Bioinformatics and next generation sequencing data analysis to identify key genes and pathways influencing in Parkinson's disease

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Abstract

Parkinson's disease (PD) is the most commonly diagnosed neurodegenerative disorder. Identification of novel prognostic and pathogenesis biomarkers plays a pivotal role in the management of the PD. Next generation sequencing (NGS) dataset from the GEO (Gene Expression Omnibus) database were used to identify differentially expressed genes (DEGs) in PD. Gene Ontology (GO) and REACTOME pathway enrichment analyses were performed to elucidate the functional roles of the DEGs. Protein-protein interaction (PPI), modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network were established. The receiver operating characteristic curve (ROC) analysis was used to explore the diagnostic values of hub genes in PD. In total, 957 DEGs were identified, of which 478 were up regulated genes and 479 were down regulated genes. GO and pathway enrichment analysis results revealed that the up regulated genes were mainly enriched in nervous system development, cell junction, transporter activity and neuronal system, whereas down regulated genes were mainly enriched in response to stimulus, cell periphery, identical protein binding and immune system. The top hub genes in the constructed PPI network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network were OTUB1, PPP2R1A, AP2M1, PIN1, USP11, CDK2, IQGAP1, NEDD4, VIM and CDK1. Furthermore, ROC analysis showed that hub genes were having good diagnostic values. We identified a series of essential genes along with the pathways that were most closely related with PD initiation and progression. Our results provide a more detailed molecular mechanism for the advancement of PD, shedding light on the potential biomarkers and therapeutic targets.

Keywords: Parkinson's disease; microRNAs; hub gene; bioinformatics analysis; biomarkers

Introduction

Parkinson's disease (PD) is the second most common type of neurodegenerative disorder and a leading cause of impairment of voluntary motor control, which places a great burden on the economy of health and reduces quality of life [1]. PD accounts for 1-2 per 1000 of the population at any time [2]. PD involves the degeneration of dopaminergic neurons in the substantia nigra of the midbrain and the advancement of neuronal Lewy Bodies [3]. Numerous factors might affect PD progression, including genetic factors [4], aging and inflammatory factors [5], and environmental factors [6]. However, how these factors affect the development of PD requires further investigation and no effective method has been developed for treatment and diagnosis. It is therefore urgent to identify novel diagnostic and prognostic biomarkers for PD.

Molecular biology investigations have identified numerous biomarkers and signaling pathways that contribute to PD, including the brain-derived neurotrophic factor (BDNF) [7], histone deacetylase 4 (HDAC4) [8], vacuolar protein sorting 35 (VPS35) [9], leucine-rich repeat kinase 2 (LRRK2) [10], phosphatidylinositol binding clathrin assembly protein (PICALM) [11], RhoA-ROCK signaling pathways [12], Nrf2 signaling pathways [13], GTPase-p38 MAPK signaling pathways [14], JAK/STAT signaling pathway [15] and PI3K/Akt signaling pathway [16]. Further investigation into the molecular events linked with PD is required.

With the advance of the human genome project, PD has been investigated at the genetic level. Next generation sequencing (NGS) technology can be used to find genes that cause early PD. NGS technology has the characteristics of high sensitivity. NGS technology is extensively used in disease diagnosis [17] and novel therapeutic target screening [18]. At present, NGS technology was used to find potential biomarkers that affect the advancement of diseases in studies [19]. NGS technology plays an important role in elucidating gene expression in PD [20]. However, the pathogenesis of PD remains unclear.

In this investigation, we explored novel biomarkers for PD diagnosis and targeting therapies. We manipulated the NGS data of GSE135036 [21] dataset from the GEO (Gene Expression Omnibus) (<http://www.ncbi.nlm.nih.gov/geo/>)

[22] database to distinguish differentially expressed genes (DEGs) between PD and normal control. gene ontology (GO) and pathway enrichment analysis were done to elucidate the functions of the DEGs. The hub genes, miRNAs (micro RNA) and TFs (transcription factors) related to the pathogenesis of PD were chosen by protein-protein interaction (PPI) network, modules, miRNA-hub gene regulatory network and TF-hub gene regulatory network. Receiver operating characteristic curve (ROC) analysis was performed to validate the hub genes, which could be used as molecular biomarkers or diagnostic or therapeutic targets for PD therapy. Collectively, our investigation will help the advancement of a genetic diagnosis for PD and more effective measures of prevention and interference.

Materials and methods

Data resources

The GEO database is a public genome database. In this investigation, NGS dataset GSE135036 [21] was downloaded from the GEO database. GSE135036 was based on Illumina NextSeq 500 (Homo sapiens) platform. GSE135036 dataset contained 25 samples, including 13 PD samples and 12 normal control samples.

Identification of DEGs

The DESeq2 package of R software [23] was used for the screening of differentially expressed genes (DEGs) with the criteria of fold change > 0.513 for up regulated genes, fold change < -0.61 for down regulated genes and adjusted $P < 0.05$. The results were visualized as a volcano plot and heat map using the ggplot2 and gplot in R software.

GO and pathway enrichment analyses of DEGs

We used GO analysis (<http://www.geneontology.org>) [24] to explore the potential functions of the DEGs. GO is a widely used bioinformatics tool to identify genes and study-related biological processes. Three terms comprised the GO analysis, including cellular component (CC), biological process (BP), and molecular function (MF). We employed KEGG to search for potential pathways of the overlapping DEGs. REACTOME (<https://reactome.org/>) [25] is a database to study gene functions and pathways from big datasets sourced from high-throughput experiments. g:Profiler (<http://biit.cs.ut.ee/gprofiler/>) [26], an online biological

database, was used to analyze the GO and REACTOME terms. A value of $p < 0.05$ was considered significant.

Construction of the PPI network and module analysis

The HIPPIE interactome (<http://cbdm-01.zdv.uni-mainz.de/~mschaefer/hippie/index.php>) is a database for searching between known proteins and predicting the interactions between proteins [27]. We used it to build PPI network for DEGs. The interaction networks were visualized with Cytoscape software version 3.8.2 (<http://www.cytoscape.org/>) [28]. Centrality analysis includes analyzing the degree [29], betweenness [30], stress [31] and closeness [32] of network nodes. Cytoscape plug-in Network Analyzer was used to calculate the values of degree, betweenness, stress and closeness to predict the key genes [33]. Functional modules in the network were identified by using the plug-in PEWCC1 [34] of Cytoscape.

miRNA-hub gene regulatory network construction

miRNet database (<https://www.mirnet.ca/>) [35] is a comprehensive database, which provides the largest available set of predicted and experimentally validated miRNA-hub gene interactions. Additionally, it not only records miRNA binding sites in the entire sequence of genes but also compared this information with the binding sites of 14 existing miRNA-hub gene prediction programs: TarBase, miRTarBase, miRecords, miRanda (S. mansoni only), miR2Disease, HMDD, PhenomiR, SM2miR, PharmacomiR, EpimiR, starBase, TransmiR, ADmiRE, and TAM 2.0. Cytoscape software version 3.8.2 [28] was used to construct a miRNA-hub gene regulatory network and analyze the interactions of the miRNAs and hub genes.

TF-hub gene regulatory network construction

NetworkAnalyst database (<https://www.networkanalyst.ca/>) [36] is a comprehensive database, which provides the largest available set of predicted and experimentally validated TF-hub gene interactions. Additionally, it not only records TF binding sites in the entire sequence of genes but also compared this information with the binding sites of existing TF-hub gene prediction program

Jasper. Cytoscape software version 3.8.2 [28] was used to construct a TF-hub gene regulatory network and analyze the interactions of the TFs and hub genes.

Receiver operating characteristic curve (ROC) analysis

Receiver operating characteristic (ROC) curves were adopted to analyze the diagnostic value of the hub genes for PD. To check hub genes' diagnostic values, we plotted ROC curves and determined area under the curve (AUC) with “pROC” R package [37]. The hub genes with the highest AUC value were consistent as having the key power for diagnosing PD.

Results

Identification of DEGs

To explore the role of systems biology in the pathogenesis of PD, we analyzed NGS data of GSE135036 by DESeq2 package of R software. NGS results from GSE135036, candidate DEGs were screened using the criteria of fold change > 0.513 for up regulated genes, fold change < -0.61 for down regulated genes and adjusted $P < 0.05$. There were 957 DEGs in GSE135036. These DEGs included 478 up regulated genes and 479 down regulated genes between PD and normal control samples (Fig. 1 and Table 1). Hierarchical clustering analysis revealed a clear distinction of DEGs between patients with PD and normal control (Fig. 2).

GO and pathway enrichment analyses of DEGs

In order to better understand the biological function of DEGs, we conducted GO and REACTOME pathway enrichment analysis by g:Profiler. GO results showed that up and down regulated genes significantly enriched in nervous system development, cell communication and response to stimulus of BP, cell junction, membrane, cell periphery and cytoplasm of CC, and transporter activity, protein binding, identical protein binding and molecular transducer activity of MF (Table 2). Moreover, REACTOME pathway enrichment analysis showed that the up and down regulated genes were enriched in neuronal system, transmission across chemical synapses, immune system and cytokine signaling in immune system (Table 3).

Construction of the PPI network and module analysis

To investigate the molecular mechanism of PD from a systematic perspective, PPI network was built to examine the relationship between proteins. PPI network was built by HIPPIE interactome for DEGs. There were 4092 nodes and 7138 edges in the visualization network using the Cytoscape (Fig. 3). Based on the high node degree, betweenness centrality, stress centrality and closeness centrality the top hub genes, including OTUB1, PPP2R1A, AP2M1, PIN1, USP11, CDK2, IQGAP1, NEDD4, VIM and CDK1, were identified in the PPI network (Table 4). PEWCC1 was used to identify the significant cluster modules in the PPI network and the top 2 modules were selected (Fig. 4A and 4B). Following GO and REACTOME pathway screening, the module 1 (7 nodes and 15 edges) was revealed to be associated with neuronal system and nervous system development and the module 2 (20 nodes and 41 edges) was revealed to be associated with immune system, muscle contraction, signaling by NTRK1 (TRKA), response to stimulus and cell communication.

miRNA-hub gene regulatory network construction

miRNA-hub gene regulatory network was built by miRNet for hub genes. The miRNA-hub gene regulatory network of hub genes was constructed with 2432 (miRNA: 2135; hub gene: 297) nodes and 14589 edges (Fig. 5). AP2M1 was targeted by 69 miRNAs (ex; hsa-mir-3911), PIN1 was targeted by 56 miRNAs (ex; hsa-mir-199b-5p), PPP2R1A was targeted by 46 miRNAs (ex; hsa-mir-6779-5p), SCN2B was targeted by 46 miRNAs (ex; hsa-mir-4722-3p), OTUB1 was targeted by 45 miRNAs (ex; hsa-mir-1908-5p), FKBP5 was targeted by 88 miRNAs (ex; hsa-mir-3654), CDK2 was targeted by 78 miRNAs (ex; hsa-mir-1296-5p), PLSCR1 was targeted by 75 miRNAs (ex; hsa-mir-1304-5p), YAP1 was targeted by 56 miRNAs (ex; hsa-mir-548d-5p) and CDK1 was targeted by 52 miRNAs (ex; hsa-mir-103a-3p) (Table 5).

TF-hub gene regulatory network construction

TF-hub gene regulatory network was built by NetworkAnalyst for hub genes. The TF-hub gene regulatory network of hub genes was constructed with 372 (TF: 85; hub gene: 287) nodes and 2217 edges (Fig. 6). DLG3 was targeted by 17 TFs (ex; FOXC1), COPS7A was targeted by 15 TFs (ex; IRF2), GABARAPL1 was targeted by 15 TFs (ex; PPARG), MAP1LC3A was targeted by 14 TFs (ex; GATA2),

OTUB1 was targeted by 12 TFs (ex; ARID3A), BCL6 was targeted by 17 TFs (ex; FOXL1), FKBP5 was targeted by 17 TFs (ex; SREBF1), CDK1 was targeted by 14 TFs (ex; NFIC), CDK2 was targeted by 14 TFs (ex; POU2F2) and SYK was targeted by 13 TFs (ex; PRDM1) (Table 5).

Receiver operating characteristic curve (ROC) analysis

A ROC curve was plotted to evaluate the diagnostic value of OTUB1, PPP2R1A, AP2M1, PIN1, USP11, CDK2, IQGAP1, NEDD4, VIM and CDK1 (Fig. 7). The AUCs for the 10 hub genes were 0.943, 0.934, 0.874, 0.846, 0.854, 0.931, 0.929, 0.869, 0.940 and 0.860, respectively (Fig. 7). This analysis demonstrated that the 10 hub genes had a diagnostic role in PD.

Discussion

PD is a neurodegenerative disease characterized by tremor and bradykinesia. However, the exact mechanisms linked with PD are not clear. It has been demonstrated that tic factors play key roles in the advancement of PD. However, owing to lack of validated genetic targets, no possible therapeutic agents have been reported for the effective and safe treatment of the disease, so our goal was to find the key DEGs, associated pathways, and models that might be used as potential novel biomarkers or therapeutic targets for PD.

In the present investigation, integrated bioinformatics analysis of NGS data (GSE135036) was used to find the potential key genes related to PD. By performing DEGs analysis, 478 up regulated and 479 down regulated genes were successfully identified. Previous studies have demonstrated that VGF (VGF nerve growth factor inducible) [38] and SST (somatostatin) [39] are linked with the development mechanisms of Huntington's disease. VGF (VGF nerve growth factor inducible) [40] and RRM2 [41] expression has significant diagnosis value in amyotrophic lateral sclerosis patients and acts as potential targets for amyotrophic lateral sclerosis targeted therapy. The recent studies have reported the identification of VGF (VGF nerve growth factor inducible) [42], CRH (corticotropin releasing hormone) [43], NPAS4 [44] and SST (somatostatin) [45] biomarkers in schizophrenia. Altered CRH (corticotropin releasing hormone) [46] and SST (somatostatin) [47] expression levels are associated with PD and are considered to be a biomarker and therapeutic target for PD. CRH (corticotropin releasing

hormone) [48] and SST (somatostatin) [49] were shown to participate in facilitating Alzheimer's disease. Kämpfel et al. [50] and Basivireddy et al. [51] found that biomarkers, including CRH (corticotropin releasing hormone) and SST (somatostatin) positively correlate with multiple sclerosis. CRH (corticotropin releasing hormone) [52] and SST (somatostatin) [53] have been reported to be altered expression in autism spectrum disorder. DUSP4 [54] have been reported to be related to epilepsy. These findings suggested that these genes might participate in the occurrence and development of PD.

