaffl, 2001).  $\Delta C_{t,\text{adjusted}}$  is the difference between the adjusted  $C_t$  ( $C_{t,\text{measured}} \times E$ ) for the target transcript and the geometric mean of the adjusted  $C_t$  values for the three reference genes and  $\Delta\Delta C_t$  is defined as the difference between the  $\Delta C_t$  for the SMA sample and the  $\Delta C_t$  for the control sample.

## Immunoblot

Protein extracts were generated from cell pellets as described previously (Gentillon et al., 2017). Protein extracts from treated cells (15  $\mu\text{g}$  protein/lane) were resolved from miniPROTEAN TGX gradient precast acrylamide gels (BioRad) via electrophoresis as described previously (Gentillon et al., 2017). The resolved proteins were then transferred onto PVDF membranes via electroblotting. Immunoblotting was completed as described in (Gentillon et al., 2017). The following primary antibodies were used in this study: mouse anti-SMN mAb (1:2000; clone 8, BD Biosciences) and mouse anti- $\beta$ -actin mAb (1:10,000; clone AC15, Sigma-Aldrich, St. Louis, MO). The horseradish peroxidase-conjugated anti-mouse and anti-rabbit secondary antibodies (1:5000); Rockland Immunochemicals, Inc., Gilbertsville, PA). After extensive washing, the bound antibody was detected by chemiluminescence using either Western Sure ECL Substrate (LiCor, Lincoln, NE) or SuperSignal West Femto (Thermo Scientific) kits and captured with the C-DiGit Blot Scanner (LiCor). Band intensities, defined as the band signal divided by the band area, were measured using the Image Studio™ Lite software (LiCor). The measured band areas were the same for each sample on a blot.

Band intensities for the target protein (SMN) were divided by those for the reference protein ( $\beta$ -actin) to obtain normalized band intensities. To measure the relative protein level for a sample, the normalized band intensity for the drug-treated sample was divided by the normalized band intensity for the control sample (DMSO-treated cells).

## Microarray

cDNAs from treated RNA samples—with RNA integrity numbers greater than 9.0—were prepared using the GeneChip WT PLUS Reagent Kit (Applied Biosystems, Foster City, CA). Double-stranded cDNA was synthesized from 100 ng total RNA using a random primer which incorporated a T7 promoter. This double-stranded cDNA was then used as a template to generate cRNA via a 16 hr in-vitro transcription reaction followed by purification with magnetic beads. Single stranded cDNA was regenerated from this cRNA through a random primed reverse transcription using a dNTP mix containing dUTP. After RNA hydrolysis with RNase H, the cDNA was purified using magnetic beads and then enzymatically fragmented with a mixture of uracil-DNA glycosylase (UDG) and apyrimic/apyrimidinic endonuclease 1 (APE1). This fragmented cDNA was then end-labeled with a biotinylated dideoxynucleotide using terminal transferase. Fragmented, biotinylated cDNA was added to a hybridization cocktail, denatured, loaded on a Clariom D human GeneChips and hybridized for 16 hours at 45 °C and 60 rpm. Following hybridization, the chips were washed and stained using the pre-programmed FS450\_0001 protocol. The stained chips were scanned at 532 nm with a GeneChip Scanner 3000 (Applied Biosystems).

The resultant data were analyzed with the TAC 4.0 software (Applied Biosystems). The raw data have been deposited into the NCBI Gene Expression Omnibus (GEO) (Barrett et al., 2013) under the accession number GSE179861. Identification of biological pathways and upstream regulators was completed using Ingenuity Pathway Analysis (IPA version 21901358; QIAGEN Redwood City, Inc., Redwood City, CA) as described previously (Maeda et al., 2014). Biological function and canonical pathways were determined to be over-represented using the Fisher exact test with a false discovery

rate (FDR) correction ( $p \leq 0.05$ ). Upstream regulators were considered as being activated if their z-scores were greater than or equal to 2.0 or inhibited if they were less than or equal to -2.0 (Krämer et al., 2014).

## Statistical Analysis

Data are expressed as mean  $\pm$  standard error. Parametric data were analyzed by ANOVA with a Holm-Sidak (expression analysis) *post hoc* test. Statistical significance was set at  $p \leq 0.05$ . Comparisons between data were performed with Sigma Plot v.12.0 or SPSS v.22.0.

## RESULTS

### Effects of NHE Inhibitors on *SMN2* Exon 7 Alternative Splicing

To determine the effect of NHE inhibitors on increasing *SMN2* expression, we first examined their effects on the inclusion of *SMN2* exon 7. Using a *SMN2* exon 7 splicing reporter assay established in motor neuron-like NSC-34 cells (Andreassi et al., 2001), we measured the effects of amiloride, DMA, EIPA, HMA, cariporide and zoniporide (**Figure 1**) on  $\beta$ -lactamase (BLA) activity—a marker for *SMN2* exon 7 inclusion. The EIPA and HMA significantly increased exon 7 inclusion, as shown by an increase in the  $\lambda_{460\text{nm}}$  to  $\lambda_{530\text{nm}}$  fluorescence ratio, in these reporter cells (**Figure 2A**). Amiloride, cariporide and zoniporide, on the other hand, significantly reduced BLA activity.

We also examined the effect of NHE inhibitors on the inclusion of exon 7 in *SMN2* mRNAs in a SMA intracellular environment by using patient-derived fibroblasts. GM03813 type II SMA fibroblasts (Scudiero et al., 1986) were treated with different concentrations of amiloride, DMA, EIPA, HMA, zoniporide or cariporide for 5 days. After treatment, *SMN2* exon 7 inclusion was measured via RT-PCR using primers spanning exons 6 through 8 of *SMN2*. *Collagen IIIA* (*COL3A*) transcript levels were used as a loading control as it is highly and constitutively expressed in fibroblast cells (Heier et al., 2007). As shown in **Figure 2B**, the proportion of *FL-SMN* (top band) relative to *SMN $\Delta$ 7* (bottom band) transcripts was increased in SMA fibroblasts treated with EIPA and HMA but not in any of the



other NHE inhibitors. HMA was more potent at increasing *SMN2* exon 7 inclusion than EIPA (**Figure 2C**).

There are 5 different isoforms of SLC9A-type  $\text{Na}^+/\text{H}^+$  antiporters (*NHE1*, *NHE2*, *NHE3*, *NHE4* and *NHE5*) that are present on the plasma membrane (Masereel et al., 2003). Using RT-PCR, we determined the SLC9A isoform expression profiles for NSC-34 cells as well as for GM03813 and GM03814 fibroblasts. NSC-34 cells as well as fibroblast cell lines express predominantly *NHE1* and *NHE5* (**Supplemental Figure 1**).

### Effects of NHE Inhibitors on *SMN2* Expression in Type II SMA Fibroblasts

We treated GM03813 type II SMA fibroblasts with different concentrations (0.1 – 10  $\mu\text{M}$ ) of the NHE inhibitors for 5 days. *FL-SMN* and *SMN $\Delta$ 7* transcript levels were measured by qPCR. EIPA and HMA significantly increase *FL-SMN* mRNA levels in GM03813 cells to about 80% of the amount of *FL-SMN* seen in carrier fibroblasts (GM03814) (**Figure 3A**). Amiloride, cariporide and zoniporide, however, reduced the abundance of *FL-SMN* transcripts in SMA fibroblasts. EIPA was the only NHE inhibitor that significantly reduced the levels of *SMN $\Delta$ 7* mRNA in treated cells (**Figure 3B**). To demonstrate that these observations were not unique to a single SMA cell line, we measured the effects of the NHE inhibitors on *FL-SMN* and *SMN $\Delta$ 7* transcript levels in two other type II SMA fibroblast lines— GM22592 and AIDHC-SP22. EIPA and HMA also increased *FL-SMN* transcripts in GM22592 and AIDHC-SP22 cells, indicating that their effects on *SMN2* mRNA regulation are cell-line independent (**Figure 3C**). *SMN $\Delta$ 7* transcript levels were also reduced in AIDHC-SP22 and GM22592 fibroblasts treated with EIPA or HMA (**Figure 3D**).

We measured SMN protein levels of GM03813 type II SMA fibroblasts treated with the aforementioned NHE inhibitors for 5 days (**Figure 4**). Amiloride, cariporide and zoniporide had marginal effects on SMN protein levels in these cells. EIPA and HMA increased SMN protein levels in GM03813 fibroblasts with EIPA showing a maximal effect at 10  $\mu\text{M}$  while the maximal effect of HMA was observed at 1  $\mu\text{M}$ . Interestingly, DMA also increased SMA protein levels in SMA fibroblasts even

though it had no effect on *FL-SMN* mRNA levels nor on exon 7 inclusion. This observation suggests that the DMA affects SMN gene regulation at a different level from EIPA and HMA.

### **Effects of NHE Inhibitors on Alternative Splicing of *Striatin-3 (STRN3)* and *Forkhead Box Protein M1 (FOXM1)* in SMA Fibroblasts**

We measured the effects of the NHE inhibitors on the alternative splicing of other transcripts—aside from *SMN2*—that are affected by the pyridopyridinone RG7800 (Ratni et al., 2016; Woll et al., 2016) in order to determine if EIPA and HMA operate via a similar mechanism to promote exon 7 inclusion. *Striatin-3 (STRN3)* has a similar pre-mRNA structure to the *SMN2* exon 7:intron 7 junction and RG7800 increases the inclusion of *STRN3* exons 8 and 9 (Naryshkin et al., 2014; Sivaramakrishnan et al., 2017). There are 3 isoforms of *forkhead box protein M1 (FOXM1)* generated by alternative splicing of exons Va and VIIa: *FOXM1A* (which contains both exons Va and VIIa), *FOXM1B* (which contains neither exon) and *FOXM1C* (which contains only exon Va) (Liao et al., 2018). RG7800 increased the abundance of *FOXM1A* while reducing *FOXM1C* levels (Ratni et al., 2018).

The levels of *STRN3* and *FOXM1* splice variants were measured in GM03813 type II SMA fibroblasts treated with amiloride, EIPA, HMA or RG7800 for 5 days. EIPA and HMA had no effect on the amount of *FL-STRN3* mRNA while amiloride significantly increased *FL-STRN3* transcript levels (**Figure 5A**). RG7800 also increased the abundance of *FL-STRN3* transcripts in treated SMA fibroblasts. Interestingly, all NHE inhibitors tested increased *STRN3Δ89* mRNA levels (**Figure 5B**) while RG7800 reduced the amount of *STRN3Δ89* transcripts. None of the NHE inhibitors increased the levels of *FOXM1A* in SMA fibroblasts (**Figure 5C**). EIPA but not amiloride nor HMA significantly decreased *FOXM1C* transcript levels in SMA fibroblasts (**Figure 5D**). *FOXM1B* transcripts could not be detected in fibroblast samples (data not shown). Predictably, RG7800 increased relative *FOXM1A* levels and reduced the amount of *FOXM1C* transcript levels in treated cells (**Figures 5C and 5D**). The

mechanism of action of EIPA and HMA on the alternative splicing of *SMN2* exon 7, therefore, is distinct from that used by RG7800.

### Effects of NHE Inhibitors on Expression of Regulators of *SMN2* Exon 7 Splicing

To understand the mechanism of action for the increased inclusion of exon 7 in *SMN2* transcripts induced by EIPA and HMA, we first examined the effects of NHE inhibitors on the expression of previously identified proteins that modulate the splicing of *SMN2* at exon 7. We focused on the following splicing regulators: hnRNP-A1 (Doktor et al., 2011; Harahap et al., 2012; Kashima et al., 2007a; Kashima et al., 2007b), SF2/ASF (SRSF1) (Cartegni et al., 2006; Cartegni and Krainer, 2002; Wee et al., 2014), hTra2 $\beta$ 1 (SRSF10) (Chen et al., 2015; Helmken and Wirth, 2000; Hofmann et al., 2000; Hofmann and Wirth, 2002), SaM68 (KHDRBS1) (Pagliarini et al., 2015; Pedrotti et al., 2010) and SRp20 (SRSF3) (Helmken et al., 2003). The transcript levels of these splicing factors were measured in type II SMA fibroblasts treated with NHE inhibitors or DMSO for 5 days. *hnRNP-A1* transcript levels were significantly reduced in GM03813 cells treated with DMA, EIPA, HMA and zoniporide (**Figure 6A**). DMA, EIPA, HMA and cariporide reduced *SF2/ASF* levels in SMA fibroblasts (**Figure 6B**). Cariporide was the only NHE inhibitor to increase *hTra2 $\beta$ 1* mRNA levels (**Figure 6C**). HMA significantly reduced *SaM68* transcript levels in SMA fibroblasts (**Figure 6D**). EIPA, HMA, cariporide and zoniporide decreased *SRp20* mRNA levels while DMA increased *SRp20* transcript levels (**Figure 6E**). Interestingly, *hnRNP-A1*, *hTra2 $\beta$ 1* and *SRp20* mRNA levels are significantly elevated in GM03813 type II SMA fibroblasts relative to GM03814 carrier fibroblasts (**Figures 6A, 6C and 6E**). While the NHE inhibitors differentially regulate the expression of splicing factors which regulate *SMN2* exon 7 inclusion, there was no correlation between the differential expression of any of these splicing factors and the enhanced inclusion of *SMN2* exon 7 induced by EIPA or HMA in SMA fibroblasts.

### Identification of Differentially Expressed Transcripts in SMA Fibroblasts Treated with EIPA

To understand the molecular mechanisms by which EIPA enhances *SMN2* exon 7 inclusion, we compared the transcriptomes of GM03813 type II SMA fibroblasts treated with 10  $\mu$ M EIPA against those treated with DMSO as well as against those treated with 10  $\mu$ M amiloride, which did not increase *SMN2* exon 7 inclusion. Principal component analysis (PCA) correctly distributed each of the samples within their treatment groups (**Figure 7A**). Hierarchical clustering of the identified transcripts from amiloride-treated (**Figure 7B**) and EIPA-treated (**Figure 7C**) fibroblasts showed consistent differential expression between each treatment group. Amiloride treatment of GM03813 SMA fibroblasts altered the levels of 1269 transcripts when compared against DMSO-treated cells (**Figure 7D** and **Supplementary Table 1A**). There were 999 differentially expressed transcripts in SMA fibroblasts treated with 10  $\mu$ M EIPA when compared against those cells exposed to DMSO (**Figure 7E** and **Supplementary Table 1B**). To identify those differentially expressed transcripts that may be relevant to *SMN2* alternative splicing, we compared the EIPA transcriptome against the amiloride transcriptome and identified 839 EIPA-unique differentially expressed transcripts (**Figure 7F** and **Supplementary Table 1C**).

Ingenuity Pathways Analysis (IPA) (Krämer et al., 2014) uses a manually curated literature database to determine the biological relevance of differentially expressed transcripts. There were 165 canonical pathways that were significantly overrepresented (Fisher's exact test p-value  $\leq 0.05$ ) in EIPA-treated SMA fibroblasts relative to amiloride-treated cells (**Supplementary Table 2**), with the top 12 overrepresented pathways shown in **Figure 7G**. Most of the top 12 overrepresented pathways contained Ras-family GTPases (*RAP2A*, *RAP1A* and *MRAS*) and subunits of the phosphatidylinositol-4-phosphate 3-kinase (*PIK3R1*, *PIK3C2G* and *PIK3CB*). Upstream Regulator Analysis (URA) (Krämer et al., 2014) can identify potential upstream molecules that may be responsible for EIPA-mediated differential gene expression. UPA identified 19 potential upregulators (10 of which were activated and 9 were inhibited) in EIPA-treated SMA fibroblasts relative to amiloride-treated fibroblasts (**Figure 7H** and **Supplementary Table 3**). Thrombospondin-1 (*THBS1*) and *DHCR7* are overrepresented target molecules in this analysis.

Transcriptome arrays can also provide important information about differential splicing in response to drug treatment. There were 10307 splicing events that were differentially expressed in amiloride-treated GM03813 SMA fibroblasts while EIPA treatment showed 8307 differentially expressed splicing events. Of those events, only 352 were classifiable as either intron retention, alternative 5' donor, alternative 3' acceptor or cassette exon events in amiloride-treated cells and 251 in EIPA-treated cells (**Figure 7I**). The splicing index (SI) is a measure of exon expression that is normalized to the expression level of that gene (Clark et al., 2007). In EIPA-treated cells, there was an increase in the *SMN2* exons 6 and 7 splice junction (JUC0500051219; SI = +2.34,  $p = 0.0031$ ) and a decrease in *SMN2* exons 6 and 8 splice junction (JUC0500051223; SI = -2.68;  $p = 0.0086$ ). Amiloride treatment, however, did not significantly alter the abundance of either splice junction. The amount of *SMN2* exon 7 inclusion was, therefore, increased in EIPA-treated SMA fibroblasts.

To validate our microarray analysis, we used biological replicates of type II SMA fibroblasts (Fang and Cui, 2011) that were treated with either 10  $\mu$ M EIPA, 10  $\mu$ M HMA, 10  $\mu$ M amiloride, 1  $\mu$ M RG7800 or DMSO. We focused on the following transcripts: *TIA1* (**Figure 8A**; 2.06-fold decrease), *FABP3* (**Figure 8B**; 6.44-fold increase), *DHCR7* (**Figure 8C**; 2.07-fold decrease), *TRPV4* (**Figure 8D**; 2.13-fold decrease), *ATXN1* (**Figure 8E**; 2.58-fold decrease) and *PRKAR2B* (**Figure 8F**; 2.15-fold increase). The differential expressions of these transcripts, with respect to direction, in response to EIPA treatment were validated in the biological replicates. Transcripts that are differentially expressed only in EIPA- and HMA-treated SMA fibroblasts would potentially provide insights into the molecular mechanisms underlying EIPA- and HMA-induced *SMN2* exon 7 inclusion. *FABP3* (**Figure 8B**) transcript levels were markedly increased in cells treated with EIPA and HMA but not with amiloride or RG7800. EIPA and HMA as well as RG7800 reduced *TIA1* transcript levels (**Figure 8A**) in SMA fibroblasts. For the remaining transcripts, the direction of change in response to EIPA treatment was different from that to HMA, i.e. increased in EIPA-treated cells but decreased in HMA-treated cells.

## DISCUSSION

Because of the inverse relationship between SMA severity and *SMN2* copy number, *SMN2* is a primary target of SMA treatment and drug discovery through multiple mechanisms including promoter activation and increased exon 7 inclusion of *SMN2* pre-mRNA transcripts (Cherry et al., 2014). Many structurally distinct small molecules such as EIPA (Yuo et al., 2008), the pyridopyrimidinones RG7800 and RG7916 (Feng et al., 2016; Naryshkin et al., 2014; Ratni et al., 2018; Ratni et al., 2016; Sivaramakrishnan et al., 2017; Wang et al., 2018; Woll et al., 2016) and NVS-SM1 (Palacino et al., 2015) increase *SMN2* expression by enhancing exon 7 inclusion. EIPA is a derivative of amiloride and inhibits the activity of the SLC9A family of Na<sup>+</sup>/H<sup>+</sup> antiporters (Kleyman and Cragoe Jr, 1988). In this study, we examined the effects of amiloride derivatives like EIPA and HMA as well as other NHE inhibitors on *SMN2* alternative splicing of exon 7. EIPA and HMA but none of the other SCL9A inhibitors tested increase *SMN2* exon 7 inclusion via a novel mechanism not involving previously identified regulators of *SMN2* exon 7 splicing.

There are 5 different isoforms of SLC9A-type Na<sup>+</sup>/H<sup>+</sup> antiporters that are localized to the plasma membrane in mammalian cells (Masereel et al., 2003). NHE1 is ubiquitously expressed in most mammalian cell types while NHE5 is primarily expressed in neurons and skeletal muscle (Donowitz et al., 2013). Tissue distribution profiles of *NHE1* and *NHE5* in humans and mice show strong expression in the tissues from which the cell lines used in this study were derived, i.e. brain and skin (Cheng et al., 2019; Fagerberg et al., 2014; Yue et al., 2014). EIPA and the related amiloride analogue HMA are potent inhibitors of the NHE1 and NHE5 isoforms (Kleyman and Cragoe Jr, 1988; Masereel et al., 2003; Szabó et al., 2000). Cariporide and zoniporide, on the other hand, are selective inhibitors of NHE1 (Masereel et al., 2003).

EIPA modulates neuronal plasticity and LTP in mice (Rönicke et al., 2009). NHE5 has been shown to be involved in neuronal excitation and long-term potentiation by negatively regulating dendrite spine growth in an activity-dependent manner (Diering et al., 2011). NHE5 knockout mice display enhanced learning and memory and increased BDNF/TrkB-mediated signaling (Chen et al., 2017). NHE5 also regulates the membrane trafficking of the receptor tyrosine kinase Met and  $\beta$ 1 integrins in

glioma cells (Fan et al., 2016; Kurata et al., 2019). NHE5 is positively regulated by AMP-activated protein kinase (AMPK) in neuronal as well as non-neuronal cells (Jinadasa et al., 2014). NHE5 membrane localization is regulated by phosphatidylinositol 3-kinase (PI3K) activity and the actin cytoskeleton (Szász et al., 2002). In addition to these roles in neuronal signaling, NHE5 regulates autophagy in neuronal cells (Togashi et al., 2013). Based on our observations, the selectivity of EIPA and HMA in increasing *SMN2* exon 7 inclusion may result from inhibition of a specific NHE isoform, in this case *NHE5*. The regulation of alternative splicing by *NHE5* has not been previously reported; future studies using gene knockdown approaches in SMA model systems will further elucidate the role of *NHE5* in *SMN2* exon 7 splicing. It is possible that selective inhibition of *NHE5* may not be sufficient to increase *SMN2* exon 7 inclusion. To address this possibility, future studies would determine if inhibition of other NHE isoforms, like *NHE1*, would be necessary for or would augment *SMN2* alternative splicing resulting from inhibition of *NHE5*.

The pyridopyridinone RG7800—which is undergoing clinical trials with SMA patients—increases *SMN2* exon 7 inclusion by binding to an exonic splice enhancer (ESE2) element present on the 5' splice site of the exon 7:intron 7 junction (Ratni et al., 2016; Sivaramakrishnan et al., 2017; Woll et al., 2016). Binding at these sites facilitates the binding of U1 snRNPs by dissociation of the inhibitory splicing factor hnRNP-G. *STRN3* has a similar pre-mRNA structure to the *SMN2* exon 7:intron 7 junction and RG7800 increases the inclusion of *STRN3* exons 8 and 9 (Naryshkin et al., 2014; Sivaramakrishnan et al., 2017). We show that EIPA and HMA have no effect on exon 8 and 9 inclusion in *STRN3* transcripts. Furthermore, EIPA and HMA do not modulate the alternative splicing of *FOXN1*, another transcript whose splicing is modulated by RG7800 (Ratni et al., 2018). These data suggest that EIPA and HMA modulate *SMN2* exon 7 alternative splicing via a mechanism that is distinct from the pyridopyridinones.

NHE antiporters regulate the cellular pH in mammalian cells (Masereel et al., 2003; Putney et al., 2002). Alterations in pH have been shown to affect the splicing of multiple mRNA transcripts including tenascin C and *SMN2* (Borsi et al., 1995; Chen et al., 2008). Low extracellular pH increases *SMN2*

exon 7 skipping while a high extracellular pH promotes exon 7 inclusion (Chen et al., 2008). The decrease in exon 7 inclusion at low pH may be the result of diminished nuclear localization of hnRNP-A1, a splicing factor that prevents exon 7 inclusion via binding to an exonic enhancer element (Chen et al., 2008). EIPA (Yuo et al., 2008) and elevating extracellular pH (Chen et al., 2008) increase the nuclear localization of the splicing factor SRp20. In this study, we did not identify any relationship between the differential expression of any of these splicing factors and the enhanced inclusion of *SMN2* exon 7 induced by EIPA or HMA in SMA fibroblasts. Furthermore, the effects of EIPA and HMA on *SMN2* exon 7 alternative splicing may not be linked with regulation of cellular pH as other NHE1-selective inhibitors like cariporide and zoniporide do not alter *SMN2* exon 7 splicing. The effects of EIPA and HMA on *SMN2* alternative splicing may be mediated by a novel mechanism.

TIA1 is a splicing factor that has been shown to increase *SMN2* exon 7 levels (Singh et al., 2011). Loss of *Tia1* worsens disease progression in female, but not male, SMA-like mice (Howell et al., 2017). We show here that EIPA and HMA decrease *TIA1* mRNA levels in SMA fibroblasts even though these compounds increase *SMN2* exon 7 inclusion. Muscle biopsies from patients with Welander distal myopathy that harbor a point mutation in *TIA1* (TIA1(E384K)) have reduced *FL-SMN2* transcript levels but elevated *SMNΔ7* transcript levels (Klar et al., 2013); however, a recent report (Carrascoso et al., 2019) has shown that mutant TIA1 only modestly affects *SMN2* exon 7 alternative splicing in different cell types. Future studies will elucidate the role of NHE5 inhibition by EIPA and HMA on *TIA1* expression and the regulation of *TIA1* expression on the modulation *SMN2* exon 7 alternative splicing.

*FABP3* transcript levels were markedly elevated in SMA fibroblasts treated with EIPA or HMA but not by other NHE inhibitors. *FABP3* is robustly expressed in neurons, as well as other non-neural tissues, and is responsible for intracellular transport of long chain polyunsaturated fatty acids (Falomir-Lockhart et al., 2019; Liu et al., 2010). *FABP3* increases the aggregation of α-synuclein within dopaminergic neurons of the substantia nigra pars compacta, which leads to cell death and neurodegeneration (Shioda et al., 2014). In murine GABAergic neurons within the anterior cingulate



cortex, FABP3 modulates the expression of glutamic acid decarboxylase (*Gad67*) by differential promoter methylation (Yamamoto et al., 2018). Further studies examining the effect of increased *FABP3* expression on *SMN2* alternative splicing would provide important insights into a novel mechanism of gene regulation.

While EIPA and HMA are potent inhibitors of NHE-type antiporters (Masereel et al., 2003), it is possible their mode of action with respect to *SMN2* exon 7 inclusion may be separate from NHE inhibition. Certain amilorides can also inhibit different types of  $\text{Ca}^{2+}$ -activated non-specific cation channels like ASIC1A (acid-sensing ion channel 1A) or TRPP3 (transient receptor potential P3, also known as polycystin-2) (Dai et al., 2007; Leng et al., 2016). It is possible that the effects of EIPA and HMA on *SMN2* alternative splicing may be mediated by inhibition of these other channels. To address this possibility, SMA fibroblasts and other cellular models can be treated with more specific ASIC1A or TRPP3 inhibitors, like phenamil and benzamil (Dai et al., 2007; Leng et al., 2016) to monitor their effects on *SMN2* exon 7 inclusion.

SMA can now be considered an actionable disease since there are currently 3 therapies approved by the FDA for SMA patients: nusinersen (Finkel et al., 2017; Mercuri et al., 2018), risdiplam (Baranello et al., 2021) and onasemnogene abeparvovec (Mendell et al., 2017). Despite these exciting advances, other therapies are needed, particularly if they are complementary to current therapeutic options. Traditional small molecule therapies have been the mainstay of the pharmaceutical industry for several important reasons. Small molecule inducers of *SMN2* expression could serve as complementary therapies for SMA patients who are either not good candidates or poor responders to biologic therapies. NHE5 inhibitors like EIPA and HMA may be able to serve this complementary role but they will need to be tested in animal models for SMA. The identification of more precisely targets for therapeutic development will ultimately lead to additional drug candidates for the treatment of SMA which can be used either alone or in combination with existing SMA therapies.

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## AUTHORSHIP CONTRIBUTIONS

Participated in research design: Kanda and Butchbach

Conducted experiments: Kanda and Moulton

Contributed new reagents or analytic tools: Butchbach

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Wrote or contributed to the writing of the manuscript: Kanda, Moulton and Butchbach

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## FOOTNOTES

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No author has an actual or perceived conflict of interest with the contents of this article.

## FIGURE LEGENDS

**Figure 1. Chemical structures of the SLC9A-type sodium-proton exchanger (NHE) inhibitors tested.**

**Figure 2. Effects of NHE inhibitors on *SMN2* alternative splicing. (A)** *SMN2* exon 7 inclusion reporter cells (NSC-34:*SMN2*:Mg2:bla5.3) were treated with varying concentrations of the NHE inhibitors amiloride, DMA, EIPA, HMA, cariporide or zoniporide (1 nM - 10  $\mu$ M; n=4/dose) or DMSO for 19 hours.  $\beta$ -Lactamase (BLA) activity was measured fluorimetrically. **(B-C)** Effect of NHE inhibitors on *SMN2* exon 7 inclusion in type II SMA fibroblasts. Type II SMA fibroblasts (GM03813) were treated with varying concentrations (100 nM – 10  $\mu$ M; n=3/group) of NHE inhibitors or DMSO for 5 days (n=3/treatment group). After total RNA isolation, samples were analyzed for relative amounts of *FL-SMN* and *SMN $\Delta$ 7* transcripts by RT-PCR and agarose gel electrophoresis. *COL3A* served as a loading control in this assay. The relative amounts of *FL-SMN* and *SMN $\Delta$ 7* transcripts were also measured on carrier fibroblasts (GM03814). The asterisk (\*) denoted a statistically significant ( $p < 0.05$ ) difference between NHE inhibitor- and vehicle-treated cells.

**Figure 3. Effects of NHE inhibitors on expression of *FL-SMN* and *SMN $\Delta$ 7* mRNA transcripts in SMA patient-derived fibroblasts.** GM03813 type II SMA fibroblasts were treated with different concentrations of NHE inhibitors (100 nM – 10  $\mu$ M; n=3/dose) or DMSO for 5 days. Changes in *FL-SMN* **(A)** or *SMN $\Delta$ 7* **(B)** transcript levels were measured via quantitative RT-PCR with *ACTB*, *GAPDH*, and *RPLP0* serving as reference transcripts. *FL-SMN* and *SMN $\Delta$ 7* transcript levels were also measured in GM03814 carrier fibroblasts. Changes in *FL-SMN* **(C)** or *SMN $\Delta$ 7* **(D)** transcript levels were measured in two other type II SMA fibroblast lines (GM22592 and AIDHC-SP22) treated with NHE inhibitors (10  $\mu$ M; n=3/inhibitor) for 5 days. All transcript levels were expressed relative to

DMSO-treated GM03813 cells (dashed line). The asterisk (\*) denoted a statistically significant ( $p < 0.05$ ) difference between NHE inhibitor- and vehicle-treated cells.

**Figure 4. Effects of NHE inhibitors on SMN protein levels in SMA fibroblasts.** GM03813 type II SMA fibroblasts were treated with different concentrations of NHE inhibitors (100 nM – 10  $\mu$ M;  $n=3$ /dose) or DMSO for 5 days. Changes in SMN protein levels were measured via immunoblot using  $\beta$ -actin as a reference protein. SMN protein levels were also measured in GM03814 carrier fibroblasts.

**Figure 5. Effects of the NHE inhibitors on alternative splicing of *striatin-3* (*STRN3*) and *forkhead box protein M1* (*FOXM1*) in type II SMA fibroblasts.** GM03813 type II SMA fibroblasts were treated with 10  $\mu$ M amiloride, 10  $\mu$ M EIPA, 10  $\mu$ M HMA, 1  $\mu$ M RG7800 or DMSO ( $n=3$ /group) for 5 days. The levels of *full-length STRN3* (*FL-STRN3*; **A**), *STRN3* lacking exons 8 and 9 (*STRN3 $\Delta$ 89*; **B**), *FOXM1* containing exons Va and VIIa (*FOXM1A*; **C**) and *FOXM1* containing exon Va (*FOXM1C*; **D**) transcripts were measured in total RNA extracted from treated cells by quantitative RT-PCR. All transcript levels were expressed relative to DMSO-treated GM03813 cells (dashed line). The asterisk (\*) denoted a statistically significant ( $p < 0.05$ ) difference between drug- and vehicle-treated cells.

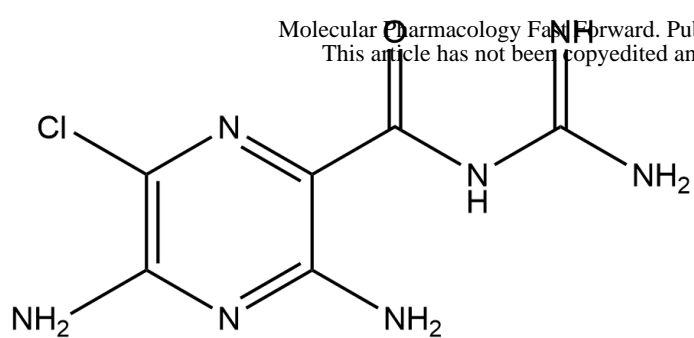
**Figure 6. Effects of NHE inhibitors on the expression of splicing regulators involved in *SMN2* exon 7 alternative splicing.** GM03813 type II SMA fibroblasts were treated with 10  $\mu$ M NHE inhibitors (amiloride, DMA, EIPA, HMA, cariporide or zoniporide) or DMSO ( $n=3$ /group) for 5 days. *hnRNP-A1* (**A**), *SF2/ASF* (**B**), *hTRA2 $\beta$ 1* (**C**), *SaM68* (**D**) and *SRp20* (**E**) transcript levels were measured in total RNA extracted from treated cells by quantitative RT-PCR. Transcript levels were also measured in GM03814 carrier fibroblasts. All transcript levels were expressed relative to DMSO-treated GM03813 cells (dashed line). The asterisk (\*) denoted a statistically significant ( $p < 0.05$ ) difference between drug- and vehicle-treated cells.



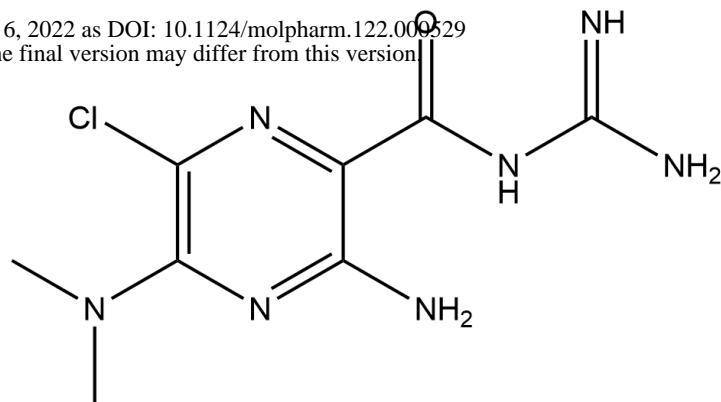
**Figure 7. Identification of differentially expressed transcripts in type II SMA fibroblasts treated with amiloride or EIPA.** GM03813 type II SMA fibroblasts were treated with 10  $\mu$ M amiloride, 10  $\mu$ M EIPA or DMSO (n=3/group) for 5 days and their RNA pools were analyzed for differential transcript expression using Clariom D human transcriptome arrays. **(A)** Principal component analysis (PCA) of samples treated with amiloride (purple), EIPA (red) or DMSO (blue). Hierarchical clustering analysis of amiloride vs. DMSO **(B)** and EIPA vs. DMSO **(C)**. Volcano plots of amiloride vs. DMSO **(D)** and EIPA vs. DMSO **(E)** type II SMA fibroblast transcriptomes. Significantly upregulated transcripts are shown in red while significantly downregulated transcripts are shown in blue. **(F)** Venn diagram showing the similarities and differences between the amiloride vs. DMSO (red) and EIPA vs. DMSO (blue) transcriptomes. The overlap between these two transcriptomes is shown in purple. **(G)** The top dozen canonical pathways—out of 165—that were significantly over-represented in the EIPA-unique transcriptome. The numbers next to the pathway lines represent the number of differentially expressed molecules for each pathway. **(H)** The upstream regulators that are significantly and uniquely differentially regulated in EIPA-treated type II SMA fibroblasts. **(I)** Distributions of the categorized differential splicing events between amiloride vs. DMSO and EIPA vs. DMSO transcriptomes.

