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Andrew Block April 10, 2016

Peripheral cytokine-induced CNS immune activation and effects on mesolimbic dopamine
by

Andrew Block

Jennifer Felger, PhD
Adviser

Neuroscience and Behavioral Biology Department

Jennifer Felger, PhD
Adviser

Steven Bossinger, PhD
Committee Member

Kate O'Toole, PhD
Committee Member

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Abstract

Peripheral cytokine-induced CNS immune activation and effects on mesolimbic dopamine

By Andrew Block

Peripheral administration of inflammatory cytokines such as interferon alpha (IFNα) has been shown to reliably induce depressive behaviors in humans and non-human primates (NHPs) that are related to reduced motivation and anhedonia. Peripheral administration of inflammatory cytokines and cytokine-inducers (e.g. endotoxin) has also been shown to reduce neural activation of the ventral striatum to hedonic reward in humans. Our previous work in NHPs suggests that the effects of peripheral inflammation on reward circuitry and behavior may by due to decreased availability and release of dopamine. However, the immunologic and neurobiologic mechanisms by which peripheral cytokines affect the dopamine system is currently unknown. Herein immune activation was assessed in relation to effects on the dopamine system in the ventral and dorsal striatum in post-mortem brain tissue from rhesus monkeys (aged 10-14 yrs) exposed to chronic IFNα (20 $MIU/m^2$ s.c. for 4 weeks, n=7) compared to saline control (n=4). Significantly less tissue content of dopamine was observed in the nucleus accumbens (p=0.004) and putamen (p=0.009) of IFNα-treated animals. Whole-gene expression analysis revealed induction of limited immune signaling pathways by IFNα in association with activation of immune cells primarily in vascular and meningeal compartments in or near putamen. Whole genome and targeted analysis also revealed alterations in genes related to dopamine neurotransmission and receptor signaling. These results support our previous findings of decreased striatal dopamine release in IFNα-treated monkeys, and indicate that effects of peripheral IFNα on brain dopamine are likely driven by peripheral immune cells trafficking to the CNS.

Peripheral cytokine-induced CNS immune activation and effects on mesolimbic dopamine

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# Table of Contents

# Introduction

Mood disorders currently affect more than 20% of the general population in the United States (Kessler et al., 2003). One such mood disorder is major depression. While some treatment options do exist, more than 30% of those with depression fail to achieve remission of their symptoms (Fava et al., 2006, Mathew and Charney, 2009). Thus, more work is needed to better understand the pathophysiological pathways of depression.

There is evidence of a cause and effect relationship between depressive symptoms and inflammation (Felger and Lotrich, 2013, Felger and Miller, 2014). For example, elevated levels of inflammatory cytokines and other markers of innate immune activation have been consistently observed in the blood and cerebrospinal fluid of patients with major depression (Raison et al., 2006, Raison et al., 2013a, Raison et al., 2013b). Moreover, peripheral administration of inflammatory cytokines has been shown to induce depressive symptoms in both humans and laboratory animals (Haroon et al., 2012). For instance, chronic administration of interferon (IFN)α, an antiviral inflammatory cytokine that was used as an effective treatment for Hepatitis C virus (Dorr, 1993), causes clinical depression and symptoms of anhedonia in many patients (Capuron and Miller, 2004). Additionally, administration of IFNα to laboratory animals, such as non-human primates (NHPs), has been shown to induce both depressive and anhedonic-like behavior (Felger et al., 2007, Felger et al., 2013b). Anhedonia, a deficit in feelings such as pleasure and motivation, is a core symptom of depression as well as an indicator of dysfunction in the dopaminergic reward system (Hickie et al., 1999, Treadway and Zald, 2011, Tye et al., 2013).

Neuroimaging studies in humans have found that inflammatory cytokines decrease neural activation of the ventral striatum to hedonic reward, which correlated with self reported increases in depressive symptoms and reduced motivation (Eisenberger et al., 2010, Capuron et al., 2012); an effect that appears to be mediated by cytokine-induced decreases in mesolimbic dopamine (Capuron et al., 2012, Felger and Miller, 2012, Felger et al., 2013b). Indeed, decreased release of striatal dopamine in NHPs administered IFNα has been found by *in vivo* microdialysis, which correlated with decreased effort-based sucrose consumption, a measure of anhedonia in NHPs (Felger et al., 2013b). Interestingly, IFNα-induced decreases in dopamine release in NHPs were reversed by administration of the dopamine precursor levodopa (L-DOPA) via reverse microdialysis (Felger et al., 2015). Inflammatory cytokines may disrupt dopamine production by inhibition of the enzyme co-factor tetrahydrobioterin (BH4), which is required for the conversion of phenylalanine to tyrosine by phenylalanine hydroxylase and tyrosine to L-DOPA by tyrosine hydroxylase (Neurauter et al., 2008). Additionally, inflammation-related decreases in BH4 can cause oxidative stress, which can lead to even less BH4 being available for dopamine synthesis (Cunnington and Channon, 2010). Furthermore, patients that have had chronic peripheral administration of IFNα have shown evidence of reduced BH4 activity (Neurauter et al., 2008, Zoller et al., 2012, Felger et al., 2013a), implicating the loss of BH4 as a potential factor in the loss of dopamine synthesis and release. In addition, previous studies in NHPs have also found a decrease in dopamine 2 receptor (D2R) but not dopamine transporter (DAT) binding following chronic IFNα administration, suggesting that cytokines and immune activation may also reduce dopamine receptor expression or function (Felger et al., 2013b).

Mechanistically, peripherally administered cytokines are thought to access the central nervous system (CNS) and may activate microglia and astroglia in the brain. This activation of brain immune cells may then cause local cytokine production of cytokines. For example, when IFNα is administered peripherally over several weeks, concentrations of the inflammatory cytokines interleukin (IL)-6 and tumor necrosis factor (TNF) and their soluble receptors are significantly elevated in the cerebrospinal fluid (CSF) in humans and NHPs administered IFNα (Felger et al., 2007, Raison et al., 2009). IFNα also causes the production of monocyte chemotactic protein-1 (MCP-1), a chemokine that recruits monocytes and macrophages to the CNS (Collins et al., 1985, Smith et al., 1985, Raison et al., 2009). Previous studies in post-mortem brain tissue from depressed suicides indicate increased macrophage recruitment to perivascular spaces and selective activation or priming of microglia in the neighboring parenchyma of the prefrontal cortex (Torres-Platas et al., 2014). However, no previous study has investigated the pattern of immune cell activation in the brains of IFNα-treated subjects, or in the basal ganglia of depressed suicides. Therefore, it is unknown whether peripheral inflammatory cytokines like IFNα affect dopamine synthesis, release, and/or receptor signaling through direct effects across the blood brain barrier, or whether changes may be driven in part by accumulation of peripheral cells in perivascular and meningeal spaces or activation of local brain immune cells.

Thus, in this study, we tested the hypotheses that chronic IFNα administration was associated with increased accumulation of perivascular and meningeal macrophages, selective activation of local microglial, and increased inflammatory signaling, in association with decreased tissue content of dopamine and genes related to dopamine synthesis, metabolism or receptor signaling. To determine the immunological and neurotransmitter mechanisms by which chronic exposure to inflammatory cytokines may affect dopamine function, post-mortem tissue from NHPs chronically administered IFNα compared to controls was examined for tissue content of dopamine by high performance liquid chromatography (HPLC), microglia and peripheral immune cell activation by immunofluorescence and confocal microscopy, and changes in gene expression related to inflammatory and neurotransmitter signaling through targeted and genome wide analyses using RNA-sequencing (RNA-seq).

# Methods

## Subjects and Brain Tissue Collection

Post-mortem brain tissue from rhesus monkeys (*Macaca mulatta*) aged 10-14 yrs administered pegylated IFNα 20 MIU/$m^2$ s.c. (rHu-IFNα-2b (Schering-Plough, Kenilworth, NJ)) between 0700 hours and 1000 hours, 5 days per week for 4 weeks (n=7, 3 female), similar to the treatment schedule of patients receiving IFNα monotherapy for malignant melanoma (Musselman et al., 2001), were compared to controls administered saline in equivalent volumes for 4 weeks (n=4, 2 female). All brains were collected following transcardial perfusion with cold 0.9% saline with heparin. The left hemisphere was fixed in cold 4% PFA, sunk in increasing concentrations of sucrose (10 to 30%) in 0.1 M phosphate buffer (PB), and stored at −80° C until sectioning. The right hemisphere was blocked for micro-dissections for RNA extraction and HPLC of neurotransmitters, and stored at -80°C until analysis.

## HPLC for Tissue Dopamine Concentrations

Samples extract from basal ganglia tissue was outsourced to Briansonline.org for quantification of dopamine by HPLC with electrochemical detection according to established procedures (Felger and Miller, 2012, Raison et al., 2013a). Desired portions of brain tissue were dissected on dry ice and weighed. Each portion of tissue was then placed in a solution of 0.5 Molar perchloric acid and .01% (w/v) ascorbic acid for each gram of brain tissue at 4°C. The solution was then homogenized using a tissue homogenizer (PowerGen 125, Fisher Scientific). The homogenates were then centrifuged at 4°C for 30 mins at 13,000 rpm. The supernatant was then aliquoted and stored at -80°C until analysis. Concentrations of dopamine were determined by using electrochemical detection using an internal standard. Samples (10 µl) were mixed with 20 µl internal standard (3,4-Dihydroxybenzylamine, DHBA), 20 µl was injected onto the LC system by an automated sample injector (Gilson XL233, Gilson, France). Chromatographic separation was performed on a reversed phase Hypersil BDS C18 (150 x 2.1 mm, 3 µm) analytical column (Thermo Scientific, keystone, USA) held at a temperature of 32.5º C. Components were separated using isocratic sodium acetate buffer, pH=4.1. Detection was performed using a potentiostate (Antec Leyden, model Intro, The Netherlands) fitted with a glassy carbon electrode set at +600 mV vs. Ag/AgCl (Antec Leyden, the Netherlands).

Gene Expression

Changes in the transcriptome induced by IFNα compared to control in the caudate and putamen were assessed by RNA-seq in collaboration with Dr. Bosinger, Yerkes NHP Genomics Core. RNA was isolated from microdissected brain tissue stored at -80 in RNAlater, and isolated with RNeasy Mini Kits (Qiagen, Hilden, Germany). RNA-seq was then run on two flowcells of an Illumina HiSeq1000. Reads were aligned to the MacaM version 7 assembly of the Indian rhesus macaque genome (Zimin et al., 2014). Alignment was performed using STAR version 2.4.0g1 (Dobin et al., 2013). Parameters were set using the annotation as a splice junction reference. Transcript abundance estimates were calculated with htseq-count version 0.6.1p1 (Anders et al., 2015). Normalization was performed using DESeq2 version 1.6.3 (Love et al., 2014), producing a both a normalized read count table and a regularized log expression table. There was an average of 19-20 million reads per sample, single end. DESeq2 was also used for differential expression estimation between treated and control samples for each brain region. A false discovery rate (FDR) <5% was maintained to identify genes most likely to be differentially expressed while controlling the rate of false-positives. Additionally, differentially expressed gene transcripts were defined as having a ≥20% difference (1.2 fold change) (Cole et al., 2003, Miller et al., 2008, Mehta et al., 2013, Torres et al., 2013), and were therefore highly predictive based on both statistical significance (p value) as well as biological effect size (fold change). Identified genes were examined for significantly represented pathways and transcription factor networks in Metacore. Compared with microarray, this read depth allows significantly more power to detect differentially expressed genes. A targeted analysis of genes related to the dopamine neurotransmitter system (Bibb, 2005, Bonci and Hopf, 2005) was also conducted as described below in statistical analysis.

Immunofluorescence

The fixed hemisphere was blocked and sectioned at 50-60 micron using either a freezing microtome or Vibratome 1500. Sections were then stored in cryoprotectant solution at −20°C until staining. Sections were rinsed in phosphate-buffered saline (pH 7.6; PBS) and blocked in 0.5% bovine serum albumin (BSA) with PBS at room temperature. Slices were then incubated in primary antibody in tris-buffered saline (TBS), 0.1% Triton-X, and .1% BSA overnight at ~4°C while on a shaker. Sections were then rinsed and incubated with secondary fluorescent antibodies in the dark for 1 hour at room temperature. For macrophage/microglia stain, rabbit anti-Iba-1 was used (Wako, 019-19741) at 1:2000. For the microglia stain, mouse anti-human B-lymphocytes was used (HLA-DR/MHC-II) (MP Biomedicals, 0869302) at 1:200. For staining of endothelial cells in the brain vasculature, anti-Von Willebrand factor was used (abcam, ab6994) at 1:200. Sections were then counterstained with a nuclear stain, DAPI. Sections were mounted, dehydrated, and smooth cover-slipped with an antifade mount solution (Fluro-gel, Electron Microscopy Sciences). Slides were stored in a slide box at 4°C until imaging. Images were acquired using a Leica TCS SP8 confocal system with Hybrid Detector (HyD) (Emory University Winship Cancer Institute). Images were analyzed by collapsing serial Z stacks into a single image using Image J software (NIH, Bethesda, MD).

Statistics

For HPLC data and targeted analyses of dopamine-related gene expression, all statistically analyses were conducted using SPSS (IBM, Armonk, NY). To assess dopamine concentrations in the nucleus accumbens, caudate and putamen in IFNα versus control animals, we used both a one-way multivariate analysis of variance (MANOVA) with between subject contrasts, as well as two tailed independent t-tests and Bonferroni correction for multiple comparisons ($\alpha/3$). Potential group outliers were examined using two-sided Grubbs' tests ("Outlier Calculator" tool in GraphPad). To assess the effect of IFNα versus control on the D2R (gene symbol DR2D) and DAT (gene symbol SLC63A), individual t-tests were conducted separately. Pearson's product-moment correlation coefficient was used to examine relationships between genes expression and dopamine concentrations. All tests were two-tailed with $\alpha$ of .05.

# Results

Brain tissue from all 11 NHPs (n=4 control, 7 IFNα treated) was used for HPLC and RNAseq experiments. Fixed tissue from 6 animals, 3 administered IFNα and 3 controls (1 female and 2 males per group), was used for microscopy.

## Decreased Tissue Content of Dopamine in Nucleus Acumbens and Putamen

Samples were extracted from three regions of the basal ganglia (nucleus acumbens, caudate and putamen) and dopamine content was analyzed using HPLC. There was no significant main effect of treatment between control and treated animals as assessed by MANOVA ($F[3,9]=2.99$, $p=0.105$). However, independent t-tests demonstrated that there was a significant difference of means for the putamen between control (M=53.80, SD= 9.44) and treated (M=33.67, SD= 9.44) groups ($t= -3.089$, df=9, $p=0.013$; Bonferroni corrected $p=0.039$) (**Figure 1)**. However, Grubbs' test indicated that one sample from each group was a significant outlier in data from the nucleus accumbens ($p > 0.05$). When these statistical outliers were removed, a significant main effect of treatment was revealed by MANOVA ($F[3,9]=17.30$, $p=0.005$) (**Figure S1**). Between-subject contrast demonstrated significantly decreased dopamine in both nucleus accumbens ($p=0.004$) and putamen ($p=0.009$). Individual t-tests also indicated significant difference in means between the control (M= 17.23, SD= 0.92) and treated (M= 5.72, SD= 4.69) animals in the nucleus accumbens ($t= -4.13$, df=9, $p=0.004$; Bonferroni corrected $p=0.012$).

Changes in Inflammatory and Neurotransmitter-related Gene Expression, Whole Genome Analysis

Genome wide analysis was used to determine genes that were significantly differentially regulated in the brains of IFNα-treated compared to control animals. A threshold of ±1.20 fold change and an adjusted p-value of 0.05 was used as a cut off. Genes that were significantly differentially regulated at this threshold in putamen and caudate, respectively, are listed in **Tables S1 & S2**. In putamen, 1878 genes were differentially regulated by IFNα treatment. Of these genes, 922 were up-regulated and 956 were down-regulated by IFNα. In caudate, 187 genes were differentially regulated by IFNα treatment. Of these genes, 165 were up-regulated and only 22 were down-regulated by IFNα.

In the 922 up-regulated genes in the putamen, we observed a significant overrepresentation of genes in pathways related to development ("Thrombopoietin-regulated cell processes," "Bone morphogenetic protein (BMP) signaling," "Fibroblast growth factor receptor (FGFR) signaling pathway"), hormone signaling ("Ligand-independent activation of estrogen receptor 1 (ESR1) and estrogen receptor 2 (ESR2)," "Membrane-bound ESR1: Interaction with growth factors signaling"), and oncogenes ("Ligand independent activation of Androgen receptor in Prostate Cancer," "P53 signaling pathway," "Ovarian cancer"). Of relevance to inflammatory signaling induced by IFNα, several of these top pathways were related to nuclear factor of activated T-cells (NF-AT) signaling ("NF-AT signaling in cardiac hypertrophy"), nuclear factor-kappaB (NF-kB) ("Additional pathways of NF-kB activation in the cytoplasm"), and IFN ("IFN gamma signaling pathway") (**Figure 2A**). Of relevance to dopamine neurotransmission and other neurotransmitters that regulate dopamine, pathways related to melanocyte/ melanoma related pathways (“Melanocyte development and pigmentation,” “Aberrant B-Raf signaling in melanoma progression”), adenosine receptors (“A2B reception: action via G-protein alpha s”), and glutamate signaling through N-methyl-D-aspartate (NMDA) receptors (“NMDA dependent postsynaptic long-term potentiation in CA1 hippocampal neurons”) (**Figure 2A**). These were the top 20 significant pathways with at least 6 genes represented per pathway ($p < 2.01e-3$). In the up-regulated genes in the putamen, there was also a significant over-representation of genes regulated by a number of transcription factors. These transcription factors were primarily involved in inflammatory and immune signaling (RELA (p65 NF-kB subunit), GATA-3, FOXP3, STAT3), oncogenes (c-Myc, p53, ZNF143, c-Jun, E2F1, IRF4, EGR1), estrogen signaling (ESR1, Sp1, Androgen receptor, RFX2), and cellular processes (Oct-3/4, YY1, NANOG, SOX2, LHX2, H1F1A, C/EBPbeta, NRSF, SP3, CREB). These were the top 24 pathways that had a p-value of < 1.33e-141. The up-regulated genes related to the inflammatory and IFN relevant transcription factor, STAT3, is shown in **Figure S2**.

In the 956 down-regulated genes from the putamen, there were a significant overrepresentation of genes related to oxidative phosphorylation (“Oxidative phosphorylation,” “Ubiquinone metabolism,” “ATP/ITP metabolism”), oligodendrocyte processes (“Regulation of cytoskeleton proteins in oligodendrocyte differentiation and myelination”), and cytoskeletal modifications (“Neurofilaments,” “Slit-Robo signaling,” “Regulation of actin cytoskeleton by Rho GTPases,” “Regulation of cytoskeleton proteins”) (**Figure 2B**). These were the top 8 pathways with at least 6 genes represented per pathway ($p < 1.42e-2$).

In the 189 up-regulated genes from the caudate, a significant overrepresentation of genes in pathways involving protein folding ("Posttranslational processing of neuroendocrine peptides") and immune activation ("Lectin induced complement pathway," "Classical complement pathway") were observed (**Figure 3**). These were the top 3 pathways that had at least 3 genes represented per pathway (p< 2.94e-2). There were a variety of overrepresented genes associated with transcription factors in the up-regulated genes. These transcription factors were related to inflammatory signaling (STAT3, RElA (p65 NF-kB subunit)), oncogenes (c-Myc, p53, N-Myc, c-Jun), estrogen signaling (ESR1, Sp1, Androgen receptor, RFX2), cellular processes (Oct-3/4, H1F1A, NANOG, YY1, CREB1), and glucocorticoids (GCR, TCF7L2 (TCF4)). These were the top 15 transcription factors that had a p-value of < 4.4e-17. While 22 genes were significantly down-regulated in the caudate, none of the pathways identified as significant had more than one gene represented in the pathway. Thus, these pathways were not reported.

Decreased Expression of Dopamine-related Genes, Targeted Analysis

To examine changes in gene expression specific to dopamine synthesis, metabolism and neurotransmission, targeted analysis was performed (**Table 1 & 2**). A one-way multivariate analysis of variance (MANOVA) was conducted to determine if IFNα treatment significantly affected gene expression. In the putamen, there was significantly less expression of the dopamine and cAMP-regulated neuronal phophoprotein 32 (DARP-32) (p = 0.044). Additionally, the gene for catechol-O-methyltransferase (COMT) was significantly decreased (p=0.004). Finally, two g-protein inward rectifying potassium channels were significantly decreased in the putamen

(KCNJ4, $p<0.001$) and increased in the caudate (KCNJ16, $p=0.030$). Gene expression values from both the caudate and putamen were examined to determine whether there was a significant correlation between dopamine availability (determined via HPLC) and gene expression (via targeted expression data). In the putamen, GNG5, a gamma subunit of a g-protein is stimulated by activation of dopamine 1 and 5 receptors, was significantly decreased (-1.31 fold, $p=0.006$) and was also positively correlated with the concentration of dopamine ($r=0.696$, $df=9$, $p=0.017$).  Individual t-tests revealed that D2R was significantly decreased in the caudate (t value = 2.31, $df=8$, $p=0.050$), but not putamen ($p>0.200$). DAT was not significantly differentially expressed in either caudate or putamen (both $p>0.24$).

### Increased Activated Immune Cells in and around Perivascular and Meningeal Spaces

Brain tissue from rhesus monkeys was sliced, stained and mounted for imaging. Images were taken of the vasculature within the putamen, and of the meninges and bordering tissue of the ventral surface of the brain below the putamen and globus pallidus (**Figure S3**) In one experiment, anti-Iba-1 was used to visualize microglia and peripheral monocytes, and anti-MHC-II was used to label activated microglia and peripheral macrophages., In the putamen, there was an IFNα-driven increase in accumulation of activated peripheral immune cells expressing MHC-class-II (green/yellow cells) in what appeared to be the perivascular spaces of the vasculature. In IFNα-treated animals only, MHC class-II+ activated microglia were observed in the neighboring brain parenchyma that co-localized with Iba-1 (a classic marker for brain microglia) (**Figure 4**). Furthermore, Iba-1+ microglia that did not contain MHC class-II (red cells) of IFNα-treated animals in the putamen appeared in a “primed” state with less ramification and thicker processes. We also observed increased accumulation of activated peripheral immune MHC-class-II+ cells in the meningeal tissue that bordered the outside of the ventral surface of the brain below the putamen and globus pallidus, in IFNα-treated animals compared to controls (n=3 per group) (**Figure 4**). Moreover, MHC-class-II+ activated cells were also observed infiltrating the brain tissue parenchyma that bordered the meninges in this area in IFNα treated animals but not controls, which were found amongst the Iba-1+ cells (**Figure 4**). Anti-Von Willebrand and MHC-class-II staining was used to determine the location and relationship of activated monocytes or microglia with respect to the endothelial cells of the vasculature in the putamen. In the IFNα exposed animals, there was enlargement of the perivascular space, which also contained an increase in the accumulation of activated monocytes/macrophages (**Figure 5**). Furthermore, this experiment confirmed that activated microglia indeed present outside of the endothelial cells of the vasculature (**Figure 5**), indicating a selective activation of parenchymal microglia localized to tissue surrounding the vasculature. In the putamen of control animals, a few activated monocytes/macrophages were located inside the blood vessels (**Figure 5**). Only immune activation in the meningeal tissue on the edge of the caudate showed activate peripheral immune cells. Although accumulation of these cells were observed in IFNα-treated animals (similar to that observed below the putamen and globus pallidus in **Figure 4**), no parenchymal microglial cell activation was found in the caudate of either treated or control animals (data not shown).

## Discussion

The findings presented support the hypotheses that chronic exposure to peripheral cytokines, such as IFNα, affects the dopamine neurotransmitter system most likely via inflammatory signaling driven by recruitment of peripheral immune cells to the CNS. We observed activation of immune cells and immune signaling pathways in the basal ganglia by immunohistochemistry and gene expression analysis, respectively, along with significantly less tissue content of dopamine in the putamen and nucleus accumbens (when statistical outliers were excluded) but not caudate. These findings are particularly interesting and important because they confirmed our previous findings that peripheral administration of cytokines can decrease dopamine synthesis and release in the striatum (Capuron et al., 2012, Felger and Miller, 2012, Felger et al., 2013b). Indeed, our previous study in NHPs found decreased dopamine release after 4 weeks of IFNα as evidenced by reduced displacement of [$^{11}$C]raclopride following amphetamine administration in putamen and nucleus accumbens but not caudate. Furthermore, findings that chronic inflammatory cytokine exposure decreased striatal D2R in the caudate without affecting DAT is consistent with that of PET studies demonstrating reduced striatal D2R but not DAT following chronic IFNα exposure (Felger et al., 2013b).

Interestingly, our findings were consistent across all three techniques HPLC, gene expression and immunohistochemistry. For instance, whereas immune cell activation and increases in inflammatory signaling pathways were observed in putamen in association with decreased dopamine by HPLC, very limited immune cell or inflammatory signaling pathway activation, as well as no change in dopamine concentration, were observed in caudate. Thus, since the only other affected pathway in the caudate was neuroendocrine packaging and there did not appear to be a decrease in dopamine concentration or signaling, it is possible that another neurotransmitter, such as glutamate, may be affected. Indeed, glutamate has known interactions with striatal dopamine (Surmeier et al., 2007) and is thought to contribute to symptoms of cytokine-induced depression (Haroon et al., 2014, Haroon et al., 2016). In fact, our whole genome expression data indicated that exposure to IFNα caused significant up-regulation in of genes in the putamen related to increased NMDA receptor signaling. This could indicate negative downstream effects of inflammation-mediated increased glutamate receptor signaling on neuronal health and neural integrity through excitotoxicity. Indeed, other studies have found that activated microglia, which induce activation of the kynurenine pathway, are a major source of glutamate and quinolinic acid that can lead to depressive-like symptoms (Dantzer and Walker, 2014). The down regulation of oligodendrocyte gene expression in the putamen points to an issue with the glutamatergic signaling system as well, since oligodendrocytes are highly sensitive to excitotoxic environments and to increased inflammation (Domercq et al., 2005) (Matute, 2007). A targeted gene analysis of the glutamatergic signaling system, as well as further analysis on the kynurenine pathway, is necessary to determine the relationship between the glutamate system, peripheral cytokine administration, and its potential affects on dopaminergic signaling.