In GO function and REACTOME pathway annotation, some genes involved with regulation of neurological and immune system processes were enriched in PD samples. Signaling by NTRK1 (TRKA) [55], cardiac conduction [56], signaling by GPCR [57], immune system [58], cytokine signaling in immune system [59], interferon signaling [60] and toll-like receptor cascades [61] were responsible for development of PD. Recent studies have shown that EGR2 [62], WNT1 [63], ARC (activity regulated cytoskeleton associated protein) [64], CHRNA7 [65], SEZ6L2 [66], IL1RAPL2 [67], PER2 [68], PCDH19 [69], CNTNAP2 [70], SLC12A5 [71], CDK5 [72], ACTL6B [73], GABRD (gamma-aminobutyric acid type A receptor subunit delta) [74], CACNA1G [75], HTR2C [76], STX1A [77], ATP1A3 [78], RIMS3 [79], CNTNAP2 [80], CDH8 [81], SCAMP5 [82], SYNGR1 [83], ARHGEF9 [84], DLG3 [85], RBP4 [86], IL9 [87], S100A9 [88], HGF (hepatocyte growth factor) [89], C3 [90], FKBP5 [91], GABRE (gamma-aminobutyric acid type A receptor subunit epsilon) [92], NCKAP1L [93], PIK3CG [94], ITGB3 [95], ANXA1 [96], SYNE2 [97] and DBI (diazepam binding inhibitor, acyl-CoA binding protein) [98] were closely involved with the occurrence, development, and prognosis of autism spectrum disorder. EGR2 [99], ADCYAP1 [100], CHRNA7 [101], NRN1 [102], ETV5 [103], STXBP1 [104], CAMKK2 [105], VAMP2 [106], SYNGR1 [107], NOD2 [108], TLR2 [109], BRCA2 [110] and LEF1 [111] were previously reported to be critical for the development of bipolar disorder. Accumulating evidence shows that EGR2 [112], WNT1 [113], ARC (activity regulated cytoskeleton associated protein) [114], ADCYAP1 [115], SCN5A [116], RTN4R [117], CHRNA7 [118], NRG1 (neurogranin) [119], CHRM1 [120], CCK (cholecystokinin) [121], RGS4 [122], LINGO1 [123], PAK1 [124], PCDH19 [125], NRN1 [126], CX3CL1 [127], CNTNAP2 [128], SLC12A5 [129], GAS7 [130], NTNG1 [131], RAB3A [132], STXBP1 [104], CHRNB2 [133], CDK5

[134], HTR5A [135], SLC30A3 [136], HTR3B [137], HTR2C [138], TAMALIN (trafficking regulator and scaffold protein tamalin) [139], STX1A [140], GRM2 [141], SLC1A6 [142], NPTX2 [143], CAMKK2 [144], SYP (synaptophysin) [145], VAMP2 [146], ATP1A3 [147], SV2A [148], CNTNAP2 [149], CAP2 [150], SYNGR1 [151], SNCB (synuclein beta) [152], RBP4 [153], KIF17 [154], CHI3L1 [155], CCR5 [156], C1QB [157], TLR7 [158], TLR2 [159], MNDA (myeloid cell nuclear differentiation antigen) [160], C3 [161], IL2RG [162], MICB (MHC class I polypeptide-related sequence B) [163], FKBP5 [164], NEFH (neurofilament heavy chain) [165], CELSR1 [166], APBB1IP [167], CD34 [168], BRCA2 [110], ITGB3 [169], ANXA3 [170], NQO1 [171], B2M [172], SLC39A12 [173], NEDD4 [174], COX2 [175], CFH (complement factor H) [176], TGFBR2 [177], MYD88 [178], ITGA8 [179], REST (RE1 silencing transcription factor) [180] and KCNJ10 [181] are altered expressed in schizophrenia. WNT1 [182], NRG1 (neurogranin) [183], CCK (cholecystokinin) [184], RGS4 [185], PLK2 [186], LINGO1 [187], UNC5D [188], MEF2D [189], CX3CL1 [190], PIN1 [191], RET (ret proto-oncogene) [192], NME1 [193], STX1B [194], CDK5 [195], NPTX2 [196], VAMP2 [197], PRKAR1B [198], CAP2 [150], SNCB (synuclein beta) [199], AP2M1 [200], S100A9 [201], TLR8 [202], SERPINA1 [203], CCR5 [204], NOD2 [205], TLR7 [202], HGF (hepatocyte growth factor) [206], TLR2 [207], PTPRC (protein tyrosine phosphatase receptor type C) [208], C3 [209], LAMP3 [210], GLI1 [211], GPR4 [212], TLR1 [213], OSMR (oncostatin M receptor) [214], NFATC2 [215], GPNMB (glycoprotein nmb) [216], NQO1 [217], B2M [218], TRDN (triadin) [219], HK2 [220], NEDD4 [221], ATP6 [222], COX2 [223], CASP6 [224], MYD88 [225], NFKBIA (NFKB inhibitor alpha) [226], IL13RA1 [227], ND1 [228], TP53INP1 [229], CSF1 [230], ITPKB (inositol-trisphosphate 3-kinase B) [231], ANXA1 [232], SUMO4 [233], ITGA8 [234] and REST (RE1 silencing transcription factor) [235] have been shown to be activated in PD. WNT1 [236], RTN4R [237], MEF2D [238], CX3CL1 [239], PIN1 [240], UNC13A [241], CDK5 [242], SLC30A3 [243], TUBA4A [244], BCL2A1 [245], CHI3L1 [246], SERPINA1 [247], CCR5 [248], C7 [249], S100A4 [250], C1QB [251], SPP1 [252], TLR7 [253], TLR2 [254], NEFH (neurofilament heavy chain) [255], GPNMB (glycoprotein nmb) [256], B2M [257], COX2 [258], YAP1 [259], MYD88 [260], CSF1 [261], REST (RE1 silencing transcription factor) [262], DDX58 [263], LRP4 [264] and KCNJ10 [265] contributes to the progression of amyotrophic lateral sclerosis. Previous studies had shown that the altered

expression of ADCYAP1 [266], CCK (cholecystokinin) [267], LINGO1 [268], CX3CL1 [269], NECTIN1 [270], IL9 [271], TLR8 [272], CCR5 [273], NOD2 [274], C7 [275], TLR7 [276], HGF (hepatocyte growth factor) [277], TLR2 [278], PTPRC (protein tyrosine phosphatase receptor type C) [279], C3 [280], IFI16 [281], GLI1 [282], CYBB (cytochrome b-245 beta chain) [283], TLR1 [284], NEFH (neurofilament heavy chain) [285], CLIC1 [286], PDK4 [287], NFATC2 [288], GPNMB (glycoprotein nmb) [289], CD58 [290], NQO1 [291], B2M [292], ANXA2 [293], FLT1 [294], IFIH1 [295], COX2 [296], NLRC5 [297], CFH (complement factor H) [298], YAP1 [299], MYD88 [300], IQGAP1 [301], ANXA1 [302] and DDX58 [303] were closely related to the occurrence of multiple sclerosis. Studies had shown that NEUROD6 [304], CHRNA7 [305], NRGN (neurogranin) [306], CCK (cholecystokinin) [307], RGS4 [308], SEZ6 [309], PLK2 [310], LINGO1 [311], NRN1 [312], CX3CL1 [313], CNTNAP2 [314], CALM3 [315], PIN1 [316], RAB3A [317], CHRNB2 [318], CDK5 [319], RPH3A [320], NPTX2 [321], NPTXR (neuronal pentraxin receptor) [322], SEZ6 [323], CAMKK2 [324], SYP (synaptophysin) [325], SV2A [326], PRKAR1B [198], CDH13 [327], CNTNAP2 [328], CALM3 [329], CAP2 [150], SLC10A4 [330], RBP4 [331], HPX (hemopexin) [332], CALHM1 [333], GNG13 [334], CHI3L1 [335], STC1 [336], FPR2 [337], S100A9 [338], CCR5 [339], C7 [340], CDK1 [341], HGF (hepatocyte growth factor) [342], TLR5 [343], TFPI (tissue factor pathway inhibitor) [344], TLR2 [345], C3 [346], CFI (complement factor I) [347], ALOX5AP [348], SELL (selectin L) [349], FKBP5 [350], CASP4 [351], SYK (spleen associated tyrosine kinase) [352], CGAS (cyclic GMP-AMP synthase) [353], NCKAP1L [354], CLIC1 [286], NFATC2 [355], CD34 [356], GPNMB (glycoprotein nmb) [357], CDK2 [358], TNFSF10 [359], BTK (Bruton tyrosine kinase) [360], NQO1 [361], CTSS (cathepsin S) [362], MSTN (myostatin) [363], IFITM3 [364], DOCK2 [365], BCL6 [366], COX2 [367], CASP7 [368], CFH (complement factor H) [369], YAP1 [370], TGFB2 [371], CASP6 [372], MYD88 [373], CYTB (cytochrome b) [374], RGCC (regulator of cell cycle) [375], CSF1 [376], ITPKB (inositol-trisphosphate 3-kinase B) [377], CD2AP [378], REST (RE1 silencing transcription factor) [379] and BACE2 [380] were altered expressed in patients with Alzheimer's disease. Byrne et al. [381], Lee et al. [382], Hays et al. [383], Rudinskiy et al. [384], Subbarayan et al. [385], Carnemolla et al. [386], Cherubini et al. [387], Wang et al. [388], Goto et al. [389], Bertoglio et al.

[390], Griffioen et al. [391], Larkin and Muchowski [392], Bailus et al. [393], Sharma et al. [394], Bondulich et al. [395], Wong et al. [396], Orozco-Díaz et al. [397] and Picó et al. [398] revealed that NRG1 (neurogranin), CHRM1, CCK (cholecystokinin), HPCA (hippocalcin), CX3CL1, PIN1, CDK5, GRM2, SYP (synaptophysin), SV2A, TLR2, C3, FKBP5, CGAS (cyclic GMP-AMP synthase), MSTN (myostatin), CASP6, REST (RE1 silencing transcription factor) and SLC19A3 are associated with Huntington's disease. The expression and prognosis of TUBB2A [399], PAK1 [400], PRKCG (protein kinase C gamma) [401], CACNA1G [402], ATP1A3 [403] and KCNJ10 [404] have been investigated in ataxia. SCN3B [405], PCDH19 [406], CNTNAP2 [407], STXBP1 [408], CHRNA2 [409], NAPA (NSF attachment protein alpha) [410], STX1B [411], GABRG2 [412], CAMKK2 [144], CNTNAP2 [413], ARHGEF9 [414], COX8A [415], CALHM1 [416], SLC45A1 [417], TLR5 [418] and KCNJ10 [419] could be a useful prognostic biomarker in epilepsy. The altered expression of NPTX2 [420], VAMP2 [421], PRKAR1B [422], SNCB (synuclein beta) [199], AP2M1 [423], TUBA4A [424], KIF17 [425] and SYK (spleen associated tyrosine kinase) [426] might be related to the progression of dementia. The above evidence revealed that these genes were related with disorders of the nervous system and might have a function in PD.

The PPI network and modules of DEGs was analyzed by HIPPIE interactome. After screening hub genes, these key genes related to PD prognosis, diagnosis and novel therapy were identified. Reports describe the role of OTUB1 in PD [427]. Miron et al. [428] demonstrates that PPP2R1A is up-regulated in Alzheimer's disease. However, the role of USP11, VIM, WWTR1, RASSF8 and TEAD2 in the development of PD remains unclear. Further investigations will be required to identify the relationship between these genes and PD.

miRNA-hub gene regulatory network and TF-hub gene regulatory network containing the hub genes were constructed. After screening miRNA and TFs, these key miRNA and TFs related to PD prognosis, diagnosis and novel therapies were identified. A previous study demonstrated that hsa-mir-103a-3p [429] was altered expressed in multiple sclerosis. Wu et al [430] reported that hsa-mir-103a-3p expression might be regarded as an indicator of susceptibility to autism spectrum disorder. Kurzwski et al [431] and Lou et al [432] demonstrated that the altered

expression of GATA2 and SREBF1 are associated with prognosis in patients with PD. Study have reported that patients with SREBF1 [433] expression tended to suffer from amyotrophic lateral sclerosis. SREBF1 [434] was elevated in patients with schizophrenia. These results indicated that SCN2B, PLSCR1, COPS7A, GABARAPL1, hsa-mir-3911, hsa-mir-199b-5p, hsa-mir-6779-5p, hsa-mir-4722-3p, hsa-mir-1908-5p, hsa-mir-3654, hsa-mir-1296-5p, hsa-mir-1304-5p, hsa-mir-548d-5p, FOXC1, IRF2, PPARG, ARID3A, FOXL1, NFIC (nuclear factor 1 C), POU2F2 and PRDM1 might be a potential biomarker of PD.

In conclusion, we used a series of bioinformatics analysis methods to identify the essential genes and pathways involved in PD initiation and progression from NGS containing normal control samples and PD samples. Our results provide a more detailed molecular mechanism for the advancement of PD, shedding light on the potential biomarkers and therapeutic targets. However, the interacting mechanism and function of genes need to be confirmed in further experiments.

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

No informed consent because this study does not contain human or animals participants.