**Figure 8. Validation of EIPA- and HMA-responsive transcripts in type II SMA fibroblasts.**

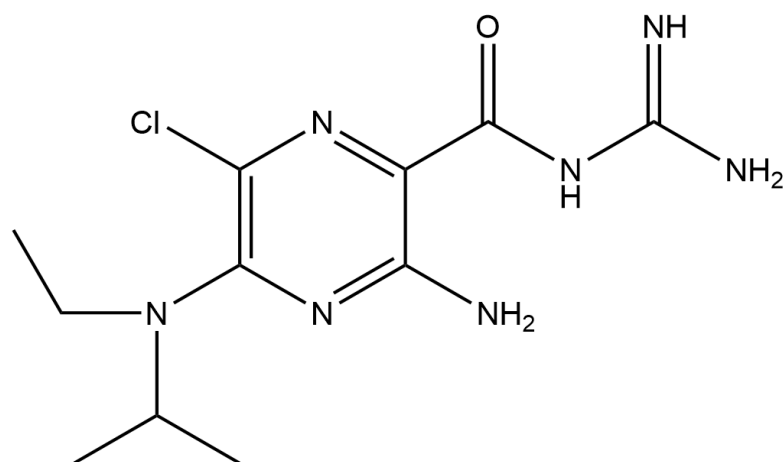
GM03813 type II SMA fibroblasts were treated with 10  $\mu$ M amiloride, 10  $\mu$ M EIPA, 10  $\mu$ M HMA, 1  $\mu$ M RG7800 or DMSO (n=3/group) for 5 days. *TIA1* **(A)**, *FABP3* **(B)**, *DHCR7* **(C)**, *TRPV4* **(D)**, *ATXN1* **(E)** and *PRKARB2* **(F)** transcript levels were measured in total RNA extracted from treated cells by quantitative RT-PCR. All transcript levels were expressed relative to DMSO-treated GM03813 cells (dashed line). The asterisk (\*) denoted a statistically significant ( $p < 0.05$ ) difference between drug- and vehicle-treated cells.



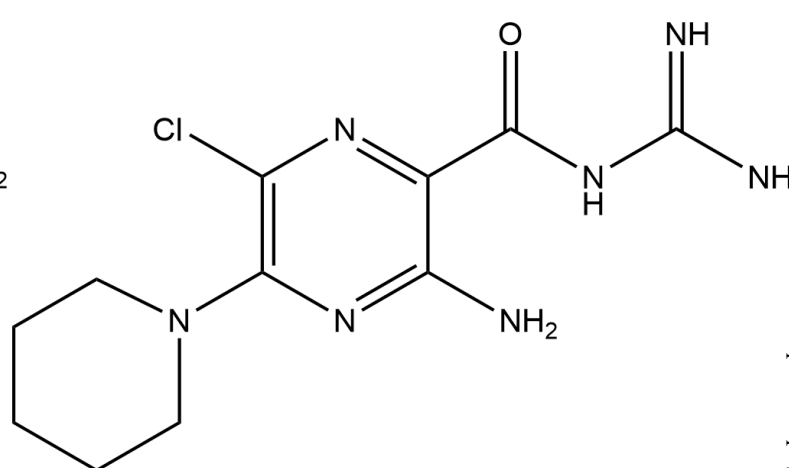
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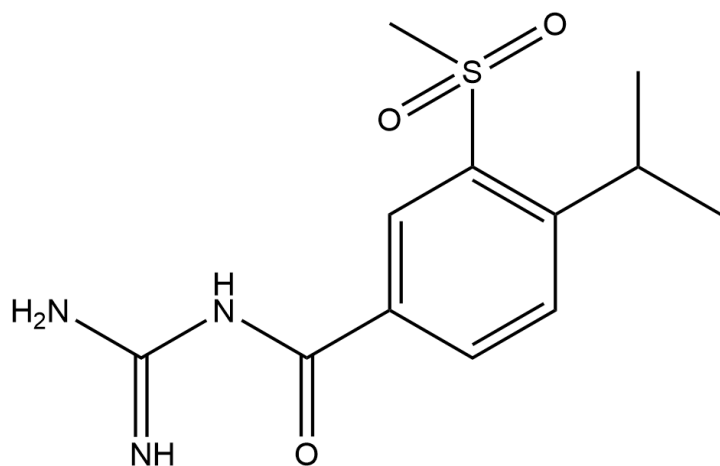
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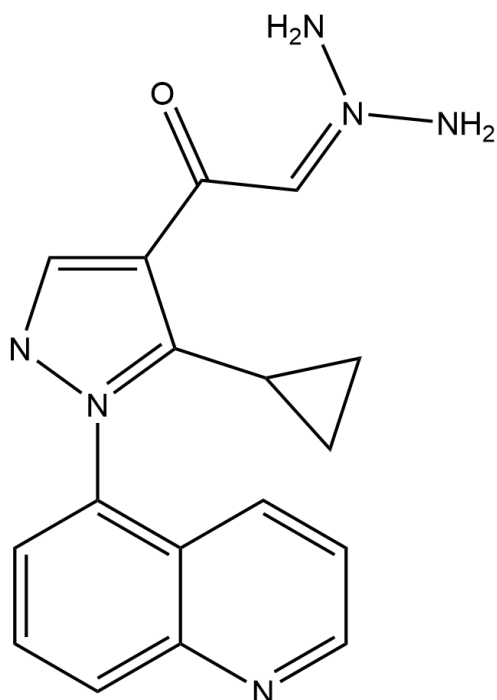
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(EIPA)**



**5-(N,N-hexamethylene)-amiloride  
(HMA)**

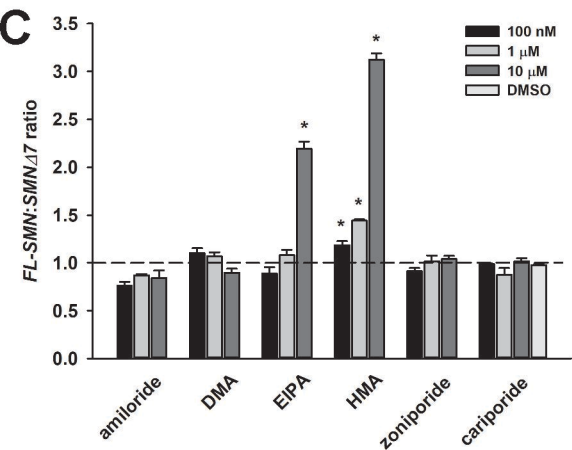
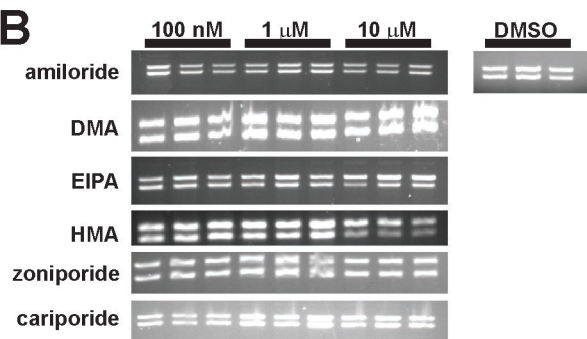
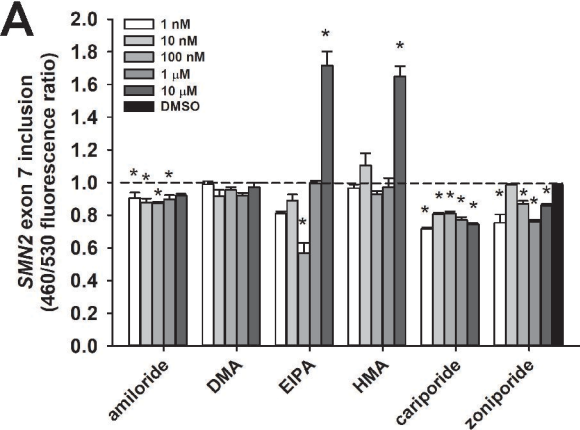


**cariporide**

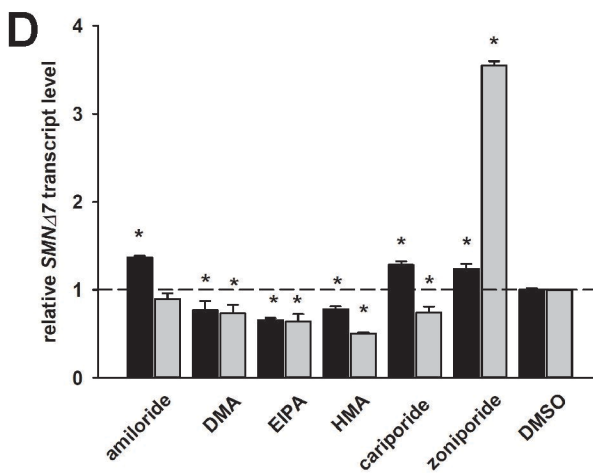
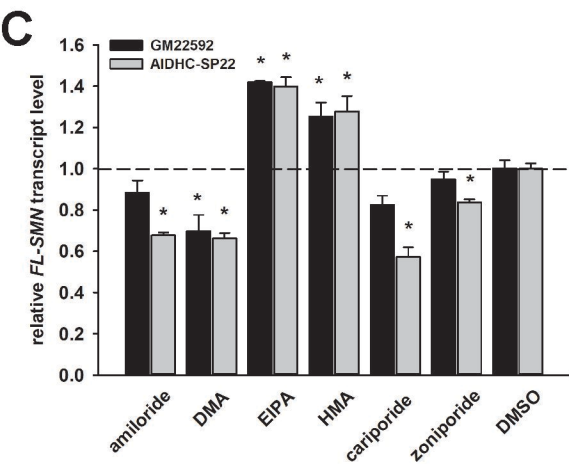
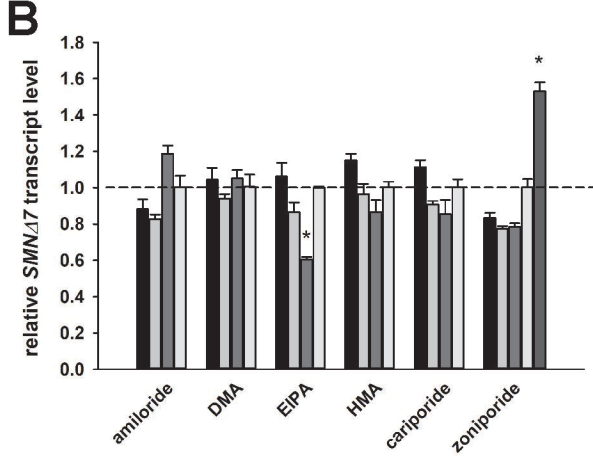
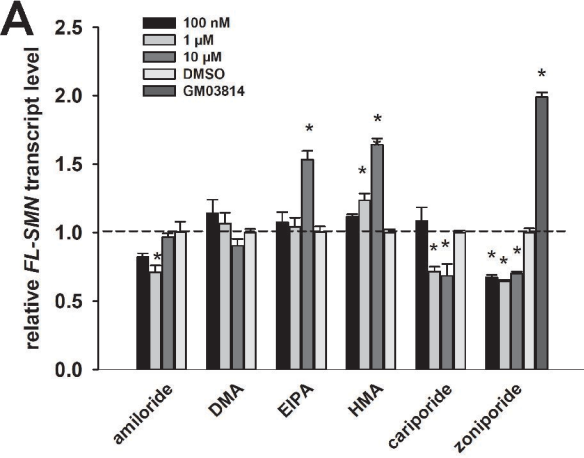


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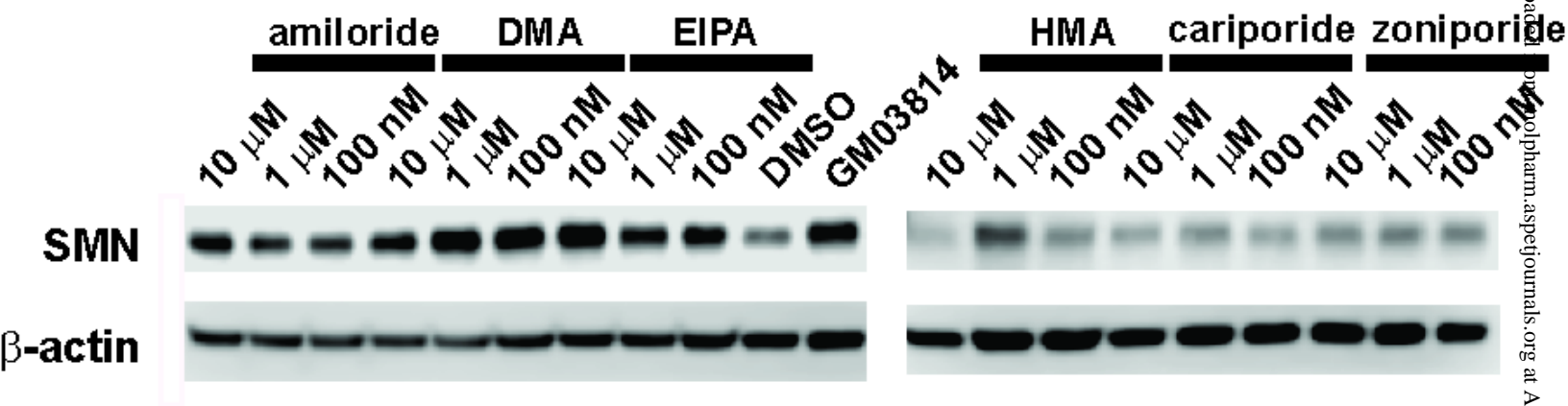
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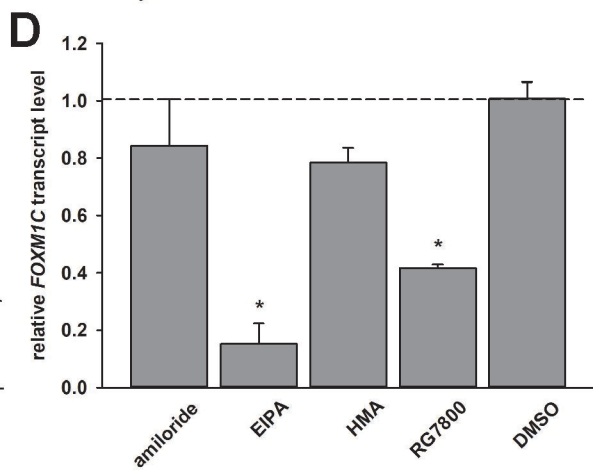
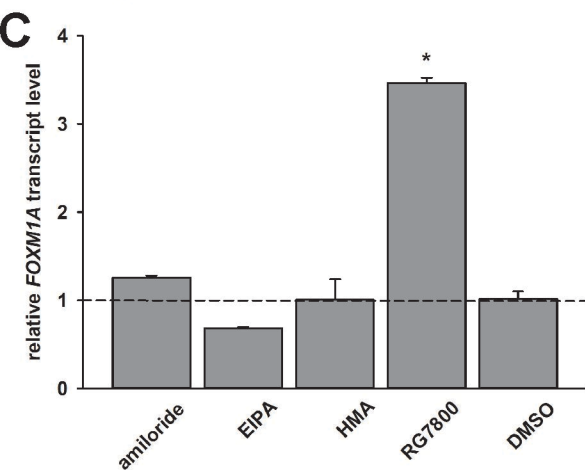
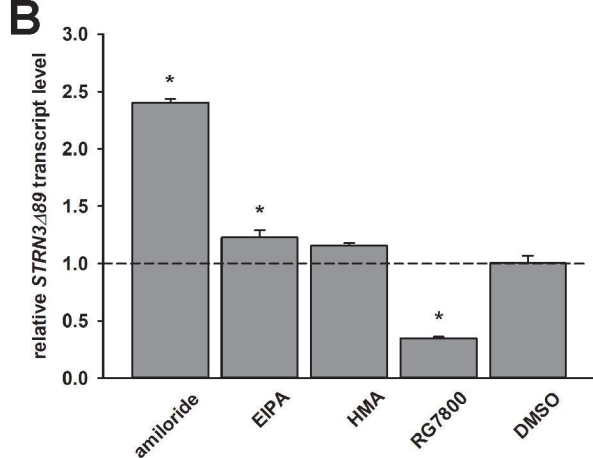
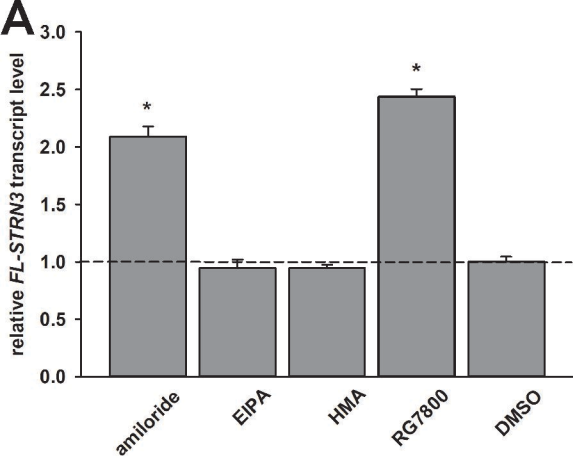
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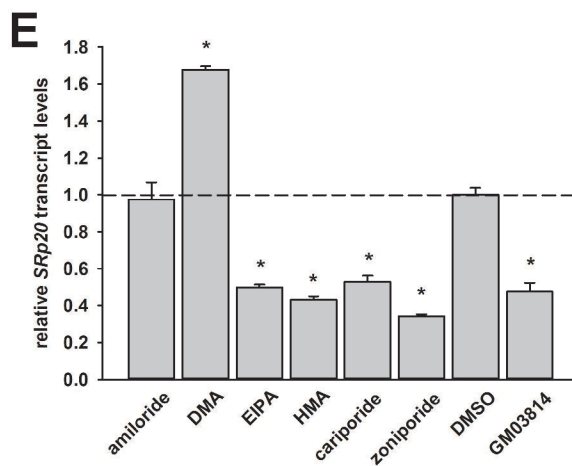
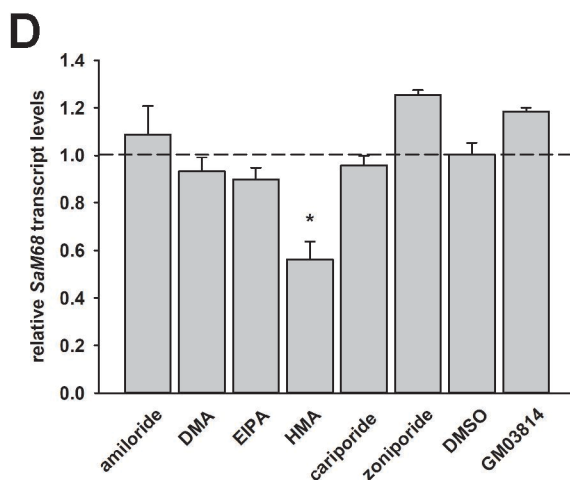
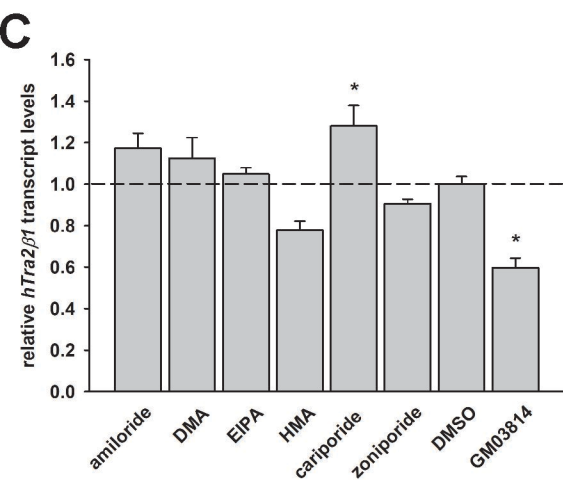
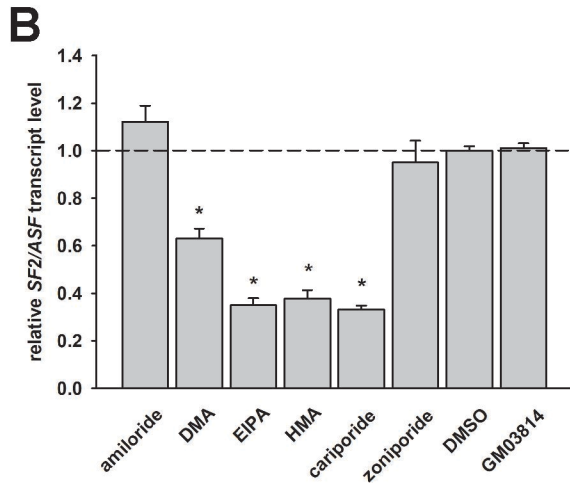
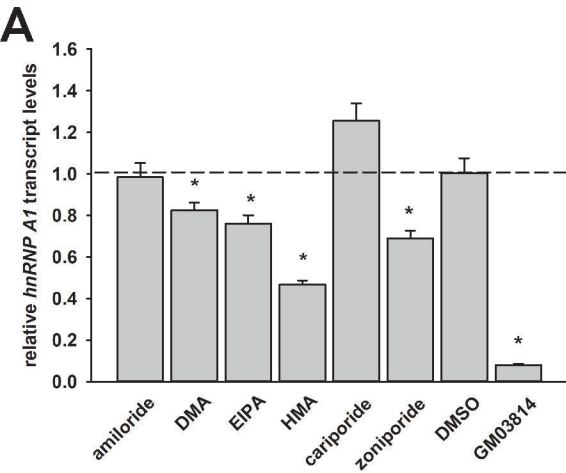
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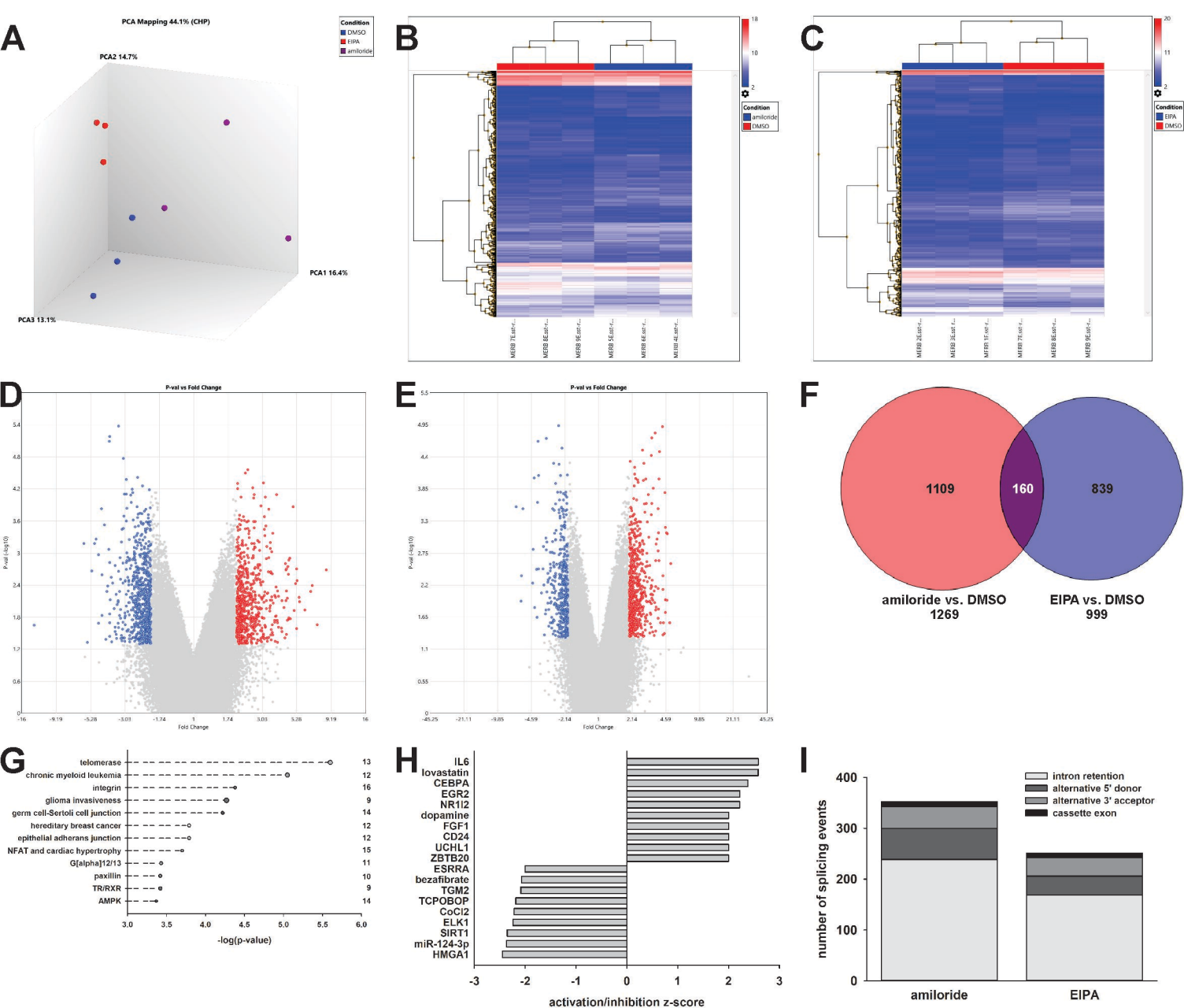
**Figure 4**



**Figure 5**

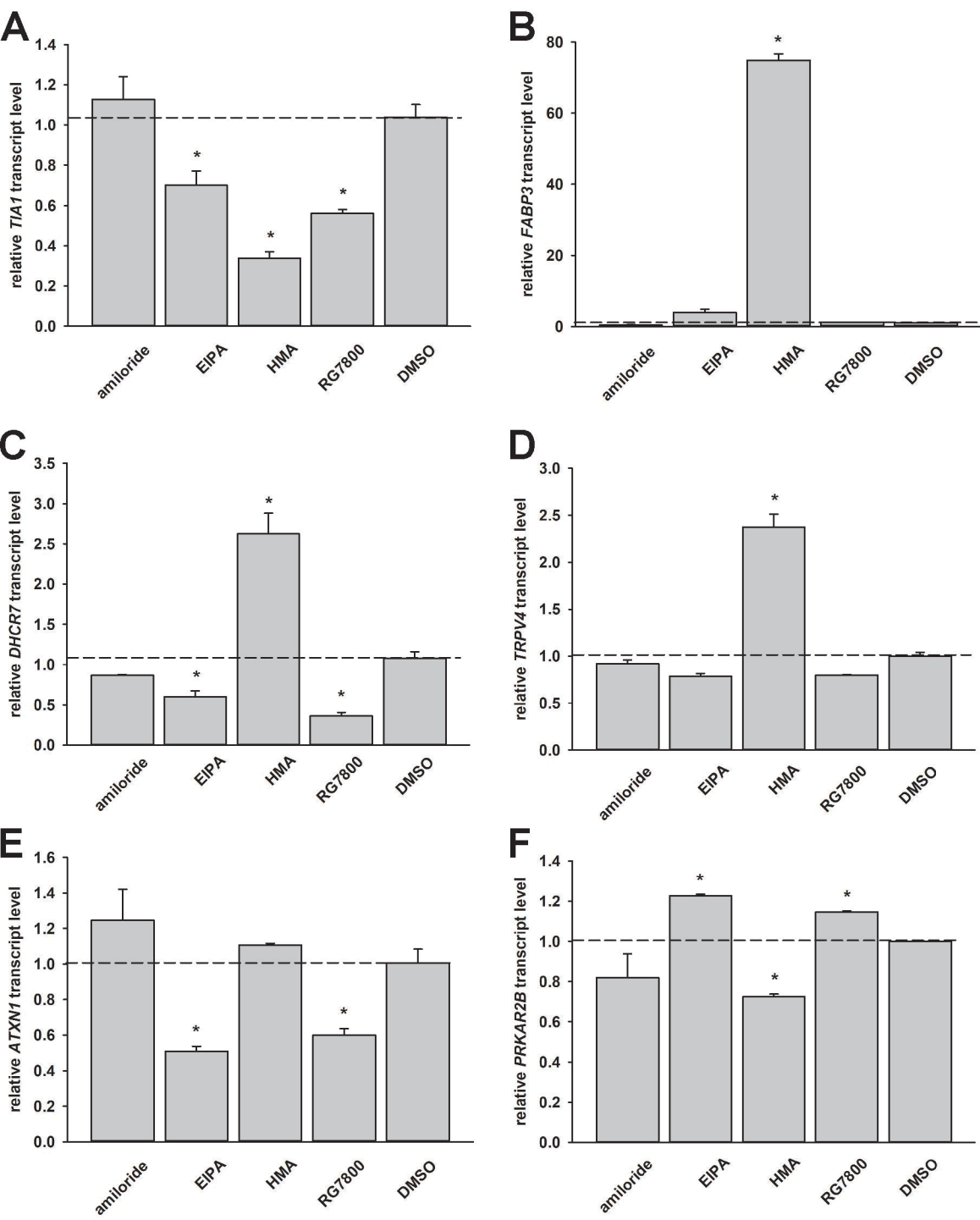


**Figure 6**



**Figure 7**





**Figure 8**

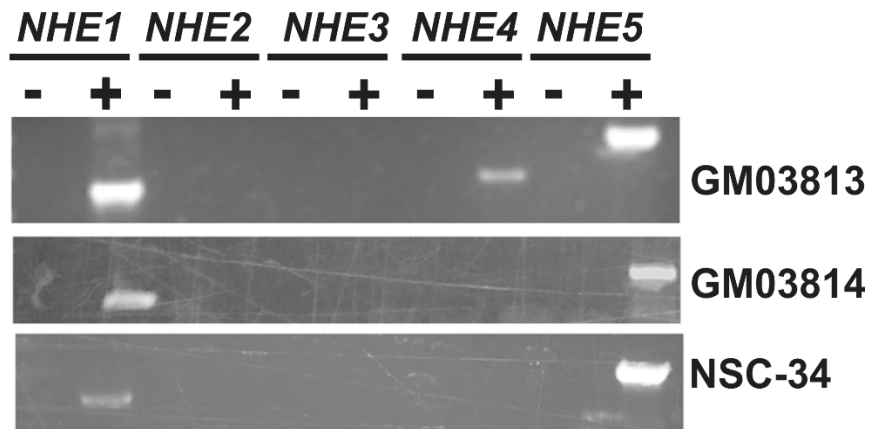
Supplemental File

Effects of inhibitors of SLC9A-type sodium-proton exchangers on *Survival Motor Neuron*  
2 (*SMN2*) mRNA splicing and expression

Sambee Kanda, Emily Moulton and Matthew E. R. Butchbach

*Molecular Pharmacology*

#MOLPHARM-AR-2022-000529



Supplemental Figure 1.

Expression of NHE isoform mRNAs in GM03813, GM03814 and NSC-34 cells.

**Supplemental Table 1.**

List of differentially expressed transcripts.

ID	DMSO Avg (log2)	EIPA Avg (log2)	DMSO Standard Deviation	EIPA Standard Deviation	Fold Change (rel to EIPA)	Fold Change (rel to DMSO)	P-val	FDR P-val	duplicate	Gene Symbol	Description
TC0100013561.hg.1	5.92	8.61	1.1	0.67	-6.44	6.44	0.0003	0.5406		FABP3	fatty acid binding protein 3, muscle and heart
TC0300010185.hg.1	9.34	11.87	1.71	0.57	-5.75	5.75	0.0044	0.6495		OXTR	oxytocin receptor
TC0700006488.hg.1	5.45	7.92	0.63	0.14	-5.56	5.56	0.0003	0.5406		GPBR1	G protein-coupled estrogen receptor 1
TC1400009798.hg.1	3.84	5.97	0.77	0.81	-4.39	4.39	0.0015	0.5917	D	NRXN3	neurexin 3
TC0500011347.hg.1	7.58	9.69	0.59	0.27	-4.32	4.32	9.11E-05	0.4854		HAPLN1	hyaluronan and proteoglycan link protein 1
TC1500008525.hg.1	3.76	5.78	0.37	1.16	-4.04	4.04	0.0228	0.7293	D	MEF2A	myocyte enhancer factor 2A
TC0X00010496.hg.1	6.28	8.27	0.21	0.58	-3.97	3.97	0.0002	0.5406		ACSL4	acyl-CoA synthetase long chain family member 4
TC0700013614.hg.1	5.08	7.04	0.59	0.24	-3.88	3.88	0.0033	0.6212		ZNF800	zinc finger protein 800
TC0800008341.hg.1	4.39	6.35	0.55	0.14	-3.87	3.87	8.23E-05	0.4854	D	STK3	serine/threonine kinase 3
TC1600008243.hg.1	3.35	5.21	0.51	0.8	-3.64	3.64	0.0087	0.6681	D	WWP2	WW domain containing E3 ubiquitin protein ligase 2
TC0400007436.hg.1	4.48	6.22	0.24	1.8	-3.34	3.34	0.0196	0.7205		CNGA1	cyclic nucleotide gated channel alpha 1
TC0M00006444.hg.1	17.71	19.41	0.39	0.15	-3.27	3.27	1.92E-05	0.4807	D	ICAM2	intercellular adhesion molecule 2
TC0M00006444.hg.1	17.71	19.41	0.39	0.15	-3.27	3.27	1.92E-05	0.4807	D	PRR29	proline rich 29
TC0400011994.hg.1	6.01	7.71	0.31	0.53	-3.26	3.26	0.0016	0.5917		INPP4B	inositol polyphosphate-4-phosphatase type II B
TC1100008544.hg.1	3.4	5.09	0.28	0.44	-3.22	3.22	0.0083	0.6679		AAMDC	adipogenesis associated Mth938 domain containing
TC1100008544.hg.1	3.4	5.09	0.28	0.44	-3.22	3.22	0.0083	0.6679		INTS4	integrator complex subunit 4
TC1900010687.hg.1	4.33	6.02	0.59	0.19	-3.22	3.22	0.0011	0.5917		ZNF780B	zinc finger protein 780B
TC0600008505.hg.1	4.37	6.03	0.57	0.28	-3.15	3.15	0.004	0.6423		RIMS1	regulating synaptic membrane exocytosis 1
TC1300007781.hg.1	3.72	5.37	0.16	0.6	-3.14	3.14	0.0056	0.6602		RAP2A	RAP2A, member of RAS oncogene family (K-REV)
TC1800007864.hg.1	3.72	5.35	0.28	0.96	-3.1	3.1	0.0319	0.7409		ENOSF1	enolase superfamily member 1
TC1200009772.hg.1	3.55	5.14	0.4	0.61	-3.01	3.01	0.0047	0.6495		C1S	complement C1s
TC1700007240.hg.1	6.09	7.67	0.54	0.54	-2.99	2.99	0.0036	0.6269		SCDP1	stearyl-CoA desaturase (delta-9-desaturase) pseudogene 1
TC1700007167.hg.1	7.02	8.6	0.56	0.54	-2.98	2.98	0.0027	0.6175	D	EPN2	epsin 2
TC0100017636.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S11	RNA, 5S ribosomal 11
TC0100017637.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S12	RNA, 5S ribosomal 12
TC0100017638.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S13	RNA, 5S ribosomal 13
TC0100017639.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S14	RNA, 5S ribosomal 14
TC0100017640.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S15	RNA, 5S ribosomal 15
TC0100017641.hg.1	12.35	13.93	0.25	0.42	-2.98	2.98	0.0017	0.5917		RNA5S16	RNA, 5S ribosomal 16
TC1400010673.hg.1	3.1	4.66	0.24	0.88	-2.96	2.96	0.0129	0.6911		SNORD114-17	small nucleolar RNA, C/D box 114-17
TC1000010702.hg.1	7.25	8.81	0.73	0.22	-2.94	2.94	0.0032	0.6196		IPMK	inositol polyphosphate multikinase
TC0200010585.hg.1	3.26	4.79	0.13	0.8	-2.89	2.89	0.0348	0.7433		CPO	carboxypeptidase O
TC1500008046.hg.1	9.03	10.55	0.46	0.23	-2.88	2.88	0.0228	0.7293	D	CEMIP	cell migration inducing protein, hyaluronan binding
TC1800006488.hg.1	5.66	7.19	0.75	0.25	-2.88	2.88	0.0062	0.6674		SMCHD1	structural maintenance of chromosomes flexible hinge domain containing 1
TC0100008912.hg.1	11.64	13.16	0.72	0.22	-2.86	2.86	0.0084	0.6679		CYR61	cysteine-rich, angiogenic inducer, 61
TC0500011232.hg.1	3.38	4.9	0.56	0.63	-2.85	2.85	0.0017	0.5917		DMGH	dimethylglycine dehydrogenase
TC1500009861.hg.1	10.63	12.13	0.57	0.22	-2.84	2.84	0.0052	0.6581		ITGA11	integrin alpha 11