Also interesting was the fact that the most significantly up-regulated pathway in the putamen were melanin related pathways. It is known that melanin, specifically neuromelanin, is a major player in Parkinson's disease and the disease's hallmark decline of dopaminergic signaling in the basal ganglia (Wilms et al., 2003, Fedorow et al., 2005). It is believed that increased levels of neuromelanin outside of the dopamine cell can cause microglial activation. Continued microglial activation exacerbates dopaminergic neurodegeneration and creates a feed forward system where increased neurodegeneration causes more neuromelanin to be present outside of a dopaminergic cell (Zhang et al., 2011). It seems likely that dopamine signaling in the putamen of IFNα-exposed animals may be affected in a similar way, except that microglia may be initially activated by chronic inflammatory stimuli to then affect neuromelanin production. Indeed, in our immunohistochemistry analysis, we have observed such activated microglia near the vasculature and meninges in the basal ganglia. Additionally, whole genome gene expression analysis demonstrated that there was down regulation of oxidative phosphorylation pathways in the putamen. This would result in a significant decrease in the amount of ATP available for metabolic processes, and thus indicative of decreased neuronal activity. To confirm if nueromelanin is accumulating in the brains of IFNα treated animals and may contribute to decreased dopamine, tissues from both groups will be compared in future assessments to see if there is an accumulation of the a black-brownish pigment in the IFNα-treated animals (Fedorow et al., 2005).

Several limitations of this work should be noted. First and foremost the small sample size, although 3-5 animals per treatment group are common in non-human primate studies (Czoty et al., 2000, Bosinger et al., 2009, Sawyer et al., 2012, Felger et al., 2013b). Additionally, the sample size of treatment was imbalanced to allow for correlation of findings between dopamine concentrations, gene expression, plasma/CSF markers and behavior in future analyses. Furthermore, additional experiments are necessary to determine whether the outliers identified in the nucleus accumbens are due to procedural issues, experimental error, or truly represent the subject's concentration of dopamine. Also, our analysis of staining of immune cells was not quantitative. Once staining is complete in all subjects, future analysis will include quantification of immunostaining for activated immune cells using Metamorph software (Chan et al., 2013). Additional staining will be conducted to determine whether gene expression changes reflect changes in protein levels for neurotransmitter-relevant proteins (e.g. dopamine and glutamate receptors), as well as for expression of other immune-related molecules and proteins relevant to neurotransmission (e.g. quinolininc acid). In terms of other future experiments, an analysis of the behavioral symptoms for these specific subjects is also needed to determine if these neuronal changes correlate with behavioral abnormalities. Additionally, cytokines and inflammatory mediators in the plasma and CSF of these monkeys will be measured to relate to immune changes in the brain. These will help determine whether blood or CSF biomarkers of inflammation, which can easily be measured in clinical samples, are representative of inflammatory processes in the brain and their potential effects on dopamine.

This work supports the hypothesis that chronic peripheral inflammation from IFNα exposure has effects on brain dopamine. Future analyses of this data to understand better the mechanisms involved in terms of potential effects on dopamine synthesis or receptor signaling may lead to novel targets for therapeutic strategies to treat the effects of inflammation on the brain and behavior.

## Tables and Figures

**Table 1**. Dopamine Targeted Gene transcripts in the Caudate and Putamen significantly changed in subjects administered IFNα (n=7) compared to controls (n=4). *=pvalue < 0.05

**Caudate**

| Gene ID | Fold Change | P-value |
|---|---|---|
| ADCY1 | 4242.44 | 0.09 |
| ADCY2 | 327.79 | 0.20 |
| ADCY3 | 2688.54 | 0.38 |
| ADCY4 | 67.27 | 0.84 |
| ADCY5 | 13276.09 | 0.12 |
| ADCY6 | 302.00 | 0.05* |
| ADCY7 | 239.25 | 0.28 |
| ADCY8 | 121.84 | 0.23 |
| ADCY9 | 875.79 | 0.52 |
| ADRB1 | 1.14 | 0.54 |
| ADRB2 | -1.25 | 0.05* |
| AKT1 | 1.01 | 0.80 |
| AKT2 | 1.06 | 0.46 |
| AKT3 | 1.01 | 0.95 |
| APP | 1.03 | 0.23 |
| ARRB1 | 1.03 | 0.58 |
| ARRB2 | 1.11 | 0.24 |
| CACNA1A | 1.08 | 0.28 |
| CACNA1G | 1.48 | 0.36 |
| CACNA1H | 1.09 | 0.25 |
| CACNA1S | 1.72 | 0.22 |
| CALM1 | -1.07 | 0.09 |
| CALM2 | -1.12 | 0.08 |
| CALM3 | -1.10 | 0.19 |
| CALML3 | 1.07 | 0.75 |
| CALML4 | 1.07 | 0.09 |
| CALML6 | -1.08 | 0.60 |
| CDK5 | -1.12 | 0.20 |
| CASP3 | -1.10 | 0.15 |
| COMT | -1.07 | 0.30 |
| CREB1 | 1.07 | 0.32 |

| | | |
|---|---|---|
| CREB3 | -1.13 | 0.07 |
| CYP2D6 | 1.11 | 0.11 |
| DDC | -1.06 | 0.85 |
| DBH | 3.20 | 0.37 |
| DRD1 | -1.14 | 0.17 |
| DRD2 | -1.22 | 0.10 |
| DRD3 | 1.10 | 0.43 |
| DRD4 | 1.30 | 0.63 |
| DRD5 | -1.08 | 0.70 |
| DUSP1 | -1.15 | 0.34 |
| FOS | 1.01 | 0.96 |
| GNAI1 | 1.23 | 0.09 |
| GNAS | 1.19 | 0.07 |
| GNG5 | -1.09 | 0.32 |
| GNG7 | -1.33 | 0.02 |
| GNG8 | 1.29 | 0.42 |
| GRK5 | 1.07 | 0.47 |
| GSK3A | -1.09 | 0.09 |
| GSK3B | 1.01 | 0.98 |
| ITPR1 | -1.15 | 0.20 |
| KCNA1 | -1.06 | 0.50 |
| KCNA2 | -1.16 | 0.72 |
| KCNA3 | 1.13 | 0.78 |
| KCNA4 | 1.03 | 0.69 |
| KCNA5 | -1.02 | 0.93 |
| KCNA6 | 1.60 | 0.08 |
| KCNJ1 | 1.63 | 0.15 |
| KCNJ10 | -1.06 | 0.42 |
| KCNJ11 | -1.01 | 0.95 |
| KCNJ12 | 1.07 | 0.61 |
| KCNJ13 | 12.16 | 0.14 |
| KCNJ14 | 1.10 | 0.66 |
| KCNJ16 | 2.18 | 0.03* |
| KCNJ2 | 1.02 | 0.87 |
| KCNJ3 | 1.75 | 0.20 |
| KCNJ4 | -1.17 | 0.14 |
| KCNJ5 | 2.60 | 0.22 |
| KCNJ6 | 1.90 | 0.30 |
| KCNJ8 | -1.23 | 0.26 |
| KCNJ9 | -1.08 | 0.25 |

| | | |
|---|---|---|
| MAOA | 1.09 | 0.32 |
| MAOB | 1.13 | 0.15 |
| MAPK1 | 1.03 | 0.70 |
| PDE10A | -1.25 | 0.18 |
| PDE4A | 1.12 | 0.11 |
| PDE4B | -1.02 | 0.66 |
| PDE4D | 1.05 | 0.58 |
| PHKA2 | 1.04 | 0.58 |
| PIK3CA | 1.04 | 0.70 |
| PIK3CG | 1.09 | 0.67 |
| PLA2G5 | -1.13 | 0.54 |
| PLCB1 | -1.15 | 0.25 |
| PLCB3 | 1.08 | 0.52 |
| PNMT | -1.22 | 0.23 |
| PPP1R1B | -1.21 | 0.06 |
| PPP3CA | -1.13 | 0.08 |
| PPP3CB | -1.06 | 0.23 |
| PPP3CC | 1.00 | 0.96 |
| PRKACA | -1.06 | 0.14 |
| SLC18A1 | 2.35 | 0.23 |
| SLC18A3 | 1.01 | 0.93 |
| SNAP25 | -1.13 | 0.11 |
| SNCA | -1.02 | 0.83 |
| SYN1 | 1.10 | 0.14 |
| SYN2 | 1.15 | 0.20 |
| SYN3 | 1.00 | 0.99 |
| YWHAZ | 1.03 | 0.46 |

**Table 2**. Dopamine Targeted Gene transcripts in the Putamen significantly changed in subjects administered IFNα (n=7) compared to controls (n=4). *=pvalue < 0.05

**Putamen**

| Gene ID | Fold Change | P-value |
|---|---|---|
| ADCY1 | 1.23 | 0.48 |
| ADCY2 | 1.13 | 0.06* |
| ADCY3 | 1.56 | 0.15 |
| ADCY4 | -1.30 | 0.64 |
| ADCY5 | -1.10 | 0.76 |

| | | |
|---|---|---|
| ADCY6 | -1.11 | 0.17 |
| ADCY7 | 1.58 | 0.80 |
| ADCY8 | -1.04 | 0.97 |
| ADCY9 | -1.28 | 0.30 |
| ADRB1 | -1.35 | 0.95 |
| ADRB2 | 1.02 | 0.69 |
| AKT1 | 1.16 | 0.33 |
| AKT2 | -1.22 | 0.73 |
| AKT3 | -1.19 | 0.01* |
| APP | 1.10 | 0.31 |
| ARRB1 | -1.02 | 0.11 |
| ARRB2 | 1.16 | 0.09 |
| CACNA1A | -1.04 | 0.16 |
| CACNA1G | 1.01 | 0.13 |
| CACNA1H | 1.11 | 0.02* |
| CACNA1S | -1.12 | 0.83 |
| CALM1 | -1.35 | 0.71 |
| CALM2 | 1.25 | 0.18 |
| CALM3 | -1.28 | 0.01* |
| CALML3 | -1.41 | 0.85 |
| CALML4 | -1.72 | 0.85 |
| CALML5 | 1.02 | 0.70 |
| CALML6 | 1.16 | 0.52 |
| CASP3 | 1.46 | 0.24 |
| CDK5 | 1.02 | 0.01* |
| COMT | 1.48 | 0.00* |
| CREB1 | -1.14 | 0.00* |
| CREB3 | 1.53 | 0.01* |
| CYP2D6 | 1.37 | 0.00* |
| DBH | 1.03 | 0.66 |
| DDC | 1.03 | 0.69 |
| DRD1 | 1.21 | 0.26 |
| DRD1_A | 1.28 | 0.26 |
| DRD2 | -1.25 | 0.20 |
| DRD3 | 1.17 | 0.36 |
| DRD4 | 1.24 | 0.61 |
| DRD5 | 1.00 | 0.59 |
| DUSP1 | 1.01 | 0.50 |
| FOS | -1.11 | 0.45 |
| GNAI1 | 1.13 | 0.22 |

| | | |
|---|---|---|
| GNAS | -1.11 | 0.44 |
| GNG5 | 1.23 | 0.01* |
| GNG7 | 1.36 | 0.74 |
| GNG8 | 1.17 | 0.67 |
| GRK5 | 1.06 | 0.94 |
| GSK3A | 1.17 | 0.03* |
| GSK3B | -1.15 | 0.01* |
| ITPR1 | 1.01 | 0.17 |
| KCNA1 | -1.08 | 0.11 |
| KCNA10 | -1.01 | 0.48 |
| KCNA2 | 1.25 | 0.04* |
| KCNA3 | 1.72 | 0.07 |
| KCNA4 | 1.17 | 0.16 |
| KCNA5 | 1.07 | 0.76 |
| KCNA6 | -1.01 | 0.24 |
| KCNA7 | -1.10 | 0.29 |
| KCNJ1 | -1.18 | 0.10 |
| KCNJ10 | 1.07 | 0.83 |
| KCNJ11 | -1.01 | 0.14 |
| KCNJ12 | -1.30 | 0.17 |
| KCNJ13 | -1.14 | 0.97 |
| KCNJ14 | 2.16 | 0.59 |
| KCNJ15 | 1.02 | 0.20 |
| KCNJ16 | -1.18 | 0.08 |
| KCNJ18 | -1.10 | 0.48 |
| KCNJ2 | -1.02 | 0.10 |
| KCNJ3 | 1.09 | 0.07 |
| KCNJ5 | 1.43 | 0.40 |
| KCNJ8 | 1.29 | 0.16 |
| KCNJ9 | 1.29 | 0.26 |
| MAOA | -1.37 | 0.25 |
| MAOB | 3.06 | 0.50 |
| MAPK1 | -1.23 | 0.08 |
| PDE10A | -1.16 | 0.18 |
| PDE4A | 1.08 | 0.71 |
| PDE4B | 1.20 | 0.53 |
| PDE4D | 1.24 | 0.12 |
| PHKA2 | 1.17 | 0.23 |
| PIK3CA | 1.22 | 0.03* |
| PIK3CG | 1.02 | 0.30 |

| | | |
|---|---|---|
| PLA2G5 | -1.32 | 0.18 |
| PLCB1 | -1.04 | 0.12 |
| PLCB3 | 1.10 | 1.00 |
| PNMT | -1.05 | 0.10 |
| PPP1R1B | 1.03 | 0.04* |
| PPP3CA | 1.06 | 0.53 |
| PPP3CB | 1.04 | 0.65 |
| PPP3CC | -1.03 | 0.14 |
| PRKACA | 1.17 | 0.80 |
| PRKACA_A | 2.27 | 0.80 |
| SLC18A1 | 2.20 | 0.43 |
| SLC18A3 | 1.18 | 0.88 |
| SNAP25 | -1.12 | 0.40 |
| SNCA | 1.22 | 0.51 |
| SYN1 | 0.00 | 0.90 |
| SYN2 | -1.05 | 0.08 |
| SYN3 | -1.30 | 0.00* |
| YWHAZ | 1.23 | 0.60 |

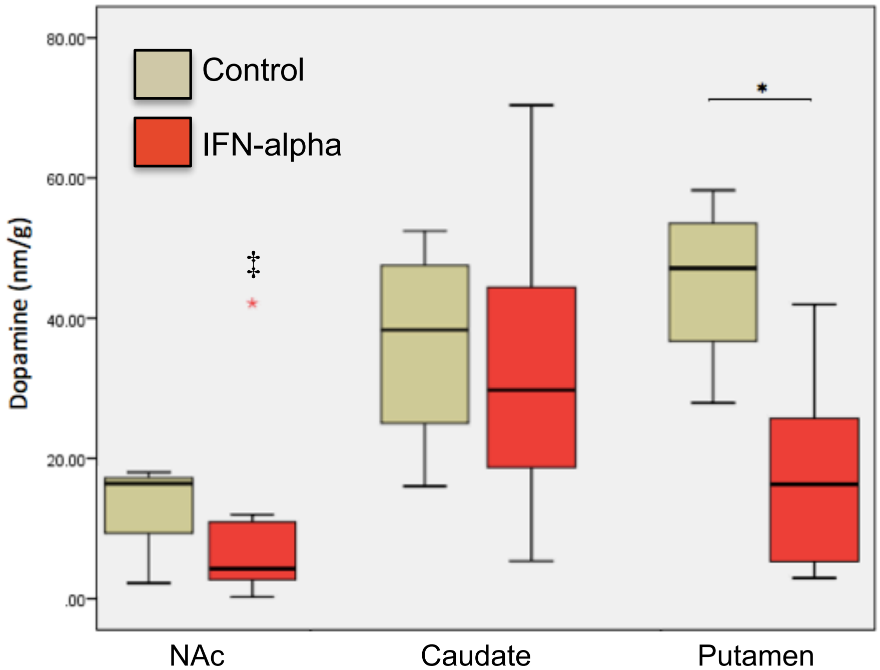
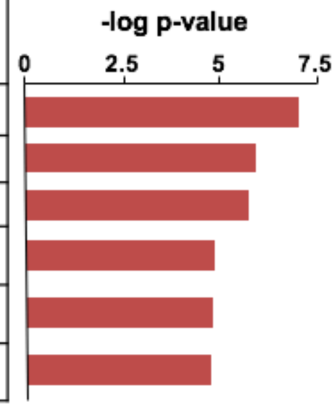



**Figure 1. Dopamine Concentrations in the Basal Ganglia.** Administration of interferon IFNα for 4 weeks (red boxes, n=7) compared to controls (tan boxes, n=4) significantly decrease tissue content of dopamine in the putamen, but not nucleus accumbens (NAc) or caudate. However, statistical outliers were observed in both IFNα and control groups in NAc. When these outliers were removed, a significant decreased in NAc dopamine was also observed. *p<0.01, ‡p<0.01 after removal of statistical outliers.

A

| Putamen | Pathways | P-value | Ratio |
|---|---|---|---|
| Up-regulated | Melanocyte development & pigmentation | 9.40e-8 | 11/49 |
| | A2B Receptor: action via G-protein alpha s | 1.15e-6 | 10/50 |
| | NF-AT signaling in cardiac hypertrophy | 1.93e-6 | 11/65 |
| | NMDA-dependent postsynaptic long-term potentiation in CA1 hippocampal neurons | 1.54e-5 | 11/80 |
| | Additional pathways of NF-kB activation (in the cytoplasm) | 1.64e-5 | 9/53 |
| | IFN gamma signaling pathway | 1.92e-5 | 9/54 |




B

| Putamen | Pathways | P-value | Ratio |
|---|---|---|---|
| Down-regulated | Oxidative Phosphorylation | 4.33e-32 | 39/105 |
| | Cytoskeleton remodeling: Neurofilaments | 8.81e-6 | 7/25 |
| | Regulation of cytoskeleton proteins in oligodendrocyte differentiation and myelination | 7.77e-5 | 9/58 |

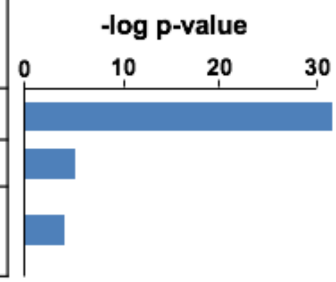



**Figure 2. Pathways significantly affected by IFNα administration in treated animals compared to controls in the putamen.** Pathways of interest that were significantly overrepresented in up-regulated (A) or down-regulated (B) genes in the putamen. Significant genes were defined as adjusted $p < 0.05$ and fold change of 1.20 cutoff.

| Caudate | Pathways | P-value | Ratio |
|---|---|---|---|
| Up-regulated | Posttranslational processing of neuroendocrine peptides | 1.05e-6 | 5/50 |
| | Lectin induced complement pathway | 8.46e-4 | 3/50 |
| | Classical complement pathway | 1.00e-3 | 3/53 |

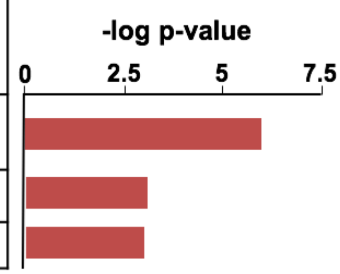



**Figure 3. Pathways significantly affected by IFNα administration in Treated animals compared to Controls in the caudate.** Pathways of interest that were significantly overrepresented in up-regulated genes in the caudate. Significant genes were defined as adjusted $p < 0.05$ and fold change of 1.20 cutoff. No significant pathways were observed in down-regulated genes from the caudate.

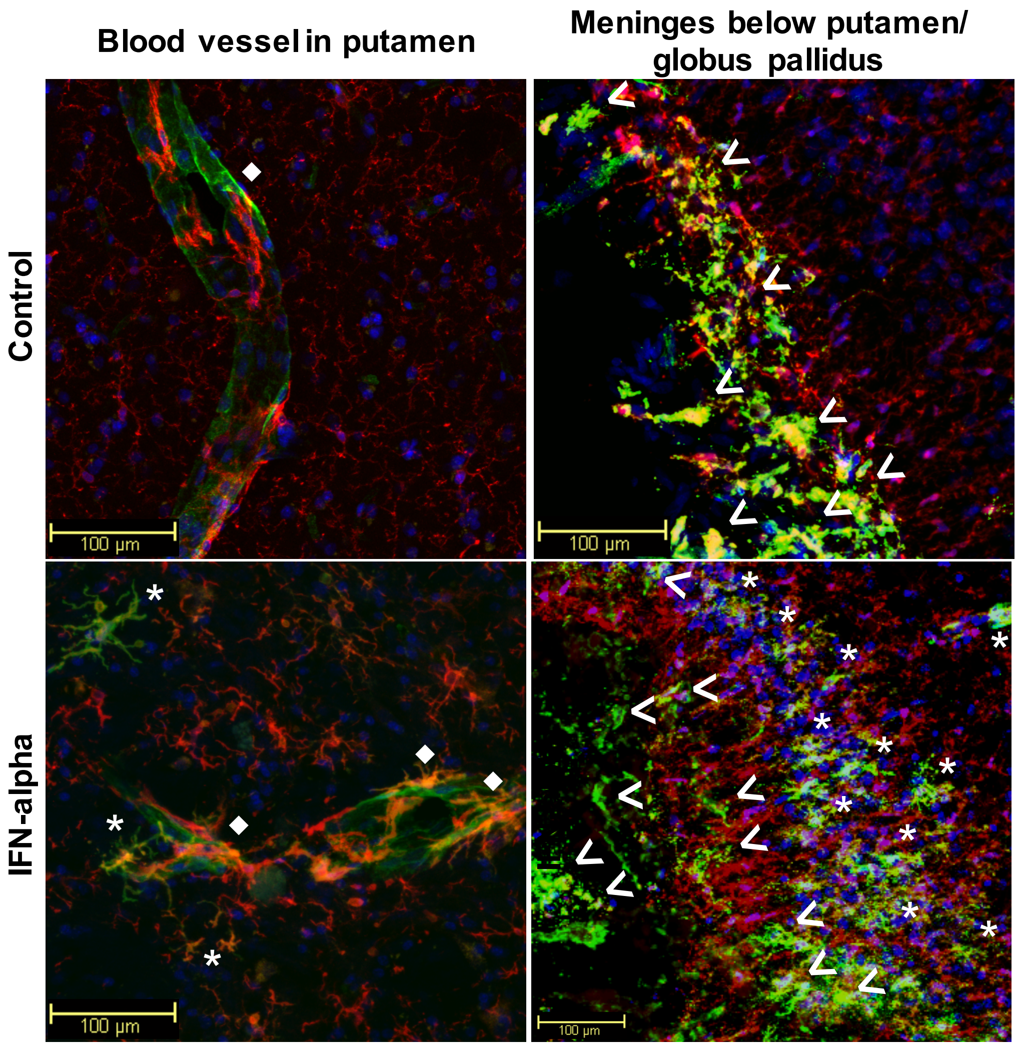



**Figure 4. Interferon IFNα increased monocyte/macrophages in perivascular and meningeal spaces and activated parenchymal microglial in basal ganglia.** In the putamen, IFNα increased accumulation of activated peripheral monocytes/macrophages (diamond = activated MHC class-II+ cells in what appeared to be perivascular spaces), and activated neighboring parenchymal microglial cells (asterisks = activated MHC class-II+ cells amongst red Iba-1+ microglia) in what was consistent with the neighboring parenchyma outside of the vasculature. Furthermore, in the putamen of IFNα-treated animals, Iba-1+ microglia that did not contain MHC class-II (red cells) were in a "primed" state with less ramification and thicker processes compared to that of controls. IFNα also increased accumulation of activated macrophages in meningeal spaces (arrow heads = activated MHC class-II+ peripheral cells in meninges and tissue border) just below the putamen and globus pallidus, and also activated immune cells in the neighboring tissue parenchyma (asterisks). Green=MHC class-II, red=Iba-1, blue=DAPI, scale bars = 100 µm

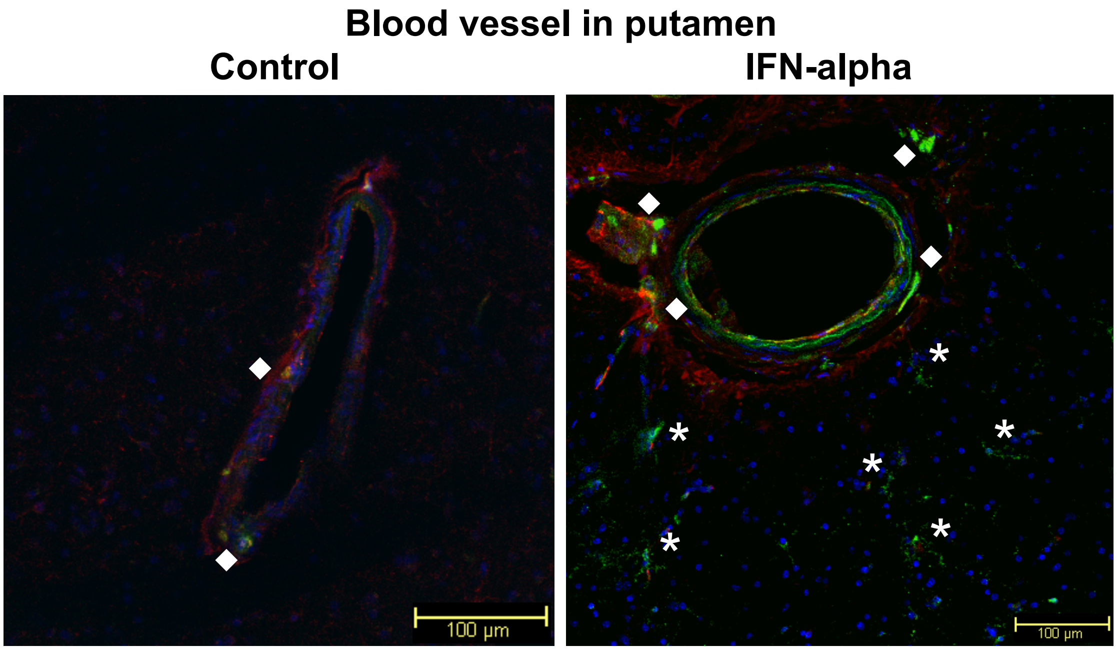



**Figure 5. Interferon IFNα increased monocyte/macrophages inside of perivascular spaces and activated parenchymal microglial in putamen outside of blood vessels.** In the putamen, anti-Von Willebrand factor staining for blood vessel endothelial cells (red) revealed large perivascular compartments in IFNα-treated animals and confirmed that they contained increased accumulation of perivascular cells (diamond = activated MHC class-II+ inside of the blood vessel endothelial cells). This experiment also confirmed the presence of activated microglial cells (asterisks = activated MHC class-II+ cells outside of the blood endothelial cells) in the neighboring parenchyma in putamen of IFNα-treated but not control animals. Green=MHC class-II, red= anti-Von Willebrand factor (endothelial cells of blood vessels), blue=DAPI, scale bars = 100 µm