Availability of data and materials

The datasets supporting the conclusions of this article are available in the GEO (Gene Expression Omnibus) (<https://www.ncbi.nlm.nih.gov/geo/>) repository. [(GSE135036) <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE135036>]

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author Contributions

B. V. - Writing original draft, and review and editing

C. V. - Software and investigation

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Tables

Table 1 The statistical metrics for key differentially expressed genes (DEGs)

Gene Symbol	logFC	pValue	adj.P.Val	tvalue	Regulation	Gene Name
LINC01833	2.212635	6.44E-05	0.004097	3.99604	Up	long intergenic non-protein coding RNA 1833
VGF	2.131639	2.00E-07	9.17E-05	5.199595	Up	VGF nerve growth factor inducible
CRH	2.103757	4.20E-05	0.00323	4.096027	Up	corticotropin releasing hormone
SLC4A1	1.796946	0.002266	0.036023	3.052926	Up	solute carrier family 4 member 1 (Diego blood group)
ALG1L	1.793344	0.000116	0.005919	3.853828	Up	ALG1 chitobiosyldiphosphodolichol beta-mannosyltransferase like
KRT5	1.778486	5.65E-05	0.003847	4.026933	Up	keratin 5
NPAS4	1.722534	0.001861	0.031987	3.111622	Up	neuronal PAS domain protein 4

DUSP4	1.680536	1.03E-07	6.61E-05	5.321414	Up	dual specificity phosphatase 4
CCDC188	1.56968	8.14E-09	1.99E-05	5.765436	Up	coiled-coil domain containing 188
SST	1.493994	2.38E-06	0.00052	4.718268	Up	somatostatin
STIM1-AS1	1.477298	0.002806	0.040879	2.98819	Up	STIM1 antisense RNA 1
LKAAEAR1	1.443122	0.00099	0.022034	3.293415	Up	LKAAEAR motif containing 1
NMBR	1.422491	0.00084	0.01994	3.339292	Up	neuromedin B receptor
KNCN	1.405007	1.29E-05	0.001551	4.361652	Up	kinocilin
TMEM132E-DT	1.372374	2.50E-08	2.85E-05	5.573417	Up	TMEM132E divergent transcript long intergenic non-protein coding RNA 1164
LINC01164	1.333661	7.57E-05	0.004516	3.957733	Up	
EGR2	1.330185	0.000487	0.014399	3.487992	Up	early growth response 2
PNOC	1.328968	0.00038	0.012598	3.553895	Up	prepronociceptin
EGR1	1.328009	3.09E-08	3.15E-05	5.536344	Up	early growth response 1
NEBL-AS1	1.327243	0.000923	0.021247	3.313065	Up	NEBL antisense RNA 1
LINC00898	1.312136	8.69E-09	1.99E-05	5.754432	Up	long intergenic non-protein coding RNA 898
ATOH7	1.302083	1.30E-05	0.001559	4.359519	Up	atonal bHLH transcription factor 7 long intergenic non-protein coding RNA 1007
LINC01007	1.295971	0.000109	0.005643	3.870309	Up	long intergenic non-protein coding RNA 1844
LINC01844	1.21576	0.001892	0.032354	3.106686	Up	
ASB2	1.203348	1.57E-06	0.000386	4.802035	Up	ankyrin repeat and SOCS box containing 2
H1-7	1.182691	0.002731	0.040317	2.996468	Up	H1.7 linker histone
SNORA5C	1.171637	0.001775	0.031151	3.125504	Up	small nucleolar RNA, H/ACA box 5C
LINC00507	1.167703	0.001675	0.030026	3.142502	Up	long intergenic non-protein coding RNA 507
RNU2-61P	1.163243	0.00242	0.037479	3.033108	Up	RNA, U2 small nuclear 61, pseudogene family with sequence similarity 163 member A
FAM163A	1.157978	0.000989	0.022033	3.293654	Up	
RN7SKP70	1.142311	0.0004	0.01304	3.539856	Up	RN7SK pseudogene 70
LOC101929473	1.139658	0.001776	0.031151	3.12534	Up	uncharacterized LOC101929473 long intergenic non-protein coding RNA 1511
LINC01511	1.12459	2.43E-05	0.002285	4.220911	Up	
NAT16	1.119217	0.000211	0.008662	3.705196	Up	N-acetyltransferase 16 (putative)
MYLK2	1.114274	0.002865	0.041426	2.981848	Up	myosin light chain kinase 2
C1QTNF4	1.109643	0.000202	0.008426	3.716351	Up	C1q and TNF related 4
GNG3	1.107955	7.41E-05	0.00445	3.962821	Up	G protein subunit gamma 3
IL11	1.104274	0.002167	0.035108	3.066305	Up	interleukin 11 long intergenic non-protein coding RNA 2395
LINC02395	1.103745	0.001607	0.029425	3.154692	Up	
SLC30A3	1.103415	1.61E-07	8.18E-05	5.239957	Up	solute carrier family 30 member 3
WNT1	1.096887	0.000584	0.01581	3.439031	Up	Wnt family member 1 long intergenic non-protein coding RNA 1166
LINC01166	1.089345	3.45E-06	0.000671	4.64193	Up	
LINC00003	1.088305	0.000667	0.017076	3.402735	Up	uncharacterized LincR-0003
TMEM200B	1.0842	0.0006	0.015989	3.431398	Up	transmembrane protein 200B
RGS8	1.066287	0.000142	0.00676	3.804452	Up	regulator of G protein signaling 8
NXPH2	1.065488	1.23E-05	0.001512	4.372983	Up	neurexophilin 2
HTR7P1	1.065194	2.60E-06	0.000545	4.700413	Up	5-hydroxytryptamine receptor 7 pseudogene 1
SPATA2L	1.064875	0.000722	0.018096	3.38103	Up	spermatogenesis associated 2 like

MPO	1.061456	0.001491	0.028188	3.176506	Up	myeloperoxidase
CALY	1.058472	2.87E-05	0.002531	4.183293	Up	calcyon neuron specific vesicular protein
CCKBR	1.057445	7.08E-10	3.25E-06	6.164244	Up	cholecystokinin B receptor
DUSP2	1.050214	0.00012	0.006039	3.845792	Up	dual specificity phosphatase 2
HTR3B	1.047519	1.47E-06	0.000368	4.815083	Up	5-hydroxytryptamine receptor 3B
CCDC184	1.044973	1.19E-05	0.00148	4.379617	Up	coiled-coil domain containing 184
KLHL14	1.044323	0.001036	0.02264	3.280668	Up	kelch like family member 14
ARC	1.043606	0.001482	0.028057	3.178254	Up	activity regulated cytoskeleton associated protein
SETBP1-DT	1.042941	9.97E-07	0.000286	4.892294	Up	SETBP1 divergent transcript
ARL4D	1.036606	2.01E-05	0.002057	4.263784	Up	ADP ribosylation factor like GTPase 4D
NPBWR2	1.033997	0.002703	0.04003	2.999628	Up	neuropeptides B and W receptor 2
IGFN1	1.033662	0.001777	0.031151	3.12525	Up	immunoglobulin like and fibronectin type III domain containing 1
ADCYAP1	1.028408	0.001253	0.025344	3.226532	Up	adenylate cyclase activating polypeptide 1
CCNO	1.024066	0.000774	0.018941	3.361922	Up	cyclin O
SPAG6	1.023468	1.55E-05	0.001779	4.322115	Up	sperm associated antigen 6
MIR381HG	1.020826	0.000146	0.006848	3.798461	Up	MIR381 host gene
PHEX-AS1	1.019008	0.000292	0.010699	3.621923	Up	PHEX antisense RNA 1
KCNF1	1.018495	3.74E-05	0.00295	4.122699	Up	potassium voltage-gated channel modifier subfamily F member 1
NCALD	1.006859	4.11E-06	0.000739	4.605993	Up	neurocalcin delta
RHEBL1	1.002658	2.96E-06	0.0006	4.673275	Up	RHEB like 1
FAM241B	1.002644	3.48E-07	0.000127	5.095148	Up	family with sequence similarity 241 member B
CRYM	0.999919	1.08E-06	0.000301	4.875934	Up	crystallin mu
PNMA5	0.999269	0.00027	0.010154	3.642726	Up	PNMA family member 5
SPEF1	0.995432	0.000171	0.007525	3.758513	Up	sperm flagellar 1
GABRD	0.994856	8.96E-05	0.005043	3.917109	Up	gamma-aminobutyric acid type A receptor subunit delta
MUC5B	0.994303	0.001389	0.026913	3.196937	Up	mucin 5B, oligomeric mucus/gel-forming
PAFAH1B2P2	0.989228	9.84E-05	0.005372	3.894498	Up	PAFAH1B2 pseudogene 2
OTOGL	0.987975	2.24E-05	0.002186	4.239516	Up	otogelin like
CACNA1G	0.984512	3.03E-07	0.000116	5.121297	Up	calcium voltage-gated channel subunit alpha1 G
NOXA1	0.983213	0.001539	0.028737	3.167143	Up	NADPH oxidase activator 1
LINC02263	0.981981	5.34E-05	0.003751	4.040023	Up	long intergenic non-protein coding RNA 2263
LRTM2	0.978132	8.06E-08	5.84E-05	5.36568	Up	leucine rich repeats and transmembrane domains 2
PCSK1	0.977999	2.17E-05	0.00217	4.246396	Up	proprotein convertase subtilisin/kexin type 1
FCRLB	0.975319	0.000161	0.007289	3.77337	Up	Fc receptor like B
SCN5A	0.972722	0.0018	0.031306	3.12137	Up	sodium voltage-gated channel alpha subunit 5
IGFBP2	0.965253	0.000417	0.013342	3.529377	Up	insulin like growth factor binding protein 2
RHOV	0.962706	0.000919	0.021187	3.314091	Up	ras homolog family member V
LOXHD1	0.961081	0.000527	0.015006	3.466415	Up	lipoxigenase homology PLAT domains 1
FAM71E1	0.959481	5.33E-05	0.003749	4.04077	Up	family with sequence similarity 71 member E1
EMILIN3	0.95933	0.001747	0.030817	3.130143	Up	elastin microfibril interfacer 3

HTR2C	0.95794	1.84E-05	0.001932	4.28366	Up	5-hydroxytryptamine receptor 2C
SLC10A4	0.955588	0.001155	0.024038	3.249775	Up	solute carrier family 10 member 4
ADAMTS8	0.950264	1.10E-07	6.61E-05	5.30901	Up	ADAM metalloproteinase with thrombospondin type 1 motif 8
PRSS16	0.948823	4.20E-06	0.000744	4.601113	Up	serine protease 16
TAMALIN	0.939267	2.40E-06	0.00052	4.716429	Up	trafficking regulator and scaffold protein tamalin
SPRED3	0.938141	9.05E-05	0.005046	3.914717	Up	sprouty related EVH1 domain containing 3
CTXN1	0.935837	0.002887	0.041605	2.979563	Up	cortexin 1
LOC101929237	0.931389	0.001255	0.025344	3.226177	Up	uncharacterized LOC101929237
RBP4	0.927886	4.67E-05	0.003439	4.071308	Up	retinol binding protein 4
SLC22A6	0.927636	5.17E-05	0.003695	4.047731	Up	solute carrier family 22 member 6
TPBGL	0.924874	0.000495	0.014532	3.483518	Up	trophoblast glycoprotein like
FFAR4	0.921381	0.00022	0.008915	3.6951	Up	free fatty acid receptor 4
TSTD1	0.921219	5.12E-05	0.003678	4.050084	Up	thiosulfate sulfurtransferase like domain containing 1
TRBC2	0.916751	0.000668	0.017077	3.402463	Up	T cell receptor beta constant 2
RTN4R	0.911203	0.001422	0.027386	3.190087	Up	reticulon 4 receptor
ICAM5	0.908596	0.0002	0.008374	3.719465	Up	intercellular adhesion molecule 5
ADTRP	0.906103	0.000339	0.011851	3.583866	Up	androgen dependent TFPI regulating protein
SLC32A1	0.905117	0.000725	0.018142	3.380095	Up	solute carrier family 32 member 1
PCDHGC5	0.903135	6.69E-10	3.25E-06	6.173303	Up	protocadherin gamma subfamily C, 5
NNAT	0.898213	1.18E-07	6.78E-05	5.296114	Up	neuronatin
TMEM59L	0.897991	1.81E-05	0.001932	4.287547	Up	transmembrane protein 59 like
SVOP	0.894023	1.26E-06	0.000333	4.84602	Up	SV2 related protein
LINC01310	0.892091	0.000676	0.017281	3.398957	Up	long intergenic non-protein coding RNA 1310
SDR9C7	0.889396	0.002464	0.037894	3.027746	Up	short chain dehydrogenase/reductase family 9C member 7
NEUROD6	0.887312	0.000503	0.014643	3.479082	Up	neuronal differentiation 6
KCNH4	0.88385	0.00053	0.015013	3.465083	Up	potassium voltage-gated channel subfamily H member 4
ADRA1D	0.882775	0.003653	0.047791	2.906695	Up	adrenoceptor alpha 1D
PPEF1	0.881533	0.000756	0.018682	3.368542	Up	protein phosphatase with EF-hand domain 1
TUBAP7	0.876317	0.002614	0.039265	3.009812	Up	tubulin alpha pseudogene 7
CHRNA7	0.869866	0.000503	0.014643	3.47891	Up	cholinergic receptor nicotinic alpha 7 subunit
RPSAP69	0.869107	9.55E-06	0.001258	4.427066	Up	ribosomal protein SA pseudogene 69
MCHR2	0.867996	3.22E-05	0.002719	4.157207	Up	melanin concentrating hormone receptor 2
GJD2	0.866984	7.81E-05	0.004602	3.950133	Up	gap junction protein delta 2
PLPPR3	0.85795	0.002565	0.038859	3.0156	Up	phospholipid phosphatase related 3
SOWAHB	0.856553	2.21E-05	0.002185	4.242315	Up	sosondowah ankyrin repeat domain family member B
MAP1LC3A	0.85541	0.000286	0.01054	3.627531	Up	microtubule associated protein 1 light chain 3 alpha
PTPRD-AS2	0.849675	0.000833	0.01982	3.341685	Up	PTPRD antisense RNA 2 (head to head)
BEST4	0.84705	0.001882	0.032248	3.108211	Up	bestrophin 4
SH2D5	0.843189	3.08E-06	0.000618	4.665614	Up	SH2 domain containing 5
TMEM221	0.843085	0.000304	0.010996	3.611761	Up	transmembrane protein 221
HPX	0.84217	0.003737	0.048438	2.899508	Up	hemopexin