TC0600010810.hg.1	3.03	4.54	0.43	0.33	-2.84	2.84	0.0011	0.5917	NEDD9	neural precursor cell expressed, developmentally down-regulated 9
TC0400011458.hg.1	3.74	5.23	0.69	0.93	-2.81	2.81	0.028	0.7374	SLC39A8	solute carrier 39 member 8; zinc transporter 8
TC1000008719.hg.1	3.56	5.04	0.65	0.96	-2.8	2.8	0.044	0.7575	GBF1	golgi brefeldin A resistant guanine nucleotide exchange factor 1
TC1700010652.hg.1	8.34	9.81	0.7	0.01	-2.77	2.77	0.0029	0.6175	KRTAP2-2	keratin associated protein 2-2
TC0600006762.hg.1	11.11	12.57	0.32	0.28	-2.76	2.76	0.0026	0.6166	MIR7641-2	microRNA 7641-2
TC1800008743.hg.1	12.76	14.21	0.84	0.32	-2.73	2.73	0.0044	0.6495	CCDC68	coiled-coil domain containing 68
TC0300013282.hg.1	9.45	10.9	0.34	0.51	-2.73	2.73	0.0137	0.6926	RNA5SP149	5S ribosomal pseudogene 149
TC0X00008054.hg.1	4.76	6.2	0.48	0.36	-2.71	2.71	0.0008	0.5917	RNF128	ring finger protein 128, E3 ubiquitin protein ligase
TC0200006730.hg.1	4.25	5.68	0.03	0.83	-2.69	2.69	0.0392	0.7497	RN7SL674P	RNA, 7SL, cytoplasmic 674, pseudogene
TC1100011234.hg.1	10.54	11.96	0.86	0.18	-2.68	2.68	0.0128	0.691	LTBP3	latent transforming growth factor beta binding protein 3
TC0100015194.hg.1	10.3	11.72	0.73	0.34	-2.67	2.67	0.0054	0.6602	SORT1	sortilin 1
TC1800006641.hg.1	2.6	4.01	0.3	0.44	-2.66	2.66	0.0003	0.5406	RALBP1	ralA binding protein 1
TC0600007087.hg.1	11.65	13.06	0.41	0.45	-2.65	2.65	0.004	0.6423	CAP2	CAP, adenylate cyclase-associated protein, 2 (yeast)
TC0900010969.hg.1	10.95	12.35	0.49	0.27	-2.65	2.65	0.0465	0.7625	CORO2A	coronin, actin binding protein, 2A
TC1000011057.hg.1	2.81	4.21	0.21	0.69	-2.64	2.64	0.0043	0.6489	ADK	adenosine kinase
TC1200010021.hg.1	10.35	11.76	0.36	0.16	-2.64	2.64	0.0011	0.5917	C12orf60	chromosome 12 open reading frame 60
TC0100007638.hg.1	10.72	12.12	0.29	0.25	-2.64	2.64	0.0001	0.5107	SERINC2	serine incorporator 2
TC1400007348.hg.1	9.48	10.87	0.63	0.07	-2.63	2.63	0.0079	0.6679	PCNX4	pecanex 4
TC0200013206.hg.1	6.28	7.67	0.35	0.32	-2.63	2.63	0.0135	0.6926	RNA5SP99	RNA, 5S ribosomal pseudogene 99
TC0300007309.hg.1	3.94	5.32	0.27	0.5	-2.6	2.6	0.0197	0.7205	SMARCC1	SWI/SNF related, matrix-associated, actin-dependent regulator of chromatin C1
TC0600011595.hg.1	12.45	13.83	0.59	0.46	-2.59	2.59	0.0028	0.6175	C6orf106	chromosome 6 open reading frame 106
TC1700007131.hg.1	3.75	5.12	0.86	0.12	-2.59	2.59	0.0154	0.7029	TBC1D28	TBC1 domain family member 28
TC0200012776.hg.1	5.65	7.02	0.55	0.39	-2.59	2.59	0.0146	0.6965	TMEM17	transmembrane protein 17
TC0600008157.hg.1	2.98	4.34	0.47	0.77	-2.57	2.57	0.0113	0.6846	ENPP5	ectonucleotide pyrophosphatase/phosphodiesterase 5
TC0800011605.hg.1	13.84	15.18	0.54	0.12	-2.53	2.53	0.03	0.7392	SAMD12	sterile alpha motif domain containing 12
TC0900006785.hg.1	2.91	4.24	0.19	0.31	-2.52	2.52	0.0002	0.5406	FOCAD	focadhesin
TC0300009844.hg.1	4.17	5.51	0.32	0.83	-2.52	2.52	0.0393	0.7507	MIR944	microRNA 944
TCUn_GL000216v200006434.hg.1	3.04	4.36	0.47	0.78	-2.5	2.5	0.0142	0.6963	U2	U2 spliceosomal RNA
TC1000012140.hg.1	4.45	5.76	0.63	0.15	-2.47	2.47	0.0482	0.7639	CTBP2	C-terminal binding protein 2
TC0X00008844.hg.1	4.09	5.39	0.75	0.16	-2.47	2.47	0.016	0.7056	IKBK	inhibitor of nuclear factor kappa B kinase subunit gamma
TC0500011131.hg.1	3.03	4.32	0.71	0.77	-2.46	2.46	0.03	0.7392	ARHGEF28	Rho guanine nucleotide exchange factor 28
TC1500008038.hg.1	13.48	14.78	0.8	0.48	-2.46	2.46	0.0097	0.6713	ARNT2	aryl-hydrocarbon receptor nuclear translocator 2
TC1500008038.hg.1	13.48	14.78	0.8	0.48	-2.46	2.46	0.0097	0.6713	MIR5572	microRNA 5572
TC0500009379.hg.1	3.28	4.57	0.32	0.1	-2.45	2.45	0.0003	0.5406	DOCK2	dedicator of cytokinesis 2
TC2000007453.hg.1	3.03	4.33	0.47	0.22	-2.45	2.45	0.0032	0.6196	HNF4A	hepatocyte nuclear factor 4 alpha
TC2000007453.hg.1	3.03	4.33	0.47	0.22	-2.45	2.45	0.0032	0.6196	MIR3646	microRNA 3646

TC0100018239.hg.1	7.76	9.04	1.04	0.74	-2.44	2.44	0.019	0.7167	GIPC2	GIPC PDZ domain containing family, member 2
TC0300012508.hg.1	8.07	9.35	0.32	0.35	-2.44	2.44	0.0108	0.6786	RNA5SP141	5S ribosomal pseudogene 141
TC1500009498.hg.1	3.65	4.93	0.43	0.71	-2.43	2.43	0.0357	0.7437	CCPG1	cell cycle progression 1
TC1000009519.hg.1	8.41	9.69	0.33	0.3	-2.43	2.43	0.0165	0.7092	DIP2C	disco interacting protein 2 homolog C
TC1100007188.hg.1	3.98	5.26	0.18	0.97	-2.43	2.43	0.0091	0.671	ELP4	elongator acetyltransferase complex subunit 4
TC0500013349.hg.1	8.13	9.41	0.4	0.3	-2.43	2.43	0.0041	0.6437	FBN2	fibrillin 2
TC1500009498.hg.1	3.65	4.93	0.43	0.71	-2.43	2.43	0.0357	0.7437	PIGB	phosphatidylinositol glycan anchor biosynthesis class B
TC0600009320.hg.1	10.33	11.61	0.63	0.7	-2.43	2.43	0.0048	0.6495	RNU1-18P	RNA, U1 small nuclear 18, pseudogene
TC1100010293.hg.1	4.48	5.75	0.23	0.86	-2.42	2.42	0.0419	0.7534	NAV2	neuron navigator 2
TC0700010738.hg.1	2.91	4.18	0.23	0.58	-2.42	2.42	0.0262	0.7354	RNU6-1085P	RNA, U6 small nuclear 1085, pseudogene
TC0300009129.hg.1	3.24	4.51	0.4	0.45	-2.41	2.41	0.0027	0.6175	HLTF	helicase-like transcription factor
TC1900010117.hg.1	3.45	4.72	0.16	0.62	-2.41	2.41	0.0031	0.6196	ZNF626	zinc finger protein 626
TC0700009339.hg.1	3.09	4.35	0.33	0.36	-2.4	2.4	0.0004	0.549	LUC7L2	LUC7 like 2, pre-mRNA splicing factor
TC0100008807.hg.1	10.4	11.67	0.52	0.25	-2.4	2.4	0.0141	0.6963	NEXN	nexilin (F actin binding protein)
TC0100017626.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S1	RNA, 5S ribosomal 1
TC0100017635.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S10	RNA, 5S ribosomal 10
TC0100017642.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S17	RNA, 5S ribosomal 17
TC0100017627.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S2	RNA, 5S ribosomal 2
TC0100017628.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S3	RNA, 5S ribosomal 3
TC0100017629.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S4	RNA, 5S ribosomal 4
TC0100017630.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S5	RNA, 5S ribosomal 5
TC0100017631.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S6	RNA, 5S ribosomal 6
TC0100017632.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S7	RNA, 5S ribosomal 7
TC0100017633.hg.1	11.72	12.98	0.22	0.26	-2.4	2.4	0.0029	0.6175	RNA5S8	RNA, 5S ribosomal 8
TC0100011197.hg.1	5.97	7.23	0.56	0.38	-2.4	2.4	0.0028	0.6175	SHISA4	shisa family member 4
TC0X00006746.hg.1	3.04	4.3	0.32	0.36	-2.39	2.39	0.0015	0.5917	BCLAF3	BCLAF1 and THRAP3 family member 3
TC2000006477.hg.1	8.46	9.71	0.47	0.18	-2.39	2.39	0.0005	0.5612	PSMF1	proteasome inhibitor subunit 1
TC0900010918.hg.1	4.66	5.9	0.33	0.17	-2.37	2.37	8.22E-05	0.4854	CDC14B	cell division cycle 14B
TC0800010264.hg.1	3.95	5.19	0.24	0.73	-2.37	2.37	0.0488	0.7642	KAT6A	lysine acetyltransferase 6A
TC0200012009.hg.1	5.19	6.43	0.48	0.41	-2.36	2.36	0.0318	0.7409	DTNB	dystrobrevin beta
TC1000008504.hg.1	10.67	11.91	0.66	0.36	-2.36	2.36	0.0018	0.5917	HELLS	helicase, lymphoid specific
TC0200016408.hg.1	5.77	7.01	0.28	0.14	-2.36	2.36	0.0002	0.5406	KCNS3	potassium voltage-gated channel, modifier subfamily S, member 3
TC2200009364.hg.1	4.66	5.9	0.61	0.36	-2.35	2.35	0.009	0.6696	CPT1B	carnitine palmitoyltransferase 1B (muscle)
TC1700010549.hg.1	3.42	4.65	0.28	0.57	-2.35	2.35	0.0081	0.6679	CWC25	CWC25 spliceosome associated protein homolog
TC0800011088.hg.1	4.02	5.25	0.6	0.79	-2.35	2.35	0.028	0.7374	RUNX1T1	RUNX1 translocation partner 1
TC0700012268.hg.1	3.12	4.35	0.04	0.68	-2.34	2.34	0.0197	0.7205	IMMP2L	IMP2 inner mitochondrial membrane peptidase subunit 2
TC0400007285.hg.1	4.29	5.51	0.35	0.44	-2.34	2.34	0.0126	0.6893	LIAS	lipoic acid synthetase
TC0200014476.hg.1	3.39	4.62	0.03	0.53	-2.34	2.34	0.0044	0.6495	LRP1B	low density lipoprotein receptor-related protein 1B
TC0300011409.hg.1	3.37	4.59	0.21	1.04	-2.34	2.34	0.0169	0.7092	MAGI1	membrane-associated guanylate kinase, WW and PDZ domain containing 1
TC0500007077.hg.1	7.17	8.4	0.7	0.37	-2.34	2.34	0.0081	0.6679	NPR3	natriuretic peptide receptor 3

TC2100006961.hg.1	6.9	8.13	0.28	0.21	-2.33	2.33	0.0016	0.5917	IFNAR1	interferon (alpha and beta) receptor 1
TC1700010651.hg.1	6.34	7.55	0.06	0.32	-2.33	2.33	0.0006	0.5837	KRTAP2-1	keratin associated protein 2-1
TC0500006786.hg.1	4.75	5.97	0.43	2.19	-2.33	2.33	0.0423	0.7546	LINC01194	long intergenic non-protein coding RNA 1194
TC0700008569.hg.1	9.63	10.84	0.73	0.64	-2.32	2.32	0.0221	0.7272	ACHE	acetylcholinesterase
TC1100008382.hg.1	5.37	6.58	0.58	0.18	-2.32	2.32	0.0107	0.6786	ARHGEF17	Rho guanine nucleotide exchange factor 17
TC0500008233.hg.1	10.01	11.22	0.23	0.2	-2.32	2.32	0.0003	0.5406	C5orf30	chromosome 5 open reading frame 30; unc119 binding
TC0700008853.hg.1	2.89	4.1	0.22	0.58	-2.32	2.32	0.0361	0.7441	FOXP2	forkhead protein box P2
TC0100006954.hg.1	5.7	6.91	0.46	0.27	-2.32	2.32	0.0042	0.6484	KAZN	kazrin, periplakin interacting protein
TC0300013106.hg.1	4.83	6.05	0.38	0.32	-2.32	2.32	0.0083	0.6679	RNU1-70P	RNA, U1 small nuclear 70, pseudogene
TC1200011896.hg.1	3.98	5.19	0.64	0.88	-2.31	2.31	0.0414	0.7524	C12orf76	chromosome 12 open reading frame 76
TC0500011352.hg.1	11.41	12.62	0.16	0.04	-2.31	2.31	0.0007	0.5837	EDIL3	EGF-like repeats and discoidin I-like domains 3
TC0800011620.hg.1	9.15	10.36	0.54	0.35	-2.31	2.31	0.0062	0.6674	ENPP2	ectonucleotide pyrophosphatase/phosphodiesterase 2
TC1700011721.hg.1	7.04	8.24	0.11	0.57	-2.31	2.31	0.0009	0.5917	FDXR	ferredoxin reductase
TC1400007540.hg.1	7.25	8.45	0.29	0.24	-2.3	2.3	0.0029	0.6175	ACTN1	actinin alpha 1
TC0X00010849.hg.1	3.37	4.57	0.22	0.61	-2.3	2.3	0.0072	0.6679	GPC4	glypican 4
TC0600010848.hg.1	2.89	4.09	0.33	0.54	-2.3	2.3	0.0181	0.7124	PHACTR1	phosphatase and actin regulator 1
TC0500008393.hg.1	2.78	3.97	0.21	0.57	-2.29	2.29	0.0133	0.6916	COMMD10	COMM domain containing 10
TC0500007509.hg.1	4.56	5.76	0.23	0.52	-2.29	2.29	0.0341	0.7424	PDE4D	phosphodiesterase 4D
TC0100009425.hg.1	3.54	4.74	0.53	0.65	-2.29	2.29	0.0166	0.7092	RAP1A	RAP1A
TC1100008050.hg.1	6.05	7.23	0.46	0.41	-2.28	2.28	0.0051	0.6578	CST6	cystatin E/M
TC0700010431.hg.1	2.74	3.93	0.53	0.81	-2.28	2.28	0.0457	0.7605	DNAH11	dynein, axonemal, heavy chain 11
TC0200008071.hg.1	11.7	12.88	0.06	0.41	-2.28	2.28	0.0056	0.6602	MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methylenetetrahydrofolate cyclohydrolase
TC0700010102.hg.1	10.32	11.5	0.62	0.2	-2.27	2.27	0.016	0.7056	SDK1	sidekick cell adhesion molecule 1
TC0400011920.hg.1	12.17	13.35	0.59	0.43	-2.27	2.27	0.0102	0.6715	SLC7A11	solute carrier 7 (anionic amino acid transporter light chain, xc- system), member 11
TC0400012988.hg.1	3.01	4.2	0.23	0.56	-2.27	2.27	0.0494	0.7657	TMEM192	transmembrane protein 192
TC0400011303.hg.1	3.55	4.72	0.4	0.55	-2.26	2.26	0.0479	0.7637	FAM13A	family with sequence similarity 13 member A
TC0500007985.hg.1	3.54	4.71	0.07	0.61	-2.26	2.26	0.0147	0.6965	LOC105379057	LOC105379057
TC0200009923.hg.1	4.07	5.25	0.13	0.66	-2.26	2.26	0.0192	0.7167	UBR3	ubiquitin protein ligase E3 component n-recogin 3
TC1100013022.hg.1	9.61	10.78	0.34	0.23	-2.25	2.25	0.0003	0.5406	FADS2	fatty acid desaturase 2
TC0100011092.hg.1	5.68	6.85	0.94	0.37	-2.25	2.25	0.0332	0.7419	LHX9	LIM homeobox 9
TC0700010377.hg.1	5.27	6.44	0.55	0.31	-2.25	2.25	0.0037	0.635	SNX13	sorting nexin 13
TC0100014652.hg.1	4.44	5.61	0.26	0.54	-2.25	2.25	0.0278	0.7374	ZZZ3	zinc finger ZZ-type containing 3
TC1300009924.hg.1	12.92	14.09	0.82	0.29	-2.24	2.24	0.0465	0.7625	GA56	growth arrest-specific 6
TC0100006564.hg.1	3.54	4.71	0.43	0.4	-2.24	2.24	0.0053	0.6602	TMEM50A	transmembrane protein 50A
TC1600006996.hg.1	5.06	6.22	0.33	0.68	-2.23	2.23	0.0404	0.7511	BFAR	bifunctional apoptosis regulator
TC0200015456.hg.1	3.32	4.47	0.34	0.57	-2.23	2.23	0.0092	0.671	BMPR2	bone morphogenic protein receptor II

TC0200008468.hg.1	6.68	7.84	0.4	0.4	-2.23	2.23	0.001	0.5917	FAHD2A	fumarylacetoacetate hydrolase domain containing 2A
TC0500007984.hg.1	2.67	3.82	0.12	0.19	-2.23	2.23	0.0002	0.5406	LOC105379057	LOC105379057
TC0200011356.hg.1	7.83	8.98	0.35	0.3	-2.22	2.22	0.0004	0.5406	GPC1	glypican 1
TC1200010005.hg.1	3.68	4.82	0.69	0.11	-2.21	2.21	0.0399	0.751	ATF7IP	activating transcription factor 7 interacting protein
TC0800007150.hg.1	8.94	10.08	0.46	0.55	-2.21	2.21	0.0015	0.5917	KIF13B	kinesin family member 13B
TC0300013886.hg.1	11.77	12.92	0.2	0.47	-2.21	2.21	0.0064	0.6674	ZIC1	Zic family member 1
TC1000010008.hg.1	4.18	5.32	0.74	0.66	-2.2	2.2	0.0051	0.6574	DNAJC1	DnaJ heat shock protein family (Hsp40) member C1
TC0600006869.hg.1	10.72	11.86	0.21	0.11	-2.2	2.2	0.001	0.5917	DSP	desmoplakin
TC1000011998.hg.1	3.22	4.35	0.25	0.51	-2.2	2.2	0.0036	0.6269	GRK5	G protein-coupled receptor kinase 5
TC0200010657.hg.1	3.31	4.45	0.47	0.55	-2.2	2.2	0.0136	0.6926	LANCL1	LanC-like 1
TC0800007998.hg.1	2.66	3.79	0.25	0.51	-2.19	2.19	0.0011	0.5917	HIGD1AP6	HIG1 hypoxia inducible domain family member 1A pseudogene 6
TC0300013941.hg.1	3.04	4.17	0.17	0.58	-2.19	2.19	0.0164	0.7092	MKRN2O5	MKRN2 opposite strand
TC0200007774.hg.1	3.14	4.27	0.28	0.38	-2.19	2.19	0.02	0.7205	WDPCP	WD repeat containing planar cell polarity effector
TC1500010203.hg.1	3.32	4.44	0.45	0.75	-2.18	2.18	0.0459	0.7609	CEMIP	cell migration inducing protein, hyaluronan binding
TC0600010160.hg.1	10.61	11.73	0.15	0.37	-2.18	2.18	0.0024	0.6041	RNA5SP226	H5S ribosomal pseudogene 226
TC0100015654.hg.1	11.9	13.02	0.47	0.42	-2.18	2.18	0.0025	0.6123	RNVU1-1	RNA, variant U1 small nuclear 1
TC0100016794.hg.1	6.39	7.51	1.02	0.6	-2.17	2.17	0.0143	0.6965	B3GALT2	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase 2
TC0600007959.hg.1	6.19	7.31	0.59	0.51	-2.17	2.17	0.0051	0.6578	DAAM2	dishevelled associated activator of morphogenesis 2
TC0100017634.hg.1	11.38	12.5	0.44	0.2	-2.17	2.17	0.0006	0.5837	RNA5S9	RNA, 5S ribosomal 9
TC0100018238.hg.1	12.9	14.01	0.61	0.28	-2.16	2.16	0.0093	0.6713	DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4
TC1000012126.hg.1	3.95	5.06	0.4	0.18	-2.16	2.16	0.02	0.7205	LHPP	phospholysine phosphohistidine inorganic pyrophosphate phosphatase
TC1200010932.hg.1	5.23	6.35	0.54	0.36	-2.16	2.16	0.006	0.6674	PTGES3	prostaglandin E synthase 3
TC0800011927.hg.1	10.21	11.32	0.44	0.49	-2.16	2.16	0.006	0.6674	RNU1-35P	RNA, U1 small nuclear 35, pseudogene
TC0100016431.hg.1	7.04	8.15	0.78	0.41	-2.16	2.16	0.027	0.7372	TNFSF4	tumor necrosis factor (ligand) superfamily, member 4
TC0900008576.hg.1	6.19	7.29	0.42	0.44	-2.15	2.15	0.0165	0.7092	ASTN2	astrotactin 2
TC0400010337.hg.1	3.33	4.43	0.5	0.31	-2.15	2.15	0.0032	0.6196	LINC02472	long intergenic non-protein coding RNA 2472
TC1100010015.hg.1	5.43	6.53	0.37	0.03	-2.15	2.15	0.0043	0.6495	NLRP10	NLR family pyrin domain containing 10
TC0700008745.hg.1	3.71	4.81	0.29	0.31	-2.15	2.15	0.0103	0.6725	PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta
TC0300008381.hg.1	7.67	8.78	0.77	0.01	-2.15	2.15	0.0402	0.751	QTRTD1	queuine tRNA-ribosyltransferase domain containing 1
TC0600011144.hg.1	3.36	4.46	0.41	0.33	-2.14	2.14	0.0172	0.7113	HIST1H4H	histone cluster 1 H4 family member h
TC1000010192.hg.1	3.77	4.87	0.47	1.3	-2.14	2.14	0.017	0.7096	JCAD	junctional cadherin 5 associated
TC0300012323.hg.1	11.05	12.15	0.44	0.06	-2.14	2.14	0.0114	0.6847	MGLL	monoglyceride lipase
TC1600009258.hg.1	5.99	7.08	0.16	0.4	-2.13	2.13	0.0184	0.7145	ALG1	chitobiosyldiphosphodolichol beta-mannosyltransferase



TC0600013361.hg.1	4.54	5.63	0.14	0.71	-2.13	2.13	0.0232	0.7299		CITED	CBP/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 1
TC0900006820.hg.1	5.91	7	0.5	0.17	-2.13	2.13	0.0014	0.5917		LINC01239	long intergenic non-protein coding RNA 1239
TC1400010214.hg.1	9.75	10.85	0.35	0.14	-2.13	2.13	0.0007	0.5837	D	MEG8	long intergenic non-protein coding RNA (Bsr)
TC1400009697.hg.1	5.18	6.27	0.4	0.26	-2.13	2.13	0.0079	0.6679		MIR4709	microRNA 4709
TC1400009697.hg.1	5.18	6.27	0.4	0.26	-2.13	2.13	0.0079	0.6679		NPC2	NPC intracellular cholesterol transporter 2
TC1900010817.hg.1	6.2	7.29	0.51	0.31	-2.13	2.13	0.0079	0.6679		PSG8	pregnancy specific beta-1-glycoprotein 8
TC0400007901.hg.1	9.43	10.52	0.52	0.15	-2.13	2.13	0.0019	0.5917		SHROOM3	shroom family member 3
TC0300013509.hg.1	2.89	3.98	0.32	0.53	-2.13	2.13	0.0048	0.6495		TP63	tumor protein p63
TC0800011956.hg.1	3.35	4.43	0.41	0.66	-2.12	2.12	0.0248	0.7317		COL22A1	collagen type XXII alpha 1 chain
TC1700011407.hg.1	3.27	4.36	0.32	0.21	-2.12	2.12	0.0002	0.5406		CYB561	cytochrome b561
TC1400007620.hg.1	2.97	4.06	0.21	0.77	-2.12	2.12	0.0133	0.6916		DCAF4	DDB1 and CUL4 associated factor 4
TC1100012777.hg.1	15.02	16.1	0.45	0.21	-2.12	2.12	0.0027	0.6175		ETS1	ETS proto-oncogene 1, transcription factor
TC1000011024.hg.1	3.33	4.42	0.38	0.69	-2.12	2.12	0.0467	0.7634		MSS51	MSS51 mitochondrial translational activator
TC0300014054.hg.1	6.79	7.88	0.21	0.49	-2.12	2.12	0.0113	0.6846		PIK3CB	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta
TC1100009397.hg.1	4.35	5.44	0.37	0.49	-2.12	2.12	0.0076	0.6679		SPA17	sperm autoantigenic protein 17
TC1300009022.hg.1	2.84	3.92	0.08	0.44	-2.12	2.12	0.0056	0.6602		SUGT1	SGT1 homolog, MIS12 kinetochore complex assembly co-chaperone
TC1200010182.hg.1	3.68	4.76	0.3	0.43	-2.11	2.11	0.005	0.6564		BHLHE41	basic helix-loop-helix family, member e41
TC1000012216.hg.1	5.11	6.19	0.28	0.31	-2.11	2.11	0.0002	0.5406		DOCK1	dedicator of cytokinesis 1
TC1000012216.hg.1	5.11	6.19	0.28	0.31	-2.11	2.11	0.0002	0.5406		FAM196A	family with sequence similarity 196 member A
TC0600006656.hg.1	4.69	5.77	0.15	0.45	-2.11	2.11	0.0072	0.6679		RIPK1	receptor interacting serine/threonine kinase 1
TC0100014621.hg.1	2.71	3.79	0.07	0.56	-2.11	2.11	0.0094	0.6713		SLC44A5	solute carrier 44 member A5
TC1300008615.hg.1	4.65	5.73	0.6	0.44	-2.11	2.11	0.0208	0.7206		SPART	spartin
TC1600008992.hg.1	4.31	5.38	0.13	0.5	-2.1	2.1	0.0122	0.6876		LMF1	lipase maturation factor 1
TC0100011096.hg.1	13.78	14.85	0.27	0.16	-2.1	2.1	0.008	0.6679		NEK7	NIMA-related kinase 7
TC0100013908.hg.1	9.66	10.73	0.13	0.31	-2.1	2.1	0.0133	0.6916		SLC2A1	solute carrier 2 member 1 (facilitated glucose transporter)
TC0600007864.hg.1	6.52	7.59	0.25	0.58	-2.1	2.1	0.0172	0.7113		TBC1D22B	TBC1 domain family, member 22B
TC1100011052.hg.1	7.08	8.15	0.2	0.4	-2.09	2.09	0.0266	0.7354		FADS3	fatty acid desaturase 3
TC0X00010036.hg.1	4.25	5.31	1.1	0.03	-2.09	2.09	0.0484	0.7639		HDAC8	histone deacetylase 8
TC2000006790.hg.1	4.99	6.05	0.33	0.53	-2.09	2.09	0.0352	0.7433		RNU1-131P	RNA, U1 small nuclear 131, pseudogene
TC1500010018.hg.1	9.43	10.5	0.52	0.12	-2.09	2.09	0.0067	0.6679		SEMA7A	semaphorin 7A
TC1100010172.hg.1	6.01	7.08	0.3	0.54	-2.09	2.09	0.0323	0.7414		SPON1	spondin 1
TC0700008539.hg.1	5.79	6.86	0.46	0.11	-2.09	2.09	0.0045	0.6495		STAG3L5P-PVRIG2P-PILRB	STAG3L5P-PVRIG2P-PILRB readthrough
TC1100007641.hg.1	5.77	6.83	0.42	0.23	-2.08	2.08	0.009	0.6696		OR5M4P	olfactory receptor, family 5, subfamily M, member 4 pseudogene
TC2000006689.hg.1	3.97	5.03	0.42	0.27	-2.08	2.08	0.0138	0.6941		SNAP25	synaptosome associated protein 25
TC1500009071.hg.1	3.2	4.26	0.28	0.41	-2.08	2.08	0.0063	0.6674		THBS1	thrombospondin 1

TC1900009363.hg.1	5.66	6.71	0.36	0.31	-2.07	2.07	0.0038	0.6395		DPP9	dipeptidyl peptidase 9
TC0800009527.hg.1	4.62	5.67	0.48	1.02	-2.07	2.07	0.0356	0.7437		ERI1	exoribonuclease 1
TC1500006775.hg.1	2.59	3.64	0.2	0.66	-2.07	2.07	0.037	0.7449		GOLGA8O	golgin A8 family member O
TC0500008539.hg.1	10.87	11.92	0.53	0.43	-2.07	2.07	0.0109	0.6793		GRAMD3	GRAM domain containing 3
TC1700006821.hg.1	5.23	6.28	0.08	0.16	-2.07	2.07	0.0004	0.5406		MYH10	myosin, heavy polypeptide 10, non-muscle
TC1200008641.hg.1	6.9	7.95	0.54	0.32	-2.07	2.07	0.0133	0.6916		NUP37	nucleoporin 37
TC0800009226.hg.1	2.8	3.84	0.28	0.75	-2.07	2.07	0.0095	0.6713		PLEC	plectin
TC0400010519.hg.1	9.89	10.94	0.43	0.13	-2.06	2.06	0.0048	0.6495		APBB2	amyloid beta (A4) precursor protein-binding, family B, member 2
TC0300006483.hg.1	9.02	10.06	0.26	0.38	-2.06	2.06	0.0003	0.5406		BHLHE40	basic helix-loop-helix family, member e40
TC1100012083.hg.1	3.35	4.39	0.17	0.49	-2.06	2.06	0.016	0.7056		CNTN5	contactin 5
TC0300007551.hg.1	3.1	4.14	0.27	0.79	-2.06	2.06	0.0229	0.7298		ERC2	ELKS/RAB6-interacting CASE family member 2
TC0200011052.hg.1	4.08	5.12	0.5	0.52	-2.06	2.06	0.0237	0.7299		PSMD1	proteasome 26S subunit, non-ATPase 1
TC0400010427.hg.1	4.36	5.4	0.35	0.53	-2.06	2.06	0.0029	0.6175		TBC1D1	TBC1 domain family, member 1
TC0300013350.hg.1	3.63	4.67	0.34	0.44	-2.06	2.06	0.0248	0.7317		YEATS2	YEATS domain containing 2
TC0200013663.hg.1	3.27	4.31	0.65	0.67	-2.05	2.05	0.0293	0.7382		CNOT1	CCR4-NOT transcription complex subunit 1
TC0900011401.hg.1	3.29	4.32	0.15	0.51	-2.05	2.05	0.0017	0.5917	D	GSN	gelsolin
TC1500009703.hg.1	11.12	12.16	0.46	0.27	-2.05	2.05	0.002	0.594		LACTB	lactamase beta
TC1200009072.hg.1	7.86	8.9	0.88	0.25	-2.05	2.05	0.0372	0.7449		TAOK3	TAO kinase 3
TC0600006922.hg.1	3.69	4.72	0.46	0.58	-2.04	2.04	0.023	0.7299		GCNT2	glucosaminyl (N-acetyl) transferase 2, I-branching enzyme
TC1700010648.hg.1	6.42	7.45	0.15	0.48	-2.04	2.04	0.0125	0.6893		KTRAP1-5	keratin associated protein 1-5
TC0300012570.hg.1	3.99	5.02	0.35	0.44	-2.04	2.04	0.0395	0.7509		MRAS	muscle Ras
TC1200012579.hg.1	5.17	6.2	0.52	0.16	-2.04	2.04	0.0044	0.6495		NTF3	neurotrophin 3
TC2200007151.hg.1	2.99	4.02	0.57	0.41	-2.04	2.04	0.01	0.6713		SYN3	synapsin III
TC2200007151.hg.1	2.99	4.02	0.57	0.41	-2.04	2.04	0.01	0.6713		TIMP3	TIMP metalloproteinase inhibitor 3
TC1700011578.hg.1	4.02	5.04	0.21	0.29	-2.03	2.03	8.21E-05	0.4854		ABCA6	ATP binding cassette subfamily A member 6
TC0900011938.hg.1	3.48	4.5	0.38	0.32	-2.03	2.03	0.0079	0.6679		C9orf116	chromosome 9 open reading frame 116 (PIERCE1)
TC0600008721.hg.1	3.58	4.6	0.22	0.56	-2.03	2.03	0.0074	0.6679		CGA	glycoprotein hormones, alpha polypeptide (CG; LH; FSH; TSH)
TC0500013107.hg.1	6.63	7.65	0.21	0.34	-2.03	2.03	0.0175	0.7113		HEIH	hepatocellular carcinoma up-regulated EZH2-associated long non-coding RNA
TC1500007102.hg.1	5.12	6.14	0.15	0.47	-2.03	2.03	0.0012	0.5917		RNU1-119P	RNA, U1 small nuclear 119, pseudogene
TC0700008262.hg.1	3.8	4.82	0.67	0.43	-2.03	2.03	0.0456	0.7602		SLC25A40	solute carrier family 25 member 40 (mitochondrial carrier protein)
TC0200012128.hg.1	3.76	4.78	0.15	0.84	-2.03	2.03	0.0132	0.6916		SPDYA	speedy/RINGO cell cycle regulator family member A
TC0300011260.hg.1	2.7	3.72	0.14	0.49	-2.02	2.02	0.0236	0.7299		ARHGEF3	Rho guanine nucleotide exchange factor 3 (GEF3)
TC0700010329.hg.1	3.3	4.31	0.12	0.28	-2.02	2.02	0.0449	0.7586		GTF3AP5	general transcription factor IIIA pseudogene 5
TC1200008027.hg.1	3.68	4.69	0.35	0.43	-2.02	2.02	0.0135	0.6926		LEMD3	LEM domain containing 3
TC0400009221.hg.1	15.46	16.47	0.65	0.23	-2.02	2.02	0.0076	0.6679		MSMO1	methylsterol monooxygenase 1