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## Supplemental Materials

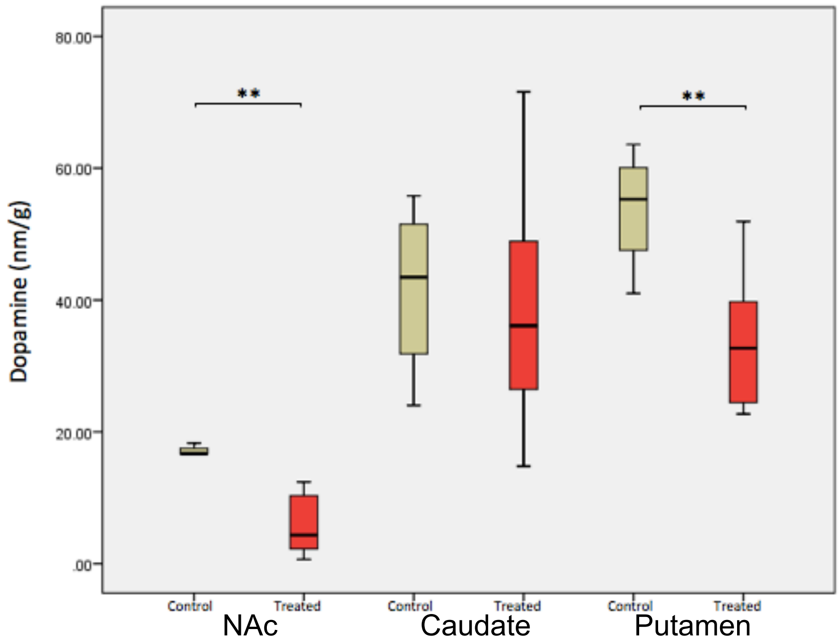


**Figure S1. Dopamine Concentration in the Basal Ganglia (outliers dropped).** After removal of statistical outliers in the nucleus accumbens (NAc), there was a significant difference in tissue dopamine content between interferon (IFN)α treated (red boxes) and control (tan boxes) animals in the NAc and putamen. ** $p < 0.01$

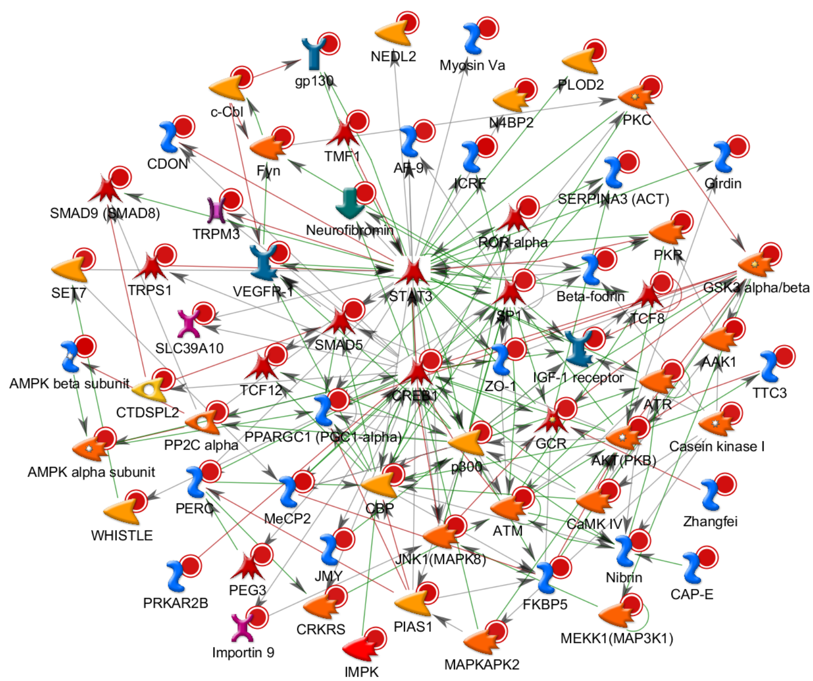


**Figure S2. Up-regulated genes in putamen in a network with the IFN-related transcription factor STAT3.** Effector genes and transcription factors that were up-regulated by interferon (IFN)α compared to control in the putamen that are significantly overrepresented in a network with the transcription factor STAT3. p= 1.44e-141.

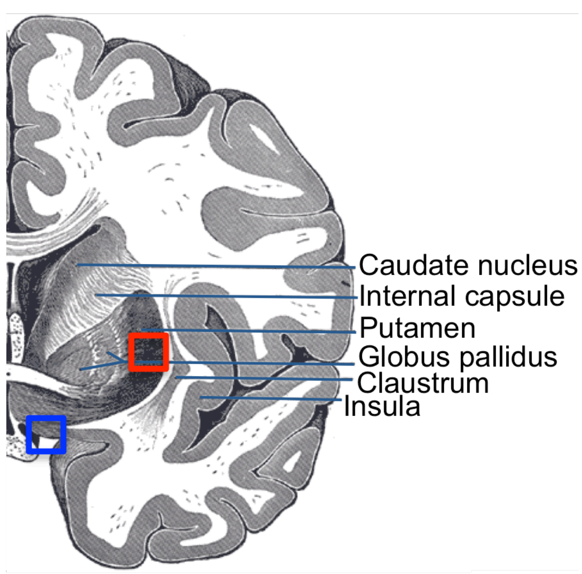


**Figure S3. Location of acquisition of confocal microscopic images in basal ganglia.** Activated immune cells were imaged in the perivascular spaces of putamen (red square) and meninges and neighboring parenchyma below the putamen and globus pallidus (blue square).

**Table S1**. Gene transcripts in the putamen significantly up- and down-regulated in subjects administered IFNα (n=7) compared to controls (n=4).

| Up-Regulated Genes | | |
|---|---|---|
| **Gene-ID** | **Fold change** | **Adjusted P-value** |
| **FAM126B** | 1.673446159 | 0.001705164 |
| **SLC30A6** | 1.654516838 | 0.001227029 |
| **LCOR** | 1.549618326 | 3.82989E-05 |
| **HCN1** | 1.545725448 | 0.004815335 |
| **SLC4A7** | 1.54095187 | 0.000260465 |
| **ARHGAP26** | 1.53279169 | 0.002184831 |
| **SKIL** | 1.528562587 | 0.007104761 |
| **UNC5D** | 1.517132822 | 0.006477586 |
| **FEM1B** | 1.511572567 | 0.007642703 |
| **FRRS1L** | 1.511290205 | 0.008109344 |
| **NFAT5** | 1.502956998 | 0.008908212 |
| **GMCL1** | 1.502232552 | 0.001842061 |
| **MAN1A2** | 1.501493718 | 0.007772611 |
| **DNAJB14** | 1.500224637 | 0.007813049 |
| **DUSP18** | 1.49927413 | 0.006953418 |
| **SYN3** | 1.494883178 | 0.005030119 |
| **RRP8** | 1.494572104 | 0.008963882 |
| **ZNF770** | 1.493366521 | 0.005146403 |
| **TRIP11** | 1.492520735 | 0.003409352 |
| **FUT9** | 1.490785077 | 0.009645686 |
| **GFOD1** | 1.488356037 | 0.009892837 |
| **LONRF3** | 1.487830816 | 0.009970324 |
| **TECPR2** | 1.485004795 | 0.009858217 |
| **UHRF1BP1** | 1.484362405 | 0.006971634 |
| **HIPK3** | 1.483350466 | 0.009858067 |
| **NRIP3** | 1.482315826 | 0.004815335 |
| **PRKAB2** | 1.481655593 | 0.009484345 |
| **ZBTB24** | 1.48145695 | 0.00586721 |
| **ITSN2** | 1.478661728 | 0.004705909 |
| **TTLL7** | 1.476879007 | 0.011290929 |
| **HOOK3** | 1.476147406 | 0.010725123 |
| **ZNF546** | 1.476138552 | 0.001841085 |
| **ZNF253** | 1.476027383 | 0.007513568 |

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|---|---|---|
| **CELF2** | 1.473694261 | 0.007388573 |
| **TMEM106B** | 1.473196442 | 0.004705909 |
| **STOX2** | 1.472714718 | 0.011758399 |
| **DOCK5** | 1.472543753 | 0.011758399 |
| **STXBP5L** | 1.47209931 | 0.008738552 |
| **SAMD12** | 1.471453704 | 0.008863773 |
| **LMBRD2** | 1.469575752 | 0.011290929 |
| **ASXL2** | 1.468980497 | 0.010802779 |
| **XKR4** | 1.468750647 | 0.008963882 |
| **AMER1** | 1.466639255 | 0.001281582 |
| **RALGPS2** | 1.464664887 | 0.008491744 |
| **PLEKHH1** | 1.464269012 | 0.00579249 |
| **NCOA2** | 1.463838981 | 0.011904999 |
| **BRAF** | 1.462138738 | 0.012970934 |
| **RUFY2** | 1.460819524 | 0.007740931 |
| **ACER2** | 1.460610488 | 0.009483478 |
| **SOGA1** | 1.457280902 | 0.01313309 |
| **HMBOX1** | 1.455210339 | 0.012144282 |
| **KLHL11** | 1.454792281 | 0.013654591 |
| **MAP3K2** | 1.452979086 | 0.009120975 |
| **VPS13C** | 1.451831563 | 0.012750185 |
| **LRCH3** | 1.44950236 | 0.007642703 |
| **NHSL2** | 1.448001993 | 0.015447614 |
| **RGP1** | 1.446084354 | 0.011904999 |
| **MAP9** | 1.444404667 | 0.015447614 |
| **SLITRK6** | 1.444261666 | 0.011904999 |
| **EPM2AIP1** | 1.443133299 | 0.007642703 |
| **NEK10** | 1.443078701 | 0.01407053 |
| **SNX29** | 1.443007421 | 0.013057252 |
| **TOR1AIP2** | 1.441975486 | 0.012810041 |
| **GRAMD1B** | 1.439512512 | 0.008963882 |
| **KIF1B** | 1.437411058 | 0.016652026 |
| **PGM2L1** | 1.437311244 | 0.00356776 |
| **SLC24A4** | 1.436039231 | 0.011535851 |
| **COL4A5** | 1.435932354 | 0.006415636 |
| **MOB1B** | 1.435151535 | 0.0154935 |
| **LRP6** | 1.433391024 | 0.017658097 |
| **PGGT1B** | 1.43324365 | 0.017033456 |
| **GFPT1** | 1.432352907 | 0.01184407 |
| **MALT1** | 1.431571305 | 0.018185236 |

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|---|---|---|
| **ZC3H8** | 1.431382947 | 0.009674447 |
| **PPP4R2** | 1.431348436 | 0.00557412 |
| **MED28** | 1.430797357 | 0.016047375 |
| **NFASC** | 1.429315301 | 0.003974097 |
| **SYT14** | 1.428900324 | 0.0154935 |
| **AGL** | 1.428146681 | 0.006283193 |
| **MDN1** | 1.427114095 | 0.004815335 |
| **SOGA3** | 1.427077772 | 0.015788454 |
| **ZNF845** | 1.426746449 | 0.009664692 |
| **TSHZ2** | 1.424816525 | 0.008738552 |
| **FNIP2** | 1.422738499 | 0.009858217 |
| **LPGAT1** | 1.421681998 | 0.003068524 |
| **EDIL3** | 1.421192665 | 0.011535851 |
| **HEATR1** | 1.420550788 | 0.008351954 |
| **BCHE** | 1.419883166 | 0.020728579 |
| **DAB1** | 1.41976807 | 0.017500413 |
| **KIAA1958** | 1.41954626 | 0.0197776 |
| **ATP7A** | 1.419310694 | 0.009484345 |
| **FAT1** | 1.418852108 | 0.008738552 |
| **C2CD3** | 1.418543512 | 0.013376019 |
| **PPM1K** | 1.417845008 | 0.006940669 |
| **CHRM3** | 1.417742917 | 0.021300163 |
| **ZFHX4** | 1.417648687 | 0.002392503 |
| **FAM169A** | 1.41647282 | 0.009790578 |
| **ZNF292** | 1.416036786 | 0.003960811 |
| **TET2** | 1.415895665 | 0.001705164 |
| **PLXNA4** | 1.415745034 | 0.020778341 |
| **LARP4** | 1.4152723 | 0.021111349 |
| **ZKSCAN8** | 1.414607706 | 0.021861218 |
| **TRUB1** | 1.414605517 | 0.019645358 |
| **RBM28** | 1.414536003 | 0.015770183 |
| **HHIP** | 1.413507224 | 0.022120754 |
| **GRM1** | 1.413236756 | 0.022120754 |
| **CLSTN2** | 1.412348482 | 0.022344274 |
| **ZNF354C** | 1.409904937 | 0.019816174 |
| **SDK2** | 1.409546347 | 0.020955744 |
| **C10orf118** | 1.409331179 | 0.009858217 |
| **ZNF462** | 1.409295972 | 0.011904999 |
| **CDH7** | 1.409224531 | 0.018845137 |
| **ERI2** | 1.408112388 | 0.007015186 |

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|---|---|---|
| **VTI1A** | 1.40809437 | 0.015146862 |
| **RNF169** | 1.407405436 | 0.015788454 |
| **MYO9A** | 1.406123167 | 0.024109681 |
| **CLMN** | 1.405926772 | 0.008544808 |
| **SLC30A4** | 1.405807931 | 0.019875258 |
| **CPEB3** | 1.40553304 | 0.004815335 |
| **ABCA5** | 1.405304879 | 0.008963882 |
| **PTPRG** | 1.404776665 | 0.01863106 |
| **PLEKHM3** | 1.404411934 | 0.019816174 |
| **UBXN7** | 1.404364453 | 0.023088572 |
| **SHPRH** | 1.404177991 | 6.0804E-05 |
| **KIAA1244** | 1.404138565 | 0.018006554 |
| **MFAP3L** | 1.403343575 | 0.02473979 |
| **NHLRC2** | 1.403121151 | 0.023787082 |
| **SEMA6D** | 1.402880747 | 0.024427672 |
| **SMG1** | 1.402789195 | 0.003321961 |
| **PREPL** | 1.402572161 | 0.015507835 |
| **TTBK2** | 1.401991898 | 0.024172564 |
| **RGS7BP** | 1.400578126 | 0.022239584 |
| **C9orf72** | 1.400168432 | 0.017356917 |
| **JRK** | 1.400096494 | 0.01184407 |
| **GRIN3A** | 1.397601818 | 0.022130072 |
| **C21orf91** | 1.397478511 | 0.024630699 |
| **ALS2CR8** | 1.396990968 | 0.011514438 |
| **ADD2** | 1.396921978 | 0.023191406 |
| **UTRN** | 1.396192636 | 0.009120975 |
| **CFLAR** | 1.395943329 | 0.012464937 |
| **TMEM41B** | 1.395812193 | 0.022520735 |
| **ABL2** | 1.395263368 | 0.0260344 |
| **GPATCH2L** | 1.394909256 | 0.024672425 |
| **TRPM3** | 1.394778299 | 0.025084018 |
| **N4BP2** | 1.394659842 | 0.018922672 |
| **PLOD2** | 1.394560973 | 0.006512065 |
| **ARFGEF2** | 1.39400149 | 0.004927559 |
| **PROX1** | 1.393962453 | 0.009674447 |
| **NYAP2** | 1.39335688 | 0.026989863 |
| **ARL5B** | 1.39313444 | 0.027105868 |
| **WDR36** | 1.392827104 | 0.000892318 |
| **KITLG** | 1.392443103 | 0.005721467 |
| **CBL** | 1.391872572 | 0.022979515 |

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|---|---|---|
| **ZNF45** | 1.391769666 | 0.006469316 |
| **INTU** | 1.391232747 | 0.006951912 |
| **HIP1** | 1.39090042 | 0.007643175 |
| **ZBTB16** | 1.390364831 | 0.023700158 |
| **ETAA1** | 1.390207642 | 0.00428854 |
| **HECW2** | 1.389944178 | 0.009674447 |
| **RASA2** | 1.389521489 | 0.02633489 |
| **IRAK3** | 1.389250731 | 0.011290929 |
| **UVSSA** | 1.389161776 | 0.024069776 |
| **AMER2** | 1.389098161 | 0.022040256 |
| **NIN** | 1.388544949 | 0.028788498 |
| **ATP11B** | 1.388440742 | 0.001227029 |
| **FERMT1** | 1.388016775 | 0.018963427 |
| **AAK1** | 1.387955946 | 0.010994693 |
| **CASC1** | 1.387773109 | 0.018631539 |
| **CLN8** | 1.386830834 | 0.009664692 |
| **SLC38A1** | 1.3865324 | 0.009858217 |
| **BRWD3** | 1.386372586 | 0.006361441 |
| **KCND3** | 1.385648822 | 0.029876874 |
| **FAM168A** | 1.385413091 | 0.016321343 |
| **SCN3A** | 1.385247875 | 0.007640433 |
| **TNKS** | 1.38419906 | 0.001705164 |
| **AFAP1** | 1.384041524 | 0.020797838 |
| **CYP7B1** | 1.383136159 | 0.020323404 |
| **ELAVL2** | 1.383004163 | 0.002212115 |
| **IGSF9B** | 1.383000293 | 0.030456202 |
| **MTR** | 1.382525376 | 0.030456202 |
| **PTPRD** | 1.382073089 | 0.024363791 |
| **AFF4** | 1.381758758 | 0.002318461 |
| **RNPC3** | 1.381668148 | 0.00648968 |
| **CDH9** | 1.381521231 | 0.025084018 |
| **ZNF16** | 1.38089655 | 0.003960811 |
| **CNTRL** | 1.380659348 | 0.021300163 |
| **MTMR9** | 1.380337192 | 0.009513256 |
| **CHD6** | 1.380011236 | 0.008926783 |
| **MARCH6** | 1.379730015 | 0.014468853 |
| **PTPLB** | 1.379197675 | 0.022120754 |
| **DIP2A** | 1.377873328 | 0.017056121 |
| **ATRN** | 1.377857463 | 0.01212472 |
| **C2CD2** | 1.377773287 | 0.02061029 |

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|---|---|---|
| **ATG2B** | 1.377018366 | 0.001281582 |
| **SLC4A8** | 1.376997555 | 0.005528176 |
| **SMCHD1** | 1.376965674 | 0.000378597 |
| **UBN2** | 1.376481973 | 0.002919494 |
| **CEP63** | 1.375736518 | 0.00648968 |
| **BMPR2** | 1.37554421 | 0.025830266 |
| **ABCC4** | 1.375302506 | 0.033247749 |
| **TTC39C** | 1.37445701 | 0.01189794 |
| **RICTOR** | 1.374257181 | 0.004197473 |
| **RALGPS1** | 1.373968923 | 0.029461297 |
| **CNTNAP5** | 1.37394254 | 0.022979515 |
| **TCEANC2** | 1.37370544 | 0.026696033 |
| **ST8SIA1** | 1.373622966 | 0.007740931 |
| **SMAD9** | 1.37285168 | 0.009858217 |
| **GRIN2A** | 1.372312062 | 0.020142188 |
| **MAML2** | 1.372157286 | 0.020778341 |
| **TARBP1** | 1.371352361 | 0.004975442 |
| **ACER3** | 1.37097776 | 0.017017924 |
| **ZNF623** | 1.370347646 | 0.010852695 |
| **ATRX** | 1.370166232 | 0.006274202 |
| **ENTPD4** | 1.369995223 | 0.0197776 |
| **CXADR** | 1.369666785 | 0.017790469 |
| **FIGN** | 1.369646099 | 0.033389338 |
| **DGKE** | 1.369106579 | 0.031800085 |
| **GABRA2** | 1.368998883 | 0.004705909 |
| **BTAF1** | 1.368496151 | 0.008906854 |
| **TTC39B** | 1.3682814 | 0.028911221 |
| **GNAQ** | 1.36777497 | 0.028764432 |
| **GEN1** | 1.367262816 | 0.031451737 |
| **ZFC3H1** | 1.367248601 | 0.002318461 |
| **VPS53** | 1.367225415 | 0.022593859 |
| **ALG11** | 1.36715763 | 0.036659577 |
| **ERBB4** | 1.365770424 | 0.025084018 |
| **ADCY10** | 1.365757735 | 0.007640433 |
| **TCP11L1** | 1.365177568 | 0.023892993 |
| **C6orf141** | 1.363798425 | 0.02140671 |
| **ATM** | 1.363771032 | 0.007553939 |
| **EXPH5** | 1.363537057 | 0.029559575 |
| **RAPH1** | 1.362450963 | 0.018185236 |
| **HAUS3** | 1.362329614 | 0.033972225 |

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|---|---|---|
| **RAB23** | 1.362209335 | 0.021192371 |
| **C4orf29** | 1.361954871 | 0.022120754 |
| **PURB** | 1.361944805 | 0.039016286 |
| **RXFP1** | 1.361753655 | 0.031975336 |
| **SLC4A10** | 1.361581172 | 0.005944049 |
| **EIF2AK2** | 1.36021149 | 0.021848687 |
| **MGA** | 1.360069567 | 0.006416367 |
| **ZNF610** | 1.359825409 | 0.028534263 |
| **CEP350** | 1.359798424 | 0.009924803 |
| **KCNH8** | 1.359758553 | 0.030180473 |
| **ZBTB40** | 1.359319913 | 0.017950273 |
| **TSSK4** | 1.359088437 | 0.03274676 |
| **UGCG** | 1.358941646 | 0.025671159 |
| **RORA** | 1.358789764 | 0.004996376 |
| **ELOVL7** | 1.358376068 | 0.025084018 |
| **ST8SIA3** | 1.358348355 | 0.018569445 |
| **PHKA1** | 1.358335252 | 0.008436737 |
| **SGPP2** | 1.358297518 | 0.024843798 |
| **OPCML** | 1.357943128 | 0.010349222 |
| **MITF** | 1.357833302 | 0.036264465 |
| **TRIM44** | 1.357583545 | 0.007889473 |
| **ZNF704** | 1.35753147 | 0.031818025 |
| **EEF2K** | 1.356714062 | 0.034310397 |
| **AKT3** | 1.356596486 | 0.016855761 |
| **KIAA1549L** | 1.356406242 | 0.000297773 |
| **GPR113** | 1.356293033 | 0.028336583 |
| **FLT1** | 1.356219666 | 0.032943229 |
| **CEP85L** | 1.35603595 | 0.041240934 |
| **ZNF780A** | 1.355898699 | 0.0331433 |
| **TMEM245** | 1.355846474 | 0.002318461 |
| **CAMSAP2** | 1.355505259 | 0.001686657 |
| **KCNQ3** | 1.355494481 | 0.041374742 |
| **MBD5** | 1.355355304 | 0.005944049 |
| **DGKH** | 1.355240391 | 0.039562163 |
| **PIAS1** | 1.355096399 | 0.034765061 |
| **PBRM1** | 1.35497157 | 0.001705164 |
| **GLRA4** | 1.354578998 | 0.042404935 |
| **MSMP** | 1.353991402 | 0.028877571 |
| **PIK3CA** | 1.353970724 | 0.017500413 |
| **CCP110** | 1.353446325 | 0.002212115 |

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|---|---|---|
| **ENTPD5** | 1.353196853 | 0.037369311 |
| **ZC3H13** | 1.353111711 | 0.011755497 |
| **LRIG2** | 1.352997324 | 0.015447614 |
| **XRN1** | 1.352892146 | 0.007947364 |
| **GUCY1A2** | 1.352519782 | 0.016261403 |
| **WSB1** | 1.35196357 | 0.001705164 |
| **ADAMTS6** | 1.351736009 | 0.021510168 |
| **SSH1** | 1.351673308 | 0.041821533 |
| **WWC2** | 1.351210796 | 0.029070016 |
| **KCNB1** | 1.351151569 | 0.030107377 |
| **NCOA3** | 1.351115492 | 0.005174853 |
| **TMF1** | 1.351083469 | 0.011421403 |
| **WDFY3** | 1.350903277 | 0.007513568 |
| **PAK3** | 1.350823142 | 0.037489112 |
| **SYNRG** | 1.350148566 | 0.007957759 |
| **SV2C** | 1.349810317 | 0.022499184 |
| **MAP3K9** | 1.349527746 | 0.045013782 |
| **LRP1B** | 1.349491192 | 0.028700037 |
| **PLXDC2** | 1.349055631 | 0.045066388 |
| **KIAA1586** | 1.348921068 | 0.035619775 |
| **CTDSPL2** | 1.347686259 | 0.004927559 |
| **INTS2** | 1.347469037 | 0.015800261 |
| **GPR83** | 1.347385404 | 0.028762545 |
| **PHC3** | 1.347040011 | 0.00356776 |
| **RASAL2** | 1.34695349 | 0.002315348 |
| **PCLO** | 1.34690658 | 0.007813049 |
| **DOPEY1** | 1.346317518 | 0.01046166 |
| **TRANK1** | 1.346159275 | 0.034765061 |
| **OGFRL1** | 1.346140288 | 0.037964311 |
| **SIPA1L1** | 1.345925984 | 0.009244314 |
| **FKBP5** | 1.345873776 | 0.039811942 |
| **ZMAT3** | 1.345526402 | 0.030786595 |
| **SMC2** | 1.345509145 | 0.029874027 |
| **PHIP** | 1.345391659 | 0.007196388 |
| **OTUD4** | 1.345171509 | 0.002315348 |
| **LPCAT2** | 1.344793502 | 0.040386875 |
| **AVL9** | 1.34473507 | 0.045854294 |
| **SECISBP2L** | 1.344455989 | 0.006692614 |
| **TNIK** | 1.344245353 | 0.019611503 |
| **AKAP6** | 1.344024105 | 0.013759989 |