REM2	0.84118	0.002474	0.037981	3.026482	Up	RRAD and GEM like GTPase 2
STX1A	0.840295	5.97E-08	4.70E-05	5.419548	Up	syntaxin 1A
FBN3	0.838099	0.003168	0.043862	2.950937	Up	fibrillin 3
NRGN	0.836966	0.000152	0.007049	3.788326	Up	neurogranin
FLG	0.835054	0.002961	0.042045	2.971792	Up	filaggrin
RPH3A	0.833674	2.01E-05	0.002057	4.26337	Up	rabphilin 3A
ABCC11	0.832149	0.001053	0.022749	3.2761	Up	ATP binding cassette subfamily C member 11
CHRM4	0.831926	2.96E-05	0.00259	4.176849	Up	cholinergic receptor muscarinic 4
CHRM1	0.830727	2.92E-06	0.000596	4.676226	Up	cholinergic receptor muscarinic 1
MUC6	0.827797	0.000358	0.012179	3.569356	Up	mucin 6, oligomeric mucus/gel-forming
TUBB2A	0.826965	4.49E-06	0.00077	4.587124	Up	tubulin beta 2A class IIa
GRM2	0.825072	1.67E-06	0.000406	4.790128	Up	glutamate metabotropic receptor 2
SYT5	0.824591	4.32E-06	0.000752	4.595506	Up	synaptotagmin 5
IQCN	0.823133	0.003026	0.042573	2.965037	Up	IQ motif containing N
LINC02774	0.823064	0.00021	0.008621	3.707149	Up	long intergenic non-protein coding RNA 2774
DCAF12L2	0.822565	0.003043	0.042738	2.963376	Up	DDB1 and CUL4 associated factor 12 like 2
BAIAP3	0.816895	0.000536	0.015074	3.462163	Up	BAI1 associated protein 3
FAM163B	0.816308	0.00206	0.033974	3.081397	Up	family with sequence similarity 163 member B
MIR770	0.806941	3.76E-05	0.00295	4.121647	Up	microRNA 770
ABCC12	0.806531	0.001094	0.023229	3.265132	Up	ATP binding cassette subfamily C member 12
OPRL1	0.804213	0.000131	0.006397	3.823901	Up	opioid related nociceptin receptor 1
OVOL2	0.798974	0.001699	0.030356	3.138353	Up	ovo like zinc finger 2
SPINT2	0.795394	0.00048	0.0143	3.49166	Up	serine peptidase inhibitor, Kunitz type 2
LBH	0.794958	0.000563	0.015483	3.448694	Up	LBH regulator of WNT signaling pathway
EFNB3	0.792388	1.32E-08	2.14E-05	5.682967	Up	ephrin B3
CCK	0.791473	0.000129	0.006316	3.828522	Up	cholecystokinin
MYOZ3	0.791347	1.61E-05	0.001828	4.3125	Up	myozenin 3
HSPBP1	0.788878	0.000165	0.007361	3.767237	Up	HSPA (Hsp70) binding protein 1
SLC22A17	0.786538	0.000164	0.00732	3.769456	Up	solute carrier family 22 member 17
FAM86JP	0.785682	0.003691	0.048039	2.903438	Up	family with sequence similarity 86, member A pseudogene
HAS1	0.784851	0.001756	0.030918	3.128622	Up	hyaluronan synthase 1
DIRAS1	0.783633	3.76E-05	0.00295	4.121518	Up	DIRAS family GTPase 1
ERFE	0.78283	0.003612	0.04751	2.910189	Up	erythroferrone
HPCA	0.781831	6.02E-06	0.000931	4.525658	Up	hippocalcin
TRIM54	0.781588	0.001968	0.03318	3.094966	Up	tripartite motif containing 54
LRRC73	0.779696	0.001789	0.03122	3.12314	Up	leucine rich repeat containing 73
GNG13	0.775401	0.002161	0.035044	3.067114	Up	G protein subunit gamma 13
CDK5R2	0.774199	0.00074	0.018434	3.374202	Up	cyclin dependent kinase 5 regulatory subunit 2
SLC1A6	0.773261	0.000217	0.008825	3.698569	Up	solute carrier family 1 member 6
RCOR2	0.77228	2.14E-05	0.002159	4.249513	Up	REST corepressor 2
PNMA8B	0.769131	7.78E-06	0.001105	4.471232	Up	PNMA family member 8B

GALNT17	0.767281	6.19E-07	0.000192	4.985139	Up	polypeptide N-acetylgalactosaminyltransferase 17
ADAMTSL1	0.766708	7.83E-05	0.004603	3.949415	Up	ADAMTS like 1
LINC01852	0.762329	0.000813	0.019577	3.348249	Up	long intergenic non-protein coding RNA 1852
CPNE6	0.757645	3.48E-08	3.42E-05	5.515443	Up	copine 6
ARF5	0.752545	9.58E-07	0.000278	4.900011	Up	ADP ribosylation factor 5
ARHGDIG	0.751133	0.003455	0.04616	2.924035	Up	Rho GDP dissociation inhibitor gamma
MAL2	0.750925	0.00053	0.015013	3.464923	Up	mal, T cell differentiation protein 2
TPBGL-AS1	0.747725	0.000381	0.012619	3.553134	Up	TPBGL antisense RNA 1
FBLL1	0.747278	0.000964	0.021756	3.300864	Up	fibrillarin like 1
COX8A	0.745665	0.000818	0.01963	3.346764	Up	cytochrome c oxidase subunit 8A
RASL10A	0.745457	1.43E-06	0.000361	4.821	Up	RAS like family 10 member A
CALHM1	0.742023	6.42E-05	0.004097	3.996832	Up	calcium homeostasis modulator 1
SLC7A4	0.741065	0.000514	0.014807	3.473391	Up	solute carrier family 7 member 4
KCNK3	0.73989	0.001144	0.023891	3.252387	Up	potassium two pore domain channel subfamily K member 3
SEZ6L2	0.739852	1.21E-05	0.001502	4.375493	Up	seizure related 6 homolog like 2
GOLGA8B	0.737827	0.002345	0.036803	3.042688	Up	golgin A8 family member B
MRPS12	0.73683	0.001616	0.029479	3.153064	Up	mitochondrial ribosomal protein S12
IL1RAPL2	0.736053	0.000358	0.012179	3.569293	Up	interleukin 1 receptor accessory protein like 2
SLC6A17	0.735556	1.00E-05	0.001308	4.416511	Up	solute carrier family 6 member 17
SLC22A24	0.730974	0.003683	0.047996	2.904107	Up	solute carrier family 22 member 24
PGLYRP1	0.728015	0.002952	0.041993	2.972729	Up	peptidoglycan recognition protein 1
IQANK1	0.727277	0.002092	0.034362	3.076802	Up	IQ motif and ankyrin repeat containing 1
EXOSC5	0.726211	3.69E-05	0.00293	4.126362	Up	exosome component 5
GPCPD1	0.725569	0.00023	0.009154	3.6833	Up	glycerophosphocholine phosphodiesterase 1
DNAJC5G	0.723975	0.001741	0.030779	3.131264	Up	DnaJ heat shock protein family (Hsp40) member C5 gamma
INSM1	0.721321	0.001391	0.026924	3.196419	Up	INSM transcriptional repressor 1
SLC6A7	0.721028	3.44E-05	0.002819	4.142033	Up	solute carrier family 6 member 7
WNT10B	0.718075	0.000183	0.007881	3.741741	Up	Wnt family member 10B
NPTX2	0.716495	0.003448	0.046123	2.924676	Up	neuronal pentraxin 2
SYT13	0.715331	1.59E-05	0.001816	4.315361	Up	synaptotagmin 13
LOC101927531	0.715119	0.000304	0.010996	3.611807	Up	uncharacterized LOC101927531
PCDHAC2	0.713742	4.13E-06	0.000739	4.6047	Up	protocadherin alpha subfamily C, 2
CDH22	0.713176	0.003097	0.043303	2.957917	Up	cadherin 22
SLC45A1	0.712508	0.000665	0.017076	3.403538	Up	solute carrier family 45 member 1
SMIM10L2B	0.712121	2.63E-05	0.002373	4.20344	Up	small integral membrane protein 10 like 2B
KLHL25	0.7114	0.001375	0.026829	3.199884	Up	kelch like family member 25
SLC8A2	0.711308	3.60E-05	0.002896	4.131753	Up	solute carrier family 8 member A2
PRMT8	0.708775	2.41E-05	0.002275	4.223027	Up	protein arginine methyltransferase 8
GPR88	0.705119	0.001332	0.026315	3.208938	Up	G protein-coupled receptor 88
ELFN2	0.70333	0.000279	0.010367	3.634355	Up	extracellular leucine rich repeat and fibronectin type III domain containing 2
IGSF3	0.702883	0.000482	0.014319	3.490622	Up	immunoglobulin superfamily member 3

TUBA1B	0.702813	0.000797	0.019313	3.353705	Up	tubulin alpha 1b
PSMG3	0.701566	0.000101	0.005414	3.888517	Up	proteasome assembly chaperone 3
SPRY4-AS1	0.701413	0.001084	0.023103	3.26777	Up	SPRY4 antisense RNA 1
VWA5B2	0.699677	0.0028	0.040854	2.988847	Up	von Willebrand factor A domain containing 5B2
MARCHF4	0.696914	4.05E-06	0.000738	4.608688	Up	membrane associated ring-CH-type finger 4
NSG2	0.695107	4.77E-05	0.003461	4.066774	Up	neuronal vesicle trafficking associated 2
NPTXR	0.694381	7.37E-05	0.004447	3.964061	Up	neuronal pentraxin receptor stum, mechanosensory transduction mediator homolog
STUM	0.692895	0.000182	0.007858	3.742894	Up	homeodomain interacting protein kinase 4
HIPK4	0.692477	0.003623	0.047557	2.90922	Up	regulator of G protein signaling 4
RGS4	0.69105	0.00061	0.016083	3.42694	Up	seizure related 6 homolog
SEZ6	0.688386	3.64E-07	0.00013	5.086728	Up	GUSB pseudogene 5
GUSBP5	0.687454	0.003388	0.045578	2.930135	Up	calcium voltage-gated channel auxiliary subunit beta 1
CACNB1	0.686313	8.13E-06	0.00113	4.461619	Up	H2A clustered histone 21
H2AC21	0.685202	0.000306	0.011024	3.610526	Up	neuronal guanine nucleotide exchange factor
NGEF	0.68419	4.76E-06	0.000799	4.575213	Up	double C2 domain alpha
DOC2A	0.684045	8.18E-05	0.004711	3.939051	Up	ubiquitin specific peptidase 11
USP11	0.682506	2.28E-08	2.73E-05	5.58935	Up	polo like kinase 2
PLK2	0.679706	3.21E-05	0.002719	4.157774	Up	transmembrane protein 121B
TMEM121B	0.679167	8.25E-07	0.000244	4.929298	Up	integrator complex subunit 5
INTS5	0.677933	0.00138	0.026881	3.19882	Up	sodium voltage-gated channel beta subunit 3
SCN3B	0.676599	2.57E-06	0.000545	4.702124	Up	CaM kinase like vesicle associated
CAMKV	0.676166	1.51E-06	0.000374	4.810257	Up	phospholipase D family member 3
PLD3	0.675655	0.000307	0.011054	3.609378	Up	cystin 1
CYS1	0.674066	0.001363	0.026672	3.202387	Up	nucleophosmin/nucleoplasmin 3
NPM3	0.673765	0.000204	0.008482	3.713911	Up	period circadian regulator 2
PER2	0.673499	3.02E-05	0.002625	4.171985	Up	exostosin like glycosyltransferase 1
EXTL1	0.672999	0.000845	0.020033	3.337759	Up	small integral membrane protein 10 like 2A
SMIM10L2A	0.672892	2.30E-05	0.002224	4.233981	Up	ring finger protein 165
RNF165	0.672744	1.61E-09	6.14E-06	6.03323	Up	solute carrier family 26 member 10
SLC26A10	0.670661	0.001998	0.033378	3.090535	Up	pyrroline-5-carboxylate reductase 3
PYCR3	0.670446	0.001408	0.027164	3.193042	Up	ECRG4 augurin precursor
ECRG4	0.669705	0.001477	0.028041	3.179068	Up	zinc finger protein 843
ZNF843	0.669329	0.002869	0.041444	2.9814	Up	interleukin 1 receptor like 2
IL1RL2	0.667346	0.002248	0.035946	3.055298	Up	NUAK family kinase 1
NUAK1	0.666452	1.96E-07	9.17E-05	5.203046	Up	leucine rich repeat and Ig domain containing 1
LINGO1	0.665604	0.000345	0.011881	3.578594	Up	opsin 3
OPN3	0.665526	0.000696	0.017674	3.391285	Up	FXYP domain containing ion transport regulator 7
FXYP7	0.664062	0.000433	0.013489	3.518977	Up	translocase of inner mitochondrial membrane 13
TIMM13	0.66333	0.001988	0.03328	3.091952	Up	transgelin 3
TAGLN3	0.66322	0.000158	0.007185	3.778598	Up	family with sequence similarity 83 member H
FAM83H	0.66238	0.002036	0.033747	3.084998	Up	