TC0700010441.hg.1	2.86	3.88	0.47	0.45	-2.02	2.02	0.0343	0.7424	RAPGEF5	Rap guanine nucleotide exchange factor 5
TC1800008358.hg.1	3.59	4.6	0.38	0.81	-2.01	2.01	0.0098	0.6713	CDH2	cadherin 2, type 1, N-cadherin (neuronal)
TC0400009001.hg.1	3.6	4.61	0.31	0.72	-2.01	2.01	0.0166	0.7092	FAM160A1	family with sequence similarity 160, member A1
TC0200006674.hg.1	8.02	9.03	0.17	0.61	-2.01	2.01	0.042	0.7539	KLF11	Kruppel-like factor 11
TC0300006520.hg.1	5.55	6.55	0.56	0.24	-2.01	2.01	0.0465	0.7625	LINC00312	long intergenic non-protein coding RNA 312
TC0500011453.hg.1	4.91	5.91	0.34	0.35	-2.01	2.01	0.0059	0.6674	LOC105379082	LOC105379082
TC1100008196.hg.1	6.19	7.19	0.6	0.26	-2.01	2.01	0.0169	0.7092	PPP6R3	protein phosphatase 6 regulatory subunit 3
TC0400010282.hg.1	7.47	8.48	0.07	0.13	-2.01	2.01	0.0019	0.594	SEL1L3	sel-1 suppressor of lin-12-like 3 (C. elegans)
TC0300009052.hg.1	2.56	3.56	0.35	0.15	-2.01	2.01	0.0093	0.6713	SLC9A9	solute carrier family 9 member A9 (NHE9)
TC0700010989.hg.1	3.05	4.06	0.3	0.35	-2.01	2.01	0.0182	0.7124	TNS3	tensin 3
TC1200007023.hg.1	3.5	4.5	0.14	0.5	-2	2	0.0186	0.7163	AEBP2	AE binding protein 2
TC0100014276.hg.1	11.83	12.83	0.65	0.09	-2	2	0.028	0.7374	DHCR24	24-dehydrocholesterol reductase
TC0500012283.hg.1	2.44	3.44	0.09	0.5	-2	2	0.0233	0.7299	HDAC3	histone deacetylase 3
TC0300012437.hg.1	3.6	4.6	0.36	0.29	-2	2	0.0144	0.6965	RNU6-726P	RNA, U6 small nuclear 726, pseudogene
TC0100011321.hg.1	4.73	3.73	0.99	0.23	2	-2	0.0371	0.7449	CNTN2	contactin 2
TC1100010131.hg.1	5.16	4.15	0.54	0.34	2	-2	0.0059	0.6653	MICAL2	microtubule associated monooxygenase, calponin and LIM domain containing 2
TC2000008499.hg.1	4.46	3.46	0.42	0.22	2	-2	0.0143	0.6965	RRBP1	ribosome binding protein 1
TC0100017872.hg.1	5	4	0.41	0.4	2	-2	0.0232	0.7299	RYR2	ryanodine receptor 2
TC1500009319.hg.1	7.93	6.93	0.84	0.44	2	-2	0.0085	0.6681	SEMA6D	semaphorin 6D
TC0100006567.hg.1	6.5	5.5	0.12	0.48	2	-2	0.004	0.6435	SKI	SKI proto-oncogene
TC1300006966.hg.1	4.87	3.87	0.29	0.27	2	-2	0.0245	0.7317	WBP4	WW domain binding protein 4
TC1100008532.hg.1	4.43	3.42	0.21	0.56	2.01	-2.01	0.0236	0.7299	AQP11	aquaporin 11
TC2200007627.hg.1	4.56	3.56	0.37	0.43	2.01	-2.01	0.0143	0.6965	ATXN10	ataxin 10
TC0500007264.hg.1	4.15	3.14	0.58	0.44	2.01	-2.01	0.016	0.7056	GHR	growth hormone receptor
TC0200011981.hg.1	3.55	2.54	0.21	0.19	2.01	-2.01	0.001	0.5917	ITSN2	intersectin 2
TC0100015523.hg.1	7.75	6.74	0.23	0.36	2.01	-2.01	0.0009	0.5917	LSP1P5	LSP1 pseudogene 5
TC0900006655.hg.1	4.38	3.37	0.14	0.41	2.01	-2.01	0.004	0.6435	LURAP1L	leucine rich adaptor protein 1-like
TC1100012041.hg.1	6.01	5.01	0.72	0.13	2.01	-2.01	0.0057	0.6602	MAML2	mastermind like transcriptional coactivator 2
TC1200007804.hg.1	4.03	3.03	0.18	0.42	2.01	-2.01	0.0256	0.7354	METTL7B	methyltransferase like 7B
TC1300009296.hg.1	4.48	3.47	0.09	0.54	2.01	-2.01	0.0307	0.7392	MYCBP2	MYC binding protein 2, E3 ubiquitin protein ligase
TC0100006995.hg.1	4.31	3.3	0.59	0.1	2.01	-2.01	0.0111	0.6811	PLEKHM2	pleckstrin homology and RUN domain containing M2
TC0300011422.hg.1	7.77	6.77	0.19	0.51	2.01	-2.01	0.0203	0.7205	RNU6-787P	RNA, U6 small nuclear 787, pseudogene
TC0700006735.hg.1	13.61	12.6	0.5	0.17	2.01	-2.01	0.0076	0.6679	SCIN	scinderin
TC1100006598.hg.1	4.37	3.36	0.53	0.2	2.01	-2.01	0.0468	0.7634	SLC22A18	solute carrier family 22, member 18
TC0800011550.hg.1	4.82	3.82	0.47	0.44	2.01	-2.01	0.0019	0.5917	TRPS1	transcriptional repressor GATA binding 1
TC0100011211.hg.1	4.29	3.27	0.31	0.47	2.02	-2.02	0.0118	0.6853	GPR37L1	G protein-coupled receptor 37 like 1
TC0600007988.hg.1	5.61	4.6	0.76	0.46	2.02	-2.02	0.0085	0.6681	NFYA	nuclear transcription factor Y
TC0900009771.hg.1	5.41	4.39	0.29	0.41	2.02	-2.02	0.0322	0.7411	PLAA	phospholipase A2 activating protein

TC0700007560.hg.1	3.97	2.96	0.42	0.33	2.02	-2.02	0.0124	0.6887	RNU1-14P	RNA, U1 small nuclear 14, pseudogene
TC0800012298.hg.1	7.96	6.94	0.23	0.45	2.02	-2.02	0.0232	0.7299	SMIM19	small integral membrane protein 19
TC1300009012.hg.1	4.7	3.68	0.29	0.33	2.02	-2.02	0.009	0.6696	THSD1	thrombospondin type 1 domain containing 1
TC1100010472.hg.1	4.19	3.17	0.23	0.34	2.03	-2.03	0.0018	0.5917	CCDC73	coiled-coil domain containing 73
TC0100008457.hg.1	3.67	2.65	0.66	0.48	2.03	-2.03	0.0479	0.7637	DAB1	reelin adaptor protein
TC0800007061.hg.1	4.62	3.6	0.45	0.34	2.03	-2.03	0.046	0.7609	DOCK5	dedicator of cytokinesis 5
TC0600008281.hg.1	10.81	9.78	0.26	0.63	2.03	-2.03	0.0058	0.6629	ELOVL5	ELOVL family member 5
TC0600007519.hg.1	4.2	3.17	0.52	0.28	2.03	-2.03	0.0036	0.6276	HCG17	HLA complex group 17 (ncRNA)
TC0700006813.hg.1	4.54	3.52	0.28	0.1	2.03	-2.03	0.0135	0.6926	HDAC9	histone deacetylase 9
TC0300010904.hg.1	6.13	5.11	0.32	0.67	2.03	-2.03	0.0386	0.7486	KIAA1143	KIAA1143
TC0100007413.hg.1	4.33	3.31	0.3	0.08	2.03	-2.03	0.0096	0.6713	MAN1C1	mannosidase alpha 1C
TC0600009326.hg.1	4.91	3.89	0.33	0.48	2.03	-2.03	0.0084	0.6679	SERINC1	serine incorporator 1
TC0200012623.hg.1	3.96	2.93	0.18	0.23	2.03	-2.03	0.0014	0.5917	SPTBN1	spectrin beta, non-erythrocytic 1
TC1200012719.hg.1	4.9	3.88	0.42	0.84	2.03	-2.03	0.0431	0.7562	WDR66	WD repeat domain 66
TC0200007063.hg.1	6.8	5.77	0.55	0.44	2.04	-2.04	0.0129	0.6911	EIF2B4	eukaryotic translation initiation factor 2B subunit delta
TC0X00007418.hg.1	4.23	3.21	0.29	0.12	2.04	-2.04	0.0006	0.5837	FAAH2	fatty acid amide hydrolase 2
TC0100017457.hg.1	8.38	7.35	0.16	0.28	2.04	-2.04	0.0008	0.5917	GTF2IP20	general transcription factor iii pseudogene 20
TC0200011281.hg.1	4.78	3.75	0.15	0.16	2.04	-2.04	0.0004	0.549	PER2	period circadian clock 2
TC0700007952.hg.1	8.24	7.22	0.19	0.37	2.04	-2.04	0.0058	0.6629	POM121	POM121 transmembrane nucleoporin
TC2200007056.hg.1	4.55	3.52	0.28	0.69	2.04	-2.04	0.0189	0.7167	RNU6-564P	RNA, U6 small nuclear 564, pseudogene
TC0500008809.hg.1	6.19	5.16	0.27	0.33	2.04	-2.04	0.0225	0.7287	RNU6-572P	RNA, U6 small nuclear 572, pseudogene
TC2200007056.hg.1	4.55	3.52	0.28	0.69	2.04	-2.04	0.0189	0.7167	SEC14L2	SEC14 like lipid binding 2
TC1000011727.hg.1	10.36	9.33	0.37	0.38	2.04	-2.04	0.0064	0.6674	SH3PXD2A	SH3 and PX domains 2A
TC0X00011259.hg.1	4.91	3.88	0.47	0.12	2.04	-2.04	0.02	0.7205	STS	steroid sulfatase (microsomal)
TC0300007015.hg.1	4.71	3.67	0.63	0.33	2.05	-2.05	0.0237	0.7299	ARPP21	cAMP regulated phosphoprotein 21
TC0100011149.hg.1	5.86	4.82	0.19	0.22	2.05	-2.05	0.0011	0.5917	CAMSAP2	calmodulin regulated spectrin associated protein family member 2
TC0800011112.hg.1	6.83	5.8	0.38	0.24	2.05	-2.05	0.0364	0.7449	FAM92A	family with sequence similarity 92 member A
TC0400009803.hg.1	5.44	4.41	0.54	0.37	2.05	-2.05	0.0227	0.7287	HTT	huntingtin
TC1400009126.hg.1	5.52	4.49	0.34	0.32	2.05	-2.05	0.0355	0.7437	L2HGDH	L-2-hydroxyglutarate dehydrogenase
TC1100009112.hg.1	4.56	3.53	0.17	0.58	2.05	-2.05	0.0114	0.6848	NNMT	nicotinamide N-methyltransferase
TC0400006642.hg.1	5.08	4.04	0.26	0.15	2.05	-2.05	4.76E-05	0.4807	STX18	syntaxin 18
TC0300008404.hg.1	4.26	3.22	0.86	0.18	2.05	-2.05	0.0448	0.7586	ZBTB20	zinc finger and BTB domain containing 20
TC0500011438.hg.1	4.74	3.7	0.29	0.26	2.06	-2.06	0.0011	0.5917	ADGRV1	adhesion G protein-coupled receptor V1
TC0600013419.hg.1	6.63	5.59	0.32	0.13	2.06	-2.06	0.0011	0.5917	AIG1	androgen induced 1
TC0500007726.hg.1	8.97	7.93	0.26	0.54	2.06	-2.06	0.0226	0.7287	BDP1	B double prime 1, subunit of RNA polymerase 3B
TC0900006753.hg.1	6.22	5.17	0.52	0.64	2.06	-2.06	0.0463	0.7616	HAUS6	HAUS augmin like complex subunit 6
TC0600009999.hg.1	4.68	3.63	0.43	0.66	2.06	-2.06	0.0292	0.7382	HSPE1P26	heat shock protein family E (Hsp10) member 1 pseudogene 26
TC0500009395.hg.1	4.17	3.13	0.65	0.4	2.06	-2.06	0.0178	0.7119	LCP2	lymphocyte cytosolic protein 2
TC0500012541.hg.1	8.41	7.36	0.45	0.19	2.06	-2.06	0.0053	0.6602	MFAP3	microfibril associated protein 3
TC0600011666.hg.1	6.94	5.9	0.24	0.13	2.06	-2.06	0.0012	0.5917	RNU1-88P	RNA, U1 small nuclear 88, pseudogene

TC0100013199.hg.1	5.07	4.03	0.7	0.37	2.06	-2.06	0.0289	0.7374	RPS15AP6	ribosomal protein S15a pseudogene 6
TC1700008571.hg.1	5.28	4.24	0.27	0.09	2.06	-2.06	0.0018	0.5917	STRADA	STE20-related kinase adaptor alpha
TC0200012990.hg.1	6.69	5.65	0.35	0.53	2.06	-2.06	0.0131	0.6916	TIA1	TIA1 cytotoxic granule associated RNA binding protein 1
TC1600009119.hg.1	4.04	3	0.48	0.27	2.07	-2.07	0.0377	0.7456	AMDHD2	amidohydrolase domain containing 2
TC0100008921.hg.1	5.82	4.77	0.2	0.06	2.07	-2.07	0.0217	0.7257	CLCA2	chloride channel accessory 2
TC1100011514.hg.1	5.22	4.17	0.48	0.35	2.07	-2.07	0.0034	0.6229	DHCR7	7-dehydrocholesterol reductase
TC0100014154.hg.1	4.68	3.63	0.27	0.2	2.07	-2.07	0.0013	0.5917	FAF1	Fas-associated factor 1
TC0100012421.hg.1	10.88	9.83	0.14	0.5	2.07	-2.07	0.0025	0.6123	FAM41C	family with sequence similarity 41, member C
TC1200008302.hg.1	5.79	4.74	0.84	0.59	2.07	-2.07	0.0454	0.7595	LIN7A	lin-7 homolog A, crumbs cell polarity complex component
TC0300009826.hg.1	4.31	3.26	0.73	0.4	2.07	-2.07	0.034	0.7423	LPP	LIM domain containing preferred translocation partner in lipoma
TC0100009702.hg.1	6.91	5.87	0.25	0.32	2.07	-2.07	0.003	0.6196	NBPF10	neuroblastoma breakpoint family member 10
TC1600009706.hg.1	5.5	4.45	0.55	0.26	2.07	-2.07	0.0056	0.6602	NPIP5	nuclear pore complex interacting protein family member B5
TC0900011331.hg.1	5.69	4.64	0.19	0.47	2.07	-2.07	0.0102	0.6715	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC0100014316.hg.1	7.46	6.41	0.54	0.6	2.07	-2.07	0.038	0.7466	PPAP2B	phosphatidic acid phosphatase 2B
TC1600009347.hg.1	7.17	6.13	0.8	0.25	2.07	-2.07	0.0164	0.7092	RNA5SP403	RNA, 5S ribosomal pseudogene 403
TC0600012620.hg.1	10.15	9.1	0.59	0.26	2.07	-2.07	0.0418	0.7532	RNU4-70P	RNA, U4 small nuclear 70, pseudogene
TSUnmapped00000505.hg.1	6.31	5.26	0.2	0.27	2.07	-2.07	0.0016	0.5917	SERTAD4-AS1	SERTAD4 antisense RNA 1
TC0500009560.hg.1	4.89	3.84	0.64	0.56	2.07	-2.07	0.0155	0.7034	SFXN1	sideroflexin 1
TC0700012463.hg.1	6.44	5.39	1.06	0.49	2.07	-2.07	0.0129	0.6911	WASL	Wiskott-Aldrich syndrome like
TC0300007975.hg.1	4.04	2.99	0.56	0.34	2.08	-2.08	0.0203	0.7205	CADM2	cell adhesion molecule 2 (SynCAM2)
TC1700010008.hg.1	4.52	3.46	0.61	0.37	2.08	-2.08	0.0228	0.7293	EPN2	epsin 2
TC0600007272.hg.1	7.11	6.05	0.44	0.56	2.08	-2.08	0.0216	0.7242	HIST1H2AC	histone cluster 1 H2A family member c
TC0100009143.hg.1	6.1	5.05	0.06	0.13	2.08	-2.08	0.02	0.7205	PTBP2	polyglutamine tract binding protein 2
TC1800007617.hg.1	6.4	5.34	0.9	0.41	2.08	-2.08	0.0062	0.6674	RTTN	rotatin
TC2000007107.hg.1	5.92	4.87	0.7	0.79	2.08	-2.08	0.0331	0.7419	TM9SF4	transmembrane 9 superfamily member 4
TC2200007198.hg.1	5.84	4.78	0.52	0.47	2.08	-2.08	0.0081	0.6679	TOM1	target of myb1 membrane trafficking protein
TC0700008901.hg.1	4.11	3.05	0.53	0.34	2.09	-2.09	0.026	0.7354	ANKRD7	ankyrin repeat domain 7
TC1600011221.hg.1	4.08	3.02	0.42	0.12	2.09	-2.09	0.0045	0.6495	MVD	mevalonate (diphospho) decarboxylase
TC1700008130.hg.1	5.14	4.08	0.51	0.32	2.09	-2.09	0.008	0.6679	NPEPP5	aminopeptidase puromycin sensitive
TC1700008131.hg.1	4.86	3.79	0.23	0.51	2.09	-2.09	0.0136	0.6926	NPEPP5	aminopeptidase puromycin sensitive
TC0200013669.hg.1	12.85	11.79	0.72	0.36	2.09	-2.09	0.0433	0.7567	RFX8	RFX family member 8, lacking RFX DNA binding domain
TC1500007386.hg.1	8.27	7.2	0.16	0.29	2.09	-2.09	0.001	0.5917	RNF111	ring finger protein 111
TC1500007386.hg.1	8.27	7.2	0.16	0.29	2.09	-2.09	0.001	0.5917	SLTM	SAFB-like, transcription modulator
TC0700010250.hg.1	3.93	2.87	0.67	0.28	2.09	-2.09	0.0343	0.7424	UMAD1	UBAP-MVB12-associated (UMA) domain containing 1
TC1100011809.hg.1	5.46	4.39	0.1	0.57	2.1	-2.1	0.0191	0.7167	ANKRD42	ankyrin repeat domain 42
TC1400009999.hg.1	6.64	5.57	0.5	0.59	2.1	-2.1	0.004	0.6437	CPSF2	cleavage and polyadenylation specific factor 2
TC0200016641.hg.1	5.19	4.12	0.31	0.08	2.1	-2.1	0.0023	0.6008	DNMT3A	DNA methyltransferase 3alpha
TC0100018570.hg.1	8.83	7.75	0.27	0.11	2.1	-2.1	0.0005	0.5735	HNRNPU	heteronuclear ribonucleoprotein U

TC0600009857.hg.1	3.71	2.64	0.5	0.42	2.1	-2.1	0.0219	0.7272	D	MTHFD1L	methylenetetrahydrofolate dehydrogenase 1-like
TC1000008643.hg.1	5.49	4.42	0.23	0.26	2.1	-2.1	0.0015	0.5917		SCD	stearoyl-CoA desaturase (delta-9-desaturase)
TC0900007520.hg.1	6.59	5.52	0.94	0.45	2.1	-2.1	0.0158	0.7053		SMC5	structural maintenance of chromosomes 5
TC0600009755.hg.1	7.4	6.33	0.53	0.53	2.1	-2.1	0.0147	0.6965		STXBPS	syntaxin binding protein 5; tomosyn
TC1300008559.hg.1	5.22	4.15	0.38	0.77	2.11	-2.11	0.045	0.7586		N4BP2L2	NEDD binding protein 2 like 2
TC0900008668.hg.1	7.31	6.23	0.36	0.01	2.11	-2.11	0.0044	0.6495		OR1H1P	olfactory receptor, family 1, subfamily H, member 1 pseudogene
TC0700012913.hg.1	7.7	6.62	0.68	0.55	2.11	-2.11	0.0152	0.7	D	OR2A1-AS1	OR2A1 antisense RNA 1
TC0300011557.hg.1	4.96	3.88	0.21	0.08	2.11	-2.11	0.0003	0.5406		PDZRN3	PDZ domain containing ring finger 3
TC1600007200.hg.1	6.67	5.59	0.32	0.36	2.11	-2.11	0.0035	0.6269		SMG1P1	SMG1 pseudogene 1
TC0600010564.hg.1	4.77	3.69	0.08	0.26	2.12	-2.12	0.0003	0.5406		BPHL	biphenyl hydrolase like
TC0100014954.hg.1	6.09	5.01	0.48	0.52	2.12	-2.12	0.0267	0.7354		CCDC18-AS1	CCDC18 antisense RNA 1
TC0400012744.hg.1	6.76	5.68	1.02	0.44	2.12	-2.12	0.015	0.6978		FRG1-DT	FRG1 divergent transcript
TC1400008934.hg.1	4.73	3.65	0.15	0.59	2.12	-2.12	0.0296	0.7392		KIAA0391	KIAA0391
TC1300009547.hg.1	4.16	3.07	0.61	0.74	2.12	-2.12	0.0353	0.7433		MBNL2	muscleblind like splicing factor 2
TC1600007181.hg.1	8.17	7.08	0.05	0.42	2.12	-2.12	0.0069	0.6679		NPIPB4	nuclear pore complex interacting protein family member B4
TC0900006557.hg.1	4.08	3	0.23	0.43	2.12	-2.12	0.0073	0.6679		PLGRKT	plasminogen receptor with a C-terminal lysine
TC1100010478.hg.1	12.19	11.11	0.11	0.41	2.12	-2.12	0.0086	0.6681		QSER1	glutamine and serine rich 1
TC0200008653.hg.1	6.48	5.4	0.63	0.49	2.12	-2.12	0.0178	0.7119	D	RFX8	RFX family member 8, lacking RFX DNA binding domain
TC0200011383.hg.1	7	5.92	0.57	0.15	2.12	-2.12	0.0078	0.6679		SNED1	sushi, nidogen and EGF-like domain 1
TC0200010145.hg.1	6.56	5.47	0.08	0.45	2.13	-2.13	0.0064	0.6674		CWC22	CWC spliceosome associated protein homolog
TC0400011117.hg.1	5.69	4.6	0.86	0.16	2.13	-2.13	0.0217	0.7257		FRAS1	Frasier extracellular matrix complex subunit 1
TC0700012622.hg.1	3.74	2.64	0.29	0.43	2.13	-2.13	0.0048	0.6495		LINC00513	long intergenic non-protein coding RNA 513
TC0100009755.hg.1	5.93	4.84	0.22	0.29	2.13	-2.13	0.0024	0.6041	D	NBPF10	neuroblastoma breakpoint family member 10
TC0100013858.hg.1	4.7	3.61	0.45	0.13	2.13	-2.13	0.0148	0.6965		SCMH1	sex comb on midleg homolog 1
TC1200011882.hg.1	6.04	4.96	0.35	0.51	2.13	-2.13	0.013	0.6916		TRPV4	transient receptor potential cation channel, subfamily C, member 4
TC0300010166.hg.1	4.7	3.61	0.51	0.34	2.14	-2.14	0.0353	0.7433		GRM7	metabotropic glutamate receptor 7
TC0900011402.hg.1	5.35	4.26	0.37	0.33	2.14	-2.14	0.0021	0.594	D	GSN	gelsolin
TC1500010526.hg.1	7.29	6.19	0.27	0.36	2.14	-2.14	0.0014	0.5917		MCTP2	multiple C2 and transmembrane domain containing 2
TC0100010412.hg.1	4.52	3.43	0.33	0.16	2.14	-2.14	0.0008	0.5917		RNU5F-6P	RNA, U5F small nuclear 6, pseudogene
TC0600011533.hg.1	4.86	3.77	0.62	0.47	2.14	-2.14	0.0248	0.7317		VP52	VP52, GARP complex subunit
TC1000008756.hg.1	3.9	2.8	0.95	0.34	2.15	-2.15	0.0369	0.7449		BORCS7-ASMT	BORCS7-ASMT readthrough
TC0100012444.hg.1	8.1	7	0.14	0.52	2.15	-2.15	0.0239	0.7299		C1orf159	chromosome 1 open reading frame 159
TC1000012165.hg.1	4.35	3.24	0.31	0.22	2.15	-2.15	0.0101	0.6715		DHX32	DEAH-box helicase 32
TC1000011989.hg.1	4.06	2.96	0.37	0.36	2.15	-2.15	0.0018	0.5917		EIF3A	eukaryotic translation inhibition factor 3 subunit A
TC0100010865.hg.1	4.5	3.4	0.25	0.55	2.15	-2.15	0.0018	0.5917		LAMC1	laminin gamma-1 (LAMB2)
TC0X00007399.hg.1	12.17	11.07	0.26	0.51	2.15	-2.15	0.0271	0.7372		NBDY	negative regulator of P-body association (NoBody)

TC0100010432.hg.1	5.11	4	1.04	0.74	2.15	-2.15	0.0321	0.7409	D	PBX1	pre-B cell leukemia homeobox 1
TC1600009762.hg.1	4.38	3.27	0.53	0.15	2.15	-2.15	0.0031	0.6196		RBBP6	RB binding protein 6, ubiquitin ligase
TC0100017359.hg.1	6.37	5.26	0.4	0.71	2.15	-2.15	0.0211	0.7215		SLC30A10	solute carrier 30 member A10 (Zn2+/Mn2+-transporter)
TC0400008130.hg.1	4.11	3.01	0.52	0.35	2.15	-2.15	0.0411	0.7524		SNCA	synuclein alpha
TC1300009224.hg.1	5.89	4.78	0.18	0.5	2.15	-2.15	0.0302	0.7392		SNORD37	Small nucleolar RNA SNORD37
TC1200012081.hg.1	6.65	5.54	0.42	0.43	2.15	-2.15	0.0239	0.7299		TESC-AS1	TESC antisense RNA 1
TC0700010761.hg.1	5.93	4.82	0.46	0.55	2.16	-2.16	0.0066	0.6679		ELMO1	engulfment and cell motility 1
TC0300012240.hg.1	4.91	3.79	0.43	1.02	2.16	-2.16	0.0396	0.7509		HEG1	heart development protein with EGF-like domain 1
TC0800007146.hg.1	10.33	9.22	0.28	0.2	2.16	-2.16	0.0004	0.5476		HMBBOX1-IT1	HMBBOX1 intronic transcript 1 (non-protein coding)
TC1900008614.hg.1	6.97	5.86	0.44	0.29	2.16	-2.16	0.0093	0.6713		KLK9	kallikrein related peptidase 9
TC1400007775.hg.1	4.86	3.74	0.34	0.16	2.16	-2.16	0.0016	0.5917	D	NRXN3	neurexin 3
TC0400011472.hg.1	6.21	5.1	0.34	0.5	2.16	-2.16	0.0246	0.7317		UBE2D3	ubiquitin conjugating enzyme E2D3
TC0700011322.hg.1	4.59	3.47	0.6	0.54	2.17	-2.17	0.0185	0.7154		CCT6P3	chaperonin containing TCP1 subunit 6 pseudogene 3
TC1200011162.hg.1	4.46	3.34	0.78	0.61	2.17	-2.17	0.0332	0.7419		LINC02408	long intergenic non-protein coding RNA 2408
TC1600007163.hg.1	4.56	3.44	0.75	0.43	2.17	-2.17	0.0321	0.7411		NPIP3	nuclear pore complex interacting protein family member B3
TC0900008441.hg.1	4.23	3.11	0.39	0.19	2.17	-2.17	0.0032	0.6196		UGCG	UDP-glucose ceramide glucosyltransferase
TC1600007114.hg.1	4.56	3.44	0.75	0.43	2.17	-2.17	0.0321	0.7411		VPS35L	VPS35 endosomal protein sorting factor like
TC0500007914.hg.1	3.94	2.82	0.46	0.18	2.17	-2.17	0.0089	0.6696		ZFYVE16	zinc finger FYVE-type containing 16
TC1400009300.hg.1	4.7	3.57	0.67	0.28	2.18	-2.18	0.0003	0.6175		CCDC198	coiled-coil domain containing 198
TC0700011551.hg.1	4.49	3.37	0.65	0.37	2.18	-2.18	0.0261	0.7354		POM121C	POM121 transmembrane nucleoporin C
TC0200014741.hg.1	4.75	3.63	0.82	0.51	2.18	-2.18	0.0183	0.7133		RBMS1	RNA binding motif, single-stranded interacting protein 1
TC1700012282.hg.1	5.91	4.79	0.42	0.28	2.18	-2.18	0.0145	0.6965		SPATA20	spermatogenesis associated 20
TC1500008523.hg.1	5.76	4.63	0.06	0.47	2.19	-2.19	0.0086	0.6681	D	MEF2A	myocyte enhancer factor 2A
TC1200006997.hg.1	4.74	3.61	0.63	0.44	2.19	-2.19	0.029	0.7375		PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma
TC0500012144.hg.1	5.27	4.14	0.26	0.68	2.19	-2.19	0.0413	0.7524		SIL1	SIL1 nucleotide exchange factor
TC0700010541.hg.1	6.07	4.94	0.36	0.41	2.19	-2.19	0.0045	0.6495		SNX10	sorting nexin 10
TC0200012966.hg.1	6.28	5.15	0.29	0.46	2.2	-2.2	0.0285	0.7374		AAK1	AP2-associated kinase 1
TC1400010594.hg.1	9.17	8.03	0.58	0.45	2.2	-2.2	0.0059	0.6653		FAM177A1	family with sequence similarity 177 member A1
TC1400008262.hg.1	6.35	5.21	0.51	0.26	2.2	-2.2	0.017	0.7096	D	MEG8	long intergenic non-protein coding RNA (Bsr)
TC0200009697.hg.1	5.3	4.16	0.62	0.4	2.2	-2.2	0.0129	0.6911		RPRM	represso, TP53 dependent G2 arrest mediator homolog
TC1400008369.hg.1	5.57	4.44	0.55	0.22	2.2	-2.2	0.007	0.6679		TRAF3	TNF receptor associated factor 3
TC2000008958.hg.1	3.96	2.82	1.26	0.33	2.2	-2.2	0.0392	0.7497		TRPC4AP	transient receptor potential cation channel, subfamily C, member 4 associated protein
TC0700011467.hg.1	4.59	3.46	0.41	0.18	2.2	-2.2	0.0039	0.6395		TYW1B	tRNA-gamma-synthetizing protein 1 homolog B
TC1900007244.hg.1	5.93	4.79	0.51	0.97	2.21	-2.21	0.0192	0.7167		CYP4F2	cytochrome P450 family 4 subfamily F member 2

TC1100013032.hg.1	5.97	4.83	0.85	0.33	2.21	-2.21	0.0054	0.6602	DNAJC4	DnaJ (Hsp40) homolog, subfamily C, member 4
TC0500009101.hg.1	6.08	4.94	0.1	0.72	2.21	-2.21	0.0313	0.7392	SMIM3	small integral membrane protein 3
TC0900010975.hg.1	15.59	14.43	0.1	0.43	2.22	-2.22	0.0019	0.5917	GABBR2	gamma-aminobutyric acid (GABA) B receptor, 2
TC0X00010427.hg.1	4.43	3.28	0.5	0.27	2.22	-2.22	0.003	0.6194	MORF4L2	mortality factor 4 like 2
TC0600011864.hg.1	5.98	4.83	0.04	0.33	2.22	-2.22	0.0002	0.5406	PTK7	protein tyrosine kinase 7
TC1800008130.hg.1	3.98	2.83	0.16	0.49	2.22	-2.22	0.0028	0.6175	PTPN2	protein tyrosine phosphatase, non-receptor type 2
TC1400010390.hg.1	4.89	3.73	0.2	0.14	2.23	-2.23	0.0004	0.5406	AHNAK2	AHNAK nucleoprotein 2
TC1200006490.hg.1	4.17	3.01	0.54	0.23	2.23	-2.23	0.0299	0.7392	CACNA1C	calcium voltage-gated channel subunit alpha 1 C (CaV1.2)
TC0300011900.hg.1	4.16	3	0.37	0.15	2.23	-2.23	0.0001	0.5236	CBLB	Cbl proto-oncogene B
TC1600008624.hg.1	8.68	7.52	0.39	0.59	2.23	-2.23	0.0244	0.7317	CDH13	cadherin 13
TC1200010968.hg.1	4.24	3.09	0.5	0.28	2.23	-2.23	0.0361	0.7448	DDIT3	DNA-damage-inducible transcript 3
TC0100010417.hg.1	7.97	6.82	0.61	0.39	2.23	-2.23	0.0284	0.7374	PBX1	pre-B cell leukemia homeobox 1
TC0500011993.hg.1	4.5	3.34	0.63	0.63	2.23	-2.23	0.0253	0.7354	RAPGEF6	Rap guanine nucleotide exchange factor 6
TC0200014599.hg.1	11.6	10.44	0.49	0.37	2.23	-2.23	0.0237	0.7299	RND3	Rho family GTPase 3; RhoE
TC0800011611.hg.1	15.81	14.65	0.08	0.38	2.23	-2.23	0.0016	0.5917	TNFRSF11B	tumor necrosis factor receptor superfamily, member 11b
TC0200012348.hg.1	5.58	4.42	0.26	0.62	2.24	-2.24	0.0006	0.5837	HNRNPA1P57	heterogeneous nuclear ribonucleoprotein A1 pseudogene 57
TC1000009893.hg.1	4.39	3.23	0.5	0.34	2.24	-2.24	0.004	0.6423	ITGA8	integrin alpha 8
TC1900007012.hg.1	5.03	3.87	0.45	0.33	2.24	-2.24	0.0055	0.6602	LDLR	low density lipoprotein receptor
TC0700013221.hg.1	6.09	4.92	0.57	0.72	2.24	-2.24	0.0442	0.7576	LMBR1	limb development membrane protein 1
TC0200009990.hg.1	4.11	2.95	0.72	0.19	2.24	-2.24	0.0351	0.7433	MAP3K20	mitogen activated protein kinase kinase kinase 20
TC1900007012.hg.1	5.03	3.87	0.45	0.33	2.24	-2.24	0.0055	0.6602	MIR6886	microRNA 6886
TC0100007399.hg.1	6.29	5.13	0.62	0.84	2.24	-2.24	0.0161	0.7073	TMEM50A	transmembrane protein 50A
TC0100010067.hg.1	9.06	7.89	0.45	0.48	2.24	-2.24	0.0303	0.7392	UBAP2L	ubiquitin associated protein 2 like (NICE 4)
TC1500009432.hg.1	4.78	3.61	0.35	0.07	2.25	-2.25	0.0039	0.641	DMXL2	Dmx like 2
TC0700010429.hg.1	4.22	3.05	0.4	0.14	2.25	-2.25	0.0025	0.6123	DNAH11	dynein, axonemal, heavy chain 11
TC0400007700.hg.1	4.81	3.64	0.44	0.21	2.25	-2.25	0.0123	0.6878	MIR1269A	microRNA 1269a
TC0200013903.hg.1	9.43	8.26	0.46	0.08	2.25	-2.25	0.0009	0.5917	RGPD8	RNABP2-like and GRIP domain containing 8
TC2200007678.hg.1	4.63	3.46	0.57	0.45	2.25	-2.25	0.0273	0.7372	TBC1D22A	TBC1 domain family member 22A
TC1500009535.hg.1	4.74	3.57	1.12	0.33	2.25	-2.25	0.0326	0.7414	TCF12	transcription factor 12
TC0900008530.hg.1	12.35	11.18	0.39	0.28	2.25	-2.25	0.0013	0.5917	TNC	tenascin C
TC1700009906.hg.1	4.5	3.32	0.69	0.17	2.26	-2.26	0.0333	0.7419	CCDC114A	coiled coil domain containing 114A
TC0200012539.hg.1	9.32	8.14	0.58	0.16	2.26	-2.26	0.0096	0.6713	PPP1R21	protein phosphatase 1 regulatory subunit 21 (KLRAQ1)
TC0800011544.hg.1	8.97	7.79	0.72	0.54	2.26	-2.26	0.0159	0.7056	TRPS1	transcriptional repressor GATA binding 1
TC1600006596.hg.1	4.87	3.69	0.73	0.05	2.27	-2.27	0.0302	0.7392	CASKIN1	CASK interacting protein 1
TC0800006812.hg.1	4.52	3.34	0.53	0.28	2.27	-2.27	0.0205	0.7205	DLC1	DLC1 Rho GTPase activating protein
TC0900008563.hg.1	5.83	4.65	0.54	0.16	2.27	-2.27	0.0018	0.5917	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC0500008119.hg.1	5.08	3.9	0.59	0.2	2.27	-2.27	0.0036	0.6269	RNU6-308P	RNA, U6 small nuclear 308, pseudogene