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|---|---|---|
| **TAF2** | 1.343949567 | 0.001705164 |
| **DMXL1** | 1.343568057 | 0.011775813 |
| **RC3H2** | 1.343562735 | 0.031648258 |
| **RAPGEF6** | 1.343311995 | 0.000378597 |
| **GSK3B** | 1.342824154 | 0.033288852 |
| **ANKRD52** | 1.342750264 | 0.029906945 |
| **BROX** | 1.342539824 | 0.030107377 |
| **ZNF236** | 1.342426936 | 0.010802779 |
| **PDZD8** | 1.342273787 | 0.030456202 |
| **PDS5B** | 1.34221681 | 0.005174853 |
| **MKL2** | 1.341878164 | 0.00428854 |
| **ERCC6L2** | 1.341754937 | 0.036611182 |
| **ODF2L** | 1.341376854 | 0.028214042 |
| **CENPF** | 1.341110589 | 0.038918656 |
| **CCSAP** | 1.340481881 | 0.021249213 |
| **WDFY2** | 1.340429331 | 0.042660196 |
| **BTBD7** | 1.339984329 | 0.046615139 |
| **AKAP11** | 1.339834457 | 0.013287069 |
| **TTPAL** | 1.339754242 | 0.024843798 |
| **KCNT2** | 1.339656692 | 0.040911557 |
| **CCDC80** | 1.339621123 | 0.035171404 |
| **ST18** | 1.339615861 | 0.008280206 |
| **ZNF33B** | 1.339496903 | 0.021249213 |
| **PITPNC1** | 1.339365108 | 0.028687065 |
| **PDPR** | 1.33922579 | 0.047017737 |
| **BDP1** | 1.339144521 | 0.038201547 |
| **SLC39A10** | 1.33890159 | 0.027867855 |
| **CAMK4** | 1.338884397 | 0.042548855 |
| **RAD54L2** | 1.338707457 | 0.037382551 |
| **POLK** | 1.338490045 | 0.039496042 |
| **DHX33** | 1.338091829 | 0.017950273 |
| **SLC12A6** | 1.337729122 | 0.024522575 |
| **TRMT44** | 1.337422331 | 0.035910039 |
| **PANK3** | 1.337055906 | 0.049403561 |
| **DCTN5** | 1.336548891 | 0.04050057 |
| **MED13** | 1.33647864 | 0.011498263 |
| **KLHL28** | 1.336379068 | 0.007947364 |
| **MAPK8** | 1.336331282 | 0.021300163 |
| **ZNF778** | 1.335910755 | 0.047451056 |
| **ZFP30** | 1.335593738 | 0.026199537 |

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|---|---|---|
| **RGS17** | 1.335486624 | 0.043209514 |
| **CLVS2** | 1.335386558 | 0.042126687 |
| **DYNC2H1** | 1.334783031 | 0.031547632 |
| **KAT6A** | 1.333941296 | 0.013722216 |
| **RIF1** | 1.333891887 | 0.040806463 |
| **ZNF609** | 1.333778644 | 0.004197473 |
| **OAS3** | 1.333663576 | 0.044758482 |
| **KIAA1109** | 1.333329207 | 0.014461968 |
| **CSMD1** | 1.332787764 | 0.018922672 |
| **LIMS1** | 1.332526083 | 0.039409174 |
| **HELZ** | 1.332508093 | 0.003882908 |
| **ZNF354B** | 1.332390294 | 0.025299478 |
| **USP45** | 1.331591819 | 0.030111451 |
| **PRKCI** | 1.330996956 | 0.004862503 |
| **LACC1** | 1.330967435 | 0.044729241 |
| **DMXL2** | 1.330891311 | 0.012347375 |
| **NF1** | 1.330445014 | 0.007640433 |
| **TRAF5** | 1.330108518 | 0.024408017 |
| **ACAP2** | 1.330045044 | 0.000283858 |
| **DICER1** | 1.329675031 | 0.011758399 |
| **ATE1** | 1.329373639 | 0.028627382 |
| **AASDH** | 1.32904139 | 0.007740931 |
| **RGS8** | 1.329007793 | 0.032711986 |
| **RNF168** | 1.328744908 | 0.039562163 |
| **SLC46A3** | 1.328199198 | 0.009858217 |
| **PTAR1** | 1.328006934 | 0.021861218 |
| **WDR37** | 1.327971923 | 0.003585441 |
| **SUSD5** | 1.327544746 | 0.034490759 |
| **PCYOX1** | 1.327510177 | 0.009464122 |
| **PCDHA9** | 1.32706052 | 0.038114863 |
| **ZBTB44** | 1.326149783 | 0.001227029 |
| **PVR** | 1.326096501 | 0.037974114 |
| **PCDHGC4** | 1.325579209 | 0.033831034 |
| **SORT1** | 1.32552064 | 0.034707422 |
| **MYO5A** | 1.325275713 | 0.009858217 |
| **IGF1R** | 1.325269597 | 0.009419791 |
| **ZNF81** | 1.325250976 | 0.048759874 |
| **PNMA2** | 1.32517149 | 0.038132417 |
| **CYP2D6** | 1.325034188 | 0.004927559 |
| **HTR2C** | 1.324899052 | 0.009306156 |

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|---|---|---|
| **CALCRL** | 1.324729381 | 0.039551961 |
| **CHD9** | 1.324024605 | 0.019816174 |
| **ARL5A** | 1.323699393 | 0.009120975 |
| **IQSEC3** | 1.323609991 | 0.00933751 |
| **SNX19** | 1.323559959 | 0.015698753 |
| **PLCXD3** | 1.322993421 | 0.033213799 |
| **PIGN** | 1.321605535 | 0.029876874 |
| **CPD** | 1.321502026 | 0.008926783 |
| **SLK** | 1.321303025 | 0.015103475 |
| **GRIP1** | 1.321053362 | 0.011775813 |
| **DHFR** | 1.320684047 | 0.010072491 |
| **SYT11** | 1.320611306 | 0.041936058 |
| **C14orf101** | 1.320313593 | 0.014284071 |
| **SMC5** | 1.319455935 | 0.0053165 |
| **YPEL2** | 1.319311613 | 0.033477246 |
| **SHROOM2** | 1.319174368 | 0.007772611 |
| **CDH19** | 1.319083017 | 0.021333769 |
| **PCDH7** | 1.318752058 | 0.011759109 |
| **PTPN4** | 1.318643406 | 0.004197473 |
| **AFF2** | 1.318591142 | 0.049869657 |
| **ZNF605** | 1.318402754 | 0.019645358 |
| **RFX7** | 1.318301024 | 0.011904999 |
| **KLHL36** | 1.318218859 | 0.045690716 |
| **ST8SIA4** | 1.318194242 | 0.028271767 |
| **FRMD5** | 1.318030896 | 0.013946966 |
| **PPIG** | 1.317972165 | 0.024550139 |
| **CREBZF** | 1.317628938 | 0.010344235 |
| **ZC3H6** | 1.317482694 | 0.006361441 |
| **SPATA13** | 1.317103112 | 0.018922672 |
| **ATAD2B** | 1.317008994 | 0.033867719 |
| **MED23** | 1.316531233 | 0.005581278 |
| **DIP2B** | 1.316500018 | 0.010444402 |
| **FNIP1** | 1.316481791 | 0.008738552 |
| **C2orf49** | 1.316330683 | 0.0260344 |
| **C5orf24** | 1.315975789 | 0.001705164 |
| **PLEKHA1** | 1.315856538 | 0.001705164 |
| **PXK** | 1.315812834 | 0.006283193 |
| **ZCCHC6** | 1.315531802 | 0.010233583 |
| **ATP8A1** | 1.31538828 | 0.006274202 |
| **ZMYM5** | 1.314927633 | 0.018610351 |

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|---|---|---|
| **BOD1L1** | 1.314658192 | 0.01509225 |
| **ZDHHC21** | 1.314629271 | 0.010349222 |
| **SMAD5** | 1.313513337 | 0.007640433 |
| **FBXL20** | 1.313131914 | 0.026476768 |
| **LARP1B** | 1.31294737 | 0.009858217 |
| **STX17** | 1.312850129 | 0.005864323 |
| **MTF1** | 1.312666201 | 0.026690313 |
| **MKLN1** | 1.312554967 | 0.038543469 |
| **PRKD3** | 1.312310557 | 0.022495251 |
| **TRAK2** | 1.312107016 | 0.003321961 |
| **IL6ST** | 1.312005193 | 0.017585805 |
| **PCDHB16** | 1.311974277 | 0.03364734 |
| **BIRC6** | 1.311939324 | 0.019962663 |
| **MIB1** | 1.311367719 | 0.006628549 |
| **FCHO2** | 1.31043578 | 0.01611736 |
| **RBM12B** | 1.310066128 | 0.011775813 |
| **INADL** | 1.309858981 | 0.028627382 |
| **TRIM66** | 1.309544442 | 0.013366911 |
| **DPY19L4** | 1.309129955 | 0.039616959 |
| **WHSC1L1** | 1.309073821 | 0.020955744 |
| **GMEB1** | 1.308770256 | 0.024869825 |
| **MORC3** | 1.308750741 | 0.005357908 |
| **CEP120** | 1.308489015 | 0.002214478 |
| **SYNJ1** | 1.308411402 | 0.004927559 |
| **PARP11** | 1.307571942 | 0.022706352 |
| **PRRC2C** | 1.307438048 | 0.011775813 |
| **CNTN1** | 1.307238405 | 0.043209514 |
| **SLC36A1** | 1.307172401 | 0.045707545 |
| **PEX5L** | 1.307172104 | 0.038605702 |
| **LIMD1** | 1.307137379 | 0.028600617 |
| **TOM1L1** | 1.306936499 | 0.034802506 |
| **QSER1** | 1.306892357 | 0.015262895 |
| **ZBTB6** | 1.306715968 | 0.041724696 |
| **ARHGEF12** | 1.306709965 | 0.013654591 |
| **PIKFYVE** | 1.306665943 | 0.013302586 |
| **NETO1** | 1.306501457 | 0.017356917 |
| **SCN1A** | 1.306356051 | 0.037396945 |
| **ZNF385D** | 1.306247663 | 0.04706971 |
| **IPP** | 1.306141854 | 0.039551961 |
| **CEP68** | 1.305647244 | 0.012259313 |

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|---|---|---|
| **SLC6A15** | 1.305578105 | 0.033213799 |
| **TM7SF3** | 1.305445016 | 0.029768662 |
| **MAP3K1** | 1.305371155 | 0.010349222 |
| **EEA1** | 1.305188541 | 0.017585805 |
| **CDH22** | 1.304948256 | 0.024733332 |
| **RSF1** | 1.304928968 | 0.047561271 |
| **NKTR** | 1.304813751 | 0.017179796 |
| **HEATR5A** | 1.304659664 | 0.048712798 |
| **SLC24A2** | 1.304386301 | 0.032133256 |
| **ATP13A3** | 1.30399994 | 0.003960811 |
| **PGAP1** | 1.303899062 | 0.045530897 |
| **XPO4** | 1.303882541 | 0.018300826 |
| **TRIM33** | 1.302576984 | 0.007422927 |
| **CNOT6L** | 1.301747963 | 0.006512065 |
| **AGAP1** | 1.301639847 | 0.004705909 |
| **ZNF595** | 1.301520316 | 0.013302586 |
| **SYNM** | 1.301097805 | 0.024700299 |
| **MED13L** | 1.301007659 | 0.018504389 |
| **ZC3H12C** | 1.300961293 | 0.0208074 |
| **VAV3** | 1.300558866 | 0.039841286 |
| **FUBP1** | 1.300523122 | 0.004906666 |
| **FRYL** | 1.300422217 | 0.020004919 |
| **CHL1** | 1.300018498 | 0.024636896 |
| **DENND4A** | 1.29974734 | 0.031387825 |
| **TMTC1** | 1.299520892 | 0.008196469 |
| **TMEM135** | 1.299195271 | 0.042837347 |
| **RBM33** | 1.298089836 | 0.007367696 |
| **ZFYVE16** | 1.297789591 | 0.012434463 |
| **WDR17** | 1.29728398 | 0.024843798 |
| **LPHN2** | 1.29722057 | 0.008929516 |
| **L3MBTL3** | 1.297144929 | 0.02061029 |
| **KIAA1432** | 1.297091692 | 0.004705909 |
| **GDAP1** | 1.296804952 | 0.003337376 |
| **TRIM68** | 1.29673987 | 0.049439942 |
| **RAB3C** | 1.296453726 | 0.037111037 |
| **EFR3A** | 1.296172083 | 0.006355846 |
| **FAM135A** | 1.296055238 | 0.037627102 |
| **ALG9** | 1.295593551 | 0.017398009 |
| **GATAD2B** | 1.295280206 | 0.019083741 |
| **KIDINS220** | 1.295156793 | 0.013931684 |

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|---|---|---|
| **GPR155** | 1.295114518 | 0.008223442 |
| **ZNF658** | 1.294173762 | 0.031986542 |
| **PPIL4** | 1.294172815 | 0.045377024 |
| **DST** | 1.294039716 | 0.020778341 |
| **HSPA4L** | 1.293404484 | 0.030438333 |
| **KSR2** | 1.293379456 | 0.034310397 |
| **ZNF518A** | 1.293339632 | 0.018845137 |
| **PTPRB** | 1.29294998 | 0.033780542 |
| **SEL1L** | 1.2928251 | 0.018601129 |
| **RNF165** | 1.29250758 | 0.04071399 |
| **SERTAD4** | 1.292261943 | 0.035313712 |
| **BCAP29** | 1.292091357 | 0.022747603 |
| **MFSD1** | 1.292024177 | 0.010022857 |
| **SPEN** | 1.291633835 | 0.009858217 |
| **ZNF175** | 1.291590821 | 0.01273978 |
| **ITGB8** | 1.291502362 | 0.037964311 |
| **LYST** | 1.291296459 | 0.021300163 |
| **SPTBN1** | 1.291234929 | 0.019773717 |
| **GIT2** | 1.291187639 | 0.039681624 |
| **ITGA6** | 1.291133834 | 0.039827396 |
| **TMEM246** | 1.290131112 | 0.027765088 |
| **CASP8AP2** | 1.290029462 | 0.011314611 |
| **ZNF451** | 1.289997263 | 0.006512065 |
| **CDON** | 1.289469092 | 0.022120754 |
| **ZFHX3** | 1.28926781 | 0.006274202 |
| **EP400** | 1.289162059 | 0.005864323 |
| **NR1D2** | 1.28882512 | 0.006940669 |
| **ASH1L** | 1.288357369 | 0.018961771 |
| **KIAA2026** | 1.28818451 | 0.008738552 |
| **STXBP5** | 1.288120698 | 0.008738552 |
| **NAV2** | 1.287626504 | 0.017790469 |
| **KLHL32** | 1.287574474 | 0.048480668 |
| **CPEB4** | 1.287389406 | 0.013057252 |
| **LRP12** | 1.287079341 | 0.008544808 |
| **CREBRF** | 1.286683112 | 0.005743726 |
| **C5orf51** | 1.286634386 | 0.011547303 |
| **ZBTB10** | 1.286387996 | 0.034071093 |
| **MYCBP2** | 1.286213035 | 0.024069776 |
| **CCNT1** | 1.286067841 | 0.010994693 |
| **NECAB1** | 1.286046388 | 0.012276413 |

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|---|---|---|
| **SLITRK4** | 1.285986933 | 0.014461968 |
| **GPR63** | 1.285785285 | 0.044647289 |
| **HAUS6** | 1.285489819 | 0.030786595 |
| **ZNF518B** | 1.285410397 | 0.017790469 |
| **ARL15** | 1.285205106 | 0.027122779 |
| **KCNQ2** | 1.285138915 | 0.043257316 |
| **NR2C2** | 1.28513648 | 0.005071953 |
| **ARFGEF1** | 1.284673137 | 0.006951912 |
| **BBX** | 1.284631715 | 0.016830547 |
| **MPP7** | 1.284315482 | 0.025145719 |
| **SESN3** | 1.284259021 | 0.007740931 |
| **SLC25A46** | 1.284054734 | 0.035627426 |
| **DHX36** | 1.284051517 | 0.005764462 |
| **CREB5** | 1.284050088 | 0.036110367 |
| **SREK1** | 1.283733299 | 0.004705909 |
| **UNC5C** | 1.28372201 | 0.024843798 |
| **CHM** | 1.28354499 | 0.00933751 |
| **GABRA4** | 1.283229939 | 0.020003817 |
| **SCAF11** | 1.283222917 | 0.00933751 |
| **MAP1B** | 1.282997666 | 0.006283193 |
| **ZNF737** | 1.282452115 | 0.047763479 |
| **C14orf37** | 1.281994034 | 0.041704015 |
| **FRMPD4** | 1.281963821 | 0.024889015 |
| **SLC12A2** | 1.28168136 | 0.016830547 |
| **STAM2** | 1.281600544 | 0.040192028 |
| **CDK6** | 1.281427665 | 0.029926471 |
| **EP300** | 1.281347465 | 0.020986884 |
| **BAZ2B** | 1.281224895 | 0.04050057 |
| **KBTBD7** | 1.280644215 | 0.04853813 |
| **ZNF667** | 1.280356336 | 0.042404935 |
| **HS6ST2** | 1.280287055 | 0.01509225 |
| **MID2** | 1.28010887 | 0.022941189 |
| **SPATA5** | 1.280046174 | 0.04087647 |
| **DNMT3A** | 1.279538564 | 0.039616959 |
| **C1orf173** | 1.279120299 | 0.029461297 |
| **WNK3** | 1.278957177 | 0.028983145 |
| **KIAA0226** | 1.278656143 | 0.027403715 |
| **FBN1** | 1.277612131 | 0.032368366 |
| **SLC4A4** | 1.277324436 | 0.01238385 |
| **CSMD2** | 1.277284695 | 0.038141254 |

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|---|---|---|
| **SCN2A** | 1.277134804 | 0.029926471 |
| **KLHL24** | 1.276968863 | 0.004927559 |
| **TRPS1** | 1.276689206 | 0.021107666 |
| **TMTC3** | 1.276385002 | 0.016094265 |
| **B3GALNT2** | 1.275972786 | 0.02600648 |
| **SLC30A1** | 1.27593246 | 0.04325497 |
| **MPDZ** | 1.275776198 | 0.044214917 |
| **ADAM10** | 1.27542896 | 0.037152417 |
| **TCF12** | 1.274957952 | 0.008223442 |
| **ZBTB43** | 1.274756544 | 0.010349222 |
| **PALM2** | 1.274479832 | 0.022979515 |
| **DOCK10** | 1.27427879 | 0.024888775 |
| **PRDM2** | 1.27402379 | 0.008929516 |
| **RSPRY1** | 1.273534705 | 0.041572276 |
| **VCPIP1** | 1.272754461 | 0.011904999 |
| **ARID5B** | 1.272553502 | 0.006283193 |
| **SLC35B4** | 1.272469132 | 0.024843798 |
| **HECTD2** | 1.272239112 | 0.011392688 |
| **TRIM2** | 1.272012678 | 0.007813049 |
| **ZNF558** | 1.271957285 | 0.028881801 |
| **PHACTR2** | 1.271615507 | 0.020469329 |
| **ETNK1** | 1.271510418 | 0.001307559 |
| **ATXN7** | 1.27130681 | 0.015371098 |
| **HOOK1** | 1.271219202 | 0.00356776 |
| **IPMK** | 1.271058094 | 0.010725123 |
| **ZDHHC20** | 1.270894224 | 0.025084018 |
| **ZKSCAN1** | 1.27078748 | 0.040844685 |
| **PPP2R5E** | 1.270646672 | 0.028267614 |
| **FAM91A1** | 1.270436253 | 0.004845055 |
| **ZNF286A** | 1.26991823 | 0.020797838 |
| **INPP4B** | 1.269568243 | 0.037974114 |
| **SYNJ2** | 1.269174342 | 0.009516825 |
| **MYSM1** | 1.269073067 | 0.030622276 |
| **FGD4** | 1.268539675 | 0.049991064 |
| **ZXDA** | 1.26852417 | 0.046488061 |
| **MON2** | 1.26753678 | 0.011904999 |
| **PPARGC1A** | 1.266578984 | 0.018504389 |
| **ACSL3** | 1.266493661 | 0.010740563 |
| **UBR2** | 1.266093637 | 0.008896528 |
| **ATP11A** | 1.265883954 | 0.031423199 |

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| **NMD3** | 1.265711229 | 0.019258381 |
| **PRKAR2B** | 1.26547271 | 0.040746781 |
| **TGFBRAP1** | 1.265100032 | 0.038583507 |
| **WDFY1** | 1.265044791 | 0.0197776 |
| **AHCTF1** | 1.264701904 | 0.018963427 |
| **CSRNP3** | 1.264526001 | 0.047017737 |
| **STARD13** | 1.264340496 | 0.038062101 |
| **DCX** | 1.264327805 | 0.005528176 |
| **SMURF2** | 1.264287551 | 0.034780685 |
| **NSD1** | 1.264217413 | 0.00708908 |
| **PEAK1** | 1.264130575 | 0.033213799 |
| **G2E3** | 1.264061995 | 0.011904999 |
| **KIAA1107** | 1.2638373 | 0.033129238 |
| **TBC1D12** | 1.263526492 | 0.018845137 |
| **MCF2** | 1.262972554 | 0.011758399 |
| **CCDC88A** | 1.262816474 | 0.01843272 |
| **ERCC4** | 1.262618136 | 0.012494107 |
| **ARHGAP32** | 1.261862171 | 0.022503896 |
| **PLXNA2** | 1.261838177 | 0.044688937 |
| **KDM6A** | 1.261771758 | 0.011514438 |
| **TAB3** | 1.261482675 | 0.013376019 |
| **MGAT4A** | 1.260535105 | 0.007177071 |
| **SNX13** | 1.260411138 | 0.015598748 |
| **LIMCH1** | 1.260339686 | 0.008929516 |
| **PPP1R12B** | 1.260278536 | 0.014951896 |
| **HACE1** | 1.260159298 | 0.021910856 |
| **TNKS2** | 1.260082002 | 0.01154469 |
| **ERC1** | 1.259628931 | 0.016917525 |
| **ABCC5** | 1.259111766 | 0.017697646 |
| **NBEAL1** | 1.258499833 | 0.047500506 |
| **FAM208A** | 1.258070187 | 0.013528136 |
| **MANEA** | 1.2579844 | 0.020314828 |
| **FRS2** | 1.257849778 | 0.016830547 |
| **C11orf30** | 1.257260389 | 0.022120754 |
| **RAPGEF5** | 1.25704955 | 0.01617865 |
| **KIF21B** | 1.256971261 | 0.030180473 |
| **APC** | 1.256669648 | 0.028700037 |
| **ANKRD17** | 1.256606792 | 0.009791123 |
| **RPE** | 1.256569012 | 0.013063266 |
| **UTP14C** | 1.25646869 | 0.009483478 |

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|---|---|---|
| **PEG3** | 1.25512053 | 0.045712194 |
| **FZD4** | 1.255019595 | 0.024404766 |
| **SEMA4D** | 1.254938311 | 0.020048282 |
| **DHX8** | 1.254836363 | 0.029906945 |
| **KIAA1715** | 1.254725453 | 0.022120754 |
| **HUWE1** | 1.254482164 | 0.020627408 |
| **TBC1D8B** | 1.254317513 | 0.028762545 |
| **ZNF507** | 1.254224016 | 0.009858217 |
| **HCFC2** | 1.254215856 | 0.019976196 |
| **MFAP3** | 1.253776224 | 0.00978058 |
| **GLTSCR1L** | 1.253717853 | 0.026349829 |
| **ARID4B** | 1.253507199 | 0.00579249 |
| **TANC2** | 1.253245369 | 0.011755497 |
| **NUFIP2** | 1.252858541 | 0.009858217 |
| **UGGT1** | 1.252770835 | 0.005528176 |
| **CEP170** | 1.252625863 | 0.04540026 |
| **PRKAA1** | 1.252474882 | 0.015264404 |
| **TACC1** | 1.252402518 | 0.009858217 |
| **IQCE** | 1.251778509 | 0.009068636 |
| **PPIP5K2** | 1.251436908 | 0.029559575 |
| **ASAP1** | 1.251360007 | 0.035197882 |
| **UBR4** | 1.251346119 | 0.019200024 |
| **LONRF2** | 1.251340991 | 0.020406554 |
| **AMIGO1** | 1.25125313 | 0.03167939 |
| **ATRNL1** | 1.251249243 | 0.037843038 |
| **FMR1** | 1.251231648 | 0.007008428 |
| **LPPR4** | 1.250999357 | 0.028788498 |
| **KIAA1671** | 1.250853025 | 0.039099141 |
| **SENP5** | 1.250686236 | 0.025145719 |
| **NBN** | 1.250000199 | 0.012375988 |
| **TAOK1** | 1.249798148 | 0.016335896 |
| **FRMD4B** | 1.249202258 | 0.021440816 |
| **PCNX** | 1.249109225 | 0.018995172 |
| **PPARGC1B** | 1.249009231 | 0.044647289 |
| **GPR12** | 1.248985247 | 0.024838192 |
| **KBTBD6** | 1.248832329 | 0.013104295 |
| **HERC2** | 1.248221584 | 0.008908212 |
| **CASD1** | 1.248118108 | 0.020731913 |
| **FOXN3** | 1.247892888 | 0.031986542 |
| **SPIN3** | 1.247871624 | 0.010894901 |