CAMKK2	0.662207	8.37E-06	0.001151	4.455606	Up	calcium/calmodulin dependent protein kinase kinase 2
RHBDD2	0.661935	0.000323	0.011415	3.596229	Up	rhomboid domain containing 2
RTL8C	0.661341	0.000524	0.014965	3.467967	Up	retrotransposon Gag like 8C
CLSTN3	0.661263	3.12E-05	0.002668	4.164495	Up	calsyntenin 3
LZTS1	0.660794	0.00046	0.013961	3.502917	Up	leucine zipper tumor suppressor 1
ASMTL	0.658189	4.50E-06	0.00077	4.586643	Up	acetylserotonin O-methyltransferase like
SYT12	0.657803	7.41E-05	0.00445	3.962805	Up	synaptotagmin 12
PAK6	0.65675	0.00023	0.009154	3.683477	Up	p21 (RAC1) activated kinase 6
LYRM9	0.656544	0.000141	0.006744	3.806235	Up	LYR motif containing 9
ENO2	0.655341	4.74E-05	0.003458	4.068169	Up	enolase 2
DCTPP1	0.654944	0.000891	0.020803	3.322974	Up	dCTP pyrophosphatase 1
RBM3	0.654476	0.003382	0.045551	2.930681	Up	RNA binding motif protein 3
CHCHD2	0.653998	3.13E-06	0.00062	4.662194	Up	coiled-coil-helix-coiled-coil-helix domain containing 2
SPRYD3	0.650124	5.26E-06	0.000851	4.55414	Up	SPRY domain containing 3
KCNIP3	0.648476	0.000541	0.015092	3.459506	Up	potassium voltage-gated channel interacting protein 3
SYN	0.647508	1.14E-05	0.00144	4.388625	Up	synaptophysin
HPCAL1	0.646778	0.000649	0.016826	3.410186	Up	hippocalcin like 1
ATP6V0E2	0.646404	0.000115	0.005894	3.856466	Up	ATPase H+ transporting V0 subunit e2
C17orf107	0.646091	0.000384	0.012692	3.55099	Up	chromosome 17 open reading frame 107
STOML1	0.645355	0.000486	0.014399	3.488589	Up	stomatin like 1
IGSF8	0.644994	0.001726	0.030613	3.133796	Up	immunoglobulin superfamily member 8
PAK1	0.6446	8.58E-05	0.00488	3.927526	Up	p21 (RAC1) activated kinase 1
ST6GAL2	0.64444	2.44E-05	0.002287	4.219959	Up	ST6 beta-galactoside alpha-2,6-sialyltransferase 2
PNCK	0.6433	0.002253	0.035955	3.054701	Up	pregnancy up-regulated nonubiquitous CaM kinase
SCN2B	0.643055	2.00E-05	0.002057	4.265334	Up	sodium voltage-gated channel beta subunit 2
CORO1A	0.642552	0.000993	0.022057	3.292434	Up	coronin 1A
SYNGR3	0.642483	0.000342	0.011867	3.581276	Up	synaptogyrin 3
PCDH1	0.642386	8.94E-07	0.000262	4.913608	Up	protocadherin 1
POP7	0.642121	0.000667	0.017076	3.40291	Up	POP7 homolog, ribonuclease P/MRP subunit
TRIM67	0.641558	0.000952	0.021622	3.304215	Up	tripartite motif containing 67
PPP1R14C	0.640426	0.000164	0.00732	3.769433	Up	protein phosphatase 1 regulatory inhibitor subunit 14C
DLK2	0.639578	0.001207	0.024751	3.237222	Up	delta like non-canonical Notch ligand 2
PIGZ	0.635922	1.27E-05	0.001547	4.365041	Up	phosphatidylinositol glycan anchor biosynthesis class Z
NRSN1	0.635858	9.97E-05	0.0054	3.891254	Up	neurensin 1
NAT14	0.633433	0.002358	0.036899	3.04105	Up	N-acetyltransferase 14 (putative)
CCNA1	0.633374	0.002938	0.041978	2.974174	Up	cyclin A1
ADGRB2	0.633335	0.002806	0.040879	2.988175	Up	adhesion G protein-coupled receptor B2
CIRBP	0.633167	0.002021	0.033557	3.087148	Up	cold inducible RNA binding protein
TMIE	0.632303	0.002008	0.033447	3.089019	Up	transmembrane inner ear
TBCC	0.632039	2.88E-05	0.002531	4.182841	Up	tubulin folding cofactor C
RHOBTB2	0.631338	3.04E-05	0.002625	4.170476	Up	Rho related BTB domain containing 2

TMEM38A	0.630823	3.55E-05	0.002875	4.135105	Up	transmembrane protein 38A
VAMP2	0.630349	1.22E-06	0.000326	4.852353	Up	vesicle associated membrane protein 2
STMN3	0.630257	0.002968	0.04208	2.970986	Up	stathmin 3
ATP1A3	0.630237	0.000991	0.022042	3.292943	Up	ATPase Na ⁺ /K ⁺ transporting subunit alpha 3
NSG1	0.629552	0.00068	0.01736	3.397454	Up	neuronal vesicle trafficking associated 1 potassium voltage-gated channel subfamily B member 2
KCNB2	0.6271	2.21E-05	0.002185	4.24216	Up	
NLRP1	0.62667	0.000976	0.021884	3.29739	Up	NLR family pyrin domain containing 1
TUBA4A	0.626034	0.000629	0.016441	3.418969	Up	tubulin alpha 4a
PTPN3	0.625855	6.03E-05	0.003997	4.011688	Up	protein tyrosine phosphatase non-receptor type 3
TENM2	0.625289	3.43E-05	0.002814	4.143087	Up	teneurin transmembrane protein 2
PCDH19	0.62376	0.001579	0.029104	3.159716	Up	protocadherin 19
NMNAT2	0.623416	3.58E-06	0.000686	4.634428	Up	nicotinamide nucleotide adenyltransferase 2
RIMS3	0.623123	6.45E-05	0.004097	3.995805	Up	regulating synaptic membrane exocytosis 3
NRN1	0.623104	0.002649	0.039607	3.00582	Up	neurtin 1
SV2A	0.623085	1.68E-05	0.001876	4.303091	Up	synaptic vesicle glycoprotein 2A calcium/calmodulin dependent protein kinase IV
CAMK4	0.622566	0.000412	0.013274	3.532277	Up	
COPS7A	0.622008	3.34E-05	0.002779	4.149115	Up	COP9 signalosome subunit 7A
UNC5D	0.621766	2.23E-05	0.002186	4.240741	Up	unc-5 netrin receptor D
HR	0.62154	0.002581	0.038945	3.013632	Up	HR lysine demethylase and nuclear receptor corepressor
SHISAL1	0.621252	6.95E-06	0.001029	4.495065	Up	shisa like 1
ATP6V0B	0.620476	0.001433	0.027526	3.188004	Up	ATPase H ⁺ transporting V0 subunit b
PNMA3	0.619918	0.000206	0.00855	3.711134	Up	PNMA family member 3
C1orf115	0.618116	4.34E-05	0.003272	4.088554	Up	chromosome 1 open reading frame 115
FLJ33534	0.617924	0.003139	0.043598	2.953769	Up	uncharacterized LOC285150
VIPR1	0.614155	5.35E-07	0.000177	5.013206	Up	vasoactive intestinal peptide receptor 1 protein phosphatase 2 scaffold subunit Aalpha
PPP2R1A	0.613768	0.000244	0.009491	3.668319	Up	
LAMB3	0.611764	0.001681	0.030087	3.141529	Up	laminin subunit beta 3
MEG9	0.61146	0.001654	0.029823	3.146289	Up	maternally expressed 9 calcium voltage-gated channel auxiliary subunit gamma 3
CACNG3	0.611001	1.50E-05	0.001737	4.329255	Up	
BAIAP2-DT	0.610293	1.13E-05	0.001434	4.390522	Up	BAIAP2 divergent transcript
PRKCG	0.609658	0.001206	0.024751	3.237449	Up	protein kinase C gamma
BFSP1	0.609396	0.000224	0.008988	3.690554	Up	beaded filament structural protein 1
MEF2D	0.606269	6.74E-08	5.15E-05	5.397881	Up	myocyte enhancer factor 2D
DNAL4	0.605999	2.41E-05	0.002275	4.222628	Up	dynein axonemal light chain 4
TRIB3	0.605755	0.001122	0.02356	3.258079	Up	tribbles pseudokinase 3
RAB40C	0.604893	0.003641	0.047664	2.907676	Up	RAB40C, member RAS oncogene family
EMD	0.601995	0.0005	0.014605	3.480747	Up	emerin
SULT4A1	0.601165	0.000401	0.01304	3.539695	Up	sulfotransferase family 4A member 1 family with sequence similarity 131 member A
FAM131A	0.600311	2.56E-05	0.002346	4.209238	Up	
CX3CL1	0.599497	0.000207	0.008554	3.710645	Up	C-X3-C motif chemokine ligand 1
PRKAR1B	0.597876	0.000537	0.015074	3.461641	Up	protein kinase cAMP-dependent type I regulatory subunit beta

NBL1	0.597287	0.000242	0.009453	3.671087	Up	NBL1, DAN family BMP antagonist
CA10	0.594811	0.000868	0.02041	3.330142	Up	carbonic anhydrase 10
ENC1	0.594616	0.000124	0.006135	3.838121	Up	ectodermal-neural cortex 1
VSTM5	0.594469	0.000167	0.007396	3.764855	Up	V-set and transmembrane domain containing 5
NRSN2	0.593309	3.98E-05	0.003093	4.108674	Up	neurensin 2
PARM1	0.593043	0.000798	0.019321	3.353347	Up	prostate androgen-regulated mucin-like protein 1
FNDC5	0.592705	0.000123	0.006115	3.839376	Up	fibronectin type III domain containing 5
CLCA4-AS1	0.592668	0.000464	0.014026	3.500632	Up	CLCA4 antisense RNA 1
KLHL26	0.591733	0.003862	0.049477	2.889178	Up	kelch like family member 26
MN1	0.591269	0.001017	0.022363	3.285848	Up	MN1 proto-oncogene, transcriptional regulator
ADRA1B	0.59109	0.001072	0.022962	3.270814	Up	adrenoceptor alpha 1B
NDUFA4	0.590831	0.000401	0.01304	3.539444	Up	NDUFA4 mitochondrial complex associated
ATP2B1-AS1	0.590095	0.001336	0.026326	3.208062	Up	ATP2B1 antisense RNA 1
MICOS13	0.588719	0.002569	0.038862	3.015075	Up	mitochondrial contact site and cristae organizing system subunit 13
ATP6V1B2	0.584358	0.000316	0.011233	3.601498	Up	ATPase H+ transporting V1 subunit B2
CDH13	0.584249	0.001336	0.026326	3.208071	Up	cadherin 13
GNG4	0.583564	1.48E-05	0.001721	4.332212	Up	G protein subunit gamma 4
EFR3B	0.582314	5.26E-05	0.003722	4.043684	Up	EFR3 homolog B
CNTNAP2	0.581828	0.000394	0.012919	3.544118	Up	contactin associated protein 2
SPIN2B	0.579472	0.000374	0.012428	3.558105	Up	spindlin family member 2B
GGT7	0.579166	0.001134	0.023749	3.254946	Up	gamma-glutamyltransferase 7
CAMK1	0.578944	0.001382	0.026881	3.198379	Up	calcium/calmodulin dependent protein kinase I
ETV5	0.577556	0.00176	0.03096	3.128034	Up	ETS variant transcription factor 5
FLRT1	0.577462	0.0024	0.03727	3.035678	Up	fibronectin leucine rich transmembrane protein 1
KIF17	0.576033	0.000158	0.007197	3.777749	Up	kinesin family member 17
RAB36	0.57552	6.83E-05	0.004226	3.981992	Up	RAB36, member RAS oncogene family signal transducer and activator of transcription 4
STAT4	0.575097	0.00093	0.021351	3.310765	Up	transcription 4
CALM3	0.574971	0.000342	0.011867	3.581292	Up	calmodulin 3
SLC12A5	0.574925	0.000795	0.019294	3.354481	Up	solute carrier family 12 member 5
NRIP3	0.574464	0.002189	0.035375	3.063252	Up	nuclear receptor interacting protein 3
NIPSNAP1	0.573253	0.000187	0.008009	3.735356	Up	nipsnap homolog 1
PIN1	0.572929	0.000532	0.015024	3.464097	Up	peptidylprolyl cis/trans isomerase, NIMA-interacting 1
PHYHIP	0.572383	0.003333	0.045227	2.935187	Up	phytanoyl-CoA 2-hydroxylase interacting protein
ATP5MC1	0.571539	0.000784	0.019099	3.358505	Up	ATP synthase membrane subunit c locus 1
C11orf87	0.570198	0.000371	0.012399	3.559702	Up	chromosome 11 open reading frame 87
ARF3	0.569953	2.06E-06	0.000479	4.747897	Up	ADP ribosylation factor 3
ATP5F1B	0.569352	0.00045	0.013741	3.508912	Up	ATP synthase F1 subunit beta
CDH8	0.56886	0.000685	0.017432	3.395572	Up	cadherin 8
PTPRN	0.568466	0.000814	0.019587	3.347861	Up	protein tyrosine phosphatase receptor type N
C3orf80	0.568119	0.002463	0.037894	3.027826	Up	chromosome 3 open reading frame 80
HSD11B1L	0.567059	0.001777	0.031151	3.125094	Up	hydroxysteroid 11-beta dehydrogenase 1 like