TC0300009603.hg.1	5.25	4.06	0.32	0.19	2.28	-2.28	0.001	0.5917		MFN1	mitofusin 1
TC0100009839.hg.1	5.42	4.23	0.07	0.5	2.28	-2.28	0.0015	0.5917	D	NBPF10	neuroblastoma breakpoint family member 10
TC0500007644.hg.1	5.61	4.43	0.67	0.74	2.28	-2.28	0.0086	0.6681		PIK3R1	phosphoinositol 3-kinase, regulatory subunit 1
TC2000006674.hg.1	5.04	3.86	0.93	0.19	2.28	-2.28	0.0078	0.6679		PLCB4	phospholipase C, beta 4
TC0300012659.hg.1	4.87	3.68	0.32	0.7	2.28	-2.28	0.0361	0.7441		TFDP2	transcription factor Dp-2
TC1800008828.hg.1	6.44	5.24	0.85	0.45	2.29	-2.29	0.0261	0.7354	D	CCBE1	collagen and calcium binding EGF domains 1
TC1500008048.hg.1	4.94	3.74	0.37	0.33	2.29	-2.29	0.0017	0.5917	D	CEMIP	cell migration inducing protein, hyaluronan binding
TC0600006737.hg.1	4.16	2.96	0.64	0.16	2.29	-2.29	0.0194	0.7195		ECI2	enoyl-CoA delta isomerase 2
TC0100007667.hg.1	5.22	4.02	0.51	0.3	2.29	-2.29	0.0157	0.7053		KPNA6	karyopherin (importin) subunit alpha 6
TC1400008556.hg.1	7.25	6.05	0.09	0.35	2.29	-2.29	0.0005	0.5735		LINC01297	long intergenic non-protein coding RNA 1297
TC0100007762.hg.1	4.44	3.25	0.35	0.67	2.29	-2.29	0.018	0.7124		SFPQ	splicing factor proline and glutamine rich
TC0700008055.hg.1	4.3	3.11	0.23	0.37	2.29	-2.29	0.0468	0.7634		STAG3L1	stromal antigen 3-like 1 (pseudogene)
TC1500009210.hg.1	5.26	4.07	0.31	0.56	2.29	-2.29	0.0158	0.7056		TMEM62	transmembrane protein 62
TC0500008121.hg.1	8.09	6.89	0.49	0.55	2.3	-2.3	0.0031	0.6196		ARSK	arylsulfatase family, member K
TC0600008666.hg.1	4.3	3.1	0.37	0.61	2.3	-2.3	0.0142	0.6965		ME1	malic enzyme 1, NADP(+)-dependent, cytosolic
TC2100007387.hg.1	5.66	4.46	0.62	0.16	2.3	-2.3	0.0098	0.6713		PTTG1IP	pituitary tumor-transforming 1 interacting protein
TC0300012289.hg.1	5.38	4.17	0.14	0.54	2.3	-2.3	0.0033	0.6212		TXNRD3	thioredoxin reductase 3
TC1700008114.hg.1	5.31	4.1	0.58	0.62	2.31	-2.31	0.0299	0.7392		LRRC37A17P	leucin rich repeat containing 37 member A17, pseudogene
TC1400010261.hg.1	5.16	3.95	0.21	0.59	2.31	-2.31	0.0375	0.7454		MOK	MOK protein kinase
TC1400008629.hg.1	6.35	5.15	0.21	0.34	2.31	-2.31	9.36E-05	0.4854		SUPT16H	SPT16 homolog, facilitates chromatin remodeling subunit
TC1700007512.hg.1	5.04	3.83	0.17	0.32	2.32	-2.32	0.0005	0.5674		C17orf75	chromosome 17 open reading fram 75
TC1600008344.hg.1	4.58	3.37	0.8	0.25	2.32	-2.32	0.0131	0.6916		LINC01572	long intergenic non-protein coding RNA 1572
TC0500008850.hg.1	4.43	3.21	0.53	0.33	2.33	-2.33	0.01	0.6713		CYSTM1	cystein-rich transmembrane module containing 1
TC1800008659.hg.1	7.24	6.03	0.77	0.09	2.33	-2.33	0.0356	0.7437		DYM	dymeclin
TC1400008277.hg.1	7.63	6.4	0.41	0.23	2.33	-2.33	0.0011	0.5917		MIR495	microRNA 495
TC0500012345.hg.1	7.43	6.21	0.42	1.03	2.33	-2.33	0.0469	0.7635		NR3C1	nuclear receptor subfamily 3C1; glucocorticoid receptor alpha
TC2100006865.hg.1	6.38	5.15	0.41	0.51	2.34	-2.34	0.0024	0.6041		BACH1	BTB domain and CNC homolog 1
TC2100006865.hg.1	6.38	5.15	0.41	0.51	2.34	-2.34	0.0024	0.6041		GRIK1	ionotropic glutamate receptor, kainate subtype 1
TC0600009567.hg.1	4.54	3.31	0.46	0.67	2.34	-2.34	0.0436	0.7571		PEX7	peroxisomal biogenesis factor 7
TC1200007965.hg.1	6.46	5.23	0.24	0.36	2.34	-2.34	0.0019	0.5917		PPM1H	protein phosphatase, Mg2+/Mn2+ dependent 1H
TC0400011536.hg.1	4.57	3.34	0.61	0.22	2.35	-2.35	0.0097	0.6713		DKK2	dickkopf WNT signaling pathway inhibitor 2
TC0300010671.hg.1	5.01	3.78	0.37	0.66	2.35	-2.35	0.0238	0.7299		FBXL2	F-box and leucine-rich repeat protein 2
TC1700010677.hg.1	3.96	2.73	0.27	0.54	2.35	-2.35	0.0019	0.594		KRT19	keratin 19, type I

TC0600010132.hg.1	7.6	6.37	0.69	0.19	2.35	-2.35	0.0121	0.6866	D	QKI	quaking homology KH domain RNA binding
TC1000009629.hg.1	5.9	4.66	0.39	0.12	2.36	-2.36	0.0002	0.5406		LINC00702	long intergenic non-protein coding RNA 702
TC0900008548.hg.1	8	6.77	0.42	0.45	2.36	-2.36	0.0253	0.7354	D	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC1900010341.hg.1	4.8	3.56	0.67	0.26	2.36	-2.36	0.0108	0.6786		RNA5SP471	5S ribosomal pseudogene 471
TC0300009993.hg.1	6.72	5.48	0.78	0.3	2.36	-2.36	0.0059	0.6653		SDHAP1	succinate dehydrogenase complex flavoprotein subunit A pseudogene 1
TC0100009844.hg.1	7.59	6.34	0.37	0.28	2.37	-2.37	0.0005	0.575	D	NBPF10	neuroblastoma breakpoint family member 10
TC0200008857.hg.1	4.72	3.48	0.84	0.35	2.37	-2.37	0.0119	0.6853		RGPD6	RNABP2-like and GRIP domain containing 6
TC0200008920.hg.1	4.72	3.48	0.84	0.35	2.37	-2.37	0.0119	0.6853	D	RGPD8	RNABP2-like and GRIP domain containing 8
TC1300009892.hg.1	4.68	3.43	0.45	0.21	2.38	-2.38	0.0083	0.6679		F10	coagulation factor X
TC1400008284.hg.1	6.92	5.67	0.29	0.63	2.38	-2.38	0.005	0.6538		MIR300	microRNA 300
TC0200015091.hg.1	4.69	3.43	0.3	0.36	2.38	-2.38	0.0048	0.6495		SESTD1	SEC14 and spectrin domain 1
TC1900008695.hg.1	6.55	5.29	0.38	0.42	2.38	-2.38	0.0064	0.6674		ZNF610	zinc finger protein 610
TC0900010769.hg.1	4.82	3.57	0.11	0.44	2.39	-2.39	0.0027	0.6175		NFIL3	nuclear factor, interleukin 3 regulated
TC0700007134.hg.1	5.88	4.62	0.57	0.38	2.39	-2.39	0.0009	0.5917		NT5C3A	5'-nucleotidase, cytosolic IIIA
TC1700007774.hg.1	5.55	4.29	0.52	0.38	2.39	-2.39	0.0133	0.6916		PSMD3	proteasome 26S subunit, non-ATPase 3
TC0500010556.hg.1	4.09	2.83	0.52	0.52	2.4	-2.4	0.0352	0.7433		C9	complement C9
TC0200012526.hg.1	5.4	4.13	0.4	0.47	2.4	-2.4	0.0296	0.7392		FBXO11	F-box protein 11
TC1200010611.hg.1	4.75	3.48	0.44	0.41	2.41	-2.41	0.0048	0.6495		KMT2D	lysine methyltransferase 2D
TC1400008309.hg.1	4.66	3.39	0.46	0.27	2.41	-2.41	0.0015	0.5917		MIR656	microRNA 656
TC0800009528.hg.1	4.84	3.57	0.42	0.29	2.41	-2.41	9.87E-05	0.4854		RNU7-55P	RNA, U7 small nuclear 55 pseudogene
TC1000007525.hg.1	4.75	3.48	0.61	0.09	2.42	-2.42	0.0138	0.6945		BMS1P1	BMS1, ribosome biogenesis factor pseudogene 1
TC0600006688.hg.1	4.65	3.37	0.68	0.19	2.42	-2.42	0.0022	0.594		SLC22A23	solute carrier 22 member 23
TC0300011833.hg.1	3.79	2.51	0.51	0.35	2.43	-2.43	0.014	0.6958		CMSS1	cms1 ribosomal small subunit homolog
TC1500007316.hg.1	4.46	3.18	0.56	0.21	2.43	-2.43	0.0065	0.6679		RFX7	regulatory factor X7
TC0100013499.hg.1	6.91	5.63	0.17	0.76	2.43	-2.43	0.0331	0.7419		SRSF4	serine and arginine rich splicing factor 4 (SRP75)
TC0900008971.hg.1	6.66	5.37	0.8	0.55	2.44	-2.44	0.0046	0.6495		ABL1	ABL proto-oncogene 1, non-receptor tyrosine kinase
TC0200007761.hg.1	7.41	6.12	0.58	0.45	2.44	-2.44	0.0488	0.7642		EHBP1	EH domain binding protein 1; NACSIN
TC1700012404.hg.1	5.88	4.6	0.68	0.33	2.44	-2.44	0.0204	0.7205		KTRAP1-1	keratin associated protein 1-1
TC1900008125.hg.1	4.38	3.08	0.29	0.24	2.45	-2.45	0.0009	0.5917		CYP2A6	cytochrome P450 family 2 subfamily A member 6
TC1400008273.hg.1	6.4	5.11	0.35	0.35	2.45	-2.45	0.0051	0.6574		MIR329-2	microRNA 329-2
TC1800007344.hg.1	6.51	5.22	0.27	0.51	2.45	-2.45	0.0172	0.7113		MIR4528	microRNA 4528
TC0200007942.hg.1	4.01	2.72	0.57	0.28	2.45	-2.45	0.0016	0.5917		PCBP1-AS1	PCBP1 antisense RNA 1
TC0500011289.hg.1	4.86	3.57	0.85	0.15	2.45	-2.45	0.0431	0.7562		RASGRF2	RAS protein-specific guanine nucleotide-releasing factor 2
TC1000011495.hg.1	5.06	3.76	0.2	0.62	2.45	-2.45	0.0078	0.6679		SORBS1	sorbin and SH3 domain containing 1
TC0700012186.hg.1	5.45	4.16	0.51	0.39	2.46	-2.46	0.0053	0.6593		CCDC71L	coiled-coil domain containing 71 like
TC1700008441.hg.1	6.28	4.98	0.42	0.34	2.47	-2.47	0.0115	0.6849		PPM1E	protein phosphatase, Mg2+/Mn2+ dependent 1E

TC0100014498.hg.1	4.28	2.96	0.45	0.3	2.49	-2.49	0.0054	0.6602		SGIP1	SH3 domain GRB2 like endophilin interacting protein 1
TC1000009819.hg.1	11.24	9.91	0.36	0.35	2.5	-2.5	0.0005	0.5735		CAMK1D	calcium/calmodulin-dependent protein kinase ID
TC0600008339.hg.1	5.04	3.72	0.7	0.57	2.5	-2.5	0.0242	0.7313		DST	dystonin
TC1700008453.hg.1	4.39	3.07	0.57	0.23	2.5	-2.5	0.0016	0.5917		GDPD1	glycerophosphodiester phosphodiesterase domain containing 1
TC0100006744.hg.1	4.08	2.76	0.59	0.33	2.5	-2.5	0.0028	0.6175		RERE	arginine-glutamate dipeptide repeats
TC0400007581.hg.1	6.94	5.61	0.71	0.35	2.52	-2.52	0.0154	0.7022		CEP135	centrosomal protein 135
TC1200008538.hg.1	4.16	2.83	0.27	0.28	2.52	-2.52	0.0007	0.5837		ELK3	ELK, ETS transcription factor
TC1000007005.hg.1	5.9	4.57	0.45	0.57	2.52	-2.52	0.0014	0.5917		RNU6-413P	RNA, U6 small nuclear 413, pseudogene
TC1700011452.hg.1	4.15	2.82	0.65	0.49	2.52	-2.52	0.0126	0.6893		SMURF2	SMAD specific E3 ubiquitin protein ligase 2
TC0800009820.hg.1	5.58	4.24	0.14	0.71	2.52	-2.52	0.0012	0.5917		XPO7	exportin 7
TC1100008849.hg.1	6.82	5.48	0.3	0.62	2.53	-2.53	0.0306	0.7392		CEP57	centrosomal protein 57
TC0100014317.hg.1	6.98	5.64	0.86	0.3	2.53	-2.53	0.0244	0.7317	D	PPAP2B	phosphatidic acid phosphatase 2B
TC1000007104.hg.1	4.63	3.29	0.68	0.17	2.53	-2.53	0.006	0.6674		RAB1B	RAB1B, member RAS oncogene family
TC1100010535.hg.1	5.95	4.61	0.39	0.5	2.54	-2.54	0.0023	0.6012		PAMR1	with muscle regeneration 1
TC1400010653.hg.1	11.27	9.92	0.32	0.45	2.56	-2.56	0.0013	0.5917	D	MEG8	long intergenic non-protein coding RNA (Bsr)
TC0800011264.hg.1	4.87	3.51	0.25	0.76	2.56	-2.56	0.0184	0.7147		PABPC1	poly(A) binding protein cytoplasmic 1
TC0X00010094.hg.1	7.56	6.2	0.3	0.76	2.56	-2.56	0.0073	0.6679		SLC16A2	solute carrier family 16 member 2 (MCT8)
TC0900008561.hg.1	6.72	5.36	0.16	0.57	2.57	-2.57	0.0005	0.5735	D	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC0600010131.hg.1	4.28	2.92	1.06	0.18	2.57	-2.57	0.0118	0.6853	D	QKI	quaking homology KH domain RNA binding
TC0800007226.hg.1	4.41	3.05	0.74	0.24	2.57	-2.57	0.0112	0.6837		RNA5SP263	5S ribosomal pseudogene 263
TC0600010894.hg.1	4.01	2.64	0.57	0.46	2.58	-2.58	0.0147	0.6965		ATXN1	ataxin 1
TC0300006881.hg.1	4.39	3.02	0.39	0.65	2.59	-2.59	0.011	0.6799		SLC4A7	solute carrier 4 member A7; sodium bicarbonate transporter (NBC3)
TC0500009065.hg.1	5.6	4.21	0.6	0.26	2.61	-2.61	0.0148	0.6967		CSNK1A1	casein kinase 1 alpha 1
TC1900011512.hg.1	5.42	4.04	0.46	0.45	2.61	-2.61	0.0204	0.7205		ZSCAN5A	zinc finger and SCAN domain containing 5A
TC2000009461.hg.1	5.73	4.34	0.8	0.41	2.62	-2.62	0.045	0.7586		ATP9A	ATPase, class II, type 9A
TC0700012263.hg.1	6.5	5.12	0.66	0.35	2.62	-2.62	0.0027	0.6175		LRRN3	leucine-rich repeat neuronal 3
TC0900007116.hg.1	12.82	11.42	0.58	0.31	2.63	-2.63	0.0036	0.6269		CCIN	calicin
TC0900007603.hg.1	4.41	3.01	0.84	0.27	2.64	-2.64	0.0344	0.7424		CARNMT1	carnocine N-methyltransferase 1
TC1100007112.hg.1	6.03	4.63	0.18	0.51	2.65	-2.65	0.0216	0.7245		BBOX1	gamma-butyrobetaine hydroxylase 1
TC1700007618.hg.1	7.6	6.19	0.24	0.51	2.65	-2.65	0.0075	0.6679		CCL3	C-C motif chemokine ligand 3
TC0M00006445.hg.1	5.32	3.91	0.47	0.41	2.65	-2.65	0.0111	0.6807	D	ICAM2	intercellular adhesion molecule 2
TC0M00006445.hg.1	5.32	3.91	0.47	0.41	2.65	-2.65	0.0111	0.6807	D	PRR29	proline rich 29
TC1300009376.hg.1	4.84	3.43	0.52	0.44	2.65	-2.65	0.0101	0.6715		SLTRK1	SLIT and NTRK like family member 1
TC0800008151.hg.1	5.48	4.07	0.43	0.5	2.66	-2.66	0.0016	0.5917		RMDN1	regulator of microtubule dynamics 1
TC0400008463.hg.1	5.27	3.85	0.5	0.89	2.67	-2.67	0.0087	0.6681		PRDM5	PR/SET domain 5
TC1200011245.hg.1	5.2	3.79	0.67	0.14	2.67	-2.67	0.0085	0.6679		PTPRB	protein tyrosine phosphatase, receptor type, B
TC1400010647.hg.1	13.46	12.04	0.76	0.48	2.69	-2.69	0.0096	0.6713		BDKRB2	bradykinin receptor B2
TC1000011923.hg.1	6.88	5.46	0.4	0.51	2.69	-2.69	0.0011	0.5917		GFRA1	GDNF family receptor alpha 1

TC1600010779.hg.1	4.7	3.27	0.43	0.26	2.69	-2.69	0.0033	0.6196	HYDIN	HYDIN, axonemal central pair apparatus protein
TC1700010942.hg.1	4.79	3.35	0.68	0.68	2.7	-2.7	0.0172	0.7113	EFCAB13	EF-hand calcium binding domain 13
TC0400010627.hg.1	5.2	3.76	0.4	0.29	2.7	-2.7	3.06E-05	0.4807	FRYL	FRY like transcription coactivator
TC1600008242.hg.1	4.3	2.87	0.27	0.42	2.7	-2.7	0.0096	0.6713	D WWP2	WW domain containing E3 ubiquitin protein ligase 2
TC0900007518.hg.1	9.91	8.47	0.42	0.43	2.71	-2.71	0.0017	0.5917	MAMDC2	MAM domain containing 2
TC0800008340.hg.1	6.35	4.91	0.34	0.81	2.72	-2.72	0.0104	0.6742	D STK3	serine/threonine kinase 3
TC1700011016.hg.1	5.2	3.76	0.87	0.36	2.72	-2.72	0.041	0.7524	UBE2Z	ubiquitin conjugating enzyme E2 Z
TC0300012081.hg.1	6.22	4.77	0.44	0.33	2.74	-2.74	0.0016	0.5917	LSAMP	limbic system associated membrane protein
TC0600006833.hg.1	4.28	2.82	0.64	0.54	2.75	-2.75	0.0157	0.7053	LY86-AS1	LY86 antisense RNA 1
TC0500006738.hg.1	4.63	3.17	0.58	0.27	2.75	-2.75	0.0196	0.7205	MARCH6	membrane-associated ring-CH-type finger 6
TC0700012912.hg.1	5.42	3.96	0.96	0.04	2.75	-2.75	0.0483	0.7639	D OR2A1-AS1	OR2A1 antisense RNA 1
TC1800008781.hg.1	4.64	3.18	0.84	0.31	2.76	-2.76	0.0149	0.6973	ATP8B1	ATPase, aminophospholipid transporter, class I, type 8B, member 1
TC1600009946.hg.1	5.16	3.69	0.77	0.55	2.77	-2.77	0.0036	0.6269	KCTD13	potassium channel tetramerization domain containing 13
TC0900008465.hg.1	11.24	9.77	0.31	0.37	2.78	-2.78	0.0001	0.4854	HSDL2	hydroxysteroid dehydrogenase like 2
TC0600013560.hg.1	4.55	3.08	0.6	0.31	2.78	-2.78	0.0013	0.5917	D MTHFD1L	methylenetetrahydrofolate dehydrogenase 1 like
TC1400008245.hg.1	8.03	6.56	0.57	0.34	2.78	-2.78	0.0053	0.6602	SNORD113-1	small nucleolar RNA, C/D box 113-1
TC1600011166.hg.1	5.94	4.45	0.31	0.92	2.81	-2.81	0.0081	0.6679	C16orf95	chromosome 16 open reading frame 95
TC1900011262.hg.1	5.91	4.41	0.46	0.56	2.83	-2.83	0.0038	0.6395	SIGLEC29P	sialic acid binding Ig like lectin 29, pseudogene
TC0400010477.hg.1	5.52	4	0.92	0.15	2.87	-2.87	0.0301	0.7392	UBE2K	ubiquitin conjugating enzyme E2K
TC0800011539.hg.1	8.82	7.29	0.65	0.62	2.88	-2.88	0.0372	0.7449	D TRPS1	transcriptional repressor GATA binding 1
TC0700011581.hg.1	10.37	8.83	1.42	0.62	2.9	-2.9	0.0263	0.7354	DTX2P1-UPK3BP1-PMS2P11	DTX2P1-UPK3BP1-PMS2P11 readthrough, transcribed pseudogene
TC1000009135.hg.1	4.42	2.88	0.66	0.18	2.91	-2.91	0.0045	0.6495	ATE1	arginyltransferase 1
TC1400008247.hg.1	9.76	8.21	0.64	0.18	2.91	-2.91	0.0096	0.6713	SNORD113-2	small nucleolar RNA, C/D box 113-2
TC0800008784.hg.1	6.31	4.77	0.33	0.53	2.91	-2.91	9.42E-05	0.4854	WASHC5	WASH complex subunit 5
TC2000009715.hg.1	12.79	11.25	0.87	0.58	2.92	-2.92	0.0098	0.6713	CDH4	cadherin 4
TC2000006823.hg.1	7.17	5.63	0.44	0.37	2.92	-2.92	0.003	0.6194	ZNF133	zinc finger protein 133
TC0900007776.hg.1	6.46	4.91	0.92	0.26	2.94	-2.94	0.012	0.6866	NAA35	N(alpha)-acetyltransferase 35, NatC auxiliary subunit
TC0600013116.hg.1	5.99	4.42	0.5	0.23	2.97	-2.97	0.0025	0.6123	ECHDC1	ethylmalonyl-CoA decarboxylase 1
TC0100009147.hg.1	5.3	3.72	0.17	0.64	2.98	-2.98	0.0122	0.6876	D PTBP2	polyglutamine tract binding protein 2
TC0300009176.hg.1	4.87	3.29	0.71	0.84	3	-3	0.0204	0.7205	CLRN1-AS1	CLRN1 antisense RNA 1
TC1600009837.hg.1	6.85	5.26	0.43	0.66	3.02	-3.02	0.003	0.6175	GTF3C1	general transcription factor IIIC subunit 1
TC0700007767.hg.1	7.11	5.48	0.38	0.26	3.09	-3.09	0.0002	0.5406	ZNF679	zinc finger protein 679
TC0900011305.hg.1	8.14	6.49	0.38	0.04	3.14	-3.14	0.0009	0.5917	D TNC	tenascin C
TC1400010178.hg.1	8.79	7.13	0.53	0.43	3.17	-3.17	0.0047	0.6495	EVL	Enah/Vasp-like
TC0700008330.hg.1	6.46	4.8	0.96	0.61	3.18	-3.18	0.012	0.6866	FAM133B	family with sequence similarity 133 member B
TC0300010726.hg.1	5.07	3.36	0.21	0.83	3.27	-3.27	0.0091	0.671	LRRFIP2	leucine rich repeat (in flightless) interacting protein 2

TC1400010648.hg.1	10.7	8.99	0.91	0.43	3.28	-3.28	0.0132	0.6916		BDKRB1	bradykinin receptor B1
TC0300013137.hg.1	5.16	3.45	1.21	0.3	3.28	-3.28	0.0201	0.7205		FNDC3B	fibronectin type III domain containing 3B
TC0900008551.hg.1	7.21	5.49	0.48	0.1	3.29	-3.29	0.0004	0.5406	D	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC1400008244.hg.1	9.41	7.69	0.95	0.68	3.3	-3.3	0.0065	0.6674	D	MEG8	long intergenic non-protein RNA (Bsr)
TC1300009298.hg.1	5.01	3.29	0.77	0.39	3.3	-3.3	0.0089	0.6696	D	MYCBP2	MYC binding protein 2, E3 ubiquitin protein ligase
TC1100012095.hg.1	16.62	14.9	1.29	1.15	3.3	-3.3	0.0333	0.7419		PGR	progesterone receptor
TC0800011541.hg.1	6.87	5.14	0.34	0.83	3.31	-3.31	3.73E-05	0.4807	D	TRPS1	transcriptional repressor GATA binding 1
TC1700011061.hg.1	5.48	3.75	1.18	0.39	3.32	-3.32	0.0067	0.6679		FAM117A	family with sequence similarity 117 member A
TC1300009980.hg.1	5.52	3.79	0.32	0.16	3.32	-3.32	1.86E-05	0.4807		LMO7	LIM domain 7
TC1500007387.hg.1	4.99	3.24	0.55	0.35	3.35	-3.35	0.0003	0.5406	D	RNF111	ring finger protein 111
TC1500007387.hg.1	4.99	3.24	0.55	0.35	3.35	-3.35	0.0003	0.5406	D	SLTM	SAFB-like, transcription modulator
TC0300012378.hg.1	8.59	6.82	0.81	1.12	3.4	-3.4	0.0115	0.6848		CNBP	CCHC-type zinc finger, nucleic acid binding protein
TC0200009077.hg.1	5.27	3.5	1.02	0.22	3.41	-3.41	0.04	0.751		PTPN4	protein tyrosine phosphatase, nonreceptor type 4
TC0900011306.hg.1	5.74	3.97	0.73	0.95	3.42	-3.42	0.0093	0.6713	D	TNC	tenascin C
TC1400009289.hg.1	5.85	4.06	0.59	0.21	3.45	-3.45	0.0001	0.5406		OTX2-AS1	OTX1 antisense RNA 1
TC1600007203.hg.1	5.48	3.66	0.86	0.3	3.54	-3.54	0.008	0.6679	D	NPIP85	nuclear pore complex interacting protein family member B5
TC1300007131.hg.1	5.85	4.01	0.49	0.62	3.57	-3.57	0.0126	0.6893		MED4	mediator complex subunit 4
TC0900008623.hg.1	7.94	6.09	0.42	0.11	3.6	-3.6	1.54E-05	0.4807		B3GNT10	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 10 pseudogene
TC1400008248.hg.1	6.65	4.79	0.72	0.44	3.63	-3.63	0.0067	0.6679		SNORD113-3	small nucleolar RNA, C/D box 113-3
TC0500011272.hg.1	5.78	3.92	0.57	0.89	3.64	-3.64	0.0168	0.7092		RNU6-211P	RNA, U6 small nuclear 211, pseudogene
TC1300009178.hg.1	5.02	3.16	0.86	0.46	3.65	-3.65	0.0387	0.7486		LINC00364	long intergenic non-protein coding RNA 364
TC0600011086.hg.1	8.5	6.62	0.39	1.43	3.68	-3.68	0.0151	0.6997		CMAHP	cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene
TC0X00009102.hg.1	4.84	2.96	0.45	0.46	3.69	-3.69	0.0013	0.5917		GPM6B	glycoprotein M6B
TC1500009662.hg.1	5.17	3.26	0.56	0.24	3.76	-3.76	0.001	0.5917		RORA	RAR-related orphan receptor alpha
TC0900010881.hg.1	7.62	5.67	0.43	0.48	3.86	-3.86	0.0016	0.5917		FANCC	Fanconi anemia complementation group C
TC0100012205.hg.1	5.33	3.38	1.15	0.35	3.86	-3.86	0.0236	0.7299		SDCCAG8	serologically defined colon cancer antigen 8
TC1100012133.hg.1	9.85	7.89	0.69	0.56	3.88	-3.88	0.0008	0.5917		MMP3	matrix metalloproteinase 3
TC1400006715.hg.1	4.9	2.91	0.29	0.29	3.97	-3.97	3.22E-05	0.4807		PCK2	phosphoenolpyruvate carboxylase 2
TC0500007703.hg.1	5.64	3.62	0.94	0.81	4.05	-4.05	0.028	0.7374		NAIP	NLR family apoptosis inhibitory protein
TC0200016651.hg.1	12.53	10.44	0.41	0.34	4.26	-4.26	1.20E-05	0.4807		CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1
TC1600009698.hg.1	5.45	3.35	0.38	0.84	4.29	-4.29	0.0075	0.6679		EEF2K	eukaryotic elongation factor-2 kinase
TC0100014568.hg.1	4.89	2.79	3.06	0.32	4.3	-4.3	0.0453	0.7593		HHLA3	HERV-H LTR-associated 3

TC0800011540.hg.1	7.65	5.54	0.91	1.09	4.33	-4.33	0.028	0.7374	D	TRPS1	transcriptional repressor GATA binding 1
TC1800008830.hg.1	15.16	13.01	1.87	0.62	4.45	-4.45	0.0428	0.7556	D	CCBE1	collagen and calcium binding EGF domains 1
TC0400011187.hg.1	5.69	3.52	0.75	0.81	4.53	-4.53	0.0186	0.7163		SEC31A	Sec31 homolog A
TC0800006784.hg.1	6.39	4.2	1.2	0.07	4.56	-4.56	0.0113	0.6846		ALG1L12P	asparagine-linked glycosylation 1-like 12, pseudogene
TC1700011577.hg.1	9.62	7.43	0.78	0.86	4.57	-4.57	0.0006	0.5837		ABCA9	ATP binding cassette subfamily A member 9
TC0900008545.hg.1	8.08	5.86	0.46	0.65	4.64	-4.64	0.0008	0.5917	D	PAPPA	pregnancy-associated plasma protein A, pappalysin 1
TC2000007581.hg.1	5.1	2.87	0.71	0.86	4.68	-4.68	0.0114	0.6847		SULF2	sulfatase 2
TC0100014528.hg.1	7.4	5.15	0.4	0.66	4.75	-4.75	0.0008	0.5917		DIRAS3	DIRAS family, GTP-binding RAS-like 3
TC1200012203.hg.1	7.84	5.48	0.91	0.48	5.12	-5.12	0.0027	0.6175		ANAPC5	anaphase promoting complex subunit 5

## **Supplemental Table 2**

Ingenuity canonical pathways in EIPA-unique transcriptome.

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score	Molecules
Telomerase Signaling	5.04E+00	1.14E-01	2.333	ETS1,RAP2A,HDAC9,HDAC8,PIK3R1,ABL1,PIK3C2G,RAP1A,PTGES3,HDAC3,MRAS,PIK3CB,ELK3
Chronic Myeloid Leukemia Signaling	4.47E+00	1.08E-01	NaN	RAP2A,HDAC9,IKBK,HDAC3,HDAC8,PIK3R1,CTBP2,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Integrin Signaling	3.84E+00	7.58E-02	3.742	RAP2A,PIK3R1,DIRAS3,ITGA8,WASL,PIK3C2G,ABL1,GSN,RAP1A,DOCK1,RND3,ITGA11,MRAS,PIK3CB,NEDD9,ACTN1
Glioma Invasiveness Signaling	3.79E+00	1.18E-01	2.333	RAP2A,TIMP3,RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,RAP1A
Germ Cell-Sertoli Cell Junction Signaling	3.69E+00	8.05E-02	NaN	RAP2A,PIK3R1,DIRAS3,WASL,PIK3C2G,GSN,RAP1A,EPN2,CDH2,RND3,SORBS1,MRAS,PIK3CB,ACTN1
Epithelial Adherens Junction Signaling	3.33E+00	8.22E-02	NaN	RAP2A,MYH10,EPN2,CDH2,MAGI1,LMO7,SORBS1,WASL,MRAS,BMPR2,RAP1A,ACTN1
Hereditary Breast Cancer Signaling	3.30E+00	8.16E-02	NaN	RAP2A,HDAC9,HDAC3,HDAC8,PIK3R1,PIK3C2G,MRAS,PIK3CB,SMARCC1,FANCC,RAP1A,HLTF
Role of NFAT in Cardiac Hypertrophy	3.13E+00	6.79E-02	3.317	RAP2A,HDAC9,HDAC8,CAMK1D,PIK3R1,MEF2A,PIK3C2G,CSNK1A1,CACNA1C,RAP1A,PLCB4,PRKAR2B,HDAC3,MRAS,PIK3CB
Paxillin Signaling	3.05E+00	8.70E-02	2.828	RAP2A,DOCK1,ITGA11,PIK3R1,ITGA8,PIK3C2G,MRAS,PIK3CB,RAP1A,ACTN1
TR/RXR Activation	2.97E+00	9.18E-02	NaN	F10,HDAC3,LDLR,SLC2A1,PIK3R1,PIK3C2G,SLC16A2,PIK3CB,ME1
G12/13 Signaling	2.94E+00	7.86E-02	1.508	RAP2A,CDH2,IKBK,CDH4,PIK3R1,MEF2A,PIK3C2G,MRAS,PIK3CB,RAP1A,CDH13
AMPK Signaling	2.82E+00	6.57E-02	1.732	SLC2A1,STRADA,PIK3R1,CPT1B,PIK3C2G,PRKAR2B,PCK2,TBC1D1,MRAS,PIK3CB,SMARCC1,EEF2K,HNF4A,HLTF
Renal Cell Carcinoma Signaling	2.73E+00	9.30E-02	2.646	ETS1,RAP2A,SLC2A1,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Calcium Signaling	2.69E+00	6.63E-02	2.828	RAP2A,MYH10,HDAC9,TP63,HDAC8,CAMK1D,RYR2,MEF2A,CACNA1C,RAP1A,PRKAR2B,HDAC3,GRIK1
NF- $\kappa$ B Signaling	2.57E+00	6.70E-02	3.464	RAP2A,TRAF3,IKBK,RIK1,GHR,PIK3R1,PIK3C2G,MRAS,BMPR2,PIK3CB,RAP1A,TNFRSF11B
Cancer Drug Resistance By Drug Efflux	2.56E+00	1.11E-01	NaN	mir-154,RAP2A,PIK3R1,MRAS,PIK3CB,RAP1A
NF- $\kappa$ B Activation by Viruses	2.55E+00	8.70E-02	2.828	RAP2A,IKBK,RIK1,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
PEDF Signaling	2.52E+00	8.60E-02	2.828	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,TCF12
TGF- $\beta$ Signaling	2.52E+00	8.60E-02	0.816	RAP2A,RNF111,SKI,MRAS,BMPR2,SMURF2,HNF4A,RAP1A
HMGGB1 Signaling	2.48E+00	7.30E-02	3.162	RAP2A,RND3,PIK3R1,DIRAS3,KAT6A,PIK3C2G,MRAS,PIK3CB,RAP1A,TNFRSF11B
Oncostatin M Signaling	2.43E+00	1.25E-01	2.236	RAP2A,TIMP3,MMP3,MRAS,RAP1A
HGF Signaling	2.41E+00	7.63E-02	2.646	ETS1,RAP2A,DOCK1,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,ELK3
Cholesterol Biosynthesis I	2.38E+00	2.31E-01	NaN	DHCR7,DHCR24,MSMO1
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	2.38E+00	2.31E-01	NaN	DHCR7,DHCR24,MSMO1
Cholesterol Biosynthesis III (via Desmosterol)	2.38E+00	2.31E-01	NaN	DHCR7,DHCR24,MSMO1
Antiproliferative Role of Somatostatin Receptor 2	2.37E+00	8.97E-02	2.449	RAP2A,NPR3,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
GM-CSF Signaling	2.34E+00	8.86E-02	1.89	ETS1,RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
PXR/RXR Activation	2.33E+00	1.00E-01	NaN	SCD,PRKAR2B,PCK2,CYP2A6 (includes others),HNF4A,NR3C1
Prostate Cancer Signaling	2.30E+00	7.92E-02	NaN	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Superpathway of Cholesterol Biosynthesis	2.30E+00	1.48E-01	2	MVD,DHCR7,DHCR24,MSMO1
Melanoma Signaling	2.29E+00	9.84E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
CXCR4 Signaling	2.28E+00	6.47E-02	3.162	RAP2A,DOCK1,PLCB4,RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,ELMO1,RAP1A
PTEN Signaling	2.27E+00	7.26E-02	-2.828	RAP2A,IKBK,MAGI1,GHR,PIK3R1,MRAS,BMPR2,PIK3CB,RAP1A
Actin Nucleation by ARP-WASP Complex	2.25E+00	9.68E-02	2.449	RAP2A,RND3,DIRAS3,WASL,MRAS,RAP1A
STAT3 Pathway	2.25E+00	7.77E-02	2.121	RAP2A,GHR,PTPN2,MAP3K20,MRAS,BMPR2,RAP1A,IFNAR1
GDNF Family Ligand-Receptor Interactions	2.25E+00	8.54E-02	2.646	RAP2A,PIK3R1,GFRA1,PIK3C2G,MRAS,PIK3CB,RAP1A
Acute Phase Response Signaling	2.24E+00	6.40E-02	1.414	RAP2A,IKBK,RIK1,C1S,PIK3R1,C9,MRAS,PIK3CB,RAP1A,NR3C1,TNFRSF11B
SAPK/JNK Signaling	2.22E+00	7.69E-02	2.828	RAP2A,RIK1,PIK3R1,MAP3K20,PIK3C2G,MRAS,PIK3CB,RAP1A
Angiopoietin Signaling	2.22E+00	8.43E-02	1	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Non-Small Cell Lung Cancer Signaling	2.22E+00	8.43E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Neurotrophin/TRK Signaling	2.22E+00	8.43E-02	2.646	RAP2A,NTF3,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Tetrahydrofolate Salvage from 5,10-methylenetetrahydrofolate	2.19E+00	4.00E-01	NaN	MTHFD1L,MTHFD2
VEGF Signaling	2.17E+00	7.55E-02	2.646	RAP2A,EIF2B4,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,ACTN1
Fc $\gamma$ RIIB Signaling in B Lymphocytes	2.16E+00	8.24E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,CACNA1C,PIK3CB,RAP1A
G-Protein Coupled Receptor Signaling	2.16E+00	5.38E-02	NaN	RAP2A,GDPD1,PIK3R1,PIK3C2G,RAP1A,GRM7,GABBR2,PLCB4,IKBK,PRKAR2B,GPER1,NPR3,MRAS,PIK3CB,PDE4D
CNTF Signaling	2.16E+00	9.23E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Phospholipase C Signaling	2.15E+00	5.73E-02	3.606	RAP2A,HDAC9,HDAC8,DIRAS3,MEF2A,ARHGEF17,RAP1A,PLCB4,HDAC3,RND3,MRAS,ARHGEF3,LCP2
Adipogenesis pathway	2.12E+00	6.87E-02	NaN	HDAC9,HDAC3,RUNX1T1,DDIT3,HDAC8,KAT6A,CTBP2,BMPR2,PER2
Relaxin Signaling	2.11E+00	6.45E-02	2.121	IKBK,PRKAR2B,GDPD1,NPR3,PIK3R1,PIK3C2G,MRAS,PIK3CB,PDE4D,RAP1A
Erythropoietin Signaling	2.11E+00	8.05E-02	NaN	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Role of NFAT in Regulation of the Immune Response	2.10E+00	6.11E-02	3.317	RAP2A,PLCB4,IKBK,PIK3R1,MEF2A,PIK3C2G,MRAS,CSNK1A1,PIK3CB,RAP1A,LCP2
Estrogen Receptor Signaling	2.08E+00	6.77E-02	NaN	RAP2A,HDAC3,PCK2,CTBP2,MRAS,RAP1A,NR3C1,MED4,PGR
IGF-1 Signaling	2.06E+00	7.21E-02	2.646	RAP2A,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,CYR61,RAP1A