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|---|---|---|
| **ZBTB1** | 1.247813353 | 0.012866146 |
| **PCMTD2** | 1.247810319 | 0.042974724 |
| **DCC** | 1.247642649 | 0.042837347 |
| **ATXN1L** | 1.247580578 | 0.017179796 |
| **RNF180** | 1.247400053 | 0.021300163 |
| **TRRAP** | 1.247346632 | 0.030092009 |
| **CADM2** | 1.247270036 | 0.007640433 |
| **RNF19A** | 1.247200512 | 0.011904999 |
| **RAB11FIP2** | 1.246947799 | 0.007947364 |
| **EIF5A2** | 1.246585544 | 0.048149624 |
| **GOSR1** | 1.246514996 | 0.009837756 |
| **SMC1A** | 1.246409081 | 0.016665762 |
| **ZBTB38** | 1.246313962 | 0.00933751 |
| **ARNT** | 1.246071861 | 0.022790993 |
| **AQR** | 1.246018568 | 0.047504944 |
| **PARP4** | 1.246002346 | 0.038201547 |
| **XK** | 1.245695227 | 0.047843982 |
| **TTC3** | 1.244287414 | 0.004705909 |
| **C5orf42** | 1.244261287 | 0.034490759 |
| **RAD50** | 1.243738131 | 0.028222741 |
| **KIAA0895** | 1.24346969 | 0.042245446 |
| **BAZ2A** | 1.243390837 | 0.025299478 |
| **LIN52** | 1.242848204 | 0.028267614 |
| **KANSL1L** | 1.242606707 | 0.009650066 |
| **PHC1** | 1.242528547 | 0.024926507 |
| **RBM41** | 1.242496775 | 0.009975717 |
| **LEMD3** | 1.242433731 | 0.019083741 |
| **NUP153** | 1.242386814 | 0.034490759 |
| **MYT1L** | 1.241996774 | 0.028490089 |
| **SMARCAD1** | 1.241902653 | 0.007947364 |
| **B4GALT6** | 1.241323819 | 0.022040256 |
| **DIS3** | 1.241029798 | 0.022236163 |
| **ZNF772** | 1.240979437 | 0.034390387 |
| **FBXO42** | 1.240806079 | 0.040806463 |
| **CERS6** | 1.240631567 | 0.011068238 |
| **APBB2** | 1.239618168 | 0.042404935 |
| **PHF6** | 1.239616844 | 0.011758399 |
| **CDK17** | 1.239362744 | 0.003960811 |
| **KIAA0947** | 1.239031399 | 0.021510168 |
| **MACF1** | 1.238977655 | 0.036611182 |

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|---|---|---|
| **TNPO1** | 1.238946475 | 0.012144282 |
| **FAM199X** | 1.238884456 | 0.006283193 |
| **LRRC7** | 1.238842232 | 0.017790469 |
| **GPD2** | 1.238625311 | 0.032943229 |
| **ASCC3** | 1.238393038 | 0.025145719 |
| **USP36** | 1.23828859 | 0.049103485 |
| **FAT3** | 1.238281987 | 0.030491366 |
| **PPM1A** | 1.237786392 | 0.005379835 |
| **TMEM56** | 1.237732154 | 0.01843272 |
| **CHD1** | 1.237184845 | 0.008738552 |
| **ERCC6** | 1.236385775 | 0.032288351 |
| **TOPBP1** | 1.236331258 | 0.015244012 |
| **EYA3** | 1.236171549 | 0.039959033 |
| **PPM1H** | 1.236141691 | 0.013376019 |
| **DIXDC1** | 1.235923675 | 0.021643751 |
| **RALGAPA1** | 1.235554763 | 0.034274483 |
| **CREB1** | 1.235195209 | 0.007643175 |
| **ZNF280D** | 1.234965735 | 0.011755497 |
| **HERC1** | 1.234680811 | 0.048937224 |
| **STAG2** | 1.234351061 | 0.026707587 |
| **PIK3C2B** | 1.234231206 | 0.027451534 |
| **SBNO1** | 1.234126429 | 0.031975336 |
| **EDEM3** | 1.234065472 | 0.038132417 |
| **UBXN2B** | 1.234019404 | 0.007640433 |
| **ARHGEF7** | 1.233470204 | 0.022593859 |
| **IPO9** | 1.233432747 | 0.017033456 |
| **ZNF224** | 1.233138397 | 0.030456202 |
| **ABCA8** | 1.232948714 | 0.035078673 |
| **DLGAP1** | 1.232943614 | 0.025299478 |
| **DENND5B** | 1.232424019 | 0.042974724 |
| **RPS6KC1** | 1.232381238 | 0.004815335 |
| **PNISR** | 1.232133562 | 0.019442042 |
| **NCOA6** | 1.231818655 | 0.002328705 |
| **UFL1** | 1.231762686 | 0.015001581 |
| **PIK3R3** | 1.231507066 | 0.022120754 |
| **STT3B** | 1.231406077 | 0.023760021 |
| **SON** | 1.230611445 | 0.010349222 |
| **ZNF841** | 1.230587986 | 0.022593859 |
| **STK4** | 1.23033319 | 0.025084018 |
| **JMY** | 1.230157131 | 0.015774316 |

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|---|---|---|
| **TMEM178B** | 1.229904183 | 0.044049095 |
| **ZZZ3** | 1.229683651 | 0.0154935 |
| **SEC22C** | 1.229625515 | 0.00557412 |
| **USP13** | 1.229261827 | 0.024172564 |
| **ZBTB11** | 1.229147632 | 0.034319095 |
| **USP24** | 1.228993059 | 0.0254104 |
| **HECTD1** | 1.228344125 | 0.022979515 |
| **KIAA1841** | 1.228211654 | 0.039099141 |
| **RUNX1T1** | 1.228167629 | 0.028188019 |
| **DOCK3** | 1.227892487 | 0.012420195 |
| **SH3PXD2A** | 1.227172626 | 0.028490089 |
| **FRY** | 1.226639046 | 0.006749576 |
| **ELMSAN1** | 1.22659878 | 0.041198245 |
| **RAPGEF2** | 1.226200023 | 0.025576935 |
| **MXD1** | 1.225619326 | 0.018848125 |
| **DNM3** | 1.225351642 | 0.022120754 |
| **VLDLR** | 1.225297732 | 0.015262895 |
| **ZEB1** | 1.225294435 | 0.018569445 |
| **CREBBP** | 1.225211739 | 0.024843798 |
| **KAT6B** | 1.225073597 | 0.023671884 |
| **CLIP4** | 1.224556671 | 0.025299478 |
| **SEC24A** | 1.224519944 | 0.037152417 |
| **TJP1** | 1.224463676 | 0.026579975 |
| **SPRY3** | 1.224135697 | 0.0372105 |
| **UBR5** | 1.224045884 | 0.040633654 |
| **RAP1GAP2** | 1.223999496 | 0.040386875 |
| **ZNF655** | 1.223795495 | 0.023809367 |
| **PPP1R2** | 1.223711086 | 0.009494836 |
| **GABRG2** | 1.223688216 | 0.038583507 |
| **YLPM1** | 1.222272414 | 0.01509225 |
| **NR3C1** | 1.22204784 | 0.038576747 |
| **PRRC2B** | 1.22157409 | 0.015082084 |
| **FAM178A** | 1.22125426 | 0.013057252 |
| **SPECC1** | 1.221199196 | 0.042993582 |
| **CDK12** | 1.220972135 | 0.043045425 |
| **SLC3A1** | 1.220421452 | 0.047986903 |
| **CHIC1** | 1.220190388 | 0.00499119 |
| **CHAMP1** | 1.220050466 | 0.015056659 |
| **NPHP3** | 1.219901081 | 0.040806463 |
| **JPH1** | 1.21965894 | 0.032133256 |

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|---|---|---|
| **PCF11** | 1.219575472 | 0.022294975 |
| **CEP104** | 1.219441101 | 0.022120754 |
| **GABRB2** | 1.219412595 | 0.034765061 |
| **MAPK10** | 1.218253966 | 0.02061029 |
| **ANK3** | 1.218188728 | 0.008738552 |
| **KLHDC5** | 1.218067465 | 0.015160482 |
| **FAM76B** | 1.217661087 | 0.048937224 |
| **UPRT** | 1.217410939 | 0.045712194 |
| **WAPAL** | 1.217187164 | 0.012918559 |
| **PKN2** | 1.217066693 | 0.029842595 |
| **UBR1** | 1.217025927 | 0.034310397 |
| **SPAG9** | 1.216894873 | 0.043312737 |
| **ZFYVE26** | 1.216832306 | 0.020384098 |
| **MLLT3** | 1.216735075 | 0.030033624 |
| **ZFP91** | 1.216530517 | 0.005143666 |
| **UHMK1** | 1.216337346 | 0.029909873 |
| **TAF1** | 1.216241611 | 0.02473979 |
| **ATF6** | 1.215913209 | 0.032496254 |
| **OCRL** | 1.215804007 | 0.024295157 |
| **USP32** | 1.215579413 | 0.042112092 |
| **CCDC66** | 1.215546949 | 0.021510168 |
| **GRIA2** | 1.215396164 | 0.037880394 |
| **EPG5** | 1.21510216 | 0.040069905 |
| **CHD2** | 1.214744098 | 0.016830547 |
| **SCN8A** | 1.214244469 | 0.031975336 |
| **TFDP2** | 1.21414274 | 0.022120754 |
| **ATP6V1A** | 1.213964065 | 0.036385322 |
| **CACNB4** | 1.213901198 | 0.043335822 |
| **GPRASP1** | 1.213820312 | 0.040806463 |
| **ZNF398** | 1.213746115 | 0.025084018 |
| **PCYT1B** | 1.213743448 | 0.019816174 |
| **ANKFY1** | 1.213718728 | 0.012840137 |
| **ATR** | 1.213697548 | 0.028911221 |
| **FAM115A** | 1.213351499 | 0.039562163 |
| **ZNF644** | 1.213230589 | 0.020986884 |
| **CCSER2** | 1.213181575 | 0.02038572 |
| **CIT** | 1.212896157 | 0.007697271 |
| **LATS1** | 1.212610583 | 0.024427672 |
| **CLIP1** | 1.212497047 | 0.021000091 |
| **TSNAX** | 1.212370117 | 0.039616959 |

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| **ATIC** | 1.212309523 | 0.032051314 |
| **TRIP12** | 1.212273811 | 0.018642178 |
| **RBM25** | 1.212243175 | 0.035618859 |
| **SPATS2** | 1.211355402 | 0.023034374 |
| **CPSF6** | 1.210924564 | 0.028956163 |
| **LBR** | 1.210274323 | 0.027748588 |
| **GALC** | 1.210212422 | 0.048090535 |
| **RLIM** | 1.209983505 | 0.022344274 |
| **FBXO28** | 1.209743639 | 0.005528176 |
| **LPIN2** | 1.209633739 | 0.001705164 |
| **IDS** | 1.209200018 | 0.028914709 |
| **PHF3** | 1.209128468 | 0.038201547 |
| **ZNF445** | 1.20908181 | 0.027351121 |
| **POGZ** | 1.208803487 | 0.0260344 |
| **TXLNG** | 1.208647518 | 0.025084018 |
| **PHF8** | 1.208624154 | 0.038019273 |
| **USP8** | 1.207952525 | 0.028700037 |
| **MICAL3** | 1.2078995 | 0.0208074 |
| **KDM3A** | 1.207739325 | 0.008481259 |
| **CDK19** | 1.207625529 | 0.038605702 |
| **AKAP10** | 1.207239516 | 0.016830547 |
| **CDK13** | 1.207186304 | 0.011758399 |
| **TRIM23** | 1.207090969 | 0.007718681 |
| **SP1** | 1.207018792 | 0.033767591 |
| **SRCIN1** | 1.20673612 | 0.038396482 |
| **FRMD4A** | 1.206534742 | 0.02036697 |
| **ZC3H11A** | 1.206455975 | 0.017500413 |
| **SETD7** | 1.206286751 | 0.026349829 |
| **LRRC58** | 1.206000724 | 0.028267614 |
| **IREB2** | 1.205877925 | 0.013528136 |
| **PRKCE** | 1.205503956 | 0.041845896 |
| **CSNK1G3** | 1.205256761 | 0.039208454 |
| **VPS37A** | 1.205106812 | 0.045399573 |
| **RAB33B** | 1.204945429 | 0.041907979 |
| **CENPC1** | 1.204849229 | 0.045690716 |
| **ZNF540** | 1.204803861 | 0.044941921 |
| **PNMAL1** | 1.204486923 | 0.031296614 |
| **BTBD3** | 1.204290233 | 0.0197776 |
| **IBTK** | 1.204265539 | 0.010478752 |
| **RPRD2** | 1.204062218 | 0.018642178 |

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|---|---|---|
| **MLL5** | 1.203969696 | 0.038370049 |
| **MECP2** | 1.203680846 | 0.030585393 |
| **PRPF4B** | 1.203668084 | 0.028600617 |
| **NUPL1** | 1.203275152 | 0.016222844 |
| **SLC31A1** | 1.20317689 | 0.028895225 |
| **TTC14** | 1.201950767 | 0.025671159 |
| **ARHGAP21** | 1.201910619 | 0.02473979 |
| **RALGAPB** | 1.201838068 | 0.02600648 |
| **PRR14L** | 1.201336437 | 0.02956126 |
| **DNM3** | 1.225351642 | 0.022120754 |
| **VLDLR** | 1.225297732 | 0.015262895 |
| **ZEB1** | 1.225294435 | 0.018569445 |
| **CREBBP** | 1.225211739 | 0.024843798 |
| **KAT6B** | 1.225073597 | 0.023671884 |
| **CLIP4** | 1.224556671 | 0.025299478 |
| **SEC24A** | 1.224519944 | 0.037152417 |
| **TJP1** | 1.224463676 | 0.026579975 |
| **SPRY3** | 1.224135697 | 0.0372105 |
| **UBR5** | 1.224045884 | 0.040633654 |
| **RAP1GAP2** | 1.223999496 | 0.040386875 |
| **ZNF655** | 1.223795495 | 0.023809367 |
| **PPP1R2** | 1.223711086 | 0.009494836 |
| **GABRG2** | 1.223688216 | 0.038583507 |
| **YLPM1** | 1.222272414 | 0.01509225 |
| **NR3C1** | 1.22204784 | 0.038576747 |
| **PRRC2B** | 1.22157409 | 0.015082084 |
| **FAM178A** | 1.22125426 | 0.013057252 |
| **SPECC1** | 1.221199196 | 0.042993582 |
| **CDK12** | 1.220972135 | 0.043045425 |
| **SLC3A1** | 1.220421452 | 0.047986903 |
| **CHIC1** | 1.220190388 | 0.00499119 |
| **CHAMP1** | 1.220050466 | 0.015056659 |
| **NPHP3** | 1.219901081 | 0.040806463 |
| **JPH1** | 1.21965894 | 0.032133256 |
| **PCF11** | 1.219575472 | 0.022294975 |
| **CEP104** | 1.219441101 | 0.022120754 |
| **GABRB2** | 1.219412595 | 0.034765061 |
| **MAPK10** | 1.218253966 | 0.02061029 |
| **ANK3** | 1.218188728 | 0.008738552 |
| **KLHDC5** | 1.218067465 | 0.015160482 |

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| **FAM76B** | 1.217661087 | 0.048937224 |
| **UPRT** | 1.217410939 | 0.045712194 |
| **WAPAL** | 1.217187164 | 0.012918559 |
| **PKN2** | 1.217066693 | 0.029842595 |
| **UBR1** | 1.217025927 | 0.034310397 |
| **SPAG9** | 1.216894873 | 0.043312737 |
| **ZFYVE26** | 1.216832306 | 0.020384098 |
| **MLLT3** | 1.216735075 | 0.030033624 |
| **ZFP91** | 1.216530517 | 0.005143666 |
| **UHMK1** | 1.216337346 | 0.029909873 |
| **TAF1** | 1.216241611 | 0.02473979 |
| **ATF6** | 1.215913209 | 0.032496254 |
| **OCRL** | 1.215804007 | 0.024295157 |
| **USP32** | 1.215579413 | 0.042112092 |
| **CCDC66** | 1.215546949 | 0.021510168 |
| **GRIA2** | 1.215396164 | 0.037880394 |
| **EPG5** | 1.21510216 | 0.040069905 |
| **CHD2** | 1.214744098 | 0.016830547 |
| **SCN8A** | 1.214244469 | 0.031975336 |
| **TFDP2** | 1.21414274 | 0.022120754 |
| **ATP6V1A** | 1.213964065 | 0.036385322 |
| **CACNB4** | 1.213901198 | 0.043335822 |
| **GPRASP1** | 1.213820312 | 0.040806463 |
| **ZNF398** | 1.213746115 | 0.025084018 |
| **PCYT1B** | 1.213743448 | 0.019816174 |
| **ANKFY1** | 1.213718728 | 0.012840137 |
| **ATR** | 1.213697548 | 0.028911221 |
| **FAM115A** | 1.213351499 | 0.039562163 |
| **ZNF644** | 1.213230589 | 0.020986884 |
| **CCSER2** | 1.213181575 | 0.02038572 |
| **CIT** | 1.212896157 | 0.007697271 |
| **LATS1** | 1.212610583 | 0.024427672 |
| **CLIP1** | 1.212497047 | 0.021000091 |
| **TSNAX** | 1.212370117 | 0.039616959 |
| **ATIC** | 1.212309523 | 0.032051314 |
| **TRIP12** | 1.212273811 | 0.018642178 |
| **RBM25** | 1.212243175 | 0.035618859 |
| **SPATS2** | 1.211355402 | 0.023034374 |
| **CPSF6** | 1.210924564 | 0.028956163 |
| **LBR** | 1.210274323 | 0.027748588 |

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| **GALC** | 1.210212422 | 0.048090535 |
| **RLIM** | 1.209983505 | 0.022344274 |
| **FBXO28** | 1.209743639 | 0.005528176 |
| **LPIN2** | 1.209633739 | 0.001705164 |
| **IDS** | 1.209200018 | 0.028914709 |
| **PHF3** | 1.209128468 | 0.038201547 |
| **ZNF445** | 1.20908181 | 0.027351121 |
| **POGZ** | 1.208803487 | 0.0260344 |
| **TXLNG** | 1.208647518 | 0.025084018 |
| **PHF8** | 1.208624154 | 0.038019273 |
| **USP8** | 1.207952525 | 0.028700037 |
| **MICAL3** | 1.2078995 | 0.0208074 |
| **KDM3A** | 1.207739325 | 0.008481259 |
| **CDK19** | 1.207625529 | 0.038605702 |
| **AKAP10** | 1.207239516 | 0.016830547 |
| **CDK13** | 1.207186304 | 0.011758399 |
| **TRIM23** | 1.207090969 | 0.007718681 |
| **SP1** | 1.207018792 | 0.033767591 |
| **SRCIN1** | 1.20673612 | 0.038396482 |
| **FRMD4A** | 1.206534742 | 0.02036697 |
| **ZC3H11A** | 1.206455975 | 0.017500413 |
| **SETD7** | 1.206286751 | 0.026349829 |
| **LRRC58** | 1.206000724 | 0.028267614 |
| **IREB2** | 1.205877925 | 0.013528136 |
| **PRKCE** | 1.205503956 | 0.041845896 |
| **CSNK1G3** | 1.205256761 | 0.039208454 |
| **VPS37A** | 1.205106812 | 0.045399573 |
| **RAB33B** | 1.204945429 | 0.041907979 |
| **CENPC1** | 1.204849229 | 0.045690716 |
| **ZNF540** | 1.204803861 | 0.044941921 |
| **PNMAL1** | 1.204486923 | 0.031296614 |
| **BTBD3** | 1.204290233 | 0.0197776 |
| **IBTK** | 1.204265539 | 0.010478752 |
| **RPRD2** | 1.204062218 | 0.018642178 |
| **MLL5** | 1.203969696 | 0.038370049 |
| **MECP2** | 1.203680846 | 0.030585393 |
| **PRPF4B** | 1.203668084 | 0.028600617 |
| **NUPL1** | 1.203275152 | 0.016222844 |
| **SLC31A1** | 1.20317689 | 0.028895225 |
| **TTC14** | 1.201950767 | 0.025671159 |

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| **ARHGAP21** | 1.201910619 | 0.02473979 |
| **RALGAPB** | 1.201838068 | 0.02600648 |
| **PRR14L** | 1.201336437 | 0.02956126 |
| **GPRASP1** | 1.213820312 | 0.040806463 |
| **ZNF398** | 1.213746115 | 0.025084018 |
| **PCYT1B** | 1.213743448 | 0.019816174 |
| **ANKFY1** | 1.213718728 | 0.012840137 |
| **ATR** | 1.213697548 | 0.028911221 |
| **FAM115A** | 1.213351499 | 0.039562163 |
| **ZNF644** | 1.213230589 | 0.020986884 |
| **CCSER2** | 1.213181575 | 0.02038572 |
| **CIT** | 1.212896157 | 0.007697271 |
| **LATS1** | 1.212610583 | 0.024427672 |
| **CLIP1** | 1.212497047 | 0.021000091 |
| **TSNAX** | 1.212370117 | 0.039616959 |
| **ATIC** | 1.212309523 | 0.032051314 |
| **TRIP12** | 1.212273811 | 0.018642178 |
| **RBM25** | 1.212243175 | 0.035618859 |
| **SPATS2** | 1.211355402 | 0.023034374 |
| **CPSF6** | 1.210924564 | 0.028956163 |
| **LBR** | 1.210274323 | 0.027748588 |
| **GALC** | 1.210212422 | 0.048090535 |
| **RLIM** | 1.209983505 | 0.022344274 |
| **FBXO28** | 1.209743639 | 0.005528176 |
| **LPIN2** | 1.209633739 | 0.001705164 |
| **IDS** | 1.209200018 | 0.028914709 |
| **PHF3** | 1.209128468 | 0.038201547 |
| **ZNF445** | 1.20908181 | 0.027351121 |
| **POGZ** | 1.208803487 | 0.0260344 |
| **TXLNG** | 1.208647518 | 0.025084018 |
| **PHF8** | 1.208624154 | 0.038019273 |
| **USP8** | 1.207952525 | 0.028700037 |
| **MICAL3** | 1.2078995 | 0.0208074 |
| **KDM3A** | 1.207739325 | 0.008481259 |
| **CDK19** | 1.207625529 | 0.038605702 |
| **AKAP10** | 1.207239516 | 0.016830547 |
| **CDK13** | 1.207186304 | 0.011758399 |
| **TRIM23** | 1.207090969 | 0.007718681 |
| **SP1** | 1.207018792 | 0.033767591 |
| **SRCIN1** | 1.20673612 | 0.038396482 |

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|---|---|---|
| **FRMD4A** | 1.206534742 | 0.02036697 |
| **ZC3H11A** | 1.206455975 | 0.017500413 |
| **SETD7** | 1.206286751 | 0.026349829 |
| **LRRC58** | 1.206000724 | 0.028267614 |
| **IREB2** | 1.205877925 | 0.013528136 |
| **PRKCE** | 1.205503956 | 0.041845896 |
| **CSNK1G3** | 1.205256761 | 0.039208454 |
| **VPS37A** | 1.205106812 | 0.045399573 |
| **RAB33B** | 1.204945429 | 0.041907979 |
| **CENPC1** | 1.204849229 | 0.045690716 |
| **ZNF540** | 1.204803861 | 0.044941921 |
| **PNMAL1** | 1.204486923 | 0.031296614 |
| **BTBD3** | 1.204290233 | 0.0197776 |
| **IBTK** | 1.204265539 | 0.010478752 |
| **RPRD2** | 1.204062218 | 0.018642178 |
| **MLL5** | 1.203969696 | 0.038370049 |
| **MECP2** | 1.203680846 | 0.030585393 |
| **PRPF4B** | 1.203668084 | 0.028600617 |
| **NUPL1** | 1.203275152 | 0.016222844 |
| **SLC31A1** | 1.20317689 | 0.028895225 |
| **TTC14** | 1.201950767 | 0.025671159 |
| **ARHGAP21** | 1.201910619 | 0.02473979 |
| **RALGAPB** | 1.201838068 | 0.02600648 |
| **PRR14L** | 1.201336437 | 0.02956126 |
| **GPRASP1** | 1.213820312 | 0.040806463 |
| **ZNF398** | 1.213746115 | 0.025084018 |
| **PCYT1B** | 1.213743448 | 0.019816174 |
| **ANKFY1** | 1.213718728 | 0.012840137 |
| **ATR** | 1.213697548 | 0.028911221 |
| **FAM115A** | 1.213351499 | 0.039562163 |
| **ZNF644** | 1.213230589 | 0.020986884 |
| **CCSER2** | 1.213181575 | 0.02038572 |
| **CIT** | 1.212896157 | 0.007697271 |
| **LATS1** | 1.212610583 | 0.024427672 |
| **CLIP1** | 1.212497047 | 0.021000091 |
| **TSNAX** | 1.212370117 | 0.039616959 |
| **ATIC** | 1.212309523 | 0.032051314 |
| **TRIP12** | 1.212273811 | 0.018642178 |
| **RBM25** | 1.212243175 | 0.035618859 |
| **SPATS2** | 1.211355402 | 0.023034374 |

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|---|---|---|
| **CPSF6** | 1.210924564 | 0.028956163 |
| **LBR** | 1.210274323 | 0.027748588 |
| **GALC** | 1.210212422 | 0.048090535 |
| **RLIM** | 1.209983505 | 0.022344274 |
| **FBXO28** | 1.209743639 | 0.005528176 |
| **LPIN2** | 1.209633739 | 0.001705164 |
| **IDS** | 1.209200018 | 0.028914709 |
| **PHF3** | 1.209128468 | 0.038201547 |
| **ZNF445** | 1.20908181 | 0.027351121 |
| **POGZ** | 1.208803487 | 0.0260344 |
| **TXLNG** | 1.208647518 | 0.025084018 |
| **PHF8** | 1.208624154 | 0.038019273 |
| **USP8** | 1.207952525 | 0.028700037 |
| **MICAL3** | 1.2078995 | 0.0208074 |
| **KDM3A** | 1.207739325 | 0.008481259 |
| **CDK19** | 1.207625529 | 0.038605702 |
| **AKAP10** | 1.207239516 | 0.016830547 |
| **CDK13** | 1.207186304 | 0.011758399 |
| **TRIM23** | 1.207090969 | 0.007718681 |
| **SP1** | 1.207018792 | 0.033767591 |
| **SRCIN1** | 1.20673612 | 0.038396482 |
| **FRMD4A** | 1.206534742 | 0.02036697 |
| **ZC3H11A** | 1.206455975 | 0.017500413 |
| **SETD7** | 1.206286751 | 0.026349829 |
| **LRRC58** | 1.206000724 | 0.028267614 |
| **IREB2** | 1.205877925 | 0.013528136 |
| **PRKCE** | 1.205503956 | 0.041845896 |
| **CSNK1G3** | 1.205256761 | 0.039208454 |
| **VPS37A** | 1.205106812 | 0.045399573 |
| **RAB33B** | 1.204945429 | 0.041907979 |
| **CENPC1** | 1.204849229 | 0.045690716 |
| **ZNF540** | 1.204803861 | 0.044941921 |
| **PNMAL1** | 1.204486923 | 0.031296614 |
| **BTBD3** | 1.204290233 | 0.0197776 |
| **IBTK** | 1.204265539 | 0.010478752 |
| **RPRD2** | 1.204062218 | 0.018642178 |
| **MLL5** | 1.203969696 | 0.038370049 |
| **MECP2** | 1.203680846 | 0.030585393 |
| **PRPF4B** | 1.203668084 | 0.028600617 |
| **NUPL1** | 1.203275152 | 0.016222844 |