PCDHGC4	0.566825	1.08E-05	0.00138	4.400827	Up	protocadherin gamma subfamily C, 4
SCAMP5	0.566451	0.000568	0.015575	3.446565	Up	secretory carrier membrane protein 5
SATB2-AS1	0.566214	6.35E-05	0.004086	3.99943	Up	SATB2 antisense RNA 1
DDX28	0.566055	0.00381	0.049004	2.893516	Up	DEAD-box helicase 28
SYT16	0.565556	0.000156	0.007138	3.781458	Up	synaptotagmin 16
HINT1	0.564742	0.000244	0.009491	3.668672	Up	histidine triad nucleotide binding protein 1
CYC1	0.564287	0.003586	0.047276	2.912466	Up	cytochrome c1
NAA80	0.562087	0.001467	0.027995	3.181115	Up	N-alpha-acetyltransferase 80, NatH catalytic subunit
YIF1B	0.562073	0.003136	0.043598	2.954102	Up	Yip1 interacting factor homolog B, membrane trafficking protein
NECTIN1	0.56181	0.000666	0.017076	3.403301	Up	nectin cell adhesion molecule 1
ACOT7	0.561622	0.000715	0.017971	3.383686	Up	acyl-CoA thioesterase 7
PGAP3	0.561312	0.000474	0.014191	3.495314	Up	post-GPI attachment to proteins phospholipase 3
ARSG	0.560845	5.61E-06	0.000892	4.540598	Up	arylsulfatase G
GAS7	0.56032	1.31E-07	7.33E-05	5.278071	Up	growth arrest specific 7
PIM2	0.559592	0.000752	0.018661	3.369836	Up	Pim-2 proto-oncogene, serine/threonine kinase
EOLA2	0.558484	0.000287	0.010556	3.626787	Up	endothelium and lymphocyte associated ASCH domain 2
H4C3	0.55825	0.00294	0.041978	2.973952	Up	H4 clustered histone 3
NDN	0.558194	0.000213	0.008711	3.703379	Up	necdin, MAGE family member
PODXL2	0.557048	0.001268	0.025485	3.223131	Up	podocalyxin like 2
IER5	0.556778	0.002226	0.035715	3.058279	Up	immediate early response 5
TSPYL5	0.556176	4.76E-06	0.000799	4.574983	Up	TSPY like 5
DMKN	0.556165	0.000313	0.011178	3.604409	Up	dermokine
MELTF	0.555344	0.00185	0.031886	3.113384	Up	melanotransferrin
CDIPT	0.554982	0.002878	0.041525	2.980479	Up	CDP-diacylglycerol--inositol 3-phosphatidyltransferase
CAP2	0.554587	0.000998	0.02211	3.291084	Up	cyclase associated actin cytoskeleton regulatory protein 2
RBP2	0.554399	0.002324	0.036609	3.045307	Up	retinol binding protein 2
SYNGR1	0.554115	0.001295	0.025814	3.217152	Up	synaptogyrin 1
AP1S1	0.552652	0.000925	0.021273	3.312492	Up	adaptor related protein complex 1 subunit sigma 1
DMTN	0.552086	0.001831	0.031712	3.116423	Up	dematin actin binding protein
PIANP	0.550773	0.00182	0.031579	3.118092	Up	PILR alpha associated neural protein
CRHR1	0.550694	0.002679	0.039762	3.002326	Up	corticotropin releasing hormone receptor 1
PPOX	0.548804	0.00029	0.010613	3.624354	Up	protoporphyrinogen oxidase
NTNG1	0.548229	0.001874	0.032169	3.109467	Up	netrin G1
ZFR2	0.548113	0.001977	0.033227	3.093695	Up	zinc finger RNA binding protein 2
CRY2	0.547983	2.26E-06	0.000515	4.728386	Up	cryptochrome circadian regulator 2
SNCB	0.547273	0.001516	0.028437	3.171613	Up	synuclein beta
ASS1	0.546931	0.002907	0.041695	2.977397	Up	argininosuccinate synthase 1
RAB3A	0.546661	0.001026	0.02248	3.28326	Up	RAB3A, member RAS oncogene family
B4GAT1	0.543905	2.55E-05	0.002346	4.210207	Up	beta-1,4-glucuronyltransferase 1
KATNB1	0.543621	0.002795	0.040794	2.989458	Up	katanin regulatory subunit B1
STXBP1	0.543085	5.92E-06	0.000922	4.529375	Up	syntaxin binding protein 1

SLC8A3	0.542718	8.93E-06	0.001204	4.441588	Up	solute carrier family 8 member A3
RNF187	0.542402	0.001711	0.030457	3.13624	Up	ring finger protein 187
OTUB1	0.542172	0.000611	0.016083	3.426627	Up	OTU deubiquitinase, ubiquitin aldehyde binding 1
KLHDC3	0.542157	0.000345	0.011881	3.578619	Up	kelch domain containing 3
CHRN2	0.541491	0.000314	0.011191	3.603464	Up	cholinergic receptor nicotinic beta 2 subunit
RND1	0.541448	0.00077	0.01891	3.363207	Up	Rho family GTPase 1
MEX3B	0.541264	0.002197	0.035416	3.06229	Up	mex-3 RNA binding family member B adaptor related protein complex 2 subunit mu 1
AP2M1	0.540869	5.38E-05	0.003754	4.038527	Up	
SNU13	0.539696	0.00036	0.012221	3.567648	Up	small nuclear ribonucleoprotein 13
PTPN5	0.539316	0.00024	0.009423	3.673178	Up	protein tyrosine phosphatase non-receptor type 5
ATP6AP1	0.539037	0.000627	0.016423	3.419526	Up	ATPase H ⁺ transporting accessory protein 1 GABA type A receptor associated protein like 1
GABARAPL1	0.539014	0.000143	0.00676	3.803709	Up	
PPL	0.538549	7.93E-05	0.004619	3.946436	Up	periplakin
PCP4L1	0.538368	0.003183	0.043946	2.949534	Up	Purkinje cell protein 4 like 1
PSMB5	0.537933	0.000276	0.010322	3.636747	Up	proteasome 20S subunit beta 5
SLC17A7	0.5365	0.000222	0.008953	3.692842	Up	solute carrier family 17 member 7 FHF complex subunit HOOK interacting protein 1B
FHIP1B	0.536474	5.91E-05	0.003973	4.016568	Up	
NAPA	0.536199	0.000601	0.015989	3.431062	Up	NSF attachment protein alpha amyloid beta precursor protein binding family B member 3
APBB3	0.536081	0.000835	0.019852	3.341	Up	translocase of inner mitochondrial membrane 17B
TIMM17B	0.53556	0.001665	0.029949	3.144235	Up	
ZNF710	0.534718	0.000602	0.015989	3.430676	Up	zinc finger protein 710
NELL1	0.534473	8.46E-05	0.004839	3.930994	Up	neural EGFL like 1
ZMYND12	0.53421	0.003212	0.044162	2.946723	Up	zinc finger MYND-type containing 12
TRIM66	0.533979	2.93E-07	0.000116	5.12774	Up	tripartite motif containing 66
MDH1B	0.532329	0.003014	0.042457	2.96635	Up	malate dehydrogenase 1B
ARHGEF9	0.530615	3.66E-06	0.000686	4.62961	Up	Cdc42 guanine nucleotide exchange factor 9
CPNE7	0.530277	0.001282	0.025631	3.220031	Up	copine 7
FIBP	0.530223	0.000862	0.020331	3.332225	Up	FGF1 intracellular binding protein
RET	0.529698	0.002897	0.04168	2.978507	Up	ret proto-oncogene trafficking protein particle complex subunit 1
TRAPPC1	0.528748	0.000639	0.016635	3.414474	Up	
TARBP1	0.527945	0.000992	0.022042	3.292863	Up	TAR (HIV-1) RNA binding protein 1
NEURL1B	0.527449	0.000241	0.009453	3.671134	Up	neuralized E3 ubiquitin protein ligase 1B G protein-coupled receptor associated sorting protein 2
GPRASP2	0.527069	0.000166	0.007373	3.766433	Up	
UNC13A	0.526448	3.12E-05	0.002668	4.164346	Up	unc-13 homolog A
CD200	0.526385	0.000366	0.012276	3.563246	Up	CD200 molecule
XK	0.526105	0.001959	0.033081	3.096447	Up	X-linked Kx blood group
NME1	0.526023	0.001781	0.031189	3.1245	Up	NME/NM23 nucleoside diphosphate kinase 1
CCDC113	0.525628	0.000129	0.006316	3.828348	Up	coiled-coil domain containing 113
STX1B	0.525556	0.000391	0.012879	3.545799	Up	syntaxin 1B
CDK5	0.524293	0.00155	0.028801	3.165119	Up	cyclin dependent kinase 5

SNRPB	0.523958	0.003581	0.047235	2.912928	Up	small nuclear ribonucleoprotein polypeptides B and B1
HTR5A	0.523892	0.002412	0.037385	3.034202	Up	5-hydroxytryptamine receptor 5A
HPCAL4	0.523691	0.000361	0.012247	3.566766	Up	hippocalcin like 4
MB21D2	0.523677	0.001132	0.023722	3.255477	Up	Mab-21 domain containing 2
PEF1	0.522679	0.000118	0.005954	3.851281	Up	penta-EF-hand domain containing 1
RUSF1	0.522283	0.002614	0.039265	3.009786	Up	RUS family member 1
TSPYL4	0.522091	9.78E-06	0.001282	4.421925	Up	TSPY like 4
TMEM72-AS1	0.521967	0.0013	0.025872	3.215889	Up	TMEM72 antisense RNA 1
TSHZ3	0.521488	1.97E-05	0.002049	4.267831	Up	teashirt zinc finger homeobox 3
ACTL6B	0.520435	0.000474	0.014191	3.495051	Up	actin like 6B
MAST3	0.518596	0.000221	0.008953	3.693246	Up	microtubule associated serine/threonine kinase 3
TMEM178B	0.518204	0.00019	0.008088	3.732094	Up	transmembrane protein 178B
FAM234B	0.518159	0.000179	0.007777	3.746666	Up	family with sequence similarity 234 member B
FMNL1-DT	0.517683	0.000275	0.010296	3.638086	Up	FMNL1 divergent transcript
NREP	0.516738	0.000895	0.020895	3.321501	Up	neuronal regeneration related protein
TMEM9	0.515958	0.000791	0.01922	3.356024	Up	transmembrane protein 9
GABRG2	0.51555	0.001582	0.029123	3.15922	Up	gamma-aminobutyric acid type A receptor subunit gamma2
DLG3	0.514437	6.94E-05	0.004254	3.978328	Up	discs large MAGUK scaffold protein 3
CYRIA	0.514275	0.000222	0.008962	3.692053	Up	CYFIP related Rac1 interactor A
ADGRA1	0.513877	0.001969	0.03318	3.094841	Up	adhesion G protein-coupled receptor A1
KCNS2	0.51341	0.000105	0.005584	3.878432	Up	potassium voltage-gated channel modifier subfamily S member 2
CITED2	0.513285	0.003355	0.045406	2.933199	Up	Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2
TOP2A	-5.03851	6.72E-06	0.001005	-4.5023	Down	DNA topoisomerase II alpha
DLGAP5	-5.01203	1.33E-06	0.000346	-4.83505	Down	DLG associated protein 5
MKI67	-4.58038	2.15E-07	9.26E-05	-5.18551	Down	marker of proliferation Ki-67
H1-5	-4.23005	4.98E-06	0.000818	-4.56574	Down	H1.5 linker histone, cluster member
CEP55	-3.72207	0.000235	0.009291	-3.67842	Down	centrosomal protein 55
RRM2	-3.12261	0.000371	0.012399	-3.56012	Down	ribonucleotide reductase regulatory subunit M2
FAM111B	-3.03965	0.000195	0.008246	-3.72488	Down	FAM111 trypsin like peptidase B
MTCO2P22	-2.95644	2.46E-06	0.000528	-4.71175	Down	MT-CO2 pseudogene 22
HJURP	-2.92605	6.15E-05	0.004026	-4.00714	Down	Holliday junction recognition protein
MELK	-2.74507	0.000262	0.009918	-3.65041	Down	maternal embryonic leucine zipper kinase
NDC80	-2.72879	9.38E-05	0.005184	-3.90605	Down	NDC80 kinetochore complex component
VNN1	-2.53963	3.03E-07	0.000116	-5.12187	Down	vanin 1
OR7A5	-2.42661	2.10E-08	2.73E-05	-5.60346	Down	olfactory receptor family 7 subfamily A member 5
BCL2A1	-2.37195	8.28E-05	0.004757	-3.9361	Down	BCL2 related protein A1
CHI3L1	-2.2234	4.64E-08	4.05E-05	-5.46448	Down	chitinase 3 like 1
OR7C1	-2.1649	0.001309	0.025968	-3.21405	Down	olfactory receptor family 7 subfamily C member 1
ANKRD22	-2.12449	0.00376	0.048597	-2.8976	Down	ankyrin repeat domain 22
IL9	-2.03935	2.80E-05	0.002487	-4.18897	Down	interleukin 9
SHISA3	-1.98307	4.30E-08	4.05E-05	-5.47804	Down	shisa family member 3

STC1	-1.97591	0.002283	0.036129	-3.05067	Down	stanniocalcin 1
ANGPT2	-1.94047	1.17E-12	3.22E-08	-7.10865	Down	angiopoietin 2
KNL1	-1.91429	0.000208	0.008598	-3.70885	Down	kinetochore scaffold 1
MCM10	-1.91095	0.000864	0.020359	-3.33136	Down	minichromosome maintenance 10 replication initiation factor
LOC100418888	-1.90631	2.57E-05	0.002346	-4.20818	Down	peptidase D pseudogene
FPR2	-1.8649	0.000131	0.006397	-3.82406	Down	formyl peptide receptor 2
SGO1	-1.85155	9.69E-09	2.05E-05	-5.73615	Down	shugoshin 1
S100A9	-1.83066	0.003118	0.043479	-2.95589	Down	S100 calcium binding protein A9
MPZL2	-1.8157	0.000768	0.018865	-3.36411	Down	myelin protein zero like 2
LINC00323	-1.81439	0.000175	0.007635	-3.75286	Down	long intergenic non-protein coding RNA 323
TLR8	-1.75649	0.000156	0.007139	-3.78101	Down	toll like receptor 8
MMRN1	-1.73947	0.001911	0.032615	-3.10377	Down	multimerin 1
LINC02212	-1.73696	0.000153	0.007071	-3.78546	Down	long intergenic non-protein coding RNA 2212
SERPINA1	-1.7019	0.000906	0.020995	-3.31805	Down	serpin family A member 1
LINC00397	-1.70074	0.001066	0.02291	-3.27256	Down	long intergenic non-protein coding RNA 397
KIF14	-1.69915	6.00E-05	0.003997	-4.01286	Down	kinesin family member 14
LOC100421160	-1.69472	0.000973	0.021872	-3.29822	Down	structural maintenance of chromosomes 5 pseudogene
LINC01736	-1.68032	0.000197	0.008305	-3.7222	Down	long intergenic non-protein coding RNA 1736
MT1L	-1.67121	5.55E-05	0.003828	-4.03115	Down	metallothionein 1L, pseudogene
MT1G	-1.6624	1.06E-06	0.000296	-4.88091	Down	metallothionein 1G
KCNE4	-1.64603	5.58E-05	0.003839	-4.02985	Down	potassium voltage-gated channel subfamily E regulatory subunit 4
LINC01108	-1.63308	9.88E-05	0.005382	-3.89349	Down	long intergenic non-protein coding RNA 1108
OR52B6	-1.62445	8.35E-06	0.001151	-4.45609	Down	olfactory receptor family 52 subfamily B member 6
CDA	-1.61694	0.000209	0.008598	-3.7082	Down	cytidine deaminase
LOC100419761	-1.61275	0.001381	0.026881	-3.19869	Down	zinc finger protein 654 pseudogene
CCR5	-1.60711	0.000223	0.008967	-3.69152	Down	C-C motif chemokine receptor 5
LINC02172	-1.60536	5.98E-05	0.003997	-4.01367	Down	long intergenic non-protein coding RNA 2172
LOC100419170	-1.60039	3.63E-05	0.0029	-4.1301	Down	toll like receptor 2 pseudogene
WDR64	-1.5977	0.000147	0.006907	-3.79549	Down	WD repeat domain 64
TTK	-1.58827	0.000177	0.0077	-3.74995	Down	TTK protein kinase
NOD2	-1.58663	7.76E-05	0.004587	-3.95172	Down	nucleotide binding oligomerization domain containing 2
PLAC8	-1.57911	0.00056	0.015417	-3.45041	Down	placenta associated 8
VNN2	-1.57006	9.01E-05	0.005046	-3.91579	Down	vanin 2
MT1F	-1.56862	2.05E-06	0.000479	-4.74891	Down	metallothionein 1F
GBP1	-1.56584	3.66E-06	0.000686	-4.63005	Down	guanylate binding protein 1
MS4A6A	-1.55846	0.000951	0.021608	-3.30463	Down	membrane spanning 4-domains A6A
GBP5	-1.55818	0.000167	0.0074	-3.76429	Down	guanylate binding protein 5
GBP2	-1.55692	4.63E-09	1.27E-05	-5.86006	Down	guanylate binding protein 2
SLC1A7	-1.55493	5.40E-05	0.003754	-4.03753	Down	solute carrier family 1 member 7
HPGD	-1.54539	1.79E-05	0.001932	-4.28899	Down	15-hydroxyprostaglandin dehydrogenase
C7	-1.5299	0.000975	0.021872	-3.29777	Down	complement C7