Prolactin Signaling	2.06E+00	7.87E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,NR3C1
14-3-3-mediated Signaling	2.04E+00	6.67E-02	1.667	RAP2A,PLCB4,PIK3R1,STRADA,PIK3C2G,MRAS,PIK3CB,RAP1A,SNCA
T Cell Receptor Signaling	2.03E+00	7.14E-02	NaN	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,LCP2
IL-4 Signaling	2.03E+00	7.78E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,NR3C1
Cardiac Hypertrophy Signaling	2.01E+00	5.49E-02	3.051	RAP2A,PLCB4,EIF2B4,PRKAR2B,RND3,DIRAS3,PIK3R1,MEF2A,PIK3C2G,MRAS,CACNA1C,PIK3CB,RAP1A
IL-17 Signaling	2.01E+00	7.69E-02	NaN	RAP2A,MMP3,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Endometrial Cancer Signaling	2.00E+00	8.57E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
IL-2 Signaling	2.00E+00	8.57E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Thrombopoietin Signaling	1.97E+00	8.45E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
LPS-stimulated MAPK Signaling	1.96E+00	7.53E-02	2.646	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
TWEAK Signaling	1.94E+00	1.18E-01	0	NAIP,TRAF3,IKBK,RIPK1
Chemokine Signaling	1.92E+00	8.22E-02	2.449	RAP2A,PLCB4,CAMK1D,PIK3C2G,MRAS,RAP1A
ErbB2-ErbB3 Signaling	1.89E+00	8.11E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
PDGF Signaling	1.88E+00	7.29E-02	2.646	RAP2A,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Sumoylation Pathway	1.88E+00	7.29E-02	-1.633	ETS1,RND3,DNMT3A,DIRAS3,CTBP2,NR3C1,SNCA
Glioma Signaling	1.88E+00	6.72E-02	2.646	RAP2A,CAMK1D,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
NRF2-mediated Oxidative Stress Response	1.87E+00	5.67E-02	1.342	RAP2A,DNAJB4,DNAJC4,PIK3R1,PIK3C2G,UBE2K,MRAS,PIK3CB,DNAJC1,RAP1A,BACH1
Gap Junction Signaling	1.87E+00	5.67E-02	NaN	RAP2A,PLCB4,PRKAR2B,NPR3,PIK3R1,PIK3C2G,MRAS,CSNK1A1,PIK3CB,RAP1A,GRIK1
Role of JAK1 and JAK3 in $\text{I}\beta\text{c}$ Cytokine Signaling	1.86E+00	8.00E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Molecular Mechanisms of Cancer	1.86E+00	4.65E-02	NaN	RAP2A,NAIP,PIK3R1,DIRAS3,PIK3C2G,ABL1,BMPR2,ARHGEF17,RALBP1,RAP1A,RASGRF2,PLCB4,IKBK,PRKAR2B,RND3,MRAS,PIK3CB,ARHGEF3
Ceramide Signaling	1.84E+00	7.14E-02	0.378	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,TNFRSF11B
Myc Mediated Apoptosis Signaling	1.84E+00	7.89E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
ErbB4 Signaling	1.84E+00	7.89E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
HIF1 $\pm$ Signaling	1.82E+00	6.56E-02	NaN	RAP2A,SLC2A1,MMP3,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Signaling by Rho Family GTPases	1.81E+00	5.18E-02	3.606	CDH4,PIK3R1,DIRAS3,WASL,PIK3C2G,ARHGEF17,CDH2,RND3,MAP3K20,MRAS,PIK3CB,ARHGEF3,CDH13
Ovarian Cancer Signaling	1.79E+00	6.08E-02	2.828	RAP2A,PRKAR2B,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,CGA,RAP1A
Histidine Degradation III	1.76E+00	2.50E-01	NaN	MTHFD1L,MTHFD2
RhoGDI Signaling	1.75E+00	5.68E-02	-3.162	CDH2,CDH4,RND3,DIRAS3,WASL,MRAS,ARHGEF17,ARHGEF3,DLC1,CDH13
Glucocorticoid Receptor Signaling	1.75E+00	4.71E-02	NaN	RAP2A,PIK3R1,PIK3C2G,PBX1,CCL3,NR3C1,RAP1A,PTGES3,PGR,IKBK,PCCK2,KRT19,MRAS,PIK3CB,SMARCC1,HLTF
Role of Tissue Factor in Cancer	1.75E+00	6.35E-02	NaN	RAP2A,F10,PIK3R1,PIK3C2G,MRAS,PIK3CB,CYR61,RAP1A
Melanocyte Development and Pigmentation Signaling	1.73E+00	6.80E-02	2.646	RAP2A,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
fMLP Signaling in Neutrophils	1.71E+00	6.25E-02	2.121	RAP2A,PLCB4,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
FAK Signaling	1.71E+00	6.73E-02	NaN	RAP2A,DOCK1,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Leukocyte Extravasation Signaling	1.71E+00	5.37E-02	1.508	TIMP3,EDIL3,MMP3,PIK3R1,WASL,PIK3C2G,ABL1,PIK3CB,RAP1A,DLC1,ACTN1
IL-15 Signaling	1.69E+00	7.32E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Thrombin Signaling	1.68E+00	5.31E-02	3.317	RAP2A,PLCB4,RND3,CAMK1D,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,ARHGEF3,RAP1A
PKC $\delta$ Signaling in T Lymphocytes	1.68E+00	5.81E-02	2.828	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,CACNA1C,PIK3CB,RAP1A,LCP2
Cholecystokinin/Gastrin-mediated Signaling	1.67E+00	6.60E-02	2.646	RAP2A,PLCB4,RND3,DIRAS3,MEF2A,MRAS,RAP1A
PAK Signaling	1.67E+00	6.60E-02	2.646	RAP2A,PIK3R1,WASL,PIK3C2G,MRAS,PIK3CB,RAP1A
Regulation of Cellular Mechanics by Calpain Protease	1.67E+00	8.20E-02	NaN	RAP2A,MRAS,RAP1A,CNGA1,ACTN1
Folate Transformations I	1.66E+00	2.22E-01	NaN	MTHFD1L,MTHFD2
PI3K Signaling in B Lymphocytes	1.66E+00	6.11E-02	2.828	RAP2A,PLCB4,IKBK,PIK3R1,MRAS,ABL1,PIK3CB,RAP1A
Breast Cancer Regulation by Stathmin1	1.66E+00	5.26E-02	NaN	RAP2A,PLCB4,PRKAR2B,CAMK1D,PIK3R1,PIK3C2G,MRAS,PIK3CB,ARHGEF17,ARHGEF3,RAP1A
Nitric Oxide Signaling in the Cardiovascular System	1.63E+00	6.48E-02	2.449	BDKRB2,PRKAR2B,PIK3R1,RYR2,PIK3C2G,CACNA1C,PIK3CB
IL-6 Signaling	1.62E+00	6.02E-02	2.828	RAP2A,IKBK,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,TNFRSF11B
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	1.62E+00	1.25E-01	NaN	PTPN2,CGA,IFNAR1
Small Cell Lung Cancer Signaling	1.62E+00	7.06E-02	2.236	TRAF3,IKBK,PIK3R1,PIK3C2G,ABL1,PIK3CB
Estrogen-Dependent Breast Cancer Signaling	1.62E+00	7.06E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Regulation of eIF4 and p70S6K Signaling	1.61E+00	5.66E-02	2.449	PABPC1,RAP2A,EIF2B4,PIK3R1,PIK3C2G,MRAS,EIF3A,PIK3CB,RAP1A
UVA-Induced MAPK Signaling	1.61E+00	6.42E-02	2.646	RAP2A,PLCB4,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
p53 Signaling	1.59E+00	6.36E-02	0	HDAC9,TP63,THBS1,PIK3R1,PIK3C2G,PIK3CB,RPRM
Adenine and Adenosine Salvage VI	1.58E+00	1.00E+00	NaN	ADK
Macropinocytosis Signaling	1.58E+00	6.90E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Mouse Embryonic Stem Cell Pluripotency	1.57E+00	6.31E-02	1.89	RAP2A,PIK3R1,PIK3C2G,MRAS,BMPR2,PIK3CB,RAP1A
Oleate Biosynthesis II (Animals)	1.57E+00	2.00E-01	NaN	SCD,FADS2
CREB Signaling in Neurons	1.56E+00	5.09E-02	3.162	GRM7,RAP2A,PLCB4,PRKAR2B,PIK3R1,PIK3C2G,MRAS,CACNA1C,PIK3CB,RAP1A,GRIK1
p70S6K Signaling	1.56E+00	5.84E-02	2.121	RAP2A,PLCB4,PIK3R1,PIK3C2G,MRAS,PIK3CB,EEF2K,RAP1A

P2Y Purigenic Receptor Signaling Pathway	1.54E+00	5.80E-02	2.828	RAP2A,PLCB4,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
IL-3 Signaling	1.53E+00	6.74E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
FLT3 Signaling in Hematopoietic Progenitor Cells	1.53E+00	6.74E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
JAK/Stat Signaling	1.53E+00	6.74E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Thyroid Cancer Signaling	1.53E+00	8.89E-02	NaN	RAP2A,NTF3,MRAS,RAP1A
Neuropathic Pain Signaling In Dorsal Horn Neurons	1.52E+00	6.14E-02	2.646	GRM7,PLCB4,PRKAR2B,CAMK1D,PIK3R1,PIK3C2G,PIK3CB
Lymphotoxin $\text{I}^2$ Receptor Signaling	1.51E+00	7.46E-02	2.236	TRAF3,IKBKG,PIK3R1,PIK3C2G,PIK3CB
Virus Entry via Endocytic Pathways	1.50E+00	6.09E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Glioblastoma Multiforme Signaling	1.50E+00	5.39E-02	3	RAP2A,PLCB4,RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,RAP1A
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	1.48E+00	4.55E-02	NaN	RAP2A,TRAF3,MMP3,PIK3R1,PIK3C2G,CSNK1A1,RAP1A,PLCB4,IKBKG,RIPK1,MRAS,DDK2,PIK3CB,TNFRSF11B
Insulin Receptor Signaling	1.48E+00	5.63E-02	2.121	RAP2A,EIF2B4,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
VEGF Family Ligand-Receptor Interactions	1.47E+00	6.52E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Natural Killer Cell Signaling	1.47E+00	5.98E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,LCP2
Bladder Cancer Signaling	1.45E+00	6.45E-02	NaN	RAP2A,MMP3,THBS1,MRAS,ABL1,RAP1A
HER-2 Signaling in Breast Cancer	1.43E+00	6.38E-02	NaN	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
ERK/MAPK Signaling	1.43E+00	5.03E-02	3.162	ETS1,RAP2A,DOCK1,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,ELK3
Actin Cytoskeleton Signaling	1.43E+00	4.85E-02	2.714	RAP2A,DOCK1,MYH10,PIK3R1,WASL,PIK3C2G,MRAS,PIK3CB,GSN,RAP1A,ACTN1
Assembly of RNA Polymerase III Complex	1.42E+00	1.67E-01	NaN	BDP1,GTFC31
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	1.42E+00	4.82E-02	NaN	NAIP,IKBKG,MMP3,PIK3R1,PIK3C2G,CSNK1A1,DDK2,BMPR2,PIK3CB,GSN,TNFRSF11B
PPAR $\alpha$ /RXR $\alpha$ Activation	1.40E+00	5.17E-02	-1.414	RAP2A,PLCB4,IKBKG,GHR,PRKAR2B,CPT1B,MRAS,BMPR2,RAP1A
Fc Epsilon RI Signaling	1.38E+00	5.74E-02	2.646	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,LCP2
NGF Signaling	1.38E+00	5.74E-02	2.646	RAP2A,IKBKG,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
G $\alpha$ i Signaling	1.38E+00	5.74E-02	1.134	GRM7,RAP2A,GABBR2,PRKAR2B,NPR3,MRAS,RAP1A
Acute Myeloid Leukemia Signaling	1.38E+00	6.19E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Synaptic Long Term Potentiation	1.37E+00	5.69E-02	2.449	GRM7,RAP2A,PLCB4,PRKAR2B,MRAS,CACNA1C,RAP1A
Sertoli Cell-Sertoli Cell Junction Signaling	1.35E+00	5.06E-02	NaN	SPTBN1,RAP2A,EPN2,PRKAR2B,SORBS1,MAP3K20,MRAS,RAP1A,ACTN1
G Protein Signaling Mediated by Tubby	1.33E+00	9.68E-02	NaN	PLCB4,MRAS,ABL1
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	1.32E+00	5.56E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,BMPR2,PIK3CB,RAP1A
Role of PI3K/AKT Signaling in the Pathogenesis of Influenza	1.31E+00	6.58E-02	1.342	IKBKG,PIK3R1,PIK3C2G,PIK3CB,IFNAR1
Renin-Angiotensin Signaling	1.30E+00	5.51E-02	2.646	RAP2A,PRKAR2B,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Lipoate Biosynthesis and Incorporation II	1.29E+00	5.00E-01	NaN	LIAS
Anandamide Degradation	1.29E+00	5.00E-01	NaN	FAAH2
ErbB Signaling	1.27E+00	5.83E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
CD40 Signaling	1.27E+00	6.41E-02	1.342	TRAF3,IKBKG,PIK3R1,PIK3C2G,PIK3CB
CCR3 Signaling in Eosinophils	1.26E+00	5.38E-02	2.646	RAP2A,PLCB4,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
CDK5 Signaling	1.26E+00	5.77E-02	2.449	LAMC1,RAP2A,PRKAR2B,MRAS,ABL1,RAP1A
B Cell Receptor Signaling	1.25E+00	4.84E-02	2.333	ETS1,RAP2A,IKBKG,PIK3R1,PIK3C2G,MRAS,ABL1,PIK3CB,RAP1A
Vitamin-C Transport	1.24E+00	1.33E-01	NaN	SLC2A1,TXNRD3
G $\alpha$ q Signaling	1.24E+00	5.03E-02	2.828	PLCB4,IKBKG,RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB
EIF2 Signaling	1.23E+00	4.63E-02	2.121	PABPC1,RAP2A,EIF2B4,DDIT3,PIK3R1,PIK3C2G,MRAS,EIF3A,PIK3CB,RAP1A
Circadian Rhythm Signaling	1.23E+00	8.82E-02	NaN	BHLHE41,BHLHE40,PER2
BMP signaling pathway	1.23E+00	6.25E-02	2.236	RAP2A,PRKAR2B,MRAS,BMPR2,RAP1A
Huntington's Disease Signaling	1.21E+00	4.45E-02	1.633	HDAC9,PLCB4,HDAC3,HDAC8,PSMF1,PIK3R1,HTT,PIK3C2G,PIK3CB,SNAP25,SNCA
Coagulation System	1.20E+00	8.57E-02	NaN	BDKRB2,F10,BDKRB1
G $\alpha$ s Signaling	1.18E+00	5.50E-02	2.236	PRKAR2B,GPER1,RYR2,MRAS,RAP1A,CNGA1
eNOS Signaling	1.17E+00	4.88E-02	2.449	BDKRB2,PRKAR2B,PIK3R1,AQP11,PIK3C2G,PIK3CB,CNGA1,BDKRB1
ILK Signaling	1.17E+00	4.66E-02	2.828	DOCK1,MYH10,RND3,PIK3R1,DIRAS3,PIK3C2G,PIK3CB,ACTN1,DSP
Amyotrophic Lateral Sclerosis Signaling	1.16E+00	5.45E-02	1.342	NAIP,PIK3R1,PIK3C2G,CACNA1C,PIK3CB,GRIK1
Leptin Signaling in Obesity	1.16E+00	5.95E-02	NaN	PLCB4,PRKAR2B,PIK3R1,PIK3C2G,PIK3CB
cAMP-mediated signaling	1.15E+00	4.46E-02	1.897	GRM7,GABBR2,PRKAR2B,GPER1,GDPD1,NPR3,CAMK1D,PDE4D,RAP1A,CNGA1
Adrenomedullin signaling pathway	1.15E+00	4.62E-02	3	RAP2A,PLCB4,PRKAR2B,NPR3,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
$\text{I}^3$ -linolenate Biosynthesis II (Animals)	1.14E+00	1.18E-01	NaN	FADS2,ACSL4
Mitochondrial L-carnitine Shuttle Pathway	1.14E+00	1.18E-01	NaN	CPT1B,ACSL4
Induction of Apoptosis by HIV1	1.14E+00	6.67E-02	0	NAIP,IKBKG,RIPK1,TNFRSF11B
Activation of IRF by Cytosolic Pattern Recognition Receptors	1.12E+00	6.56E-02	2	TRAF3,IKBKG,RIPK1,IFNAR1
L-carnitine Biosynthesis	1.12E+00	3.33E-01	NaN	BBOX1
1D-myo-inositol Hexakisphosphate Biosynthesis V (from Ins(1,3,4)P3)	1.12E+00	3.33E-01	NaN	IPMK
Fatty Acid $\text{I}^2$ -oxidation III (Unsaturated, Odd Number)	1.12E+00	3.33E-01	NaN	ECI2
N-acetylglucosamine Degradation I	1.12E+00	3.33E-01	NaN	AMDHD2

mTOR Signaling	1.08E+00	4.48E-02	2.828	RAP2A,RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,EIF3A,PIK3CB,RAP1A
IL-8 Signaling	1.07E+00	4.46E-02	3	RAP2A,IKBK, RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,RAP1A
Synaptic Long Term Depression	1.07E+00	4.62E-02	2.828	GRM7,RAP2A,PLCB4,NPR3,RYR2,MRAS,CACNA1C,RAP1A
Th1 and Th2 Activation Pathway	1.07E+00	4.62E-02	NaN	NFIL3,TNFSF4,BHLHE41,PIK3R1,PIK3C2G,BMPR2,PIK3CB,IFNAR1
Protein Ubiquitination Pathway	1.06E+00	4.18E-02	NaN	DNAJB4,DNAJC4,UBE2K,ANAPC5,UBE2Z,DNAJC1,SMURF2,SUGT1,PSMD1,PSMD3,UBE2D3
Ubiquinol-10 Biosynthesis (Eukaryotic)	1.06E+00	1.05E-01	NaN	MICAL2,ECHDC1
Cell Cycle: G1/S Checkpoint Regulation	1.04E+00	6.15E-02	NaN	HDAC9,HDAC3,HDAC8,ABL1
Reelin Signaling in Neurons	1.04E+00	5.49E-02	NaN	PIK3R1,PIK3C2G,PIK3CB,ARHGEF3,DAB1
Sperm Motility	1.03E+00	5.04E-02	1.633	PLCB4,PRKAR2B,MRAS,PDE4D,CNGA1,PTK7
Maturity Onset Diabetes of Young (MODY) Signaling	1.02E+00	1.00E-01	NaN	CACNA1C,HNF4A
Endoplasmic Reticulum Stress Pathway	1.02E+00	1.00E-01	NaN	DDIT3,TAOK3
Inflammasome pathway	1.02E+00	1.00E-01	NaN	NAIP,NEK7
Role of RIG1-like Receptors in Antiviral Innate Immunity	1.01E+00	7.14E-02	NaN	TRAF3,IKBK, RIPK1
Role of p14/p19ARF in Tumor Suppression	1.01E+00	7.14E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Phagosome Formation	1.01E+00	4.96E-02	NaN	PLCB4,RND3,PIK3R1,DIRAS3,PIK3C2G,PIK3CB
Î±-tocopherol Degradation	9.97E-01	2.50E-01	NaN	CYP4F2
N-acetylglucosamine Degradation II	9.97E-01	2.50E-01	NaN	AMDHD2
Rac Signaling	9.94E-01	4.92E-02	2.449	RAP2A,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Stearate Biosynthesis I (Animals)	9.91E-01	6.98E-02	NaN	DHCR24,ACSL4,HNF4A
Type II Diabetes Mellitus Signaling	9.91E-01	4.64E-02	2.236	IKBK,PIK3R1,PIK3C2G,CACNA1C,ACSL4,PIK3CB,TNFRSF11B
Apoptosis Signaling	9.83E-01	5.26E-02	-1.342	RAP2A,NAIP,IKBK,MRAS,RAP1A
Sphingosine-1-phosphate Signaling	9.82E-01	4.88E-02	2.449	PLCB4,RND3,PIK3R1,DIRAS3,PIK3C2G,PIK3CB
Role of IL-17A in Arthritis	9.72E-01	5.80E-02	NaN	IKBK,PIK3R1,PIK3C2G,PIK3CB
ERK5 Signaling	9.54E-01	5.71E-02	2	RAP2A,MEF2A,MRAS,RAP1A
IL-9 Signaling	9.46E-01	6.67E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
PPAR Signaling	9.41E-01	5.10E-02	-2.236	RAP2A,IKBK,MRAS,RAP1A,TNFRSF11B
Agrin Interactions at Neuromuscular Junction	9.22E-01	5.56E-02	NaN	LAMC1,RAP2A,MRAS,RAP1A
MSP-RON Signaling Pathway	9.22E-01	5.56E-02	NaN	KLK9,PIK3R1,PIK3C2G,PIK3CB
PI3K/AKT Signaling	9.21E-01	4.69E-02	1.633	RAP2A,IKBK,PIK3R1,MRAS,PIK3CB,RAP1A
Colorectal Cancer Metastasis Signaling	9.21E-01	4.02E-02	3.162	RAP2A,PRKAR2B,RND3,MMP3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB,RAP1A
RANK Signaling in Osteoclasts	9.14E-01	5.00E-02	2.236	IKBK,PIK3R1,PIK3C2G,PIK3CB,GSN
Folate Polyglutamylation	9.06E-01	2.00E-01	NaN	MTHFD1L
Hypoxia Signaling in the Cardiovascular System	9.06E-01	5.48E-02	NaN	IKBK,UBE2K,UBE2Z,UBE2D3
GP6 Signaling Pathway	8.98E-01	4.62E-02	2.449	LAMC1,PIK3R1,PIK3C2G,COL22A1,PIK3CB,LCP2
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	8.88E-01	4.19E-02	2.646	IKBK,RND3,PIK3R1,DIRAS3,PIK3C2G,PIK3CB,RAP1A,TNFRSF11B
Bupropion Degradation	8.88E-01	8.33E-02	NaN	CYP2A6 (includes others),CYP1B1
TNFR1 Signaling	8.84E-01	6.25E-02	NaN	NAIP,IKBK, RIPK1
UVB-Induced MAPK Signaling	8.84E-01	6.25E-02	NaN	RAP2A,MRAS,RAP1A
Regulation of the Epithelial-Mesenchymal Transition Pathway	8.79E-01	4.17E-02	NaN	ETS1,RAP2A,CDH2,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Axonal Guidance Signaling	8.77E-01	3.56E-02	NaN	RAP2A,PAPPA,NTF3,MMP3,PIK3R1,WASL,PIK3C2G,ABL1,RAP1A,DOCK1,PLCB4,SEMA6D,PRKAR2B,MRAS,PIK3CB,SEMA7A
Protein Kinase A Signaling	8.72E-01	3.65E-02	0	MYH10,GDPD1,PTPN2,RYR2,RAP1A,CNGA1,PLCB4,PTPN4,IKBK,PRKAR2B,PTPRB,CDC14B,ANAPC5,PDE4D
OX40 Signaling Pathway	8.65E-01	6.12E-02	NaN	TRAF3,TNFSF4,IKBK
Aldosterone Signaling in Epithelial Cells	8.35E-01	4.22E-02	2	PLCB4,DNAJB4,DNAJC4,PIK3R1,PIK3C2G,PIK3CB,DNAJC1
NAD Biosynthesis from 2-amino-3-carboxymuconate Semialdehyde	8.32E-01	1.67E-01	NaN	ABL1
Zymosterol Biosynthesis	8.32E-01	1.67E-01	NaN	MSMO1
IL-17A Signaling in Airway Cells	8.30E-01	5.13E-02	1	IKBK,PIK3R1,PIK3C2G,PIK3CB
Docosahexaenoic Acid (DHA) Signaling	8.10E-01	5.77E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Semaphorin Signaling in Neurons	8.10E-01	5.77E-02	NaN	RND3,DIRAS3,SEMA7A
Cyclins and Cell Cycle Regulation	8.02E-01	5.00E-02	NaN	HDAC9,HDAC3,HDAC8,ABL1
Neuroinflammation Signaling Pathway	7.95E-01	3.69E-02	3	GABBR2,TRAF3,IKBK, RIPK1,MMP3,PIK3R1,PIK3C2G,BMPR2,PIK3CB,CCL3,SNCA
Transcriptional Regulatory Network in Embryonic Stem Cells	7.92E-01	5.66E-02	NaN	KAT6A,HNF4A,HIST1H4H
Human Embryonic Stem Cell Pluripotency	7.91E-01	4.29E-02	NaN	NTF3,PIK3R1,PIK3C2G,MRAS,BMPR2,PIK3CB
Cardiac Î²-adrenergic Signaling	7.91E-01	4.29E-02	2.236	PRKAR2B,GDPD1,RYR2,MRAS,CACNA1C,PDE4D
Th2 Pathway	7.91E-01	4.29E-02	1.633	TNFSF4,BHLHE41,PIK3R1,PIK3C2G,BMPR2,PIK3CB
Thioredoxin Pathway	7.71E-01	1.43E-01	NaN	TXNRD3
Inositol Pyrophosphates Biosynthesis	7.71E-01	1.43E-01	NaN	IPMK
Dendritic Cell Maturation	7.63E-01	4.02E-02	2.646	PLCB4,IKBK,PIK3R1,PIK3C2G,PIK3CB,IFNAR1,TNFRSF11B
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	7.62E-01	4.82E-02	NaN	RAP2A,IKBK,MRAS,RAP1A
IL-7 Signaling Pathway	7.62E-01	4.82E-02	2	SLC2A1,PIK3R1,PIK3C2G,PIK3CB
iCOS-iCOSL Signaling in T Helper Cells	7.57E-01	4.42E-02	2.236	IKBK,PIK3R1,PIK3C2G,PIK3CB,LCP2

TNFR2 Signaling	7.56E-01	6.90E-02	NaN	NAIP,IKBKG
Acetone Degradation I (to Methylglyoxal)	7.56E-01	6.90E-02	NaN	CYP2A6 (includes others),CYP1B1
Growth Hormone Signaling	7.50E-01	4.76E-02	2	GHR,PIK3R1,PIK3C2G,PIK3CB
Opioid Signaling Pathway	7.46E-01	3.75E-02	2.333	RAP2A,PRKAR2B,CAMK1D,RYR2,PIK3C2G,MRAS,CACNA1C,GRK5,RAP1A
Ephrin Receptor Signaling	7.37E-01	3.95E-02	2.646	RAP2A,SORBS1,WASL,PIK3C2G,MRAS,ABL1,RAP1A
Fatty Acid $\beta$ -oxidation I	7.33E-01	6.67E-02	NaN	ECI2,ACSL4
Regulation of Actin-based Motility by Rho	7.25E-01	4.65E-02	NaN	RND3,DIRAS3,WASL,GSN
Systemic Lupus Erythematosus Signaling	7.21E-01	3.79E-02	NaN	BDKRB2,RAP2A,PIK3R1,C9,PIK3C2G,MRAS,PIK3CB,RAP1A
Pathogenesis of Multiple Sclerosis	7.18E-01	1.25E-01	NaN	CCL3
Role of JAK2 in Hormone-like Cytokine Signaling	6.90E-01	6.25E-02	NaN	GHR,HLTF
Pancreatic Adenocarcinoma Signaling	6.85E-01	4.17E-02	2	PIK3R1,PIK3C2G,ABL1,PIK3CB,RALBP1
G Beta Gamma Signaling	6.85E-01	4.17E-02	2.236	RAP2A,PRKAR2B,MRAS,CACNA1C,RAP1A
Ephrin A Signaling	6.83E-01	5.00E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Prostanoid Biosynthesis	6.73E-01	1.11E-01	NaN	PTGES3
DNA Methylation and Transcriptional Repression Signaling	6.70E-01	6.06E-02	NaN	DNMT3A,HIST1H4H
MIF-mediated Glucocorticoid Regulation	6.70E-01	6.06E-02	NaN	IKBKG,NR3C1
Neuregulin Signaling	6.67E-01	4.40E-02	2	RAP2A,PIK3R1,MRAS,RAP1A
$\beta$ -Adrenergic Signaling	6.67E-01	4.40E-02	NaN	RAP2A,PRKAR2B,MRAS,RAP1A
CD28 Signaling in T Helper Cells	6.66E-01	4.10E-02	2.236	IKBKG,PIK3R1,PIK3C2G,PIK3CB,LCP2
Th1 Pathway	6.56E-01	4.07E-02	2.236	NFIL3,PIK3R1,PIK3C2G,PIK3CB,IFNAR1
Fc $\gamma$ Receptor-mediated Phagocytosis in Macrophages and Monocytes	6.56E-01	4.35E-02	2	DOCK1,PIK3R1,PIK3C2G,LCP2
CTLA4 Signaling in Cytotoxic T Lymphocytes	6.45E-01	4.30E-02	NaN	PIK3R1,PIK3C2G,PIK3CB,LCP2
Cellular Effects of Sildenafil (Viagra)	6.29E-01	3.97E-02	NaN	MYH10,PLCB4,PRKAR2B,CACNA1C,PDE4D
Endothelin-1 Signaling	6.29E-01	3.66E-02	2.646	RAP2A,PLCB4,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A
Netrin Signaling	6.16E-01	4.62E-02	NaN	PRKAR2B,RYR2,CACNA1C
UVB-Induced MAPK Signaling	6.16E-01	4.62E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Interferon Signaling	6.15E-01	5.56E-02	NaN	PTPN2,IFNAR1
Complement System	6.15E-01	5.56E-02	NaN	C1S,C9
Superpathway of Inositol Phosphate Compounds	6.04E-01	3.51E-02	2.828	PLCB4,TNS3,IPMK,PTPN2,PIK3R1,PPM1H,PIK3C2G,PIK3CB
Tec Kinase Signaling	6.00E-01	3.70E-02	2.449	RND3,PIK3R1,DIRAS3,PIK3C2G,MRAS,PIK3CB
Acyl-CoA Hydrolysis	5.97E-01	9.09E-02	NaN	HNF4A
Dolichyl-diphosphooligosaccharide Biosynthesis	5.97E-01	9.09E-02	NaN	ALG1
Inhibition of Matrix Metalloproteases	5.81E-01	5.26E-02	NaN	TIMP3,MMP3
EGF Signaling	5.80E-01	4.41E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Caveolar-mediated Endocytosis Signaling	5.68E-01	4.35E-02	NaN	ITGA11,ITGA8,ABL1
April Mediated Signaling	5.65E-01	5.13E-02	NaN	TRAF3,IKBKG
Estrogen Biosynthesis	5.65E-01	5.13E-02	NaN	CYP2A6 (includes others),CYP1B1
Cleavage and Polyadenylation of Pre-mRNA	5.64E-01	8.33E-02	NaN	CPSF2
Mevalonate Pathway I	5.64E-01	8.33E-02	NaN	MVD
Guanosine Nucleotides Degradation III	5.64E-01	8.33E-02	NaN	NT5C3A
Pregnenolone Biosynthesis	5.64E-01	8.33E-02	NaN	MICAL2
Corticotropin Releasing Hormone Signaling	5.62E-01	3.73E-02	1.342	PRKAR2B,NPR3,MEF2A,CACNA1C,RAP1A
Xenobiotic Metabolism Signaling	5.57E-01	3.33E-02	NaN	RAP2A,CAMK1D,PIK3R1,PIK3C2G,MRAS,PIK3CB,RAP1A,CYP1B1,PTGES3
Melatonin Signaling	5.57E-01	4.29E-02	NaN	PLCB4,PRKAR2B,RORA
GNRH Signaling	5.56E-01	3.57E-02	2.236	RAP2A,PLCB4,PRKAR2B,MRAS,CACNA1C,RAP1A
nNOS Signaling in Skeletal Muscle Cells	5.50E-01	5.00E-02	NaN	RYR2,CACNA1C
Antioxidant Action of Vitamin C	5.47E-01	3.88E-02	NaN	PLCB4,IKBKG,SLC2A1,TXNRD3
Role of PKR in Interferon Induction and Antiviral Response	5.35E-01	4.88E-02	NaN	TRAF3,IKBKG
B Cell Activating Factor Signaling	5.35E-01	4.88E-02	NaN	TRAF3,IKBKG
Intrinsic Prothrombin Activation Pathway	5.35E-01	4.88E-02	NaN	KLK9,F10
Fatty Acid Activation	5.35E-01	7.69E-02	NaN	ACSL4
NAD biosynthesis II (from tryptophan)	5.35E-01	7.69E-02	NaN	ABL1
Urate Biosynthesis/Inosine 5'-phosphate Degradation	5.35E-01	7.69E-02	NaN	NT5C3A
tRNA Splicing	5.21E-01	4.76E-02	NaN	GDPD1,PDE4D
DNA Double-Strand Break Repair by Homologous Recombination	5.08E-01	7.14E-02	NaN	ABL1
Chondroitin Sulfate Degradation (Metazoa)	5.08E-01	7.14E-02	NaN	CEMIP
Adenosine Nucleotides Degradation II	5.08E-01	7.14E-02	NaN	NT5C3A