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|---|---|---|
| **SLC31A1** | 1.20317689 | 0.028895225 |
| **TTC14** | 1.201950767 | 0.025671159 |
| **ARHGAP21** | 1.201910619 | 0.02473979 |
| **RALGAPB** | 1.201838068 | 0.02600648 |
| **PRR14L** | 1.201336437 | 0.02956126 |
| **GPRASP1** | 1.213820312 | 0.040806463 |
| **ZNF398** | 1.213746115 | 0.025084018 |
| **PCYT1B** | 1.213743448 | 0.019816174 |
| **ANKFY1** | 1.213718728 | 0.012840137 |
| **ATR** | 1.213697548 | 0.028911221 |
| **FAM115A** | 1.213351499 | 0.039562163 |
| **ZNF644** | 1.213230589 | 0.020986884 |
| **CCSER2** | 1.213181575 | 0.02038572 |
| **CIT** | 1.212896157 | 0.007697271 |
| **LATS1** | 1.212610583 | 0.024427672 |
| **CLIP1** | 1.212497047 | 0.021000091 |
| **TSNAX** | 1.212370117 | 0.039616959 |
| **ATIC** | 1.212309523 | 0.032051314 |
| **TRIP12** | 1.212273811 | 0.018642178 |
| **RBM25** | 1.212243175 | 0.035618859 |
| **SPATS2** | 1.211355402 | 0.023034374 |
| **CPSF6** | 1.210924564 | 0.028956163 |
| **LBR** | 1.210274323 | 0.027748588 |
| **GALC** | 1.210212422 | 0.048090535 |
| **RLIM** | 1.209983505 | 0.022344274 |
| **FBXO28** | 1.209743639 | 0.005528176 |
| **LPIN2** | 1.209633739 | 0.001705164 |
| **IDS** | 1.209200018 | 0.028914709 |
| **PHF3** | 1.209128468 | 0.038201547 |
| **ZNF445** | 1.20908181 | 0.027351121 |
| **POGZ** | 1.208803487 | 0.0260344 |
| **TXLNG** | 1.208647518 | 0.025084018 |
| **PHF8** | 1.208624154 | 0.038019273 |
| **USP8** | 1.207952525 | 0.028700037 |
| **MICAL3** | 1.2078995 | 0.0208074 |
| **KDM3A** | 1.207739325 | 0.008481259 |
| **CDK19** | 1.207625529 | 0.038605702 |
| **AKAP10** | 1.207239516 | 0.016830547 |
| **CDK13** | 1.207186304 | 0.011758399 |
| **TRIM23** | 1.207090969 | 0.007718681 |

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|---|---|---|
| **SP1** | 1.207018792 | 0.033767591 |
| **SRCIN1** | 1.20673612 | 0.038396482 |
| **FRMD4A** | 1.206534742 | 0.02036697 |
| **ZC3H11A** | 1.206455975 | 0.017500413 |
| **SETD7** | 1.206286751 | 0.026349829 |
| **LRRC58** | 1.206000724 | 0.028267614 |
| **IREB2** | 1.205877925 | 0.013528136 |
| **PRKCE** | 1.205503956 | 0.041845896 |
| **CSNK1G3** | 1.205256761 | 0.039208454 |
| **VPS37A** | 1.205106812 | 0.045399573 |
| **RAB33B** | 1.204945429 | 0.041907979 |
| **CENPC1** | 1.204849229 | 0.045690716 |
| **ZNF540** | 1.204803861 | 0.044941921 |
| **PNMAL1** | 1.204486923 | 0.031296614 |
| **BTBD3** | 1.204290233 | 0.0197776 |
| **IBTK** | 1.204265539 | 0.010478752 |
| **RPRD2** | 1.204062218 | 0.018642178 |
| **MLL5** | 1.203969696 | 0.038370049 |
| **MECP2** | 1.203680846 | 0.030585393 |
| **PRPF4B** | 1.203668084 | 0.028600617 |
| **NUPL1** | 1.203275152 | 0.016222844 |
| **SLC31A1** | 1.20317689 | 0.028895225 |
| **TTC14** | 1.201950767 | 0.025671159 |
| **ARHGAP21** | 1.201910619 | 0.02473979 |
| **RALGAPB** | 1.201838068 | 0.02600648 |
| **PRR14L** | 1.201336437 | 0.02956126 |

| **Gene ID** | **Down-Regulated Genes**<br>**Fold Change** | **Adjusted P-value** |
|---|---|---|
| **CST3** | -1.579323303 | 0.000332706 |
| **PHLDB3** | -1.552853957 | 0.00579249 |
| **MZT2B** | -1.536438182 | 0.001008709 |
| **EGR2** | -1.529422034 | 0.005528176 |
| **C7orf50** | -1.512690694 | 0.001307559 |
| **ROMO1** | -1.50989593 | 0.001686657 |
| **CFD** | -1.503180345 | 0.007367696 |
| **SLC2A8** | -1.496112221 | 0.001281582 |
| **PARD6A** | -1.485261304 | 0.000939807 |
| **REEP6** | -1.480062655 | 0.003338795 |
| **RPL35** | -1.47099459 | 0.001281582 |

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|---|---|---|
| **PCSK1** | -1.466128483 | 0.009858217 |
| **TMEM45A** | -1.464570208 | 0.012464937 |
| **HSD17B6** | -1.462273616 | 1.20504E-07 |
| **ORAI1** | -1.459694013 | 0.00648968 |
| **ASGR1** | -1.457283189 | 0.006820981 |
| **SHD** | -1.456420438 | 0.012935763 |
| **MAMU-DRA** | -1.451049191 | 0.013528136 |
| **C8orf82** | -1.446412213 | 0.004815335 |
| **FAM83D** | -1.442107076 | 0.011392688 |
| **PTRHD1** | -1.44089265 | 0.00716266 |
| **EXOSC6** | -1.440328555 | 0.009674847 |
| **POLR2L** | -1.436581348 | 0.004705909 |
| **CCDC85B** | -1.433238859 | 0.005528176 |
| **RPS19BP1** | -1.430779623 | 0.006600468 |
| **TRAPPC5** | -1.430131101 | 0.003170335 |
| **TMED1** | -1.428991266 | 0.001987043 |
| **VMO1** | -1.427190413 | 0.011498263 |
| **HRAS** | -1.424488778 | 0.004815335 |
| **HSPE1** | -1.424430657 | 0.000283858 |
| **CRADD** | -1.419969736 | 0.001705164 |
| **CBR3** | -1.418657213 | 0.011904999 |
| **FXYD1** | -1.414282618 | 0.008544808 |
| **MYEOV2** | -1.413767577 | 0.016009534 |
| **TMEM256** | -1.413102363 | 0.012810041 |
| **DOHH** | -1.412040003 | 0.002318461 |
| **C1QL1** | -1.409538365 | 0.005379835 |
| **C16orf13** | -1.406931128 | 0.005071953 |
| **IQCA1** | -1.405564396 | 0.020920438 |
| **LAMTOR4** | -1.405378349 | 0.004610624 |
| **TMEM141** | -1.404633968 | 0.005764462 |
| **DCXR** | -1.403557606 | 0.004790873 |
| **PARD6G** | -1.403359235 | 0.017594157 |
| **CBY3** | -1.402624224 | 0.017697646 |
| **RPS2** | -1.402062675 | 0.00499119 |
| **SCAND1** | -1.397957936 | 0.004790873 |
| **APRT** | -1.395008228 | 0.006371191 |
| **MACROD1** | -1.394788601 | 0.011068238 |
| **ABT1** | -1.394319266 | 0.005286173 |
| **PRADC1** | -1.393632666 | 0.004705909 |
| **ARL2** | -1.392393176 | 0.001686657 |

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|---|---|---|
| **MRPS12** | -1.392238644 | 0.004815335 |
| **SDS** | -1.391797274 | 0.025084018 |
| **TMEM219** | -1.391014642 | 0.005864323 |
| **TXNRD2** | -1.39087805 | 0.006274202 |
| **IFT43** | -1.390248093 | 0.002318461 |
| **IGFLR1** | -1.389094429 | 0.022120754 |
| **GRHPR** | -1.389020585 | 0.002212115 |
| **TST** | -1.388657376 | 0.010994693 |
| **AURKAIP1** | -1.388290453 | 0.005101244 |
| **TMEM160** | -1.388194475 | 0.007367696 |
| **POLR2F** | -1.388120338 | 0.000283858 |
| **GDF1** | -1.386445535 | 0.003960811 |
| **RPS27L** | -1.385035365 | 0.013104295 |
| **CD74** | -1.385025644 | 0.028956163 |
| **C1orf122** | -1.383568005 | 0.004948341 |
| **CTXN1** | -1.382610081 | 0.004790873 |
| **MPST** | -1.382607405 | 0.008908212 |
| **JUNB** | -1.382476411 | 0.030778793 |
| **ALKBH7** | -1.382454944 | 0.006771791 |
| **ATP5D** | -1.381858339 | 0.00579249 |
| **COX7A1** | -1.380147454 | 0.011904999 |
| **RPS15** | -1.379182908 | 0.007553939 |
| **C2orf80** | -1.37787918 | 0.007388573 |
| **LYRM4** | -1.377518956 | 0.009484345 |
| **SSNA1** | -1.375908703 | 0.009484345 |
| **MAD2L2** | -1.375863002 | 0.001705164 |
| **AEBP1** | -1.375193871 | 0.026741357 |
| **PPIF** | -1.374916592 | 0.011904999 |
| **RAMP1** | -1.374723333 | 0.003338795 |
| **PRR7** | -1.37469023 | 0.007374591 |
| **CENPM** | -1.374517378 | 0.004927559 |
| **SIVA1** | -1.3744774 | 0.006940669 |
| **NDUFB7** | -1.374127911 | 0.004705909 |
| **SPATA2L** | -1.373763894 | 0.004815335 |
| **EGR4** | -1.373261599 | 0.028222741 |
| **FAM195A** | -1.37313051 | 0.005864323 |
| **FKBP2** | -1.373063801 | 0.006283193 |
| **GSTT1** | -1.372635492 | 0.018601129 |
| **SIRT3** | -1.372486196 | 0.002082672 |
| **SLC26A11** | -1.372392625 | 0.022991663 |

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|---|---|---|
| **JOSD2** | -1.371965946 | 0.0154935 |
| **GP1BB** | -1.371938325 | 0.017356917 |
| **PET100** | -1.371063214 | 0.003451947 |
| **MRPL24** | -1.370748079 | 0.007207603 |
| **C19orf24** | -1.370647707 | 0.009473895 |
| **ZNF593** | -1.369872072 | 0.007947364 |
| **RPS21** | -1.368103545 | 0.014535379 |
| **CHCHD5** | -1.367040361 | 0.009120975 |
| **PTPMT1** | -1.366327458 | 0.004705909 |
| **HMG20B** | -1.36526523 | 0.00648968 |
| **ZSWIM7** | -1.365225503 | 0.014084693 |
| **RNF208** | -1.364105467 | 0.002919494 |
| **TIMM13** | -1.364066131 | 0.006283193 |
| **SMKR1** | -1.363577522 | 0.004705909 |
| **LRRC24** | -1.362692381 | 0.005864323 |
| **GRASP** | -1.36188401 | 0.005143666 |
| **RND1** | -1.361243826 | 0.00716266 |
| **GCK** | -1.361040892 | 0.021643751 |
| **MPC2** | -1.360565917 | 0.00067063 |
| **SLIRP** | -1.360349714 | 0.005724196 |
| **FBLN1** | -1.358977388 | 0.023897048 |
| **PHPT1** | -1.358548344 | 0.010368881 |
| **RGS10** | -1.357214682 | 0.017500413 |
| **HSD17B10** | -1.357039736 | 0.002919494 |
| **UBE2S** | -1.356938052 | 0.004705909 |
| **MRPL52** | -1.356878388 | 0.004705909 |
| **NDUFS6** | -1.356513772 | 0.010448715 |
| **BRI3** | -1.356442418 | 0.011290929 |
| **CKS1B** | -1.356419514 | 0.020004919 |
| **BATF** | -1.356033091 | 0.010548212 |
| **FIBIN** | -1.354912539 | 0.017056121 |
| **MT3** | -1.354541544 | 0.014951896 |
| **ABHD14A** | -1.35443416 | 0.006749576 |
| **COX4I1** | -1.354220239 | 0.008738552 |
| **WDR18** | -1.354074262 | 0.003631906 |
| **ECI1** | -1.353726955 | 0.005439944 |
| **RPL12** | -1.353174482 | 0.005143666 |
| **C1QTNF4** | -1.352939105 | 0.008065485 |
| **ALKBH2** | -1.352155428 | 0.008738552 |
| **ETFB** | -1.352101039 | 0.025599792 |

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|---|---|---|
| **NDUFA7** | -1.351949968 | 0.01273978 |
| **ARC** | -1.351729203 | 0.029768568 |
| **SIK1** | -1.35134729 | 0.04391025 |
| **RPUSD3** | -1.35118096 | 0.002315348 |
| **CPLX1** | -1.350573506 | 0.018601129 |
| **LSM7** | -1.350487964 | 0.004705909 |
| **MRPS34** | -1.349856083 | 0.007015186 |
| **TUBB4B** | -1.349146319 | 0.000260465 |
| **SERF2** | -1.348867434 | 0.006283193 |
| **CDK2AP2** | -1.348650475 | 0.001686657 |
| **CYBASC3** | -1.348435091 | 0.019653 |
| **RPS9** | -1.348259737 | 0.013104295 |
| **DPM3** | -1.348142016 | 0.014164739 |
| **STUB1** | -1.347848285 | 0.003338795 |
| **NUTF2** | -1.346697807 | 0.000260465 |
| **RPUSD1** | -1.346188347 | 0.005528176 |
| **MED16** | -1.346033152 | 6.1474E-05 |
| **NLE1** | -1.345900577 | 0.002184831 |
| **APOE** | -1.344743254 | 0.005146403 |
| **B3GAT3** | -1.344727722 | 0.002988616 |
| **RNF25** | -1.344384333 | 0.004705909 |
| **PSMB4** | -1.343905224 | 0.001227029 |
| **RPS5** | -1.34385196 | 0.010802779 |
| **ITPA** | -1.343792489 | 0.010802779 |
| **NPC2** | -1.343670708 | 0.007422927 |
| **EIF3G** | -1.343568203 | 0.002318461 |
| **FRZB** | -1.343517717 | 0.0104728 |
| **EMC10** | -1.34288665 | 0.01509225 |
| **ALG1** | -1.342550192 | 0.011498263 |
| **CKB** | -1.34195482 | 0.011758399 |
| **ENDOG** | -1.341932099 | 0.010072491 |
| **ENHO** | -1.341518238 | 0.008738552 |
| **CLU** | -1.341183564 | 0.006953418 |
| **IFI30** | -1.340642977 | 0.045399573 |
| **KCNF1** | -1.33934215 | 0.008896528 |
| **UFSP1** | -1.338807242 | 0.041335063 |
| **SLC7A10** | -1.338295456 | 0.002212115 |
| **PGLS** | -1.337624875 | 0.010183285 |
| **C17orf62** | -1.337461047 | 0.003321961 |
| **ENTPD2** | -1.337234579 | 0.028687065 |

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|---|---|---|
| **MNF1** | -1.337160159 | 0.007553939 |
| **TOMM22** | -1.33691796 | 0.003338795 |
| **ZNF703** | -1.336594768 | 0.026906514 |
| **ADRA2C** | -1.336467353 | 0.011904999 |
| **DEXI** | -1.336320753 | 0.009674447 |
| **RPS23** | -1.336157009 | 0.008896528 |
| **MANF** | -1.336128383 | 0.005864323 |
| **SSR4** | -1.335751498 | 0.007367696 |
| **MATK** | -1.335322901 | 0.008431285 |
| **COX6B1** | -1.335168877 | 0.012661285 |
| **MRPS21** | -1.335057466 | 0.006274202 |
| **DUT** | -1.334928621 | 0.004497921 |
| **C20orf27** | -1.334762554 | 0.008738552 |
| **SNRPC** | -1.334716701 | 0.048615487 |
| **TIMM17B** | -1.334535578 | 0.01238385 |
| **COMMD4** | -1.333937875 | 0.00933751 |
| **SPA17** | -1.333911043 | 0.036110367 |
| **FBXW5** | -1.333523285 | 0.000977913 |
| **C19orf10** | -1.333294102 | 0.001705164 |
| **COX8A** | -1.332263862 | 0.0104728 |
| **PPDPF** | -1.332089907 | 0.010320849 |
| **TYROBP** | -1.332019071 | 0.019442042 |
| **PCDH8** | -1.331829094 | 0.025566529 |
| **GUK1** | -1.331685182 | 0.009645686 |
| **TMEM208** | -1.331488992 | 0.005999958 |
| **ZNF428** | -1.331440605 | 0.006951912 |
| **MYL6** | -1.331375046 | 0.00408181 |
| **BAD** | -1.331208351 | 0.013722216 |
| **NOSIP** | -1.330917362 | 0.012918559 |
| **RELB** | -1.330574974 | 0.029926471 |
| **PRR5** | -1.330154095 | 0.028762545 |
| **HOMER3** | -1.328958863 | 0.020532054 |
| **NDUFAF3** | -1.32829167 | 0.004815335 |
| **SERTAD1** | -1.327952643 | 0.028687065 |
| **TMUB1** | -1.327587461 | 0.006807379 |
| **POLB** | -1.327239476 | 0.001987043 |
| **H2AFJ** | -1.327199733 | 0.010802779 |
| **HSPBP1** | -1.326751058 | 0.005528176 |
| **PRDX6** | -1.326613626 | 0.008839611 |
| **KCNJ4** | -1.326575911 | 0.00648968 |

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|---|---|---|
| **GADD45GIP1** | -1.325779486 | 0.013722216 |
| **TM7SF2** | -1.325325655 | 0.021300163 |
| **KRTCAP2** | -1.324868011 | 0.010478752 |
| **NDUFA13** | -1.324433124 | 0.011112425 |
| **FAU** | -1.324351098 | 0.018601129 |
| **DUSP23** | -1.323843099 | 0.018031969 |
| **CDC34** | -1.323805236 | 0.004996376 |
| **B9D2** | -1.323731894 | 0.02037913 |
| **AGMAT** | -1.323710744 | 0.039476401 |
| **NME3** | -1.323667039 | 0.010349222 |
| **FAM181B** | -1.32357742 | 0.034490759 |
| **NOL12** | -1.323518593 | 0.007740931 |
| **BLOC1S1** | -1.323089094 | 0.006361441 |
| **MRPS17** | -1.322411819 | 0.010337378 |
| **NUBP2** | -1.321726429 | 0.016434578 |
| **SELENBP1** | -1.321685529 | 0.030989759 |
| **AIF1** | -1.321471762 | 0.028914709 |
| **MLST8** | -1.321406269 | 0.008436737 |
| **CCDC124** | -1.321112608 | 0.007015186 |
| **FBL** | -1.320827866 | 0.00716266 |
| **ANAPC15** | -1.320766544 | 0.009686658 |
| **PDLIM2** | -1.320742271 | 0.030989759 |
| **SURF1** | -1.320077911 | 0.030391073 |
| **TMEM234** | -1.319979562 | 0.039726395 |
| **C1orf86** | -1.319840454 | 0.041907979 |
| **TSPO** | -1.319712002 | 0.024473606 |
| **LIN7B** | -1.319096047 | 0.009513256 |
| **MDP1** | -1.318791207 | 0.022787837 |
| **MEA1** | -1.318781764 | 0.003000553 |
| **TECR** | -1.318542288 | 0.007015186 |
| **TALDO1** | -1.318338587 | 0.010072491 |
| **PCYT2** | -1.318246892 | 0.001705164 |
| **NHP2** | -1.318110608 | 0.00978058 |
| **VPS28** | -1.318047852 | 0.014584219 |
| **TMSB10** | -1.31772499 | 0.011904999 |
| **C9orf116** | -1.317414464 | 0.045884167 |
| **GADD45B** | -1.317297706 | 0.033910856 |
| **TMEM121** | -1.31703157 | 0.024024264 |
| **FTH1** | -1.316174176 | 0.013538157 |
| **FAM108A1** | -1.316168091 | 0.025830266 |

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|---|---|---|
| **HIGD2A** | -1.315932446 | 0.005528176 |
| **TMEM176A** | -1.315756068 | 0.0176241 |
| **SEC61G** | -1.315652447 | 0.008963882 |
| **ANAPC11** | -1.31549719 | 0.012918559 |
| **SERP2** | -1.315466963 | 0.009120975 |
| **PSMC3** | -1.315115388 | 0.012145374 |
| **EXOSC7** | -1.315096787 | 0.02157716 |
| **PHB** | -1.314949519 | 0.007642703 |
| **BUD31** | -1.314940301 | 0.011759109 |
| **TMEM205** | -1.314884941 | 0.005764462 |
| **NDUFS7** | -1.314859757 | 0.004975442 |
| **NTHL1** | -1.314357319 | 0.016830547 |
| **EDF1** | -1.314217726 | 0.009484345 |
| **ITPKA** | -1.314111124 | 0.009858217 |
| **SNTA1** | -1.313850858 | 0.010937717 |
| **SF3B5** | -1.313369269 | 0.014234648 |
| **DENND1C** | -1.312993485 | 0.048937224 |
| **RPS29** | -1.312872404 | 0.018963427 |
| **PTGES2** | -1.312587009 | 0.01238385 |
| **RHBDL1** | -1.312061554 | 0.019875258 |
| **RBFA** | -1.31199212 | 0.016358074 |
| **PEX7** | -1.311737839 | 0.022695615 |
| **MRPL51** | -1.311712625 | 0.005761571 |
| **C2orf40** | -1.311483831 | 0.032499619 |
| **H2AFX** | -1.310935613 | 0.005528176 |
| **PDRG1** | -1.31088816 | 0.00708908 |
| **AIP** | -1.310701908 | 0.001705164 |
| **SLC25A26** | -1.310382676 | 0.034599778 |
| **NR4A1** | -1.310250105 | 0.04853813 |
| **PHB2** | -1.310240067 | 0.005967608 |
| **UQCR11** | -1.309859016 | 0.039972944 |
| **PACSIN3** | -1.309735965 | 0.021440816 |
| **PNKD** | -1.309704191 | 0.008929516 |
| **TMEM223** | -1.309377527 | 0.023649965 |
| **RPS16** | -1.309232363 | 0.022120754 |
| **ECHS1** | -1.309206951 | 0.011714793 |
| **NDUFB2** | -1.309205791 | 0.017056121 |
| **AGTRAP** | -1.308684393 | 0.017639148 |
| **ZNHIT1** | -1.308479603 | 0.010183285 |
| **SPATA7** | -1.30832326 | 0.012734442 |

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|---|---|---|
| **TBCB** | -1.30812721 | 0.005174853 |
| **COX7B** | -1.308031136 | 0.002919494 |
| **UBL5** | -1.307867447 | 0.002376061 |
| **CCDC28B** | -1.307535774 | 0.016358074 |
| **PFDN5** | -1.307509618 | 0.01271268 |
| **RPL23A** | -1.307275143 | 0.021019507 |
| **DNTTIP1** | -1.306428033 | 0.01273978 |
| **TMEM54** | -1.306310065 | 0.041422552 |
| **FCER1G** | -1.306239041 | 0.042178739 |
| **RABAC1** | -1.306183447 | 0.013003832 |
| **PKIG** | -1.306000519 | 0.005721467 |
| **PQLC1** | -1.305426468 | 0.007642703 |
| **NTMT1** | -1.305080523 | 0.010919179 |
| **EIF3K** | -1.305017436 | 0.013149612 |
| **PTGDS** | -1.304575785 | 0.029569222 |
| **CCDC137** | -1.304171703 | 0.006361441 |
| **PPP1R1A** | -1.304149115 | 0.021616352 |
| **MIF** | -1.304077001 | 0.019026727 |
| **TNFSF12** | -1.303982317 | 0.023648978 |
| **ECI2** | -1.303927636 | 0.005581278 |
| **ATP5E** | -1.303648885 | 0.033801571 |
| **UQCRQ** | -1.303267096 | 0.022457893 |
| **GAL3ST3** | -1.303028312 | 0.018845137 |
| **EMC6** | -1.302928398 | 0.021300163 |
| **TOMM34** | -1.302816242 | 0.0197776 |
| **COA3** | -1.302787642 | 0.007772611 |
| **SLC25A6** | -1.302556887 | 0.024408017 |
| **PTRH1** | -1.302515033 | 0.028956163 |
| **ZNF787** | -1.30250061 | 0.006042284 |
| **RTN2** | -1.30228784 | 0.020920438 |
| **CDK5** | -1.302080625 | 0.010183285 |
| **FAM96B** | -1.301992465 | 0.008488596 |
| **RHOC** | -1.301904486 | 0.016830547 |
| **NDUFA3** | -1.30189904 | 0.027202306 |
| **MYL6B** | -1.300555581 | 0.019083741 |
| **FBXL15** | -1.300501153 | 0.022120754 |
| **PSMB3** | -1.299986988 | 0.019528828 |
| **NDUFS3** | -1.298950747 | 0.023103073 |
| **FAM89B** | -1.298337388 | 0.007642703 |
| **MRPL53** | -1.298140558 | 0.007553939 |