LOC100419447	-1.51315	0.000885	0.020712	-3.32487	Down	lysine acetyltransferase 14 pseudogene
ZNF849P	-1.51014	0.000582	0.015781	-3.44007	Down	zinc finger protein 849, pseudogene
S100A4	-1.50734	0.001119	0.023525	-3.25872	Down	S100 calcium binding protein A4
OR51B5	-1.50185	0.001317	0.026095	-3.21218	Down	olfactory receptor family 51 subfamily B member 5
ANKRD30A	-1.49293	0.00034	0.011863	-3.58301	Down	ankyrin repeat domain 30A
MGAM	-1.4739	2.09E-07	9.26E-05	-5.19088	Down	maltase-glucoamylase
PLA1A	-1.47336	0.000107	0.005616	-3.8747	Down	phospholipase A1 member A
CD180	-1.46031	0.00054	0.015092	-3.45992	Down	CD180 molecule
EEF1A1P28	-1.46017	0.000796	0.019294	-3.35425	Down	eukaryotic translation elongation factor 1 alpha 1 pseudogene 28
KIF20A	-1.45282	3.84E-05	0.002993	-4.1169	Down	kinesin family member 20A
LINC01480	-1.43053	0.000494	0.014508	-3.48424	Down	long intergenic non-protein coding RNA 1480
CDK1	-1.42371	0.00314	0.043598	-2.95364	Down	cyclin dependent kinase 1
C1QB	-1.41986	0.002463	0.037894	-3.02786	Down	complement C1q B chain
KLRC3	-1.4196	0.002762	0.040567	-2.99301	Down	killer cell lectin like receptor C3
MGAM2	-1.41904	0.003224	0.044246	-2.94552	Down	maltase-glucoamylase 2 (putative)
NEAT1	-1.40979	1.11E-10	7.67E-07	-6.45055	Down	nuclear paraspeckle assembly transcript 1
LOC100133252	-1.40228	5.00E-06	0.000818	-4.56493	Down	zinc finger protein 131 pseudogene
RNU1-1	-1.39805	0.002847	0.04128	-2.98375	Down	RNA, U1 small nuclear 1
ASH2LP3	-1.39017	0.000243	0.009479	-3.67001	Down	ASH2L pseudogene 3
BOLL	-1.38337	2.31E-05	0.002224	-4.23269	Down	boule homolog, RNA binding protein
SPP1	-1.37844	0.001542	0.028739	-3.16658	Down	secreted phosphoprotein 1
FCGR3A	-1.36226	0.003084	0.043223	-2.95928	Down	Fc fragment of IgG receptor IIIa
EFCAB13-DT	-1.35955	4.29E-05	0.003266	-4.09154	Down	EFCAB13 divergent transcript
LAMB4	-1.35501	0.000422	0.013401	-3.52577	Down	laminin subunit beta 4
RNU6-1043P	-1.34282	0.000392	0.012879	-3.54556	Down	RNA, U6 small nuclear 1043, pseudogene
KCNJ15	-1.33383	0.00132	0.026136	-3.21153	Down	potassium inwardly rectifying channel subfamily J member 15
DDIT4L	-1.32471	5.77E-06	0.000909	-4.53459	Down	DNA damage inducible transcript 4 like
TMPRSS12	-1.31678	0.001801	0.031306	-3.12121	Down	transmembrane serine protease 12
SAMSN1	-1.31589	2.73E-05	0.00245	-4.1946	Down	SAM domain, SH3 domain and nuclear localization signals 1
TNFAIP8	-1.31156	4.12E-07	0.000145	-5.06341	Down	TNF alpha induced protein 8
TFAP2C	-1.31139	0.000594	0.015952	-3.43449	Down	transcription factor AP-2 gamma
AZGP1	-1.30905	5.19E-05	0.003695	-4.04694	Down	alpha-2-glycoprotein 1, zinc-binding
HMMR	-1.30619	0.002932	0.041948	-2.9748	Down	hyaluronan mediated motility receptor
TLR7	-1.29052	6.55E-05	0.004144	-3.99202	Down	toll like receptor 7
PRRG4	-1.28905	9.14E-05	0.005072	-3.91225	Down	proline rich and Gla domain 4
TNFRSF10D	-1.28183	0.000153	0.007071	-3.78687	Down	TNF receptor superfamily member 10d
REP15	-1.2731	0.000139	0.00671	-3.80907	Down	RAB15 effector protein
FYB1	-1.26793	0.000603	0.015989	-3.43043	Down	FYN binding protein 1
SCN4A	-1.26596	0.002923	0.041845	-2.97572	Down	sodium voltage-gated channel alpha subunit 4
SLFN12	-1.26338	2.42E-09	7.39E-06	-5.96695	Down	schlafen family member 12
SLFN13	-1.26259	2.39E-06	0.00052	-4.71733	Down	schlafen family member 13

NDUFA3P4	-1.25782	0.003348	0.045378	-2.93385	Down	NADH:ubiquinone oxidoreductase subunit A3 pseudogene 4
HGF	-1.2569	0.001884	0.032253	-3.10798	Down	hepatocyte growth factor
TRIP10	-1.25553	2.52E-07	0.000105	-5.15653	Down	thyroid hormone receptor interactor 10
LOC107984827	-1.25169	0.001622	0.029529	-3.152	Down	uncharacterized LOC107984827
PPEF2	-1.2479	0.003293	0.044852	-2.93899	Down	protein phosphatase with EF-hand domain 2
LOC643342	-1.24391	0.00062	0.016275	-3.42276	Down	ATM interactor pseudogene
TLR5	-1.24339	7.18E-05	0.004373	-3.97009	Down	toll like receptor 5
LUCAT1	-1.233	0.002856	0.041362	-2.98281	Down	lung cancer associated transcript 1
MTND2P8	-1.23111	0.000664	0.017074	-3.40412	Down	MT-ND2 pseudogene 8
C9orf153	-1.22934	6.81E-05	0.004226	-3.98266	Down	chromosome 9 open reading frame 153
SULT1B1	-1.22225	0.002004	0.03344	-3.08958	Down	sulfotransferase family 1B member 1
LNCSRLR	-1.21483	0.000513	0.014807	-3.47411	Down	lncRNA sorafenib resistance in renal cell carcinoma associated
TFPI	-1.21407	2.39E-11	2.19E-07	-6.68009	Down	tissue factor pathway inhibitor
TLR2	-1.20881	6.41E-05	0.004097	-3.99701	Down	toll like receptor 2
MNDA	-1.20468	4.22E-06	0.000744	-4.60046	Down	myeloid cell nuclear differentiation antigen
RUNX3	-1.19151	0.000169	0.00746	-3.76107	Down	RUNX family transcription factor 3
PTPRC	-1.18921	9.20E-05	0.005092	-3.91084	Down	protein tyrosine phosphatase receptor type C
LVRN	-1.18869	0.000177	0.007715	-3.74907	Down	laeverin
C3	-1.18458	0.00357	0.047132	-2.91387	Down	complement C3
INSL6	-1.18047	0.001782	0.031189	-3.12436	Down	insulin like 6
IL2RG	-1.1796	0.001005	0.022151	-3.28921	Down	interleukin 2 receptor subunit gamma
TBX15	-1.17219	0.000571	0.015579	-3.4451	Down	T-box transcription factor 15
MT1M	-1.16761	0.001987	0.03328	-3.09212	Down	metallothionein 1M
CLEC2B	-1.15159	2.22E-05	0.002185	-4.242	Down	C-type lectin domain family 2 member B
LOC100127965	-1.15105	0.000312	0.011178	-3.60513	Down	ribosomal protein L7 like 1 pseudogene
CFI	-1.1494	1.18E-05	0.001476	-4.38129	Down	complement factor I
SINHCAF	-1.14665	3.07E-05	0.002639	-4.16827	Down	SIN3-HDAC complex associated factor
NIBAN1	-1.14201	6.35E-05	0.004086	-3.99941	Down	niban apoptosis regulator 1
GAS2L3	-1.14131	5.93E-06	0.000922	-4.52891	Down	growth arrest specific 2 like 3
KRBOX1-AS1	-1.14021	0.0008	0.01934	-3.35283	Down	KRBOX1 antisense RNA 1
DNAH11	-1.1318	1.75E-06	0.000419	-4.78029	Down	dynein axonemal heavy chain 11
CENPF	-1.13064	0.000115	0.005886	-3.85725	Down	centromere protein F
RNU1-134P	-1.12063	0.000246	0.009491	-3.66679	Down	RNA, U1 small nuclear 134, pseudogene
ZBTB20-AS5	-1.11876	0.000824	0.01976	-3.34454	Down	ZBTB20 antisense RNA 5
PIK3AP1	-1.11611	0.000682	0.017387	-3.39678	Down	phosphoinositide-3-kinase adaptor protein 1
TRIM5	-1.11304	1.87E-11	2.19E-07	-6.71606	Down	tripartite motif containing 5
JAML	-1.10628	0.001665	0.029949	-3.14421	Down	junction adhesion molecule like
GIMAP4	-1.09957	1.46E-08	2.23E-05	-5.6666	Down	GTPase, IMA family member 4
NUPR1	-1.0891	1.52E-05	0.001755	-4.32604	Down	nuclear protein 1, transcriptional regulator
PII5	-1.08496	0.000508	0.014733	-3.47671	Down	peptidase inhibitor 15
E2F7	-1.08082	0.000348	0.011953	-3.57637	Down	E2F transcription factor 7
NUSAP1	-1.07895	0.002026	0.033627	-3.08635	Down	nucleolar and spindle associated protein 1

METTL7B	-1.0788	0.001608	0.029425	-3.15449	Down	methyltransferase like 7B
FCGR2A	-1.07674	0.001737	0.030742	-3.13182	Down	Fc fragment of IgG receptor IIa
VCAN-AS1	-1.07553	0.001147	0.023937	-3.25162	Down	VCAN antisense RNA 1
RBM47	-1.0696	0.000346	0.0119	-3.57785	Down	RNA binding motif protein 47
CYSLTR2	-1.06853	6.28E-07	0.000192	-4.98233	Down	cysteinyl leukotriene receptor 2
LINC02181	-1.06621	0.00272	0.040195	-2.99778	Down	long intergenic non-protein coding RNA 2181
HORMAD1	-1.06471	0.00123	0.025012	-3.23179	Down	HORMA domain containing 1
TMEM213	-1.05462	0.002465	0.037896	-3.02756	Down	transmembrane protein 213
ALOX5AP	-1.05188	0.001515	0.028437	-3.17176	Down	arachidonate 5-lipoxygenase activating protein
NEB	-1.05174	1.10E-07	6.61E-05	-5.30997	Down	nebulin
S100A11	-1.0488	0.000625	0.016385	-3.42066	Down	S100 calcium binding protein A11
ADAMDEC1	-1.04762	0.0007	0.017717	-3.38951	Down	ADAM like decysin 1
LAMP3	-1.04488	0.001749	0.030825	-3.12979	Down	lysosomal associated membrane protein 3
CPVL	-1.04134	5.20E-05	0.003695	-4.04661	Down	carboxypeptidase vitellogenic like
CCDC160	-1.04131	0.000109	0.005643	-3.87071	Down	coiled-coil domain containing 160
P2RY6	-1.04067	0.001386	0.026896	-3.19753	Down	pyrimidinergic receptor P2Y6
HIGD1B	-1.03655	0.000564	0.015483	-3.44844	Down	HIG1 hypoxia inducible domain family member 1B
IHO1	-1.02756	6.05E-05	0.004001	-4.01089	Down	interactor of HORMAD1 1
FCER1G	-1.02741	0.003772	0.048658	-2.89663	Down	Fc fragment of IgE receptor Ig
MICB	-1.02036	0.000371	0.012399	-3.55966	Down	MHC class I polypeptide-related sequence B
SMTN	-1.02019	3.54E-05	0.002875	-4.13542	Down	smoothelin
IFI16	-1.01659	2.83E-07	0.000115	-5.13465	Down	interferon gamma inducible protein 16
SELL	-1.01452	3.69E-05	0.00293	-4.12591	Down	selectin L
LAPTM5	-1.01412	0.001082	0.023085	-3.26821	Down	lysosomal protein transmembrane 5
OVCH1	-1.01036	5.78E-06	0.000909	-4.53423	Down	ovochoyase 1
LPGAT1P1	-1.00861	0.001516	0.028437	-3.17165	Down	lysophosphatidylglycerol acyltransferase 1 pseudogene 1
RNU6-327P	-1.00767	0.002941	0.041978	-2.97383	Down	RNA, U6 small nuclear 327, pseudogene
FKBP5	-1.00683	1.04E-05	0.001344	-4.40766	Down	FKBP prolyl isomerase 5
DIAPH3	-1.0059	0.000246	0.009491	-3.6661	Down	diaphanous related formin 3
CASP4	-1.00535	0.000313	0.011178	-3.60411	Down	caspase 4
NMI	-1.00522	1.44E-07	7.50E-05	-5.26001	Down	N-myc and STAT interactor
ALKAL2	-1.0042	2.28E-08	2.73E-05	-5.58906	Down	ALK and LTK ligand 2
STEAP4	-1.00344	0.001373	0.026815	-3.20023	Down	STEAP4 metalloredutase
IFNE	-0.99743	0.000449	0.013741	-3.50919	Down	interferon epsilon
MIR2052HG	-0.99336	4.50E-07	0.000157	-5.04655	Down	MIR2052 host gene
ADGRL4	-0.99009	1.39E-07	7.50E-05	-5.26681	Down	adhesion G protein-coupled receptor L4
TM4SF18	-0.98989	0.000108	0.00564	-3.87235	Down	transmembrane 4 L six family member 18
SYK	-0.98607	0.001987	0.03328	-3.09213	Down	spleen associated tyrosine kinase
CGAS	-0.98593	1.65E-07	8.25E-05	-5.23514	Down	cyclic GMP-AMP synthase
RNU4ATAC18 P	-0.98511	0.002674	0.039734	-3.00288	Down	RNA, U4atac small nuclear 18, pseudogene
LINC00484	-0.98344	6.88E-05	0.004246	-3.98031	Down	long intergenic non-protein coding RNA 484
GLI1	-0.97388	0.002206	0.035494	-3.06101	Down	GLI family zinc finger 1