Nicotine Degradation III	5.07E-01	4.65E-02	NaN	CYP2A6 (includes others),CYP1B1
Role of MAPK Signaling in the Pathogenesis of Influenza	5.04E-01	4.00E-02	NaN	RAP2A,MRAS,RAP1A
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	4.94E-01	4.55E-02	NaN	MEF2A,WWP2
Dermatan Sulfate Degradation (Metazoa)	4.84E-01	6.67E-02	NaN	CEMIP
Histidine Degradation VI	4.84E-01	6.67E-02	NaN	MICAL2
Extrinsic Prothrombin Activation Pathway Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)	4.61E-01	6.25E-02	NaN	MVD
Parkinson's Signaling	4.61E-01	6.25E-02	NaN	SNCA
Role of BRCA1 in DNA Damage Response	4.57E-01	3.75E-02	NaN	SMARCC1,FANCC,HLTF
RAN Signaling	4.40E-01	5.88E-02	NaN	KPNA6
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	4.40E-01	5.88E-02	NaN	CCL3
Purine Nucleotides Degradation II (Aerobic)	4.40E-01	5.88E-02	NaN	NT5C3A
LXR/RXR Activation	4.35E-01	3.42E-02	NaN	SCD,LDLR,C9,TNFRSF11B
Nicotine Degradation II	4.34E-01	4.08E-02	NaN	CYP2A6 (includes others),CYP1B1
Amyloid Processing	4.23E-01	4.00E-02	NaN	PRKAR2B,CSNK1A1
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	4.23E-01	4.00E-02	NaN	ABL1,RPRM
Phototransduction Pathway	4.12E-01	3.92E-02	NaN	PRKAR2B,CNGA1
Cardiomyocyte Differentiation via BMP Receptors	4.02E-01	5.26E-02	NaN	BMPR2
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	4.02E-01	5.26E-02	NaN	IPMK
D-myo-inositol (1,3,4)-trisphosphate Biosynthesis	4.02E-01	5.26E-02	NaN	IPMK
Melatonin Degradation I	4.02E-01	3.85E-02	NaN	CYP2A6 (includes others),CYP1B1
3-phosphoinositide Biosynthesis	4.00E-01	3.09E-02	2,449	TNS3,PTPN2,PIK3R1,PPM1H,PIK3C2G,PIK3CB
Hepatic Cholestasis	4.00E-01	3.16E-02	NaN	IKBK,PRKAR2B,HNF4A,ATP8B1,TNFRSF11B
CCR5 Signaling in Macrophages	3.99E-01	3.45E-02	NaN	MRAS,CACNA1C,CCL3
Role of Lipids/Lipid Rafts in the Pathogenesis of Influenza	3.85E-01	5.00E-02	NaN	IFNAR1
FGF Signaling	3.69E-01	3.30E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
Death Receptor Signaling	3.69E-01	3.30E-02	NaN	NAIP,IKBK,RIK1
NAD Salvage Pathway II	3.69E-01	4.76E-02	NaN	NT5C3A
Superpathway of Melatonin Degradation	3.63E-01	3.57E-02	NaN	CYP2A6 (includes others),CYP1B1
Glutamate Receptor Signaling	3.63E-01	3.57E-02	NaN	GRM7,GRIK1
IL-1 Signaling	3.62E-01	3.26E-02	NaN	IKBK,PRKAR2B,MRAS
Tight Junction Signaling	3.57E-01	3.01E-02	NaN	CPSF2,MYH10,PRKAR2B,SNAP25,TNFRSF11B
Polyamine Regulation in Colon Cancer	3.54E-01	4.55E-02	NaN	PSMF1
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	3.54E-01	4.55E-02	NaN	CCL3
GABA Receptor Signaling	3.49E-01	3.19E-02	NaN	GABBR2,MRAS,CACNA1C
Clathrin-mediated Endocytosis Signaling	3.48E-01	2.93E-02	NaN	LDLR,PIK3R1,WASL,PIK3C2G,AAK1,PIK3CB
Superpathway of D-myo-inositol (1,4,5)-trisphosphate Metabolism	3.27E-01	4.17E-02	NaN	IPMK
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	3.15E-01	2.92E-02	2	TNS3,IPMK,PTPN2,PPM1H
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	3.15E-01	2.92E-02	2	TNS3,IPMK,PTPN2,PPM1H
Gluconeogenesis I	3.14E-01	4.00E-02	NaN	ME1
Antiproliferative Role of TOB in T Cell Signaling	3.02E-01	3.85E-02	NaN	PABPC1
Type I Diabetes Mellitus Signaling	3.00E-01	2.94E-02	NaN	IKBK,RIK1,TNFRSF11B
Pyridoxal 5'-phosphate Salvage Pathway	2.99E-01	3.12E-02	NaN	CSNK1A1,GRK5
D-myo-inositol (1,4,5)-Trisphosphate Biosynthesis	2.91E-01	3.70E-02	NaN	PLCB4
IL-12 Signaling and Production in Macrophages	2.86E-01	2.80E-02	NaN	IKBK,PIK3R1,PIK3C2G,PIK3CB
IL-15 Production	2.80E-01	3.57E-02	NaN	PTK7
Sonic Hedgehog Signaling	2.70E-01	3.45E-02	NaN	PRKAR2B
RAR Activation	2.68E-01	2.69E-02	NaN	PRKAR2B,PIK3R1,PIK3CB,SMARCC1,HLTF
Gustation Pathway	2.64E-01	2.70E-02	NaN	PRKAR2B,GDPD1,CACNA1C,PDE4D

TREM1 Signaling	2.59E-01	2.86E-02	NaN	NLRP10,CCL3
GPCR-Mediated Nutrient Sensing in Enteroendocrine Cells	2.53E-01	2.70E-02	NaN	PLCB4,PRKAR2B,CACNA1C
3-phosphoinositide Degradation	2.51E-01	2.65E-02	2	TNS3,INPP4B,PTPN2,PPM1H
Role of Wnt/GSK-3 $\beta$ Signaling in the Pathogenesis of Influenza	2.47E-01	2.78E-02	NaN	CSNK1A1,IFNAR1
GPCR-Mediated Integration of Enteroendocrine Signaling Exemplified by an L Cell	2.47E-01	2.78E-02	NaN	PLCB4,PRKAR2B
4-1BB Signaling in T Lymphocytes	2.42E-01	3.12E-02	NaN	IKBKG
Inhibition of Angiogenesis by TSP1	2.42E-01	3.12E-02	NaN	THBS1
Ephrin B Signaling	2.42E-01	2.74E-02	NaN	MRAS,ITSN2
p38 MAPK Signaling	2.39E-01	2.63E-02	NaN	DDIT3,MEF2A,EEF2K
Autoimmune Thyroid Disease Signaling	2.18E-01	2.86E-02	NaN	CGA
IL-17A Signaling in Fibroblasts	2.18E-01	2.86E-02	NaN	IKBKG
Notch Signaling	2.04E-01	2.70E-02	NaN	MAML2
Triacylglycerol Degradation	1.97E-01	2.63E-02	NaN	MGLL
IL-10 Signaling	0.00E+00	1.45E-02	NaN	IKBKG
Aryl Hydrocarbon Receptor Signaling	0.00E+00	1.49E-02	NaN	CYP1B1,PTGES3
LPS/L-1 Mediated Inhibition of RXR Function	0.00E+00	2.43E-02	NaN	CPT1B,ACSL4,CYP2A6 (includes others),FABP3,TNFRSF11B
Hepatic Fibrosis / Hepatic Stellate Cell Activation	0.00E+00	2.20E-02	NaN	MYH10,COL22A1,IFNAR1,TNFRSF11B
Mitochondrial Dysfunction	0.00E+00	1.24E-02	NaN	CPT1B,SNCA
VDR/RXR Activation	0.00E+00	1.32E-02	NaN	CST6
FXR/RXR Activation	0.00E+00	2.46E-02	NaN	PCK2,C9,HNF4A
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	0.00E+00	2.29E-02	NaN	PIK3R1,PIK3C2G,PIK3CB
MIF Regulation of Innate Immunity	0.00E+00	2.44E-02	NaN	IKBKG
CD27 Signaling in Lymphocytes	0.00E+00	1.92E-02	NaN	IKBKG
T Helper Cell Differentiation	0.00E+00	1.56E-02	NaN	TNFRSF11B
Factors Promoting Cardiogenesis in Vertebrates	0.00E+00	1.12E-02	NaN	BMPR2
Mitotic Roles of Polo-Like Kinase	0.00E+00	1.59E-02	NaN	ANAPC5
ATM Signaling	0.00E+00	1.03E-02	NaN	ABL1
Androgen Signaling	0.00E+00	2.21E-02	NaN	PRKAR2B,MRAS,CACNA1C
Primary Immunodeficiency Signaling	0.00E+00	2.56E-02	NaN	IKBKG
Communication between Innate and Adaptive Immune Cells	0.00E+00	1.33E-02	NaN	CCL3
Cdc42 Signaling	0.00E+00	8.20E-03	NaN	WASL
Retinoic acid Mediated Apoptosis Signaling	0.00E+00	1.69E-02	NaN	IFNAR1
RhoA Signaling	0.00E+00	2.46E-02	NaN	RND3,RAPGEF6,DLC1
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	0.00E+00	1.28E-02	NaN	TRAF3
Atherosclerosis Signaling	0.00E+00	8.20E-03	NaN	MMP3
Neuroprotective Role of THOP1 in Alzheimer's Disease	0.00E+00	1.79E-02	NaN	PRKAR2B,NFYA
Nur77 Signaling in T Lymphocytes	0.00E+00	2.08E-02	NaN	HDAC9
Role of Hypercytokinemia/hyperchemokine in the Pathogenesis of Influenza	0.00E+00	2.50E-02	NaN	CCL3
Dopamine-DARPP32 Feedback in cAMP Signaling	0.00E+00	2.52E-02	2	PLCB4,PRKAR2B,CSNK1A1,CACNA1C
iNOS Signaling	0.00E+00	2.27E-02	NaN	IKBKG
D-myo-inositol-5-phosphate Metabolism	0.00E+00	2.58E-02	2	PLCB4,TNS3,PTPN2,PPM1H
Phospholipases	0.00E+00	1.72E-02	NaN	PLCB4
Triacylglycerol Biosynthesis	0.00E+00	2.27E-02	NaN	PLPP3
Salvage Pathways of Pyrimidine Ribonucleotides	0.00E+00	2.15E-02	NaN	CSNK1A1,GRK5
Remodeling of Epithelial Adherens Junctions	0.00E+00	1.56E-02	NaN	ACTN1
Agranulocyte Adhesion and Diapedesis	0.00E+00	2.31E-02	NaN	MYH10,ICAM2,MMP3,CCL3
Granulocyte Adhesion and Diapedesis	0.00E+00	2.45E-02	NaN	ICAM2,MMP3,CCL3,TNFRSF11B
HIPPO signaling	0.00E+00	1.16E-02	NaN	STK3
Unfolded protein response	0.00E+00	1.85E-02	NaN	DDIT3
Wnt/Ca <sup>2+</sup> pathway	0.00E+00	1.61E-02	NaN	PLCB4
Toll-like Receptor Signaling	0.00E+00	1.33E-02	NaN	IKBKG
Wnt/ $\beta$ -catenin Signaling	0.00E+00	2.38E-02	NaN	CDH2,CSNK1A1,DKK2,BMPR2
Dopamine Receptor Signaling	0.00E+00	1.33E-02	NaN	PRKAR2B
Phagosome Maturation	0.00E+00	7.41E-03	NaN	SNAP25
Osteoarthritis Pathway	0.00E+00	2.46E-02	1	TIMP3,HDAC3,MMP3,BMPR2,SLC39A8
Sirtuin Signaling Pathway	0.00E+00	1.08E-02	NaN	SLC2A1,PCK2,CPT1B
Iron homeostasis signaling pathway	0.00E+00	7.69E-03	NaN	BMPR2



### **Supplemental Table 3**

Ingenuity upstream regulator analysis in EIPA-unique transcriptome.

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	Flags	p-value of overlap	Target molecules in dataset
pirinixic acid		chemical toxicant	Activated	2.081	bias	3.44E-02	ACSL4,C9,CDH2,CGA,CPT1B,ECI2,ELOVL5,FADS2,HNF4A,KLF11,LDLR,MGLL,NPC2,PCK2,RORA,SCD,UBE2K
beta-estradiol		chemical - endogenous mammalian	Activated	2.96	bias	9.81E-04	ADK,ARNT2,BHLHE40,BMPR2,CAP2,CDH2,CGA,CLCA2,CNBP,CPT1B,CWC25,CYP1B1,CYP2A6 (includes others),CYR61,DDIT3,DHCR7,DNAJC1,DSP,EIF3A,ENPP2,ETS1,FABP3,FADS3,GHR,GIPC2,GPC1,GPER1,HELLS,IKBK,G,INPP4B,KAT6A,KRT19,LDLR,LIN7A,LMO7,MFE2A,MGLL,MSMO1,NEDD9,NFYA,NPR3,NR3C1,OXTR,PBX1,PGR,PIK3R1,PLAA,PTBP2,PTPN2,PTTG1IP,RAP1A,RAPGEF6,RND3,RPRM,RYR2,SHISA4,SLC2A1,SNAP25,SNED1,STK3,STS,TBHS1,TIMP3,TNFRSF11B,TNS3,TP63,TRAF3,ZBTB20
8-bromo-cAMP		chemical reagent	Activated	2.761	bias	2.41E-02	ACSL4,CGA,CYP1B1,FDXR,LDLR,NFIL3,PDE4D,PGR,SLC2A1
Calcineurin protein(s)		complex	Activated	2.2	bias	7.71E-03	CBLB,CCL3,CPT1B,LIN7A,NFIL3,RNF128
PDGF BB		complex	Activated	2.383	bias	5.58E-03	BDKRB1,BDKRB2,BHLHE40,CYR61,DDIT3,ETS1,GHR,LDLR,MMP3,NEXN,NFIL3,NPR3,RND3,SCD,THBS1,TNC
Insulin		group	Activated	2.233		2.69E-01	FADS2,ME1,MMP3,NFIL3,NR3C1,PER2,PIK3R1,SCD,SLC2A1,SORBS1,Sort1
Cg		complex	Activated	3.297	bias	6.25E-04	BHLHE40,CDH2,DHCR7,DNAH11,ELK3,ENPP2,GPC1,HAPLN1,LDLR,LRP1B,LRRN3,NPR3,OXTR,PAPPA,PDE4D,PGR,PDP1,RORA,SMURF2,SNAP25
Lh		complex	Activated	2.138	bias	8.22E-05	ACTN1,ATP9A,CAP2,CSNK1A1,DHCR7,FDXR,GRK5,MSMO1,NPC2,NTF3,PDE4D,PGR,PSMD1,PSMD3,RPRM,SNAP25,THBS1,TNFRSF11B
Ins1		other	Activated	2.143	bias	2.85E-02	DDIT3,ECI2,FABP3,FADS2,LDLR,MMP3,NTF3,PGR,PIK3R1,SCD,SLC2A1,SNAP25,TIMP3
SOX4		transcription regulator	Activated	2.896	bias	1.04E-03	ARPP21,BMPR2,CDH2,EVL,HDAC8,LMO7,LRRN3,MAGI1,SEL1L3,SNX10,Sort1,THSD1
WNT1		cytokine	Activated	2.425	bias	1.47E-02	DKK2,DNAJC1,ENPP2,HNF4A,KRT19,MMP3,MRAS,ZIC1
AGT		growth factor	Activated	2.748	bias	1.02E-02	BACH1,BDKRB2,CACNA1C,CDH13,ETS1,FDXR,FOXp2,GRK5,LDLR,LPP,MSMO1,MYH10,NPR3,PIK3R1,PTBP2,SLC2A1,SNCA,UGCG,WASL
PDGFB		growth factor	Activated	2	bias	4.76E-02	CCL3,MMP3,THBS1,TNC
HIF1A		transcription regulator	Activated	3.386	bias	2.68E-02	BHLHE40,BHLHE41,CDH2,CEMIP,CYR61,ETS1,FAM13A,GHR,GPER1,HDAC3,HIST1H2AC,KRT19,QKI,RAPGEF6,SLC2A1,THBS1,TNFRSF11B
RASSF1		other	Activated	2.433		2.85E-02	BHLHE40,BMPR2,CDH2,GHR,GSN,MRAS
SP1		transcription regulator	Activated	2.486	bias	1.38E-02	CDH2,CYP1B1,DHCR24,DLC1,DNMT3A,F10,GHR,HDAC3,HNF4A,KRT19,LDLR,LTBP3,PGR,PLAA,PRKAR2B,SLC2A1,SLC39A8,SLC4A7,SMARCC1,SNAP25,TIMP3,TNC,UGCG
PTK2		kinase	Activated	2.378	bias	2.42E-04	CYR61,DSP,LDLR,LPP,THBS1,TIMP3,TNC
SREBF1		transcription regulator	Activated	3.617	bias	4.28E-04	ACSL4,BHLHE40,BHLHE41,CAMK1D,CAP2,CYP4F2,DHCR7,FABP3,FADS2,HNF4A,LDLR,MSMO1,MVD,NFIL3,PCK2,SCD
FGF10		growth factor	Activated	2.213	bias	1.07E-02	CYP1B1,LDLR,LMO7,SCD,TIMP3
TNF		cytokine	Activated	3.052	bias	1.08E-02	AAK1,ARHGEF17,BBOX1,BDKRB1,BDKRB2,BHLHE40,BHLHE41,CCL3,CDH13,CDH2,CPT1B,CYP1B1,CYR61,DDIT3,ELK3,ENPP2,ETS1,GHR,HAPLN1,HDAC9,HNF4A,ICAM2,KCTD13,LAMC1,LDLR,MAGI1,MAN1C1,MAP3K20,MMP3,MYH10,NAIP,NEDD9,NNMT,NR3C1,PAPPA,PCK2,PER2,PIK3CB,PLAA,QKI,RAPGEF5,RIPK1,RND3,RORA,SCD,SKI,SLC16A2,SLC2A1,SMURF2,SORBS1,THBS1,TIMP3,TNC,TNFRSF11B,TNS3,TRAF3,UGCG
IFI16		transcription regulator	Activated	2.236	bias	3.51E-02	CCL3,CGA,FAF1,LDLR,MTHFD2
PIK3R1	5.61	kinase	Activated	2.213	bias	4.31E-02	CCL3,DDIT3,PIK3CB,PIK3R1,SLC2A1
NR1I2		ligand-dependent nuclear receptor	Activated	2.216		8.32E-02	CYP2A6 (includes others),DHCR7,HNF4A,HTT,SCD,TNFRSF11B
ERG		transcription regulator	Activated	3.162	bias	4.23E-06	ACTN1,BDKRB1,CAMK1D,DOCK1,DOCK2,ELMO1,ETS1,ICAM2,IKBK, MAGI1, MMP3, NFIL3, PLPP3, PTPN4, RAPGEF5, RBMS1, SNCA, THBS1
TGFB1		growth factor	Activated	3.182	bias	2.30E-07	ABL1,ACTN1,ADK,AQP11,ARNT2,ATXN1,B3GALT2,BDKRB2,BHLHE40,C15,CCL3,CDH2,CDH4,CEMIP,CLCA2,CPT1B,CYB561,CYR61,DNAJB4,DNMT3A,DOCK2,DSP,ELK3,ELMO1,ETS1,FDXR,FNDC3B,GPER1,GRM7,GSN,HDAC9,HITF,HNF4A,ICAM2,ITGA11,KPNA6,KRT19,LAMC1,LANCL1,LDLR,LEMD3,LTBP3,MBNL2,mir-154,MMP3,MSMO1,MTHFD2,MVD,NEDD9,NNMT,PAPPA,PBX1,PDE4D,PHACTR1,PSMD1,RAP1A,RASGRF2,RBMS1,RERE,RNF111,RORA,SCD,SEMA7A,SKI,SLC22A18,SLC2A1,SLC39A8,SMURF2,SRSF4,TBC1D1,TCF12,THBS1,TIA1,TIMP3,TMEM17,TNC,TNFRSF11B
PLG		peptidase	Activated	2.393	bias	9.53E-03	CYR61,DOCK1,ELMO1,PIK3CB,PRKAR2B,TNFRSF11B
ZAP70		kinase	Activated	2	bias	4.76E-02	EDIL3,MYCBP2,PLEC,SCD
AR		ligand-dependent nuclear receptor	Activated	3.583	bias	3.33E-03	BMPR2,CACNA1C,CDH2,CGA,DHCR24,DHCR7,ELMO1,GA56,GSN,INPP4B,MRAS,MSMO1,MTHFD2,NR3C1,PGR,SLC39A8,SLC7A11,SMARCC1,THBS1,TIMP3,TP63
EGF		growth factor	Activated	3.031	bias	1.02E-02	ACSL4,ACTN1,CDH4,CGA,CYR61,DDIT3,ETS1,GPER1,HNF4A,KRT19,MAP3K20,MMP3,PGR,PLPP3,SCD,SLC4A7,SNAP25,THBS1,TIMP3,TNC,TP63



TGFB3		growth factor	Activated	3.358	bias	1.37E-05	BHLHE40,CDH2,CYR61,ETS1,MICAL2,MMP3,SCD,SH3PX2,2A,THBS1,TIMP3,TNC,TNFRSF11B
ELK1		transcription regulator	Activated	2.236	bias	1.26E-02	BMMPR2,MTHFD2,SLC2A1,SLC7A11,THBS1
CREBBP		transcription regulator	Activated	2.236	bias	3.57E-02	AQP11,ARHGEF3,BDKRB2,CGA,CYR61,DNAJB4,EVL,FNDC3B,GFRA1,GRAMD2B,LDLR,NR3C1,PGR,PPM1E,SLC7A11,TNC
SREBF2		transcription regulator	Activated	2.745	bias	5.39E-04	CAMK1D,CYP4F2,DHCR7,FADS2,LDLR,MSMO1,MVD,SCD
TP53		transcription regulator	Activated	3.242		1.04E-02	ACTN1,APBB2,ASTN2,ATXN1,BDKRB2,BHLHE40,BHLHE41,C9,C9orf116,CLCA2,CYR61,DDIT3,DHCR24,DHCR7,DLC1,EDIL3,ENPP2,FABP3,FAM196A,FDXR,GAS6,GSN,HDAC3,HDAC9,HTT,KAT6A,KMT2D,LPP,MBNL2,ME1,MMP3,MVD,MYH10,NPEPPS,PGR,PIK3R1,PSMD1,PSMD3,RALBP1,RAP2A,RBBP6,RND3,RPRM,SCMH1,SFPQ,SHROOM3,SLC2A1,SMURF2,SORBS1,SULF2,THBS1,TIMP3,TOM1,TP63
ESR1		ligand-dependent nuclear receptor	Activated	2.823		6.59E-04	ANAPC5,BMPR2,CAP2,CCPG1,CEP135,CGA,CSNK1A1,CYP1B1,DHCR7,DNAJC1,DST,EEF2K,ENPP2,GABBR2,GHR,GPER1,GSN,HELLS,KCTD13,KRT19,LANCL1,LDLR,LEMD3,MAGI1,MAP3K20,MYH10,NEDD9,NPR3,OXTR,PGR,PSMD3,PTPN4,PTTG1IP,RAPGEF6,RERE,RIPK1,RND3,RPRM,RRBP1,SCIN,SDCCAG8,SEC31A,SFPQ,SLC16A2,SLC39A8,SLC7A11,SMURF2,SPTBN1,STK3,TNFRSF11B,TNS3,TOM1
rosiglitazone		chemical drug	Activated	2.286	bias	4.46E-02	CGA,CPT1B,ETS1,FABP3,KLF11,MAN1C1,MGLL,PIK3R1,PLPP3,RORA,SCD,SKI,SLC2A1,SORBS1,THBS1,TNC
methotrexate		chemical drug	Activated	2.142		7.12E-02	ACSL4,CCL3,GSN,NR3C1,PBX1,PEX7,SCD,THBS1,TIMP3,TNFRSF11B
lovastatin		chemical drug	Activated	2.012	bias	2.00E-02	CYP4F2,DDIT3,DHCR7,HELLS,LDLR,MVD,TNFRSF11B
fatty acid		chemical - endogenous mammalian	Activated	2.378	bias	1.41E-02	CPT1B,CYR61,DDIT3,FADS2,LDLR,SCD,SLC2A1
forskolin		chemical toxicant	Activated	3.341	bias	2.48E-03	ACTN1,ATP9A,BHLHE40,CAP2,CDH2,CGA,CYP1B1,DDIT3,DHCR7,FDXR,GFRA1,GRK5,HAPLN1,MFN1,MMP3,MSMO1,NFIL3,NPC2,PDE4D,PGR,PRKAR2B,PSMD3,RPRM,SERINC2,SLC2A1,SLC7A11,SNAP25,THBS1,TNFRSF11B
fenofibrate		chemical drug	Activated	2.36	bias	1.97E-02	ACSL4,CDH2,CPT1B,ECI2,FADS2,LDLR,MGLL,NR3C1,PCK2,PIK3C2G,RORA,SCD
decitabine		chemical drug	Activated	4.254	bias	3.76E-05	BMPR2,CDH13,CDH2,CDH4,CYP1B1,CYP2A6 (includes others),DIRAS3,DLC1,DST,FBN2,FDXR,GFRA1,GSN,HELLS,HNF4A,LDLR,mir-154,MMP3,MOK,NR3C1,PABPC1,PER2,PGR,RASGRF2,RP
tunicamycin		chemical - endogenous non-mammalian	Activated	2.726	bias	4.40E-03	DDIT3,ETS1,HAPLN1,LMF1,MMP3,MORF4L2,MVD,PCK2,RIPK1,SCD,SLC2A1,SLC7A11
dihydrotestosterone		chemical - endogenous mammalian	Activated	3.007	bias	2.23E-04	AIG1,CDH2,CGA,CST6,DHCR24,DNMT3A,FOXP2,GAS6,GHR,GSN,HNRNP1,KRT19,LDLR,ME1,MGLL,MMP3,NPEPPS,NR3C1,OXTR,PER2,SCD,SLC25A40,SLC2A1,SLC4A7,SMARCC1,SORT1,THBS1,TIMP3
progesterone		chemical - endogenous mammalian	Activated	2.086	bias	8.21E-04	BHLHE40,CDH2,CYP1B1,CYP2A6 (includes others),DDIT3,DLC1,DNAJB4,ENPP2,GAS6,GHR,ITGA11,KLF11,LMO7,ME1,MMP3,NEDD9,NFIL3,NTF3,PER2,PGR,PIK3R1,PLPP3,PPM1H,SCD,SLC2A1,STX18,TIMP3,UGCG
ADRB		group	Inhibited	-2.333	bias	9.91E-03	ABL1,ARHGEF3,BHLHE40,DDIT3,IKBK,MSMO1,MVD,SLC7A11,TRAF3
miR-124-3p (and other miRNAs w/		mature microrna	Inhibited	-3.831	bias	1.04E-03	CD14B,CYP1B1,DHCR24,DNAJC1,ECI2,ELK3,ELOVL5,FAM177A1,GSN,LAMC1,LDLR,PTBP2,PTTG1IP,QSER1,RBMS1
mir-29		microrna	Inhibited	-2.166	bias	7.71E-03	BDKRB2,DNMT3A,ITGA11,PIK3R1,THBS1,TIMP3
miR-133a-3p (and other miRNAs w/		mature microrna	Inhibited	-2.183	bias	9.89E-03	CTBP2,FBN2,PTBP2,QKI,STK3
let-7a-5p (and other miRNAs w/se		mature microrna	Inhibited	-2.767	bias	3.81E-02	CDH2,DOCK5,DSP,FADS2,KRT19,POM121/POM121C,SCD,THBS1
FBN1		other	Inhibited	-2	bias	1.34E-03	CYR61,LTBP3,MMP3,TIMP3
POR		enzyme	Inhibited	-2.219	bias	2.41E-02	CYP2A6 (includes others),DHCR24,DHCR7,ELOVL5,FADS2,LDLR,MSMO1,MVD,SCD
KLF2		transcription regulator	Inhibited	-2.412	bias	1.59E-02	CCL3,CDH2,CYP1B1,DOCK2,MYH10,PLPP3,SLC2A1,SMURF2,THBS1
INSIG1		other	Inhibited	-2.573	bias	1.34E-02	ACSL4,CYP4F2,DHCR24,DHCR7,FADS2,LDLR,SCD
CST5		other	Inhibited	-2.183	bias	9.56E-04	ATP8B1,CEMIP,CNBP,DNAJB4,DOCK5,DSP,DTNB,ELK3,FAM133B,FRAS1,HNRNP1,INTS4,LAMC1,MYCBP2,NR3C1,SLC7A11,SRSF4
LMNB1		other	Inhibited	-2	bias	3.14E-04	DHCR7,GPC4,LDLR,MSMO1,PAPPA,SCD,SERINC1
4-(2-aminoethyl)benzenesulfonyl		chemical - protease inhibitor	Inhibited	-2	bias	7.54E-03	DDIT3,ENPP2,FBN2,TNC
U0126		chemical - kinase inhibitor	Inhibited	-2.085	bias	2.22E-02	BHLHE40,CCL3,CYP1B1,CYP2A6 (includes others),CYP4F2,DDIT3,ENPP2,ETS1,GSN,HAPLN1,LDLR,MMP3,PABPC1,PER2,PGR,RND3,THBS1,TIMP3,TNFRSF11B,TOM1
camptothecin		chemical drug	Inhibited	-2.111	bias	2.78E-02	APBB2,BDKRB1,BFAR,CCL3,EHBP1,FNDC3B,GRK5,LDLR,MBNL2,NR3C1,PBX1,PLEC,PRKAR2B,RALBP1,RAPGEF5,RBMS1,RIPK1,SPDYA,SPTBN1,STK3,TBC1D1,TNS3,TRAF3,UGCG
leukotriene A4		chemical - endogenous mammalian				2.63E-02	TNC
lopinavir		chemical drug				2.04E-03	DDIT3,TNFRSF11B

3,5-L-diiodothyronine		chemical - endogenous mammalian				1.74E-02	ME1,SCD
L-cysteine		chemical - endogenous mammalian				1.74E-02	PCK2,SCD
L-lysine		chemical - endogenous mammalian				1.33E-02	DDIT3,PCK2
L-glutamic acid		chemical - endogenous mammalian	1.698	bias		2.58E-02	CACNA1C,CDH2,FADS2,MGLL,NFIL3,SORBS1
glycerol		chemical - endogenous mammalian				3.25E-02	LDLR,NR3C1
dexamethasone phosphate		chemical drug				1.92E-02	CGA,THBS1,TNFRSF11B
estrone		chemical - endogenous mammalian				3.83E-02	PGR,PIK3R1
azide		chemical reagent				2.63E-02	SLC2A1
1-oleoyl-lysophosphatidic acid		chemical - endogenous mammalian				2.63E-02	ENPP2
phosphatidylcholine		chemical - endogenous mammalian				1.74E-02	DDIT3,SCD
linoleic acid		chemical - endogenous mammalian	1.455	bias		7.71E-03	ACSL4,CPT1B,CYP4F2,DDIT3,LDLR,SCD
meldonium		chemical drug				1.74E-02	CPT1B,LDLR
cortivazol		chemical reagent				2.63E-02	NR3C1
hydrocortisone		chemical - endogenous mammalian	-1.134			4.73E-02	ACHE,BDKRB2,BMPR2,GABBR2,NR3C1,PTPN4,TNFRSF11B
BARHL2		transcription regulator				2.63E-02	CNTN2
FFAR3		G-protein coupled receptor	-1.89	bias		2.60E-03	ADGRV1,CACNA1C,ENPP2,FADS2,GAS6,RASGRF2,SGIP1
triamcinolone acetonide		chemical drug	-0.894			2.01E-02	BHLHE40,DDIT3,ELK3,F10,LDLR,NEK7,NR3C1,SCD,SLC4A7,TBC1D1,TNFSF4
AEE 788		chemical drug				2.63E-02	PGR
Sos		group				1.68E-03	ATF7IP,DOCK1,LTBP3,MAP3K20,MMP3,NFIL3,PIK3CB,PIK3R1,RIPK1,SCD,SEMA6D,STK3,UGCG
Creb		group	-0.038	bias		9.04E-03	ADK,CACNA1C,CGA,CYR61,HTT,LDLR,LTBP3,NEDD9,NR3C1,PER2,RIPK1,RYR2,SLC7A11,TIA1,TNFRSF11B
Tgf beta		group	1.755	bias		2.05E-03	BACH1,BHLHE40,CCL3,CDH2,CYR61,F10,MMP3,NEDD9,PLP3,RNF111,RORA,RYR2,TIMP3,TNFRSF11B
RNA polymerase II		complex				1.55E-02	CAP2,CYP1B1,DDIT3,GHR,HNF4A,HNRNPULDLR,MEF2A,NBPF10 (includes others),PBX1,RND3,RPRM,SORBS1
Pka		complex	0.788	bias		1.91E-02	CDH2,DDIT3,HNF4A,LDLR,MMP3,OXTR,PDE4D,TNFRSF11B
glucose oxidase		group				2.63E-02	SLC2A1
Rock		group	1	bias		3.47E-02	ETS1,LPP,Sort1,THBS1
DNAI		group				2.63E-02	ENPP2
ziram		chemical toxicant				2.63E-02	SNCA
maslinic acid		chemical - endogenous non-mammalian				4.74E-03	ACTN1,DOCK1,ETS1,PIK3R1,PRKAR2B,SORBS1,THBS1
T3-TR-RXR		complex	1.982	bias		2.22E-02	F10,LDLR,ME1,SLC2A1
ERK		group	1.681	bias		1.39E-02	ACTN1,CGA,ETS1,IFNAR1,LDLR,MMP3,SLC2A1,SLC4A7,Sort1,SPTBN1,THBS1,UGCG
(E)-2,3',4,5'-tetramethoxystilbene		chemical drug				2.63E-02	CYP1B1
CLTA		other				2.63E-02	LDLR
FSH		complex	1.881	bias		1.49E-03	ACTN1,ATP9A,BMPR2,CAP2,CDH2,CSNK1A1,DHCR7,FDXR,GPER1,GRK5,LDLR,MSMO1,NPC2,PGR,PSMD1,PSMD3,RPRM,SLC2A1,SNAP25,THBS1,TNFRSF11B
Ces1b/Ces1c		enzyme				2.63E-02	GHR
BDNF		growth factor	0.042	bias		3.29E-03	ARPP21,BHLHE40,CYR61,GPC4,LAMC1,mir-154,mir-329,MVD,NTF3,PER2,RPRM,RYR2,SNAP25,THBS1,TNFRSF11B,TRAF3
SEN7		peptidase				1.33E-02	CACNA1C,CDH2
RHOJ		enzyme				1.08E-03	CNBP,GSN,LRP1B,RND3
NPC1		transporter				2.22E-02	DDIT3,LDLR,NPC2,SCD
MGEA5		enzyme	-0.908			4.71E-04	ACSL4,AHNAK2,BACH1,CAMK1D,CCBE1,CNOT1,DHCR7,DST,FABP3,GAS6,GPER1,GSN,MGLL,MSMO1,PIK3R1,PLPP3,RAP2A,SORBS1,THBS1,THSD1,TIMP3,TNC,TNFRSF11B
EIF2A		translation regulator				9.66E-03	DDIT3,PCK2
ZNF100		other				1.33E-02	ENPP5,NEDD9
ZNF85		transcription regulator				1.33E-02	ENPP5,NEDD9
E. coli serotype O127B8 lipopolysaccharide		chemical - endogenous non-mammalian	0.333	bias		4.76E-02	AQP11,DDIT3,GPER1,LAMC1,MMP3,PCK2,SEMA7A,SLC7A11,TNFRSF11B
ZNF254		other				1.33E-02	ENPP5,NEDD9
H2BfM		other				2.63E-02	DNMT3A
FGF21		growth factor	1.328	bias		4.71E-03	CPT1B,GHR,LDLR,ME1,SLC2A1
CHI3L1		enzyme				2.43E-02	BHLHE40,NNMT,TNC
CLEC1B		transmembrane receptor				3.25E-02	LCP2,TNC
ZBTB20	4.26	transcription regulator	0			2.05E-02	GAS6,GHR,NEDD9,NR3C1
STAT1/3/5 dimer		complex				3.83E-02	MMP3,TIMP3
MFSD2A		transporter				9.11E-06	ACSL4,DHCR7,FADS2,LDLR,MVD,SCD
RASSF8		other				1.33E-02	ENPP5,NEDD9
MIR17HG		other				3.77E-03	BMPR2,FBN2,FNDC3B,FRAS1,HEG1,PTK7,RNF111,SKI,Sort1
RDH11		enzyme				2.63E-02	NR3C1
Collagen(s)		complex	-0.849	bias		1.57E-02	CYR61,DDIT3,THBS1,TNC
ZNF431		other				1.33E-02	ENPP5,NEDD9
RBM24		other				2.63E-02	TP63
SH3TC2		other				3.64E-02	DHCR24,DHCR7,MVD