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| **FBXO44** | -1.297638521 | 0.002315348 |
| **SNRPD2** | -1.297588383 | 0.004197473 |
| **NDUFS8** | -1.297524354 | 0.011998934 |
| **RPL24** | -1.29744509 | 0.022016651 |
| **PSMB6** | -1.297422117 | 0.01189794 |
| **MPG** | -1.297074569 | 0.036922982 |
| **ADRM1** | -1.29679955 | 0.007104761 |
| **NGDN** | -1.296771172 | 0.006355846 |
| **TXNL4A** | -1.296377148 | 0.010175543 |
| **UBB** | -1.296356439 | 0.001705164 |
| **C17orf59** | -1.296188951 | 0.021793564 |
| **SRM** | -1.296056625 | 0.008109344 |
| **CD83** | -1.296004564 | 0.04831562 |
| **RPS11** | -1.295520558 | 0.019664823 |
| **RPS14** | -1.29547624 | 0.014683261 |
| **RPS19** | -1.295142554 | 0.030640533 |
| **ECH1** | -1.294855212 | 0.002315348 |
| **RPL18A** | -1.294680273 | 0.020484963 |
| **C1orf50** | -1.29466378 | 0.019505289 |
| **RPS28** | -1.294415871 | 0.039892554 |
| **PRELID1** | -1.294287917 | 0.006240872 |
| **CCDC34** | -1.294230285 | 0.016358074 |
| **ETHE1** | -1.294195715 | 0.018876175 |
| **CUTA** | -1.294064562 | 0.022706352 |
| **GAS2L1** | -1.29385997 | 0.002919494 |
| **C12orf52** | -1.293655843 | 0.008302472 |
| **RPSA** | -1.29352301 | 0.033458617 |
| **COX5B** | -1.293460039 | 0.034657669 |
| **TSEN34** | -1.293458252 | 0.007947364 |
| **U2AF1** | -1.293403817 | 0.003960811 |
| **C21orf2** | -1.293275723 | 0.028700037 |
| **ATP5G1** | -1.293195916 | 0.007642703 |
| **TOMM6** | -1.293076544 | 0.015657328 |
| **SIL1** | -1.293071567 | 0.011758399 |
| **FARS2** | -1.292769698 | 0.016478819 |
| **WDR45** | -1.29270529 | 0.007813049 |
| **PRDX5** | -1.292624408 | 0.022120754 |
| **MRPL48** | -1.29261465 | 0.005864323 |
| **RPLP2** | -1.292247033 | 0.031827418 |
| **GABARAP** | -1.292207125 | 0.010349222 |

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|---|---|---|
| **GNG3** | -1.292138346 | 0.01617865 |
| **ZFAND2B** | -1.29188305 | 0.005143666 |
| **METTL5** | -1.291851223 | 0.017585805 |
| **PSMB7** | -1.291518786 | 0.008929516 |
| **MGST3** | -1.291420283 | 0.011904999 |
| **EXOSC5** | -1.291384639 | 0.024843798 |
| **TADA3** | -1.291381538 | 0.00648968 |
| **CA11** | -1.291379045 | 0.029874027 |
| **RPS20** | -1.291349213 | 0.025090749 |
| **NUDT14** | -1.291340429 | 0.031621476 |
| **ARL4D** | -1.291228362 | 0.026087349 |
| **COX16** | -1.291149416 | 0.029319466 |
| **EXOSC1** | -1.291039284 | 0.017790469 |
| **BCAP31** | -1.291019753 | 0.002315348 |
| **TBCA** | -1.290530501 | 0.021577117 |
| **C1orf35** | -1.290524874 | 0.006940669 |
| **DMAP1** | -1.290448776 | 0.008544808 |
| **POLR3H** | -1.28989315 | 0.022120754 |
| **PCP4** | -1.289745696 | 0.028956163 |
| **CYP27A1** | -1.289496812 | 0.009278048 |
| **TOMM40** | -1.289433702 | 0.005528176 |
| **ZMYND19** | -1.289405318 | 0.016899872 |
| **PSMG4** | -1.289400119 | 0.029461297 |
| **C6orf1** | -1.28897408 | 0.008962951 |
| **PSMB1** | -1.288913685 | 0.010344235 |
| **FIS1** | -1.288847672 | 0.028741105 |
| **TWF2** | -1.288674015 | 0.007889473 |
| **POLR2J** | -1.28857932 | 0.010814494 |
| **ETNK2** | -1.28852546 | 0.049403561 |
| **APOA1BP** | -1.288502073 | 0.009721356 |
| **FNDC4** | -1.288414695 | 0.009363274 |
| **NENF** | -1.288277677 | 0.038583507 |
| **CEND1** | -1.287832681 | 0.00933751 |
| **MRPS18B** | -1.287611487 | 0.010349222 |
| **CCDC106** | -1.287591735 | 0.009023694 |
| **SERTAD3** | -1.287578798 | 0.017808515 |
| **CLTB** | -1.287362342 | 0.009858217 |
| **UBXN11** | -1.287266854 | 0.011904999 |
| **TSR3** | -1.287211856 | 0.043280808 |
| **LRRC73** | -1.286967342 | 0.014584219 |

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| **CHCHD1** | -1.286929466 | 0.007643175 |
| **RPL26L1** | -1.286838892 | 0.01509225 |
| **PES1** | -1.286723287 | 0.009674447 |
| **TAF10** | -1.286714119 | 0.008738552 |
| **JTB** | -1.286358955 | 0.011759109 |
| **HINT1** | -1.285903041 | 0.009328953 |
| **UBXN1** | -1.28588399 | 0.007772611 |
| **TFPT** | -1.285856109 | 0.034621609 |
| **RPLP1** | -1.285656138 | 0.028914709 |
| **NDUFV1** | -1.285419067 | 0.008962951 |
| **RPRML** | -1.285356449 | 0.01633502 |
| **RPS13** | -1.285130988 | 0.025090749 |
| **BPHL** | -1.285059128 | 0.019083741 |
| **MRPL54** | -1.28485792 | 0.042993582 |
| **MRPL4** | -1.284697239 | 0.00902338 |
| **AKR1B1** | -1.284577868 | 0.016091525 |
| **ZFPM1** | -1.284480163 | 0.028473573 |
| **RPL27A** | -1.28443521 | 0.032368366 |
| **GPC1** | -1.284266511 | 0.000260465 |
| **TEX264** | -1.284233953 | 0.014471142 |
| **PPP4C** | -1.284065948 | 0.005581278 |
| **PPP1CA** | -1.284014375 | 0.007581438 |
| **FADS3** | -1.283961715 | 0.015719724 |
| **SNRNP25** | -1.283930876 | 0.019645358 |
| **NAA10** | -1.283773453 | 0.007513568 |
| **RPL11** | -1.283567353 | 0.021440816 |
| **ATPIF1** | -1.283420937 | 0.024843798 |
| **TMEM258** | -1.283139753 | 0.021249213 |
| **SEC61B** | -1.283120535 | 0.02105832 |
| **DYDC2** | -1.283103346 | 0.048810609 |
| **CCM2** | -1.283096165 | 0.021300163 |
| **POLR2I** | -1.282929786 | 0.016830547 |
| **ALDH1L1** | -1.282809797 | 0.041422552 |
| **LAMTOR5** | -1.282779624 | 0.011711084 |
| **CHCHD10** | -1.282760721 | 0.024843798 |
| **MINOS1** | -1.282535359 | 0.019560867 |
| **ALG14** | -1.282451661 | 0.007697271 |
| **CLN3** | -1.282105104 | 0.014595146 |
| **MRPL11** | -1.282081213 | 0.02061029 |
| **TRAPPC2L** | -1.282069296 | 0.014584219 |

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| **UFC1** | -1.282055326 | 0.008750518 |
| **COX6A1** | -1.282046109 | 0.021188573 |
| **DOK5** | -1.281739477 | 0.016321343 |
| **COPE** | -1.281729576 | 0.015996482 |
| **C12orf57** | -1.281688067 | 0.035619775 |
| **YDJC** | -1.281650239 | 0.020004919 |
| **PRKCDBP** | -1.28143087 | 0.044490343 |
| **DNAJB11** | -1.281398515 | 0.013528136 |
| **ACTB** | -1.280871582 | 0.006685562 |
| **CYSTM1** | -1.280854956 | 0.027451534 |
| **C19orf60** | -1.280791967 | 0.047971764 |
| **ATP6V1G2** | -1.280780782 | 0.005581278 |
| **FBXO2** | -1.280596427 | 0.020986884 |
| **TMED9** | -1.280556215 | 0.004815335 |
| **C14orf2** | -1.280372395 | 0.027681777 |
| **ZNF205** | -1.280334077 | 0.024172564 |
| **CTDNEP1** | -1.280235322 | 0.004815335 |
| **GNPTG** | -1.279818939 | 0.019244817 |
| **NDUFA4** | -1.279497084 | 0.023787082 |
| **LRPAP1** | -1.279486394 | 0.049307138 |
| **PFN1** | -1.279422937 | 0.006940669 |
| **PDZD4** | -1.279332791 | 0.008929516 |
| **ATOX1** | -1.279185657 | 0.026690313 |
| **C12orf10** | -1.278955364 | 0.022787837 |
| **RPL18** | -1.278862757 | 0.04408273 |
| **COMT** | -1.278748146 | 0.004705909 |
| **ATP6V0B** | -1.278367763 | 0.006951912 |
| **CD63** | -1.278354636 | 0.0197776 |
| **NDUFS5** | -1.278349786 | 0.015160482 |
| **MED11** | -1.278104962 | 0.011775813 |
| **SAT2** | -1.278023573 | 0.038908626 |
| **ARMC5** | -1.277630736 | 0.024642063 |
| **KCTD13** | -1.277353989 | 0.008926783 |
| **PLGRKT** | -1.277273771 | 0.033247749 |
| **RPUSD2** | -1.277220242 | 0.026709583 |
| **EIF1AD** | -1.277161123 | 0.024718761 |
| **LAMTOR2** | -1.277096717 | 0.009941367 |
| **C21orf33** | -1.27704303 | 0.021300163 |
| **RPL17** | -1.27703211 | 0.034765061 |
| **CDKN2D** | -1.276896701 | 0.016830547 |

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|---|---|---|
| **DOLK** | -1.276680946 | 0.012881891 |
| **TOE1** | -1.276595947 | 0.023460099 |
| **TMEM186** | -1.276571905 | 0.008908212 |
| **COQ3** | -1.276186085 | 0.03660959 |
| **ISCA2** | -1.276101911 | 0.020986884 |
| **C11orf68** | -1.275938348 | 0.019776058 |
| **ZNF414** | -1.275678221 | 0.019179881 |
| **RPL13** | -1.275674615 | 0.033389338 |
| **DBNL** | -1.275576733 | 0.001307559 |
| **ATP5J** | -1.275557644 | 0.012004181 |
| **BAG1** | -1.275459016 | 0.017571215 |
| **MFSD12** | -1.275297011 | 0.024284592 |
| **POLD2** | -1.275216548 | 0.024427672 |
| **ARPC1B** | -1.275188864 | 0.040806463 |
| **RPL34** | -1.275098737 | 0.044505286 |
| **DUS3L** | -1.275018809 | 0.023880124 |
| **NFKBIL1** | -1.274828712 | 0.023088572 |
| **FABP5** | -1.274295367 | 0.028914709 |
| **ILVBL** | -1.274291873 | 0.010272605 |
| **C19orf43** | -1.274261766 | 0.012375988 |
| **COQ10A** | -1.274201258 | 0.02888021 |
| **SYNGR2** | -1.274181422 | 0.034957422 |
| **MIEN1** | -1.274097739 | 0.017430612 |
| **ELOF1** | -1.27400111 | 0.009970324 |
| **UQCRHL** | -1.273783118 | 0.046094476 |
| **RNF113A** | -1.273354319 | 0.032722649 |
| **STK16** | -1.27316336 | 0.004927559 |
| **NUDT16L1** | -1.272968288 | 0.014266825 |
| **ATP5O** | -1.272920309 | 0.018963427 |
| **PSMA7** | -1.272771867 | 0.0104728 |
| **GNG5** | -1.272533278 | 0.014451992 |
| **ATP5L** | -1.272393973 | 0.008738552 |
| **AP2S1** | -1.272268115 | 0.018642178 |
| **KLHDC3** | -1.272163296 | 0.005324283 |
| **TBCC** | -1.271951247 | 0.045065006 |
| **SARNP** | -1.271455452 | 0.009244314 |
| **RUVBL2** | -1.271066148 | 0.013235911 |
| **METTL23** | -1.271036136 | 0.030572645 |
| **NDUFA11** | -1.27098082 | 0.037822367 |
| **ZFPL1** | -1.27071718 | 0.007957759 |

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|---|---|---|
| **NDUFA8** | -1.270548775 | 0.016512993 |
| **ATP5I** | -1.270421815 | 0.037869434 |
| **THAP7** | -1.270412092 | 0.022294975 |
| **FKBP1B** | -1.270090483 | 0.045690716 |
| **ATRIP** | -1.270004841 | 0.024736878 |
| **NR1H2** | -1.269827426 | 0.012758353 |
| **ARF5** | -1.269433027 | 0.0154935 |
| **RPP25L** | -1.26926272 | 0.04011921 |
| **MBD3** | -1.269184223 | 0.028700037 |
| **PPIH** | -1.269175739 | 0.039004363 |
| **PELI3** | -1.269086849 | 0.029374168 |
| **NDUFB10** | -1.269079401 | 0.031539142 |
| **SNAPC2** | -1.269059763 | 0.02061029 |
| **DRAP1** | -1.268627286 | 0.008738552 |
| **STOML2** | -1.26850486 | 0.007740931 |
| **CRIP2** | -1.268424855 | 0.030585393 |
| **TRADD** | -1.268251819 | 0.013063266 |
| **PIGQ** | -1.268209748 | 0.003960811 |
| **PPIB** | -1.268176662 | 0.011904999 |
| **HAGHL** | -1.268150821 | 0.016652026 |
| **C11orf83** | -1.267945357 | 0.009858217 |
| **GIPC1** | -1.267606014 | 0.016398879 |
| **RPS3** | -1.267446084 | 0.028881801 |
| **C12orf44** | -1.267250917 | 0.017719116 |
| **MPC1** | -1.26716259 | 0.015144272 |
| **BABAM1** | -1.267086019 | 0.019560867 |
| **PTMS** | -1.267020259 | 0.022966622 |
| **MRPL28** | -1.266993402 | 0.017585805 |
| **ARHGDIA** | -1.266639779 | 0.004927559 |
| **MRPL1** | -1.266496135 | 0.012810041 |
| **FIBP** | -1.266035179 | 0.013950709 |
| **FAM32A** | -1.266004203 | 0.026144593 |
| **SHFM1** | -1.265986035 | 0.028687065 |
| **UROD** | -1.265977708 | 0.013003832 |
| **RPL27** | -1.265633281 | 0.037190358 |
| **FASTK** | -1.265412352 | 0.014358762 |
| **RBM42** | -1.265326164 | 0.019909727 |
| **NDUFB4** | -1.265246722 | 0.03153441 |
| **SYNGR3** | -1.26484478 | 0.0176241 |
| **DPCD** | -1.26476642 | 0.019059929 |

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|---|---|---|
| **PSMD4** | -1.2645179 | 0.011758399 |
| **HDDC3** | -1.264414821 | 0.04212125 |
| **C15orf61** | -1.264298317 | 0.030391073 |
| **ATP6V0E2** | -1.264027371 | 0.006940669 |
| **MORN2** | -1.263980204 | 0.028877571 |
| **ATP6V0C** | -1.263917664 | 0.009858217 |
| **AP1S1** | -1.263727021 | 0.024550139 |
| **SAE1** | -1.263526199 | 0.005114607 |
| **CSTB** | -1.263201682 | 0.013057252 |
| **SNAPC5** | -1.263145109 | 0.025358818 |
| **CNIH2** | -1.263060434 | 0.020004919 |
| **FAM69B** | -1.262903628 | 0.019505289 |
| **PLEKHO1** | -1.262476522 | 0.019083741 |
| **YIF1A** | -1.26187974 | 0.034446707 |
| **TMEM115** | -1.261848684 | 0.005528176 |
| **ZNF446** | -1.26163905 | 0.007813049 |
| **WDR83OS** | -1.261524824 | 0.011904999 |
| **RPL19** | -1.261504063 | 0.028600617 |
| **TUBB2B** | -1.261443106 | 0.003451947 |
| **GSTP1** | -1.261033979 | 0.024367059 |
| **HAGH** | -1.26089741 | 0.009858217 |
| **NDUFB11** | -1.260771046 | 0.028267614 |
| **C16orf91** | -1.260737988 | 0.040669442 |
| **PHGDH** | -1.260689372 | 0.022120754 |
| **RNASEK** | -1.26068588 | 0.020920438 |
| **DUSP14** | -1.260437528 | 0.044252174 |
| **MRPL34** | -1.260168655 | 0.037523007 |
| **RAB13** | -1.260058665 | 0.045096577 |
| **TOMM5** | -1.259796974 | 0.022495251 |
| **CNPY2** | -1.259713921 | 0.015800261 |
| **PIM3** | -1.259507179 | 0.030024342 |
| **PFDN6** | -1.259504805 | 0.015225362 |
| **MRPS11** | -1.259319176 | 0.022120754 |
| **RTN4IP1** | -1.259277835 | 0.033867719 |
| **MRPS15** | -1.259082346 | 0.012918559 |
| **ADPRHL2** | -1.258974912 | 0.0154935 |
| **TRMT112** | -1.25886869 | 0.039681624 |
| **MAGOHB** | -1.258286582 | 0.038822739 |
| **RPL37A** | -1.258277858 | 0.045401345 |
| **UBA52** | -1.258262385 | 0.041126587 |

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|---|---|---|
| **C9orf114** | -1.258222374 | 0.008648287 |
| **RFC2** | -1.257976444 | 0.030694787 |
| **CYC1** | -1.257564053 | 0.009858217 |
| **NOP16** | -1.257559737 | 0.008963882 |
| **IRF2BP1** | -1.257526893 | 0.017962228 |
| **GTF2A2** | -1.257443944 | 0.018845137 |
| **TIMM23** | -1.257134076 | 0.01079025 |
| **FAM58A** | -1.256795842 | 0.047516603 |
| **C19orf25** | -1.256691606 | 0.027546223 |
| **KXD1** | -1.256606933 | 0.028162854 |
| **CREB3** | -1.256564355 | 0.009858217 |
| **EXOSC4** | -1.256488053 | 0.025599792 |
| **ZNF358** | -1.256441034 | 0.042121016 |
| **RPL36AL** | -1.256318674 | 0.042267259 |
| **SLC25A39** | -1.256056182 | 0.007772611 |
| **HSD17B8** | -1.255939465 | 0.029722286 |
| **RNPEP** | -1.255828745 | 0.021239565 |
| **RDBP** | -1.255497457 | 0.003409352 |
| **NR2F6** | -1.255452578 | 0.017398009 |
| **KLF16** | -1.255250691 | 0.011849969 |
| **RPL21** | -1.255185014 | 0.043919796 |
| **DPY30** | -1.254975939 | 0.009858217 |
| **GFOD2** | -1.254877776 | 0.005528176 |
| **COTL1** | -1.254617038 | 0.04311743 |
| **FAM127C** | -1.25451333 | 0.030025078 |
| **TMSB4X** | -1.254343698 | 0.020627408 |
| **NDUFC1** | -1.254270299 | 0.028914709 |
| **CCDC53** | -1.253989248 | 0.017808515 |
| **LCMT1** | -1.253858145 | 0.013538157 |
| **RPL10A** | -1.25369412 | 0.038918656 |
| **CHST2** | -1.253690048 | 0.046727738 |
| **HYAL2** | -1.253430297 | 0.037342809 |
| **NAGK** | -1.25335547 | 0.013445921 |
| **UBTD1** | -1.253343148 | 0.038543469 |
| **DDRGK1** | -1.253327879 | 0.029197286 |
| **FAM189A2** | -1.253169731 | 0.042121016 |
| **USMG5** | -1.253148366 | 0.039134416 |
| **LIN37** | -1.253122636 | 0.021527012 |
| **EMC8** | -1.252933556 | 0.009858217 |
| **ST6GALNAC4** | -1.252831479 | 0.047985861 |

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|---|---|---|
| **ZNF408** | -1.252787964 | 0.022120754 |
| **GTF2H5** | -1.252564417 | 0.030751405 |
| **MRPS2** | -1.252498369 | 0.02888021 |
| **WDR83** | -1.252397147 | 0.028914709 |
| **LSM10** | -1.25222127 | 0.037852652 |
| **RABL6** | -1.25208987 | 0.015983711 |
| **GNB2** | -1.252067699 | 0.01241571 |
| **CNTFR** | -1.252000412 | 0.008634666 |
| **PGP** | -1.251758939 | 0.038132417 |
| **ZFYVE19** | -1.251596729 | 0.036110367 |
| **HMBS** | -1.251590607 | 0.038605702 |
| **PRDX4** | -1.25130918 | 0.044729241 |
| **SSU72** | -1.251287226 | 0.011787533 |
| **ATP1B3** | -1.251236685 | 0.009484345 |
| **SPAG7** | -1.251168891 | 0.022016651 |
| **LSM4** | -1.251110474 | 0.032368366 |
| **TPST2** | -1.250852361 | 0.025090749 |
| **PAFAH1B3** | -1.250815342 | 0.033458617 |
| **GRN** | -1.250405962 | 0.006512065 |
| **PFDN2** | -1.250343668 | 0.014481307 |
| **RPS6** | -1.250326966 | 0.029876874 |
| **EIF3M** | -1.250109513 | 0.004705909 |
| **SSBP1** | -1.250083646 | 0.010349222 |
| **C15orf59** | -1.249927233 | 0.029653885 |
| **ALYREF** | -1.249878581 | 0.03274676 |
| **NDUFAB1** | -1.249787665 | 0.026099846 |
| **PSMB2** | -1.249765496 | 0.006749576 |
| **PPP1R16A** | -1.249653528 | 0.012004181 |
| **SLC25A25** | -1.249646529 | 0.028222741 |
| **RPL23** | -1.249593534 | 0.038201547 |
| **MAP1LC3A** | -1.249317091 | 0.016830547 |
| **RHBDD2** | -1.249308115 | 0.021845924 |
| **ZBTB45** | -1.249210556 | 0.013254672 |
| **UBALD2** | -1.249153369 | 0.042660196 |
| **MAP2K2** | -1.248873377 | 0.012852759 |
| **BCKDHA** | -1.248815532 | 0.00716266 |
| **DYNLRB1** | -1.248671895 | 0.018569445 |
| **RUNDC3A** | -1.248548784 | 0.008738552 |
| **GAPDH** | -1.248130523 | 0.019560867 |
| **FLYWCH2** | -1.248096227 | 0.035445269 |

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|---|---|---|
| **GAS6** | -1.247498383 | 0.031351733 |
| **APEX1** | -1.247405534 | 0.005030119 |
| **COX5A** | -1.247392599 | 0.015294262 |
| **ARPC5L** | -1.24696554 | 0.015244012 |
| **TMEM147** | -1.246924395 | 0.011714793 |
| **ADCK1** | -1.246607154 | 0.039099141 |
| **NSMCE1** | -1.245883264 | 0.044224374 |
| **FAM195B** | -1.245590405 | 0.024838192 |
| **NPDC1** | -1.24546812 | 0.032246129 |
| **VIMP** | -1.245250368 | 0.017398009 |
| **PDCD5** | -1.245218984 | 0.015657328 |
| **UQCR10** | -1.245206016 | 0.021946876 |
| **CLPP** | -1.24517313 | 0.03153441 |
| **GSTM3** | -1.245100885 | 0.034319095 |
| **MRPS25** | -1.244784378 | 0.019059929 |
| **PPAPDC3** | -1.24467934 | 0.013175303 |
| **HDGFRP2** | -1.244651494 | 0.017398009 |
| **HN1** | -1.244477969 | 0.01153163 |
| **ANAPC10** | -1.244214854 | 0.040913448 |
| **TUBG1** | -1.24419894 | 0.036018978 |
| **ARPC4** | -1.244122373 | 0.042993582 |
| **CHPF** | -1.243924404 | 0.007553939 |
| **OCEL1** | -1.243857526 | 0.017356917 |
| **THAP4** | -1.243821059 | 0.010444402 |
| **PDAP1** | -1.243798735 | 0.010448715 |
| **COPS6** | -1.243790917 | 0.012467382 |
| **ATP6V1F** | -1.243621565 | 0.006628549 |
| **ATP5J2** | -1.243444106 | 0.013346689 |
| **DTNBP1** | -1.243256693 | 0.042599294 |
| **CD81** | -1.243135693 | 0.009464122 |
| **ERGIC3** | -1.243119452 | 0.010802779 |
| **CORO1A** | -1.242936384 | 0.012464937 |
| **EIF6** | -1.242816832 | 0.028189645 |
| **TMEM126A** | -1.242606501 | 0.019816174 |
| **PMM1** | -1.242569307 | 0.017858769 |
| **BCKDHB** | -1.24238952 | 0.029926471 |
| **RPL8** | -1.242313472 | 0.045884167 |
| **NDUFA2** | -1.242215329 | 0.047954366 |
| **B9D1** | -1.242187525 | 0.038918656 |
| **TMEM70** | -1.242184782 | 0.030786595 |