MAN2C1		enzyme				2.63E-02	DDIT3
VGLL3		other				3.25E-02	MMP3,THBS1
PX-866		chemical drug				2.63E-02	SORT1
PON2		enzyme				2.63E-02	DDIT3
EN2		transcription regulator				9.66E-03	PLCB4,SNCA
DANCR		other				2.20E-02	CDH2,TIMP3
NEUROD6		transcription regulator				2.63E-02	CNTN2
G protein		complex				2.63E-02	CYP1B1
HNFI1± dimer		complex				2.63E-02	HNFA4A
Focal adhesion kinase		group				3.99E-02	CDH2,DSP,LPP
estrogen receptor		group		0.508		1.97E-02	CDH13,CDH4,DSP,ETS1,ICAM2,KRT19,LDLR,NEDD9,OXTR,PGR,TIMP3,TNC
arginine		chemical - endogenous					
CACNA1D		mammalian		0.594		6.67E-03	DDIT3,PKC2,PIK3R1,SCD
vasoactive intestinal peptide		ion channel				6.91E-04	CACNA1C,RYR2
MYO1C		biologic drug				1.10E-02	MMP3,SNAP25,TNFRSF11B
ZSCAN21		enzyme				2.63E-02	GSN
ATXN2		transcription regulator				2.63E-02	SNCA
SETDB1		other				2.63E-02	PABPC1
		enzyme				3.00E-02	CADM2,CBLB,PIK3C2G
SCAP		other		1.863	bias	2.60E-05	ACSL4,CYP4F2,DDIT3,DHCR7,FADS2,LDLR,MSMO1,MTHF
PRRX1		transcription regulator				1.74E-02	D2,MVD,SCD
Betacatenin/TCF		complex				4.45E-02	LPP,TNC
							DKK2,TNFRSF11B
GATA2		transcription regulator		-0.277		4.56E-03	ARNT2,ARPP21,C9,C9orf116,CCDC68,ETS1,GFRA1,HNFA4,ICAM2,MCTP2,NFIL3,PBX1,PGR,SEL1L3,SNCA,THBS1,TNFSF4
PTEN		phosphatase		0		4.08E-02	BDKRB1,CST6,CYB561,ECI2,ETS1,KRT19,MMP3,MVD,NAIP,NFIL3,PIK3R1,PLEC,RAP1A,RBBP6,SCD,THBS1,TNFRSF11B,TOM1
SYN1		transporter				2.63E-02	SYN3
IGF2R		transmembrane receptor				2.70E-02	ENPP5,NEDD9
MKL1		transcription regulator				4.73E-02	DHCR24,DNAJB4,FABP3,FADS2,PGR,TNC,WASL
RUNX3		transcription regulator		-1.408	bias	3.37E-02	CYR61,DIP2C,FAM92A,GRK5,PAPPA,TNFSF4,UGCG
Alph2		other				2.63E-02	ABL1
SRSF9		enzyme				2.63E-02	NR3C1
JUNB		transcription regulator				2.74E-02	CGA,CYP1B1,MMP3,MVD,PTBP2,SCD,TIMP3
INHBB		growth factor				3.34E-03	MMP3,THBS1,TNC
HINT1		enzyme				1.74E-02	ELOVL5,FADS2
DNMT1		enzyme				4.75E-02	DAB1,DLCL1,HDAC3,SLC7A11,TIMP3
HSP90AA1		enzyme				2.20E-02	CYP1B1,TCF12
SLK		kinase				2.63E-02	DDIT3
SOD2		enzyme				3.77E-02	CTBP2,DDIT3,GSN,MMP3,SHISA4,SORT1
CHRM1		g-protein coupled receptor				3.83E-02	ACHE,CYR61
MBTPS1		peptidase				3.83E-02	LDLR,SCD
RORA	5.17	ligand-dependent nuclear receptor				2.41E-02	ACSL4,CYP2A6 (includes others),DHCR24,FABP3,NNMT,RORA,SCD,SLC30A10,SULF2
MYOCD		transcription regulator		0.6	bias	4.98E-02	CACNA1C,CCBE1,DDIT3,LPP,PTPRB
IKBKB		kinase		1.362	bias	1.45E-02	CBLB,CCL3,CDH13,CYP1B1,ENPP2,ETS1,GRK5,MMP3,SLC16A2,TIMP3,TNC,TNFRSF11B,TP63
TCOF1		transporter				3.32E-02	BPHL,CNBP,FABP3,RGPD4 (includes others),SLC2A1
EN1		transcription regulator				3.83E-02	PLCB4,SNCA
SYN2		other				2.63E-02	SYN3
NRG4		growth factor				3.34E-03	ELOVL5,ME1,SCD
RAPGEF1		other				6.55E-03	RAP1A,RAP2A
DMD		other				3.93E-02	ACHE,AIG1,ARPP21,CDH13,KPNA6,PAMR1,PIK3CB,PLPP3
Fbxl20		enzyme				2.63E-02	SCIN,SORT1
JAKMIP1		other				2.63E-02	RIMS1
NPPB		other				4.35E-02	GABBR2
							FDXR,LDLR,MSMO1
CREM		transcription regulator				9.47E-03	BHLHE40,CGA,LDLR,MSMO1,NFIL3,NPC2,RYR2,SPATA20
ELAVL1		other		0.2	bias	4.85E-02	THBS1
SMAD7		transcription regulator		-1.89	bias	4.08E-02	ACHE,CDH2,DNMT3A,SLC7A11,TIA1,TP63
							BMPR2,CDH2,GAS6,HDAC9,LTBP3,SCD,TIMP3
LEP		growth factor		-0.553	bias	4.82E-02	CPT1B,CYR61,ELOVL5,FABP3,FADS2,LDLR,MMP3,MSMO1,NR3C1,PER2,PGR,SCD,SNAP25,THBS1,TIMP3,TNFRSF11B
CLTB		other				2.63E-02	LDLR
NGFR		transmembrane receptor				3.32E-02	LDLR,SNAP25,SORT1
CACNB2		ion channel				2.63E-02	CACNA1C
ESR2		ligand-dependent nuclear receptor		1.369		2.33E-02	ARNT2,BMPR2,CDH2,CGA,CYP2A6 (includes others),DHCR7,DNAH11,DNAJC1,ENPP2,GABBR2,KRT19,LRP1B,LRRN3,NEDD9,PGR,PLEC,RAPGEF6,TNS3
TERT		enzyme				2.08E-02	ELK3,ETS1,GSN,KRT19,MMP3,MTHFD1L,PPP6R3,SPON1
miR-221-3p (and other miRNAs w		mature microRNA				3.64E-02	DIRAS3,PIK3R1,TIMP3
mir-221		microRNA				1.10E-02	DIRAS3,PIK3R1,TIMP3
miR-217-5p (and other miRNAs w		mature microRNA				3.25E-02	SCD,TRPS1
mir-584		microRNA				2.63E-02	PHACTR1
miR-129-5p (miRNAs w/seed UUL		mature microRNA				3.25E-02	BMPR2,FNDC3B
miR-615-5p (and other miRNAs w		mature microRNA				2.63E-02	KRT19
miR-204-5p (and other miRNAs w		mature microRNA				1.92E-02	FBN2,MMP3,TRPS1
mir-384		microRNA				2.63E-02	HDAC3
mir-8		microRNA		-1.398	bias	2.09E-02	ETS1,HDAC3,MOK,MYH10,PGR,SCMH1,SULF2

miR-574-3p (miRNAs w/seed ACG)		mature microRNA				2.63E-02	TP63
mir-574		microRNA				4.00E-03	QKI,TP63
NUPR1		transcription regulator	-1.528	bias		2.26E-02	ATP8B1,CYR61,CYSTM1,DDIT3,DHCR24,ETS1,GCNT2,GRAMD2B,HDAC8,HLTF,MAGI1,MGLL,MYH10,NFIL3,PIK3R1,RBMS1,SHROOM3,SLC2A1,SLC39A8,TNS3,WASHC5
AKT1		kinase	1.026	bias		1.33E-02	DHCR7,ME1,MSMO1,MYH10,NEXN,PGR,PIK3R1,SCD,SEMA6D,SLC2A1,SLC4A7,sort1,THBS1
Twist1		transcription regulator	1.718	bias		1.52E-02	CDH2,ETS1,FBN2,GPC1,GSN,HEG1,ITGA8,PAMR1,TIMP3
NeuroG1		transcription regulator	-1.134			1.42E-03	C1S,CEMIP,DSP,FABP3,LRRN3,PAPPA,THBS1
ADCYAP1		other	0.979			1.06E-02	ACTN1,CCBE1,CGA,DNMT3A,EDIL3,ENPP2,GRK5,HAPLN1,NPR3,QKI,SLC2A1,SNAP25
MMP12		peptidase				2.20E-02	ACTN1,ADK,HNF4A,NPEPPS,PSMD1
JUN		transcription regulator	0.738	bias		2.43E-02	CGA,CYP1B1,CYR61,GAS6,HNRNP, mir-154,MMP3,MVD,NBPF10 (includes others),OXTR,PGR,PTBP2,SCD,SDK1,SULF2,THBS1,TIMP3,TNC
CREB1		transcription regulator	0.74	bias		9.53E-05	ACHE,AQP11,BHLHE40,CACNA1C,CAMK1D,CCL3,CDH13,CDH2,CGA,CYR61,DKK2,EDIL3,ERC2,GFRA1,LDLR, mir-154, mir-329,MSMO1,MVD,MYH10,NFIL3,NPC2,PER2,RPRM,RUNX1T1,SCD,SEMA7A,SERINC2,TOM1,TRPS1
SUZ12		enzyme				2.54E-02	CCPG1,EIF3A,HNF4A,PGR,PLCB4,RBMS1,TNFRSF11B,TNS3
CCT3		other				2.63E-02	HTT
ARNT		transcription regulator				2.19E-02	BHLHE40,BHLHE41,CYP1B1,CYP2A6 (includes others),HNF4A,PCK2,SLC2A1
NKX2-1		transcription regulator				2.87E-02	EDIL3,ENPP2,HELLS,QKI,SCD,SEC14L2,SH3PXD2A,THBS1,TP63
TSC2		other	-0.853	bias		3.10E-02	B3GALT2,CST6,DDIT3,GSN,PSMD1,SCD,SLC2A1
Trp53-ps		other				2.63E-02	C9orf116
FOXO4		transcription regulator				8.50E-03	DHCR24,ELOVL5,LCP2,LEMD3,PTPRB,SCD,SLC2A1
LCN2		transporter	1.982	bias		2.65E-02	ACTN1,CDH2,LDLR,SCD,TNFRSF11B
ZNF665		other				1.33E-02	ENPP5,NEDD9
CHRNA5		transmembrane receptor				2.63E-02	TP63
GH1		growth factor	1.842			1.43E-01	CDH2,DDIT3,GHR,LDLR,SKI
ZNF528		other				1.33E-02	ENPP5,NEDD9
EGFR		kinase	1.485	bias		3.36E-02	DDIT3,GHR,GPC1,KIAA0391,MMP3,PABPC1,PBX1,QTRT2,SEMA7A,SLC2A1,SLC4A7,SLC7A11,THBS1,TNC,TNFRSF11B,WASL
CLOCK		transcription regulator				3.57E-03	ACSL4,ARHGEF28,ARNT2,BHLHE40,BPHL,DDIT3,EEF2K,NFIL3,PER2,ZZZ3
TRIB3		kinase				2.71E-02	DDIT3,MTHFD2,PCK2
PPARGC1A		transcription regulator	1.484	bias		3.44E-02	CPT1B,CYP2A6 (includes others),FABP3,GAS6,HAPLN1,LDLR,ME1,MSMO1,PCK2,PIK3R1,SCD
PPP1R13L		transcription regulator				1.28E-02	DSP,SLC2A1,TP63
PML		transcription regulator	-0.97			1.91E-02	ACSL4,CDH2,CPT1B,DNAJB4,LDLR,NR3C1,PIK3CB,SCD
MFGE8		other				9.66E-03	CDH2,EDIL3
ONECUT1		transcription regulator				5.81E-03	C1S,CCDC198,FADS3,FAM117A,GBF1,HIST1H4H,HNF4A,RORA,SCD,SGIP1,SMARCC1,SUPT16H,TAOK3,TMEM62,TRPC4AP
NFE2L2		transcription regulator	1.32	bias		1.87E-02	ARHGEF3,DDIT3,DHCR7,F10,GHR,IKBK,ME1,MGLL,MORF4L2,MSMO1,PSMD1,PSMD3,PTPRB,SLC16A2,SLC2A1,SLC7A11,UBE2K
ATP2A2		transporter				4.45E-02	DDIT3,SCD
HNF4A	3.03	transcription regulator	-0.57	bias		2.23E-02	AAMDC,ABCA6,ACTN1,BPHL,C1S,CMSS1,CNBP,CPT1B,CWC25,CYP1B1,CYP2A6 (includes others),CYP4F2,DNAJB4,ECI2,ELMO1,FAHD2A,FAM117A,FDXR,GBF1,GIPC2,GSN,HDAC8,HNF4A,HSDL2,IFNAR1,INTS4,L2HGDH,LDLR,LUC7L2,N4BP2L2,NEK7,NFYA,PCK2,PLAA,PRDM5,PSMD1,PTGES3,PTK7,PTPN4,QTRT2,RAB18,RORA,SCD,SEC31A,SEMA7A,SH3PXD2A,SKI,SLC22A18,SLC25A40,STX16,SUGT1,SUPT16H,TAOK3,TCF12,TIA1,TIMP3,TM9SF4,TMEM17,TNC,TNFRSF11B,TOM1,TRPC4AP,UBE2D3,WASHC5,WASL,WBP4,ZNF133,ZSCAN5A
SP3		transcription regulator				4.90E-02	CDH2,DNMT3A,F10,GHR,LDLR,PGR,SLC39A8,SLC4A7,SMARCC1,TNC
ATF3		transcription regulator	0.371			1.99E-02	BHLHE41,CGA,DDIT3,GSN,LDLR,MMP3
Ea4		other				2.63E-02	CYP1B1
ERBB4		kinase	-0.356			1.10E-03	DDIT3,GHR,GPC1,PGR,SLC2A1,THBS1,TIMP3,TNC
HSPA9		other				1.69E-02	NAV2,NEDD9,PBX1
MAP3K1		kinase	0.418	bias		1.16E-02	LDLR,MMP3,PGR,THBS1,TNC
LPA		other				1.74E-02	GHR,NR3C1
ERBB3		kinase	-0.537			1.78E-02	GHR,MMP3,SLC4A7,THBS1,TIMP3,TNC
NPPC		other				3.25E-02	CDH2,HAPLN1
PGR	16.62	ligand-dependent nuclear receptor	1.864	bias		5.81E-03	ATXN1,CGA,CPT1B,DNAJB4,DST,GAS6,GPER1,KLF11,NEDD9,PGR,PPM1H,SLC39A8,SNAP25,TNC,UGCG
PEBP1		other				2.43E-02	BACH1,PRKAR2B,SCD
LMO4		transcription regulator				3.25E-02	PGR,RYR2
AHR		ligand-dependent nuclear receptor	-0.137			1.60E-02	ACTN1,CDH2,CYP1B1,CYP2A6 (includes others),DMXL2,FBN2,GAS6,HDAC9,LTBP3,NEDD9,NNMT,SCD,SLC2A1,THBS1,TIMP3
ZNF43		other				1.33E-02	ENPP5,NEDD9
ZNF429		other				1.33E-02	ENPP5,NEDD9
DNAJC5		other				2.63E-02	SNAP25

BDKRB2	13.46	g-protein coupled receptor			4.45E-02	BDKRB1,SNCA
HNRNPA2B1		other			3.94E-02	CEMP,GSN,NPR3,PAPPA,PBX1,PLCB4,SNAP25,TNS3
PPP1R3A		phosphatase			2.63E-02	THBS1
SATB1		transcription regulator	-0.853		8.37E-03	ACTN1,DNMT3A,ENOSF1,ETS1,LRRN3,MEF2A,PGR,PTGE
CACNB3		ion channel			2.63E-02	S3,RIPK1,TRPS1
OTX1		transcription regulator			3.25E-02	CACNA1C
VLDLR		transporter			6.55E-03	CGA,ENPP2
RNF216		enzyme			2.20E-02	DAB1,SLC2A1
EBF1		transcription regulator			3.93E-02	RIPK1,TRAF3
SUPT4H1		transcription regulator			2.63E-02	CBLB,NFIL3,PCK2,PIK3R1,PRKAR2B,RASGRF2,SCD
SIGLEC10		other			2.63E-02	HTT
MEF2C		transcription regulator	1.342	bias	3.37E-02	ETS1
HERPUD1		other			2.63E-02	CACNA1C,CCBE1,CPT1B,HDAC9,MEF2A,PTPRB,RYR2
RASGRP2		other			2.63E-02	DDIT3
RGCC		other			2.63E-02	RAP2A
RBP3		transporter			2.20E-02	CDH2,SCD
DYNC1H1		peptidase			4.45E-02	DDIT3,RIPK1
ANK2		other			2.63E-02	HTT
Cyp2g1		enzyme			2.63E-02	SPTBN1
MAP7		other			2.63E-02	CYP2A6 (includes others)
SNAI2		transcription regulator	-1.496		2.63E-02	TRPV4
TAL1		transcription regulator	1.633		1.16E-02	CYR61,DSP,TP63,TRPS1,UBE2D3
SIRT1		transcription regulator	-0.784	bias	1.26E-02	ARPP21,DOCK1,ETS1,HELLS,IFNAR1,LRRN3,MVD,NFYA,R
PAGR1		other			4.17E-02	APGEF5,STRADA,TNFSF4,TRAF3
MAPK7		kinase	0.83	bias	2.63E-02	AQP11,ARNT2,ATXN10,CDH2,CPT1B,KIF13B,LDLR,MMP3
IL13		cytokine	0.79	bias	4.17E-02	MTNFD1L,NAIP,PCK2,SKI,SLC7A11,TIMP3
TAZ		enzyme			2.63E-02	NR3C1
HDAC4		transcription regulator			3.47E-02	CDH2,DLC1,MEF2A,TP63
NR0B2		ligand-dependent nuclear receptor	-1.963	bias	4.38E-02	CCL3,DHCR24,DMXL2,ENPP2,EVL,FADS2,GAS6,GSN,MM
ADRB1		g-protein coupled receptor			2.20E-02	P3,MSMO1,SNCA,SORT1,THBS1,TNFRSF11B,TRPS1
SLC16A2	7.56	transporter			3.79E-02	AHNAK2,CDH2,CYP1B1,CYR61,ENPP2
SCX		transcription regulator	-1.98	bias	2.97E-02	CACNA1C,CAP2,HDAC9,MYH10,PPM1E,SLC2A1,SNAP25
GATA1		transcription regulator	1.982		5.31E-03	HNF4A,mir-154,mir-329,PCK2,SCD
DNMT3B		enzyme	-1.89	bias	3.64E-02	DDIT3,RYR2,THBS1
CYP51A1		enzyme			3.64E-02	CNTN2,HAPLN1,SEMA7A
HNRNPK		transcription regulator			8.58E-04	HAPLN1,MMP3,TIMP3,TNC
FOS		transcription regulator	0.555	bias	2.03E-01	ACTN1,ETS1,F10,MAMDC2,NFIL3,SCIN,SKI,SNCA
CRTC1		transcription regulator			3.73E-02	CACNA1C,CYP1B1,DDIT3,DLC1,HDAC9,RYR2,SLC16A2,SL
BRCA1		transcription regulator	1.94	bias	4.45E-02	C7A11,TIMP3
RARRES1		other			2.60E-02	DHCR24,MSMO1
alirocumab		biologic drug			2.60E-02	LDLR,LPP,MMP3,ZBTB20
SNAI1		transcription regulator	-1.413		1.59E-02	ATF7IP,CGA,DOCK1,GPRI1,LTBP3,MAP3K20,MMP3,NBP
NR3C1	7.43	ligand-dependent nuclear receptor	0.692		3.83E-02	F10 (includes others),NFIL3,NR3C1,OXTR,PGR,PIK3CB,QKI,RIPK1,SCD,S
HRAS		enzyme	-0.239	bias	2.68E-02	DK1,SEMA6D,STK3,SULF2,TNFRSF11B,UGCG
CNPY2		other			2.63E-02	CGA,NEDD9
ERBB2		kinase	0.695	bias	2.63E-02	BACH1,CYP1B1,DDIT3,ENPP2,IFNAR1,NEDD9,NR3C1,SFP
DIO2		enzyme			2.63E-02	Q,TP63
CNB-001		chemical reagent			2.63E-02	GRK5
OSM		cytokine	1.281	bias	2.63E-02	LDLR
BHLHA15		transcription regulator			1.22E-02	ACTN1,CDH2,CDH4,CLCA2,CYR61,GSN,HNF4A,TP63
GJD2		transporter			1.64E-03	ABL1,ACTN1,ARHGEF3,ATXN1,BHLHE40,CGA,CORO2A,C
RARA		ligand-dependent nuclear receptor	1.373		1.50E-02	YP2A6 (includes others),CYR61,GRM7,HNRNPU,MAP3K20,NAIP,NFIL3,NL
CDS		transmembrane receptor	1.98	bias	2.63E-02	RP10,NR3C1,NTF3,PIK3CB,PIK3R1,PPP1R21,RERE,RIPK1,
pevonedistat		chemical drug			2.63E-02	SNCA,THBS1,TIMP3,TNFRSF11B,TNFSF4,TRAF3,UBE2K,U
PCYT1A		enzyme			1.50E-02	GCG
ZBTB17		transcription regulator	1.941	bias	1.50E-02	ATXN1,CGA,DDIT3,ELK3,ETS1,FABP3,GAS6,GSN,KRT19,L
					2.63E-02	PP,MMP3,MSMO1,MTHFD1L,MYH10,NEXN,PPP6R3,SHR
					2.63E-02	OOM3,SORBS1,SPON1,THBS1,TIMP3,TOM1,TP63
					2.63E-02	LDLR
					2.37E-02	ABL1,ACSL4,BHLHE40,CDC14B,CDH2,CYB561,DDIT3,ELK
					3.64E-02	3,GAS6,GHR,GPC1,LTBP3,MMP3,NEDD9,NNMT,NPC2,PB
					2.70E-02	X1,PCK2,PTPRB,QKI,SHROOM3,SLC2A1,SLC4A7,SORBS1,
					2.70E-02	THBS1,THSD1,TIMP3,TNC
					2.70E-02	CNTN2,HAPLN1,SEMA7A
					2.70E-02	DDIT3,SLC7A11
					9.90E-03	ATP9A,BBOX1,BHLHE40,C1S,CDH2,CGA,CST6,CYP1B1,DH
					4.45E-02	CR24,KRT19,LDLR,MGLL,MMP3,MYCBP2,MYH10,PLCB4,
					2.63E-02	QKI,RAP2A,RORA,TIMP3,TNC,TNFRSF11B,TOM1
					2.63E-02	CCPG1,KRT19
					3.57E-02	ARNT2,CCPG1,GHR,HELLS,NAV2,NEDD9,RAP1A,SEC31A,
					3.57E-02	SFPQ,SLC16A2,SLC7A11,SMURF2,TNFRSF11B,TP63
					4.21E-02	CCL3,LDLR,MSMO1,PCK2
					2.20E-02	DDIT3,IFNAR1
					1.69E-02	GFRA1,GSN,SCD
					1.38E-03	BHLHE40,DDIT3,LDLR,LRRN3,SPTBN1

						BHLHE40,CCL3,CDH2,CYP1B1,CYP2A6 (includes others),CYR61,DDIT3,EDIL3,ELMO1,ENPP2,GHR,GRIK1,HAPLN1,HDAC3,HNF4A,ME1,MMP3,PIK3R1,SCD,TCF12,TI
CTNNB1		transcription regulator	1.584	bias	3.88E-02	A1,TIMP3,TNC,TNFRSF11B,TP63,UGCG,ZIC1
ZNF91		transcription regulator			1.74E-02	ENPP5,NEDD9
MYZAP		other			2.70E-02	CDH2,DSP
HIC1		transcription regulator	-1.134		1.07E-03	AHNAK2,KAZN,PLEC,SLC7A11,SNAP25,TMEM62,TNS3
Nedd4		enzyme			2.63E-02	THBS1
ZNF708		other			1.33E-02	ENPP5,NEDD9
TBX2		transcription regulator	0	bias	1.49E-02	BHLHE40,DDIT3,ELK3,HELLS,NFIL3,PRDM5
PRSS1		peptidase			2.63E-02	DDIT3
PRR13		other			2.63E-02	THBS1
RBFOX2		transcription regulator			1.33E-02	PTBP2,TIA1
PPP3R1		phosphatase			6.67E-03	CACNA1C,CPT1B,RYR2,SCD
COLQ		other			3.51E-02	ACHE,FRAS1,GPC1,GPC4,LTBP3
anti-miR-29a inhibitor		chemical reagent			2.63E-02	TIMP3
3-mercaptopicolinic acid		chemical - kinase inhibitor			2.63E-02	NR3C1
chloropromazine		chemical drug			6.62E-04	CYP4F2,DHCR7,FADS2,LDLR,MSMO1,SCD
amlodarone		chemical drug			9.50E-03	FADS2,LDLR,ME1,SCD
rilmenidine		chemical drug			2.63E-02	HTT
impromidine		chemical drug			2.63E-02	LDLR
LG100268		chemical reagent	1.718	bias	8.48E-03	CPT1B,CYP4F2,LDLR,SCD
BMS-275183		chemical drug			2.63E-02	THBS1
nelfinavir		chemical drug			3.83E-02	DDIT3,TNFRSF11B
aminoglutethimide		chemical drug			9.66E-03	BDKRB2,LDLR
SU6656		chemical toxicant			3.00E-02	DDIT3,NFIL3,TNFRSF11B
GW501516		chemical drug	1.969	bias	6.63E-03	ACSL4,CPT1B,FABP3,KRT19,SCD,SKI,THBS1
monorden		chemical - endogenous non-mammalian			3.25E-02	DDIT3,GSN
						CAP2,CYP1B1,CYP2A6 (includes others),DIRAS3,DLG1,ENPP2,GHR,GSN,HDAC3,HDAC9,LDLR,mir-154,MMP3,OXTR,PBX1,PGR,RND3,SLC2A1,SMARCC1,THBS1,TIMP3,TP63,TRAF3
trichostatin A		chemical drug	1.617	bias	2.77E-02	DHCR7,HDAC3,LDLR,PRKAR2B,SCD
clozapine		chemical drug	0.973	bias	1.36E-02	PGR
toxaphene		chemical toxicant			2.63E-02	
brefeldin A		chemical - endogenous non-mammalian	1.188		3.71E-02	CGA,DDIT3,MMP3,THBS1
sulindac sulfide		chemical drug	-1.066		9.83E-05	CYP1B1,HDAC3,KRT19,MSMO1,MTHFD2,PGR,PIK3R1,RE,RE,SPTBN1
KN 93		chemical - kinase inhibitor			3.00E-02	CACNA1C,CGA,ETS1
1,2-dithiol-3-thione		chemical reagent	0.387	bias	1.16E-02	DHCR7,F10,GHR,IKBK,MLL,MORF4L2,MSMO1,PSMD1,PSMD3,SLC16A2,UBE2K
						ACHE,ACTN1,ARNT2,CAP2,CDH13,CGA,CYP1B1,CYP2A6 (includes others),CYR61,DMXL2,HDAC3,HDAC9,KPNA6,KRT19,NEDD9,NR3C1,PGR,PRKAR2B,SLC2A1,TNC
tetrachlorodibenzodioxin		chemical toxicant	0.995		3.95E-04	CEP135,CYP4F2,DHCR7,FADS2,LDLR,ME1,MSMO1,PLEC,SCD
ritonavir		chemical drug			1.04E-02	ACHE
trichlorfon		chemical toxicant			2.63E-02	
			0.906		1.99E-02	CCL3,CEP135,CPT1B,DDIT3,ETS1,FABP3,FADS2,ME1,MM
trogilazone		chemical drug			2.63E-02	P3,NNMT,PIK3CB,PLEC,QKI,SCD,SLC2A1,SORBS1
soman		chemical toxicant			2.55E-03	IKBK
CDN1163		chemical reagent			2.63E-02	DDIT3,HNF4A,SCD
pamidronic acid		chemical drug			2.63E-02	TNFRSF11B
enclomiphene		chemical drug			2.63E-02	PGR
Gga enhancer		other			2.63E-02	CGA
mirtazapine		chemical drug			3.25E-02	HDAC3,NTF3
rosuvastatin		chemical drug			3.00E-02	DHCR7,LDLR,MVD
1-chloro-2-(2,2,2-trichloro-1-(4-chlorophenyl)-1,3,5-triazol-4-yl)ethanol		chemical toxicant			4.45E-02	ARNT2,PGR
tetracycline		chemical drug	1.982		1.04E-01	BHLHE40,ME1,RAPGEF5,SEMA6D
			-0.898	bias	2.42E-03	BBOX1,CCL3,CPT1B,CYR61,HNF4A,LDLR,MMP3,MTHFD2
SP600125		chemical - kinase inhibitor			9.66E-03	PCK2,PGR,PLEC,SCD,THBS1
dieldrin		chemical toxicant			2.09E-03	PGR,SNCA
3-methylcholanthrene		chemical toxicant			1.72E-02	CYP1B1,CYR61,ME1,NEDD9,SLC7A11
SB 216763		chemical toxicant	1.982	bias	1.72E-02	BHLHE40,CYR61,RND3,SCD
			1.76	bias	6.46E-03	BHLHE40,CNBP,CYP1B1,CYR61,DDIT3,GABBR2,KRT19,NE
4-hydroxytamoxifen		chemical drug			7.85E-03	DD9,PGR,SLC2A1,SLC39A8
ezetimibe		chemical drug				DHCR7,LDLR,MVD
SU1498		chemical - kinase inhibitor			2.20E-02	ETS1,TNFRSF11B
cobalt chloride		chemical reagent	0.555	bias	4.10E-02	BACH1,BHLHE40,BHLHE41,CYP1B1,SLC2A1
			-0.642		2.59E-03	BACH1,DDIT3,DHCR24,DHCR7,DNMT3A,ME1,MSMO1,SCD,SLC7A11,TP63
						ABL1,AEBP2,ASTN2,ATXN1,BHLHE41,C9orf116,CDC14B,CPT1B,DDIT3,DMXL2,DNMT3A,DOCK1,EEF2K,FADS3,FA
cisplatin		chemical drug	-0.214	bias	2.26E-03	M117A,FDXR,FNDC3B,GHR,HDAC9,KRT19,MAML2,MBN
		chemical - endogenous mammalian			4.45E-02	L2,PRDM5,SLC2A1,SPDYA,THBS1,TIMP3,TP63,ZSCAN5A
spermidine		biologic drug			3.25E-02	KRT19,PTPN2
triptorelin		biologic drug			4.45E-02	CGA,PGR
icatibant		chemical - endogenous mammalian			6.91E-04	BDKRB2,LDLR
enalaprilat						

steroid		chemical - endogenous mammalian				3.99E-02	CYR61,NR3C1,TNC
genistein		chemical drug	0.916	bias		1.40E-02	ABCA9,ADK,BDKRB1,C17orf75,CYP4F2,DIRAS3,HDAC3,LCP2,LDLR,MMP3,NPC2,NR3C1,PGR,PIK3R1,SORT1,TNFRSF11B,VP552
isoquercitrin		chemical drug				5.31E-03	DHCR7,LDLR,MSMO1
daidzein		chemical drug	0.816	bias		2.10E-02	ADK,C17orf75,LCP2,LDLR,PIK3R1,VP552
naringenin		chemical - endogenous non-mammalian				3.00E-02	LDLR,NR3C1,PGR
hesperetin		chemical drug				2.55E-03	DHCR24,LDLR,MMP3
columbamine		chemical - endogenous non-mammalian				2.63E-02	LDLR
choline		chemical - endogenous mammalian				4.35E-02	DDIT3,DNMT3A,OXTR
sphingomyelin		chemical - endogenous mammalian				1.74E-02	ELOVL5,SCD
9Z,11E-octadecadienoic acid		chemical - endogenous non-mammalian	1.091			2.38E-03	CPT1B,LDLR,SORBS1,THBS1
n-3 fatty acids		chemical drug	-0.655			2.05E-02	ADK,FADS2,PIK3R1,SCD
tridecanoic acid		chemical - endogenous mammalian				2.20E-02	DDIT3,TNC
valproic acid		chemical drug	0.301			8.82E-04	CAP2,CYP11B1,CYP2A6 (includes others),CYR61,DDIT3,DHCR7,GRM7,HAPLN1,HDAC3,LDLR,MSMO1,MVD,NFYA,NPC2,NR3C1,NTF3,PSMD1,PSMD3,PSMF1,SCD,SEL1L3,THBS1,TRAF3
10E,12Z-octadecadienoic acid		chemical - endogenous mammalian	1.491			8.89E-03	CPT1B,DDIT3,LDLR,ME1,SCD,SORBS1
mycophenolic acid		chemical drug	0.896	bias		1.88E-02	CYR61,ETS1,HDAC3,KRT19,LDLR,UGCG
P1,P4-Di(adenosine-5') tetraphosphates		chemical - endogenous mammalian				1.74E-02	NR3C1,THBS1
L-triiodothyronine		chemical - endogenous mammalian	1.471	bias		2.40E-02	ACHE,C1S,CGA,CPT1B,ENPP2,LDLR,MAMDC2,ME1,NTF3,PCK2,PGR,RYR2,SCD,SEMA7A,SORBS1
D-glucose		chemical - endogenous mammalian	1.367	bias		6.20E-03	ACHE,ATP8B1,CACNA1C,CCPG1,CPT1B,DDIT3,EIF2B4,HAPLN1,HNF4A,ITGA8,LAMC1,LDLR,mir-154,mir-329,NEXN,NR3C1,PCK2,SCD,SLC2A1,SLC39A8,SNAP25,SORBS1,THBS1,TRPS1,TRPV4
DL-fructose		chemical - endogenous mammalian				2.70E-02	NR3C1,SCD
mannose		chemical - endogenous mammalian				3.83E-02	NR3C1,THBS1
dihydroxyacetone		chemical - endogenous mammalian				2.63E-02	NR3C1
methylprednisolone		chemical drug	0.392			9.72E-03	ADK,C9,CAMK1D,CBLB,CDH13,CDH2,ELOVL5,ENPP2,EPN2,GHR,GPC1,KRT19,LDLR,ME1,MED4,NR3C1,PER2,PLAA,RND3,SLC4A7,TIMP3,UGCG
desmosterol		chemical - endogenous mammalian				2.04E-03	ACSL4,DHCR24
metribolone		chemical reagent	1.394	bias		4.40E-02	ACTN1,CYB5B1,DHCR24,INPP4B,LDLR,MGLL,NPEPPS,PD
U18666A		chemical reagent				3.25E-02	E4D,THBS1,TRPS1
cholesterol		chemical - endogenous mammalian	-0.139	bias		1.16E-02	DDIT3,DHCR7,KLF11,LDLR,ME1,MSMO1,SCD,THBS1,TIMP3
clofibric acid		chemical drug				3.25E-02	CGA,SCD
iron		chemical - endogenous mammalian	-0.225			1.38E-03	DDIT3,EIF3A,HTT,NFYA,SLC39A8,SNCA