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|---|---|---|
| **ARMC6** | -1.242105524 | 0.035724788 |
| **DPH2** | -1.241971558 | 0.019505289 |
| **BNIP1** | -1.241458405 | 0.031827418 |
| **DYNLL1** | -1.241308391 | 0.006951912 |
| **CNPY3** | -1.241237526 | 0.016917489 |
| **TPI1** | -1.241102142 | 0.022120754 |
| **RFNG** | -1.241066696 | 0.027546223 |
| **ZNF580** | -1.240765573 | 0.039892554 |
| **UBXN6** | -1.24071839 | 0.022120754 |
| **C11orf73** | -1.240659195 | 0.01617121 |
| **DGCR6** | -1.240512305 | 0.030456202 |
| **SEC13** | -1.240325098 | 0.008738552 |
| **RPL30** | -1.24024807 | 0.046260463 |
| **EMG1** | -1.240140878 | 0.034263132 |
| **FKBP8** | -1.240136897 | 0.018922672 |
| **FIZ1** | -1.240075269 | 0.037687034 |
| **FAM131A** | -1.239932253 | 0.010342725 |
| **HYPK** | -1.239849632 | 0.038918656 |
| **MRPS7** | -1.239726826 | 0.039134416 |
| **ITM2C** | -1.239591513 | 0.040603126 |
| **ATP5H** | -1.238894016 | 0.032171464 |
| **WDR61** | -1.238845656 | 0.010017199 |
| **MRPL17** | -1.238679088 | 0.020920438 |
| **POLR2D** | -1.238205162 | 0.013057252 |
| **PSMB5** | -1.238026579 | 0.026952933 |
| **TMEM222** | -1.237897535 | 0.01381491 |
| **TTYH1** | -1.237869834 | 0.029070016 |
| **ERH** | -1.237592015 | 0.00499119 |
| **C22orf32** | -1.237560014 | 0.047088313 |
| **PCGF1** | -1.237492945 | 0.025145719 |
| **ASNA1** | -1.237328067 | 0.023296736 |
| **SLC39A3** | -1.236829141 | 0.028600617 |
| **IMP3** | -1.236766532 | 0.025671159 |
| **NIT2** | -1.236587792 | 0.0374955 |
| **NCBP2** | -1.236461409 | 0.020920438 |
| **PSMC5** | -1.236222726 | 0.011498263 |
| **RPL14** | -1.2353477 | 0.042886974 |
| **SH3BGRL3** | -1.235329917 | 0.043815715 |
| **SMARCB1** | -1.233963229 | 0.007772611 |
| **BANF1** | -1.23392921 | 0.019512243 |

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|---|---|---|
| **TMEM203** | -1.233910399 | 0.027351121 |
| **PPP2R1A** | -1.23381369 | 0.005138683 |
| **APOO** | -1.233685766 | 0.018705136 |
| **KATNB1** | -1.233022992 | 0.008196469 |
| **ACP6** | -1.232886367 | 0.028700037 |
| **RALY** | -1.232755866 | 0.021249213 |
| **CHMP2A** | -1.232406009 | 0.033149902 |
| **MRPS18A** | -1.232243448 | 0.038918656 |
| **CTNNBIP1** | -1.232183688 | 0.029926471 |
| **LSM5** | -1.232080848 | 0.042993582 |
| **PEX5** | -1.232037194 | 0.004705909 |
| **MRPL55** | -1.232011732 | 0.047619884 |
| **RNASEH2C** | -1.23160709 | 0.023450715 |
| **TBC1D22A** | -1.231430974 | 0.049098717 |
| **PSMD8** | -1.231259024 | 0.01273978 |
| **DDX39A** | -1.230968884 | 0.02772169 |
| **NTAN1** | -1.230903275 | 0.017356917 |
| **C19orf52** | -1.230874122 | 0.032943229 |
| **R3HDM4** | -1.230249738 | 0.018845137 |
| **INO80C** | -1.230079583 | 0.016316215 |
| **MFSD5** | -1.229914658 | 0.035478828 |
| **TBRG4** | -1.229838974 | 0.005864323 |
| **TUFM** | -1.22982608 | 0.010478752 |
| **CDK5R2** | -1.229786974 | 0.034807 |
| **FAM50A** | -1.229412854 | 0.02888021 |
| **SPINT2** | -1.229307136 | 0.030456202 |
| **PSENEN** | -1.229184448 | 0.020408319 |
| **PSMA5** | -1.229134147 | 0.011498263 |
| **ATP6V0E1** | -1.229019343 | 0.040038984 |
| **CAMK1** | -1.228465447 | 0.013057252 |
| **CECR5** | -1.228162773 | 0.023907939 |
| **C1QBP** | -1.227865463 | 0.022824776 |
| **ZCCHC9** | -1.227787875 | 0.015788454 |
| **TMEM59L** | -1.227527561 | 0.02325175 |
| **UQCRC1** | -1.227388294 | 0.014174151 |
| **MAF1** | -1.22737577 | 0.01154469 |
| **CYTH2** | -1.22730383 | 0.012918559 |
| **DCTPP1** | -1.227204536 | 0.049098717 |
| **RPS25** | -1.227168651 | 0.049502172 |
| **SNRPA1** | -1.226775877 | 0.024843798 |

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| **TSG101** | -1.226698511 | 0.016028012 |
| **SPNS1** | -1.226616271 | 0.007813049 |
| **BTF3** | -1.22626361 | 0.02641307 |
| **NTPCR** | -1.225978448 | 0.017041105 |
| **NDUFB6** | -1.225938307 | 0.035724788 |
| **NDUFA6** | -1.225740623 | 0.048612388 |
| **SMARCD3** | -1.225647122 | 0.0197776 |
| **BRK1** | -1.225639176 | 0.008896528 |
| **CAPNS1** | -1.225454828 | 0.017414744 |
| **MED19** | -1.22537852 | 0.023867025 |
| **TMEM134** | -1.225186693 | 0.025642165 |
| **STK11** | -1.225119474 | 0.012464937 |
| **GALNT11** | -1.225050446 | 0.017398009 |
| **LAMTOR1** | -1.225015083 | 0.047763479 |
| **PUF60** | -1.224881753 | 0.009172436 |
| **CRIPT** | -1.22485586 | 0.007202827 |
| **MRFAP1** | -1.22458724 | 0.010825742 |
| **SNRPB** | -1.224570824 | 0.044490343 |
| **RAB24** | -1.22455909 | 0.033149902 |
| **GLRX5** | -1.224484491 | 0.039134416 |
| **CFDP1** | -1.224478525 | 0.029653885 |
| **DDAH2** | -1.224190479 | 0.023760021 |
| **RAB11B** | -1.224044327 | 0.034780685 |
| **NSA2** | -1.223540439 | 0.022787837 |
| **SSBP4** | -1.223509697 | 0.037142799 |
| **ATP5SL** | -1.223438248 | 0.015788454 |
| **HDAC11** | -1.223425768 | 0.026709583 |
| **SELK** | -1.223107007 | 0.019673351 |
| **CHRNB1** | -1.223005048 | 0.049445521 |
| **PEX16** | -1.222912386 | 0.048149624 |
| **NDUFS4** | -1.222838137 | 0.038062101 |
| **ACTR3B** | -1.222715914 | 0.017790469 |
| **CSNK2B** | -1.222646225 | 0.018642178 |
| **GPAA1** | -1.222363219 | 0.004197473 |
| **TH1L** | -1.22206142 | 0.002768708 |
| **LSM1** | -1.221947346 | 0.038558604 |
| **EMC7** | -1.221793878 | 0.008087146 |
| **NT5C3L** | -1.221687909 | 0.027781167 |
| **TRAPPC1** | -1.221660493 | 0.047924907 |
| **LMAN2** | -1.221402899 | 0.029003114 |

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|---|---|---|
| **GPKOW** | -1.221373997 | 0.01633502 |
| **SLC25A1** | -1.221193416 | 0.041240934 |
| **TCEAL5** | -1.221079768 | 0.028959564 |
| **PYGB** | -1.220485034 | 0.000892318 |
| **NGFRAP1** | -1.220314092 | 0.024473606 |
| **NECAP2** | -1.220280056 | 0.045309349 |
| **PRDX2** | -1.220265601 | 0.046488061 |
| **MAGOH** | -1.219998322 | 0.029953568 |
| **CTSD** | -1.219856451 | 0.012970934 |
| **PHF5A** | -1.219606439 | 0.034446707 |
| **GPS2** | -1.219563324 | 0.014899083 |
| **UQCRH** | -1.219162399 | 0.03660959 |
| **SIRT6** | -1.219088762 | 0.049566986 |
| **RNF126** | -1.218751853 | 0.043346602 |
| **ATP5G2** | -1.218528495 | 0.030391073 |
| **FAM127A** | -1.217999179 | 0.015447614 |
| **PSMD9** | -1.217742539 | 0.042837347 |
| **BSCL2** | -1.217440836 | 0.025084018 |
| **TUBB3** | -1.217383168 | 0.042121016 |
| **USE1** | -1.217375498 | 0.028700037 |
| **COMMD3** | -1.217003698 | 0.037964311 |
| **C6orf47** | -1.216987891 | 0.039099141 |
| **TMEM138** | -1.21685981 | 0.035724788 |
| **BCS1L** | -1.21685768 | 0.032368366 |
| **UBL7** | -1.216500799 | 0.033559488 |
| **GTF3C6** | -1.216326914 | 0.042079864 |
| **TUBA4A** | -1.216184674 | 0.024533652 |
| **WBSCR16** | -1.216080082 | 0.034652691 |
| **NABP2** | -1.21598464 | 0.038583507 |
| **LRFN3** | -1.215431868 | 0.033386847 |
| **FAM204A** | -1.215186463 | 0.022593859 |
| **SHARPIN** | -1.215149281 | 0.027252011 |
| **MED27** | -1.215011411 | 0.03109287 |
| **FARSA** | -1.214960057 | 0.006065727 |
| **CDC123** | -1.214872447 | 0.006940669 |
| **B4GALT2** | -1.214428255 | 0.021510168 |
| **MYL12B** | -1.213887737 | 0.010136319 |
| **ATP6V1H** | -1.213757303 | 0.021111349 |
| **RWDD1** | -1.213638253 | 0.030456202 |
| **PAGR1** | -1.213524865 | 0.028432953 |

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|---|---|---|
| **SEPT5** | -1.2132561 | 0.031621476 |
| **RAB40B** | -1.213160826 | 0.027546223 |
| **GABARAPL2** | -1.213114668 | 0.03153441 |
| **EMD** | -1.212888678 | 0.017658097 |
| **EIF5A** | -1.212585394 | 0.021880313 |
| **TIMMDC1** | -1.212425069 | 0.025062195 |
| **NDUFA12** | -1.212311032 | 0.049866006 |
| **SYT5** | -1.212026284 | 0.043280808 |
| **UBOX5** | -1.211796124 | 0.028336583 |
| **TMEM120A** | -1.211594011 | 0.016341207 |
| **DHRS7** | -1.211519179 | 0.024422699 |
| **NUCB1** | -1.210927597 | 0.008738552 |
| **PPIA** | -1.210877764 | 0.033318909 |
| **MRPL18** | -1.210122926 | 0.022970345 |
| **URM1** | -1.209951436 | 0.047101511 |
| **TACO1** | -1.209936008 | 0.030107377 |
| **CDC37** | -1.209825837 | 0.028473573 |
| **PRAF2** | -1.209640205 | 0.0108343 |
| **PLD3** | -1.209573199 | 0.021111349 |
| **CCT7** | -1.209159287 | 0.0310585 |
| **INO80B** | -1.208989039 | 0.0154935 |
| **CSPG5** | -1.208296771 | 0.011498263 |
| **VDAC2** | -1.208255575 | 0.017790469 |
| **TUBA1A** | -1.208196614 | 0.04786864 |
| **PRMT1** | -1.208066693 | 0.029874027 |
| **PTOV1** | -1.208000952 | 0.029598147 |
| **HABP4** | -1.207902126 | 0.042255696 |
| **DRG1** | -1.207899147 | 0.025090749 |
| **LYPLA2** | -1.207820942 | 0.011498263 |
| **CDK2AP1** | -1.207772196 | 0.028764432 |
| **CCDC115** | -1.207750637 | 0.04953422 |
| **RAD23A** | -1.207742279 | 0.029653885 |
| **DCTN3** | -1.207447354 | 0.043971583 |
| **CYP46A1** | -1.206990611 | 0.037943714 |
| **DNAJC19** | -1.206479866 | 0.009858217 |
| **ALG3** | -1.206079898 | 0.031296614 |
| **C1orf85** | -1.205926061 | 0.042404935 |
| **AUP1** | -1.205570143 | 0.016970415 |
| **EIF4A1** | -1.205424727 | 0.018935808 |
| **PEX14** | -1.205368184 | 0.028700037 |

| | | |
|---|---|---|
| **ARFRP1** | -1.205059577 | 0.031827418 |
| **APEH** | -1.204896054 | 0.005528176 |
| **POLDIP2** | -1.204224984 | 0.023088572 |
| **GNB2L1** | -1.204165464 | 0.040810595 |
| **SLC25A11** | -1.203902195 | 0.030572645 |
| **EGLN2** | -1.203880931 | 0.023818221 |
| **CFL1** | -1.20383833 | 0.02600648 |
| **PC** | -1.203824702 | 0.020608997 |
| **KIAA2013** | -1.2038115 | 0.025090749 |
| **UBE2M** | -1.203805776 | 0.029722165 |
| **FN3K** | -1.203664172 | 0.042970021 |
| **ARFIP2** | -1.203319233 | 0.025145719 |
| **LRRC4B** | -1.203252389 | 0.019573236 |
| **EAPP** | -1.203084915 | 0.033129238 |
| **BRMS1** | -1.203021367 | 0.039000999 |
| **SENP3** | -1.202978662 | 0.008302472 |
| **C14orf166** | -1.202850834 | 0.018876175 |
| **TUSC2** | -1.202678488 | 0.034390387 |
| **C9orf69** | -1.202633557 | 0.025084018 |
| **CD3EAP** | -1.202433783 | 0.032133256 |
| **SDF4** | -1.202420489 | 0.030763804 |
| **RBM38** | -1.201821326 | 0.02888021 |
| **BCAS2** | -1.201033049 | 0.024408017 |
| **PEBP1** | -1.200967661 | 0.028267614 |
| **RPL4** | -1.200159071 | 0.034446707 |

**Table S2**. Gene transcripts in the caudate significantly up- and down-regulated in subjects administered IFNα (n=7) compared to controls (n=4).

| | Up-Regulated Genes | |
|---|---|---|
| **Gene** | **Fold Change** | **Adjusted P-value** |
| **VSNL1** | 1.817348661 | 0.000109002 |
| **ALS2CR12** | 1.752978942 | 0.000152217 |
| **DCDC5** | 1.740066295 | 0.000126565 |
| **CCDC37** | 1.717120587 | 5.86E-06 |
| **LRRC46** | 1.691770182 | 0.000109843 |
| **ST6GALNAC2** | 1.688414149 | 0.000215684 |
| **DNALI1** | 1.686386 | 0.000302366 |
| **WDR16** | 1.665673437 | 9.46E-05 |

| | | |
|---|---|---|
| **DPYSL3** | 1.662207252 | 0.002013253 |
| **SPAG8** | 1.636663296 | 0.000678462 |
| **FAM227A** | 1.632907648 | 0.003652052 |
| **DNAH6** | 1.629293999 | 0.002266506 |
| **LRRC48** | 1.628440094 | 0.000208213 |
| **CCDC114** | 1.625264444 | 9.46E-05 |
| **ANKMY1** | 1.617215095 | 0.004956514 |
| **DNAH9** | 1.615783556 | 0.00015828 |
| **C9orf117** | 1.612700694 | 0.000507494 |
| **AGR3** | 1.610635062 | 0.000736153 |
| **CCDC108** | 1.60922459 | 0.000317384 |
| **VWA3B** | 1.609066082 | 0.00261747 |
| **RSPH4A** | 1.605543874 | 0.000402848 |
| **TCTEX1D1** | 1.604257683 | 0.001953592 |
| **OTX2** | 1.599134128 | 0.002503812 |
| **CERKL** | 1.595901578 | 0.000302366 |
| **IQCD** | 1.592433439 | 0.000109002 |
| **HYDIN** | 1.590743058 | 0.000280333 |
| **DLEC1** | 1.590365788 | 9.46E-05 |
| **WDR63** | 1.58745926 | 2.18E-05 |
| **FXYD6** | 1.586216135 | 0.005991948 |
| **TTLL9** | 1.584680336 | 0.006821024 |
| **LRRC23** | 1.583977391 | 0.001373221 |
| **CCDC80** | 1.580500299 | 0.003013556 |
| **C4A** | 1.578597828 | 0.000780953 |
| **TP73** | 1.576966973 | 0.007464268 |
| **CD24** | 1.576466835 | 0.000678462 |
| **DNAH1** | 1.572516691 | 0.000105693 |
| **NTS** | 1.570791617 | 0.000280333 |
| **KCNE1** | 1.568599641 | 0.000217715 |
| **PIFO** | 1.566899694 | 0.00387821 |
| **CCDC40** | 1.563471706 | 0.011617142 |
| **WDR52** | 1.558658568 | 0.000714425 |
| **ABI3BP** | 1.55490701 | 0.00075594 |
| **KCNJ16** | 1.554001503 | 0.014255665 |
| **FOXJ1** | 1.544237675 | 9.46E-05 |
| **MNS1** | 1.538566473 | 0.01673483 |
| **GABRQ** | 1.530195283 | 0.003298681 |
| **C20orf26** | 1.527426404 | 0.019279208 |
| **WDR96** | 1.526686212 | 0.02379065 |

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|---|---|---|
| **CLHC1** | 1.526126284 | 0.020162027 |
| **C5orf49** | 1.521595221 | 0.001874562 |
| **RBM43** | 1.518747852 | 0.018886606 |
| **FHOD3** | 1.518258223 | 0.018787808 |
| **LRRC36** | 1.514630744 | 0.002265264 |
| **C9orf24** | 1.510544382 | 0.00015828 |
| **TGFBI** | 1.506396209 | 0.006272074 |
| **TMEM52** | 1.504121648 | 0.015668772 |
| **CAPS** | 1.500198131 | 0.026007145 |
| **ARHGAP6** | 1.499315816 | 0.032482838 |
| **SORD** | 1.498503081 | 0.018787808 |
| **KRT18** | 1.498128059 | 0.001723522 |
| **CCDC33** | 1.497774346 | 0.001122055 |
| **C22orf15** | 1.497611929 | 0.00015828 |
| **GJD3** | 1.497319804 | 0.032069939 |
| **SLC9A3** | 1.495593403 | 0.037705616 |
| **C6orf165** | 1.494219396 | 0.006803712 |
| **C7orf57** | 1.492845343 | 0.000736153 |
| **GLIS3** | 1.487463069 | 0.043296938 |
| **CCDC42B** | 1.487326303 | 0.039358868 |
| **CCDC19** | 1.485162812 | 0.000302366 |
| **DNAI1** | 1.484009292 | 0.026007145 |
| **CROCC** | 1.483721108 | 0.043296938 |
| **AK1** | 1.483251511 | 0.033099259 |
| **TTC18** | 1.481027628 | 0.047300226 |
| **MORN5** | 1.48080167 | 0.000280333 |
| **BTBD11** | 1.480517733 | 0.032532062 |
| **C20orf96** | 1.479251004 | 0.034531248 |
| **CD36** | 1.477987041 | 0.000507494 |
| **CELSR1** | 1.475397218 | 0.049979951 |
| **EFCAB1** | 1.475121591 | 0.002995558 |
| **ZCCHC12** | 1.474884616 | 0.02720269 |
| **HPCAL1** | 1.474134007 | 0.03676603 |
| **FAM83H** | 1.47273554 | 0.039621889 |
| **IL5RA** | 1.470641114 | 0.000105993 |
| **PI15** | 1.468597589 | 0.00015828 |
| **IQGAP2** | 1.467987777 | 0.017858261 |
| **GLI1** | 1.464180388 | 0.034973098 |
| **C2orf62** | 1.464095447 | 0.000287624 |
| **WDR65** | 1.462716739 | 0.004401297 |

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|---|---|---|
| **RGS6** | 1.462378479 | 0.049655786 |
| **UBXN10** | 1.462112703 | 0.02862895 |
| **ZNF16** | 1.460983129 | 0.000507494 |
| **DZIP1L** | 1.459412153 | 0.002013253 |
| **DNAI2** | 1.457367698 | 0.012139025 |
| **TTC16** | 1.456589492 | 0.02720269 |
| **DNAH2** | 1.455936659 | 0.002333771 |
| **SLC6A7** | 1.450780576 | 0.048569724 |
| **TNFRSF11B** | 1.44940426 | 0.000714425 |
| **DCDC2** | 1.447315306 | 0.02720269 |
| **GMNC** | 1.443504304 | 0.036122479 |
| **GRAMD2** | 1.442703758 | 0.022724373 |
| **MAPK15** | 1.442265595 | 0.000217715 |
| **DTHD1** | 1.44160173 | 0.010189024 |
| **SPATA18** | 1.437976464 | 0.000678462 |
| **C11orf88** | 1.436669305 | 0.000620043 |
| **SLC28A1** | 1.435901678 | 0.007561131 |
| **WEE1** | 1.428876143 | 0.039667143 |
| **PNMA5** | 1.426731821 | 0.001122055 |
| **SLC47A2** | 1.419267371 | 0.00015828 |
| **SPAG6** | 1.41899184 | 0.015817686 |
| **CCDC81** | 1.415620271 | 0.006323771 |
| **TRPC4** | 1.414681579 | 0.0293486 |
| **RORC** | 1.412342785 | 0.011561484 |
| **TYMP** | 1.411567374 | 0.007272768 |
| **FAM92B** | 1.410285663 | 0.000881796 |
| **FAM81B** | 1.407121351 | 0.000280333 |
| **TMEM61** | 1.400253372 | 0.017306195 |
| **RSPH10B** | 1.39953624 | 0.039358868 |
| **IRX3** | 1.393089418 | 0.02720269 |
| **PLOD2** | 1.381606657 | 0.024894528 |
| **KNCN** | 1.376869478 | 0.000678462 |
| **C11orf70** | 1.376763442 | 0.013759611 |
| **ARMC3** | 1.376037694 | 0.000678462 |
| **VSIG8** | 1.374075957 | 0.02720269 |
| **NPY2R** | 1.37034313 | 0.039494564 |
| **UNC5CL** | 1.370342381 | 0.001535813 |
| **ZNF608** | 1.367507122 | 0.041495694 |
| **SMAD9** | 1.364200777 | 0.048569724 |
| **C2orf61** | 1.361164171 | 0.013299518 |

| | | |
|---|---|---|
| **CLEC3A** | 1.360801264 | 0.010596677 |
| **L3MBTL3** | 1.356635583 | 0.021835843 |
| **C9orf135** | 1.354722057 | 0.00801321 |
| **ZBBX** | 1.349017395 | 0.002333771 |
| **FAM9B** | 1.346760557 | 0.041495694 |
| **ADRA2B** | 1.343829021 | 0.032958188 |
| **VWA5B1** | 1.342948132 | 0.004401297 |
| **GUCA1A** | 1.336789835 | 0.005579948 |
| **MORN3** | 1.328191353 | 0.023289956 |
| **CP** | 1.327784502 | 0.018936725 |
| **LDLRAD2** | 1.321612836 | 0.008124339 |
| **BARX2** | 1.321000756 | 0.017939739 |
| **SPATA17** | 1.31124825 | 0.039358868 |
| **ODF3B** | 1.310720178 | 0.008115443 |
| **FNDC1** | 1.308431115 | 0.044690543 |
| **HDC** | 1.307845163 | 0.009146593 |
| **TRPA1** | 1.298660736 | 0.004401297 |
| **SHROOM2** | 1.295118025 | 0.045493982 |
| **ANKRD10** | 1.284604386 | 0.036122479 |
| **SLC27A2** | 1.280415646 | 0.015817686 |
| **ADCYAP1** | 1.278402992 | 0.037705616 |
| **GSTA3** | 1.278212127 | 0.005103224 |
| **RASSF9** | 1.276080976 | 0.012769485 |
| **FHAD1** | 1.274464186 | 0.005674735 |
| **FAM183A** | 1.273327427 | 0.003471947 |
| **ATIC** | 1.272768359 | 0.036122479 |
| **LY6G6F** | 1.254058324 | 0.012119471 |
| **LY6G6D** | 1.252532846 | 0.049655786 |
| **RIBC2** | 1.251614863 | 0.014493287 |
| **CCDC60** | 1.243278493 | 0.011562918 |
| **C1orf158** | 1.241029566 | 0.008711314 |
| **PIH1D3** | 1.237076824 | 0.011429917 |
| **FAM47E** | 1.227523262 | 0.036122479 |
| **WDR38** | 1.213168236 | 0.023289956 |
| **ZNF474** | 1.206665454 | 0.035259397 |
| **CAPSL** | 1.204273277 | 0.02720269 |

**Down-Regulated Genes**

| Gene ID | Fold change | Adjusted P-value |
|---|---|---|
| **MYBPH** | -1.530821916 | 0.021835843 |
| **EGR4** | -1.490780184 | 0.02720269 |
| **CD93** | -1.453695425 | 0.046759403 |
| **HTR6** | -1.422228522 | 0.020305711 |
| **FOSL2** | -1.414460501 | 0.046200674 |
| **REEP6** | -1.391601221 | 0.038254861 |
| **MPC2** | -1.353338283 | 0.000604138 |
| **IFRD1** | -1.327556162 | 0.02720269 |
| **HAS3** | -1.315952335 | 0.019256589 |
| **ATP6V1G2** | -1.286008899 | 0.012119471 |
| **NLE1** | -1.285049947 | 0.021835843 |
| **CAMKK2** | -1.273395448 | 0.019943908 |
| **PNO1** | -1.271528021 | 0.01278501 |
| **PRKAG2** | -1.235356449 | 0.009146593 |
| **PEX5** | -1.23277581 | 0.007631107 |
| **MYBPH** | -1.530821916 | 0.021835843 |
| **EGR4** | -1.490780184 | 0.02720269 |
| **CD93** | -1.453695425 | 0.046759403 |
| **HTR6** | -1.422228522 | 0.020305711 |
| **FOSL2** | -1.414460501 | 0.046200674 |
| **REEP6** | -1.391601221 | 0.038254861 |
| **MPC2** | -1.353338283 | 0.000604138 |
| **IFRD1** | -1.327556162 | 0.02720269 |
| **HAS3** | -1.315952335 | 0.019256589 |
| **ATP6V1G2** | -1.286008899 | 0.012119471 |
| **NLE1** | -1.285049947 | 0.021835843 |
| **CAMKK2** | -1.273395448 | 0.019943908 |
| **PNO1** | -1.271528021 | 0.01278501 |
| **PRKAG2** | -1.235356449 | 0.009146593 |
| **PEX5** | -1.23277581 | 0.007631107 |