LCP1	-0.97358	0.000255	0.00975	-3.65706	Down	lymphocyte cytosolic protein 1
MT2A	-0.97289	0.000402	0.013043	-3.53846	Down	metallothionein 2A
LY75	-0.97271	0.002153	0.034976	-3.06822	Down	lymphocyte antigen 75
MT1X	-0.97074	0.001644	0.029765	-3.14793	Down	metallothionein 1X
LINC02072	-0.96901	2.57E-05	0.002346	-4.20881	Down	long intergenic non-protein coding RNA 2072
IL17RB	-0.96672	3.35E-06	0.000659	-4.64802	Down	interleukin 17 receptor B
GPR4	-0.9665	0.0032	0.044062	-2.94788	Down	G protein-coupled receptor 4
ATP8	-0.96532	0.000274	0.01027	-3.63909	Down	ATP synthase F0 subunit 8
SPN	-0.96512	0.000728	0.018194	-3.37881	Down	sialophorin
KIAA0040	-0.96207	0.001647	0.029793	-3.14747	Down	KIAA0040
RANBP3L	-0.96063	0.000772	0.018921	-3.36281	Down	RAN binding protein 3 like
DTX3L	-0.95262	3.42E-07	0.000127	-5.09867	Down	deltex E3 ubiquitin ligase 3L
CALHM5	-0.95141	9.99E-05	0.0054	-3.89085	Down	calcium homeostasis modulator family member 5
ANKRD18A	-0.94661	0.001544	0.028739	-3.16637	Down	ankyrin repeat domain 18A
GOLGA6L17P	-0.94627	0.00022	0.008915	-3.69486	Down	golgin A6 family like 17, pseudogene
SAMD9	-0.94254	2.39E-06	0.00052	-4.71736	Down	sterile alpha motif domain containing 9
MYCT1	-0.94151	2.38E-06	0.00052	-4.71798	Down	MYC target 1
CYBB	-0.9388	0.00222	0.035661	-3.05908	Down	cytochrome b-245 beta chain
TLR1	-0.93874	0.001548	0.028786	-3.16546	Down	toll like receptor 1
NEFH	-0.93787	0.000663	0.017074	-3.40442	Down	neurofilament heavy chain
BACE2	-0.93708	2.73E-06	0.000569	-4.69034	Down	beta-secretase 2
GABRE	-0.93021	0.000902	0.020983	-3.31941	Down	gamma-aminobutyric acid type A receptor subunit epsilon
SRGN	-0.92998	0.0014	0.027045	-3.19472	Down	serglycin
CELSR1	-0.92843	0.000762	0.018781	-3.36608	Down	cadherin EGF LAG seven-pass G-type receptor 1
NCKAP1L	-0.92686	0.003089	0.043274	-2.95875	Down	NCK associated protein 1 like
PARP9	-0.92283	4.89E-07	0.000168	-5.03048	Down	poly(ADP-ribose) polymerase family member 9
GBP3	-0.92164	0.000233	0.00922	-3.68074	Down	guanylate binding protein 3
TRIM38	-0.9211	3.13E-06	0.00062	-4.66206	Down	tripartite motif containing 38
SASH3	-0.92054	0.000591	0.015912	-3.43592	Down	SAM and SH3 domain containing 3
CEP152	-0.9181	2.89E-08	3.06E-05	-5.54784	Down	centrosomal protein 152
ST3GAL3-AS1	-0.91766	0.001108	0.023334	-3.26155	Down	ST3GAL3 antisense RNA 1
SP100	-0.91653	1.26E-08	2.14E-05	-5.69134	Down	SP100 nuclear antigen
CLIC1	-0.91463	2.45E-05	0.002287	-4.21914	Down	chloride intracellular channel 1
IKBIP	-0.91383	3.61E-06	0.000686	-4.63287	Down	IKBKB interacting protein
APBB1IP	-0.91296	0.00373	0.048372	-2.9001	Down	amyloid beta precursor protein binding family B member 1 interacting protein
OSMR	-0.91239	0.001259	0.025384	-3.2251	Down	oncostatin M receptor
LOC646112	-0.91226	8.71E-05	0.004941	-3.924	Down	origin recognition complex subunit 3 pseudogene
SAMD9L	-0.90998	4.51E-05	0.003352	-4.07982	Down	sterile alpha motif domain containing 9 like
SLA	-0.90389	0.00043	0.013489	-3.5207	Down	Src like adaptor
LINC02475	-0.90162	0.00145	0.027772	-3.18443	Down	long intergenic non-protein coding RNA 2475
MT1E	-0.89444	0.002351	0.036854	-3.04183	Down	metallothionein 1E

KCNJ16	-0.89303	0.001564	0.028958	-3.16256	Down	potassium inwardly rectifying channel subfamily J member 16
RPL34P5	-0.89284	0.001848	0.031874	-3.11368	Down	ribosomal protein L34 pseudogene 5
NXPE2	-0.89075	0.000385	0.012726	-3.54998	Down	neurexophilin and PC-esterase domain family member 2
PDK4	-0.88605	0.000345	0.011881	-3.57908	Down	pyruvate dehydrogenase kinase 4
NFATC2	-0.88506	1.15E-06	0.000311	-4.8637	Down	nuclear factor of activated T cells 2
ANKRD62	-0.88483	0.000197	0.008305	-3.72254	Down	ankyrin repeat domain 62
RPL7P60	-0.88298	0.001274	0.025553	-3.22176	Down	ribosomal protein L7 pseudogene 60
GNRH1	-0.87959	6.68E-07	0.000202	-4.97056	Down	gonadotropin releasing hormone 1
MAFF	-0.87886	0.003248	0.044415	-2.94327	Down	MAF bZIP transcription factor F family with sequence similarity 89 member A
FAM89A	-0.87651	0.000121	0.006039	-3.8438	Down	
CYYR1	-0.87607	3.27E-05	0.002745	-4.15365	Down	cysteine and tyrosine rich 1
CD34	-0.87586	0.000364	0.012264	-3.56472	Down	CD34 molecule
CCNA2	-0.87067	0.000173	0.00759	-3.75556	Down	cyclin A2
LRRC37A	-0.87001	0.002019	0.033543	-3.08745	Down	leucine rich repeat containing 37A
BRCA2	-0.86991	0.000278	0.010363	-3.63536	Down	BRCA2 DNA repair associated
HCLS1	-0.86901	0.00221	0.035546	-3.0604	Down	hematopoietic cell-specific Lyn substrate 1
RAB13	-0.86615	5.30E-08	4.42E-05	-5.44095	Down	RAB13, member RAS oncogene family
TFEC	-0.86545	0.00059	0.015912	-3.43631	Down	transcription factor EC
PIK3CG	-0.86445	0.000651	0.016826	-3.40957	Down	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma
SLC25A48	-0.86363	0.000517	0.014856	-3.47198	Down	solute carrier family 25 member 48
GIMAP7	-0.86351	6.31E-05	0.004086	-4.00073	Down	GTPase, IMAP family member 7
EHF	-0.86282	0.00028	0.010392	-3.63326	Down	ETS homologous factor
SLC7A11-AS1	-0.86071	0.000216	0.008813	-3.69929	Down	SLC7A11 antisense RNA 1
GBP4	-0.86046	0.000973	0.021872	-3.29823	Down	guanylate binding protein 4
CSF3R	-0.85973	0.002844	0.041272	-2.98412	Down	colony stimulating factor 3 receptor
GPNNMB	-0.85532	0.00254	0.03864	-3.01848	Down	glycoprotein nmb
ITGB3	-0.85194	0.000323	0.011415	-3.59598	Down	integrin subunit beta 3
ND3	-0.85175	4.22E-05	0.003233	-4.09517	Down	NADH dehydrogenase subunit 3
SLC7A2	-0.85126	0.000155	0.007123	-3.78239	Down	solute carrier family 7 member 2
ANXA3	-0.85083	0.000259	0.009843	-3.65321	Down	annexin A3
MAP3K8	-0.84407	6.92E-06	0.001029	-4.49612	Down	mitogen-activated protein kinase kinase kinase 8
PRELP	-0.84373	0.001523	0.028538	-3.17034	Down	proline and arginine rich end leucine rich repeat protein
EMCN	-0.84365	3.34E-05	0.002779	-4.14871	Down	endomucin
PERP	-0.84259	7.11E-06	0.001047	-4.49029	Down	p53 apoptosis effector related to PMP22
FAM111A	-0.84246	2.13E-07	9.26E-05	-5.18721	Down	FAM111 trypsin like peptidase A
COL27A1	-0.84243	0.001727	0.030623	-3.13351	Down	collagen type XXVII alpha 1 chain
CDK2	-0.83957	0.000257	0.009806	-3.65488	Down	cyclin dependent kinase 2
LOC285638	-0.83658	0.000343	0.011874	-3.58039	Down	uncharacterized LOC285638
PTAFR	-0.83578	0.003109	0.04342	-2.95677	Down	platelet activating factor receptor
SLC43A3	-0.83567	5.44E-06	0.000875	-4.54706	Down	solute carrier family 43 member 3
GIMAP2	-0.83467	0.002442	0.037728	-3.03043	Down	GTPase, IMAP family member 2

LIPH	-0.83394	0.000486	0.014399	-3.4884	Down	lipase H
ORC1	-0.8281	0.003318	0.045042	-2.93661	Down	origin recognition complex subunit 1
YES1	-0.82751	1.07E-08	2.09E-05	-5.72002	Down	YES proto-oncogene 1, Src family tyrosine kinase
NCF2	-0.82451	0.000186	0.007966	-3.73748	Down	neutrophil cytosolic factor 2
CD58	-0.82367	7.30E-06	0.001068	-4.48475	Down	CD58 molecule
NEXN	-0.82312	0.000134	0.006489	-3.81884	Down	nexilin F-actin binding protein
CARD6	-0.82251	2.62E-05	0.002373	-4.20389	Down	caspase recruitment domain family member 6
PXDC1	-0.8213	2.36E-06	0.00052	-4.71974	Down	PX domain containing 1
MTCO1P40	-0.82053	0.000753	0.018665	-3.36952	Down	MT-CO1 pseudogene 40
RASSF8	-0.81999	1.36E-06	0.000349	-4.8314	Down	Ras association domain family member 8
TNFSF10	-0.81915	0.000938	0.02141	-3.30842	Down	TNF superfamily member 10
MTATP6P1	-0.81521	0.000106	0.005585	-3.87745	Down	MT-ATP6 pseudogene 1
ITGA10	-0.81341	7.55E-05	0.004516	-3.95831	Down	integrin subunit alpha 10
ZIC5	-0.81205	8.90E-05	0.005029	-3.91873	Down	Zic family member 5
BTK	-0.81154	0.003463	0.046184	-2.92336	Down	Bruton tyrosine kinase
PRKX	-0.81076	2.81E-06	0.000576	-4.68458	Down	protein kinase X-linked
TRIM21	-0.80991	2.17E-05	0.00217	-4.24708	Down	tripartite motif containing 21
NQO1	-0.80936	2.77E-05	0.002474	-4.19165	Down	NAD(P)H quinone dehydrogenase 1
FGF11	-0.80712	0.001443	0.027665	-3.18594	Down	fibroblast growth factor 11
TEAD2	-0.80581	0.001956	0.033063	-3.09679	Down	TEA domain transcription factor 2
B2M	-0.80307	2.14E-05	0.002159	-4.25	Down	beta-2-microglobulin
TRDN	-0.80304	0.001169	0.0242	-3.24636	Down	triadin
MYOF	-0.80162	2.33E-05	0.002232	-4.23082	Down	myoferlin
SLC39A12	-0.7989	0.000141	0.006744	-3.80664	Down	solute carrier family 39 member 12
ADGRE2	-0.79867	0.002636	0.039477	-3.00731	Down	adhesion G protein-coupled receptor E2
ANXA2	-0.79731	0.002332	0.03667	-3.04429	Down	annexin A2
RNU6-125P	-0.79696	0.002988	0.042255	-2.96895	Down	RNA, U6 small nuclear 125, pseudogene
ADAM28	-0.7952	0.002881	0.041539	-2.98021	Down	ADAM metalloproteinase domain 28
FLT1	-0.79515	0.000576	0.01567	-3.44278	Down	fms related receptor tyrosine kinase 1
MECOM	-0.79448	1.26E-05	0.001547	-4.36666	Down	MDS1 and EVI1 complex locus
TGFBR1	-0.7937	0.000294	0.010741	-3.62058	Down	transforming growth factor beta receptor 1
IRAK3	-0.79303	0.000163	0.007315	-3.77043	Down	interleukin 1 receptor associated kinase 3
GNG11	-0.79254	1.66E-05	0.001872	-4.30633	Down	G protein subunit gamma 11
RPS8P7	-0.79199	0.001137	0.02378	-3.25432	Down	ribosomal protein S8 pseudogene 7
FLI1	-0.7911	2.47E-05	0.002294	-4.21772	Down	Fli-1 proto-oncogene, ETS transcription factor
DNA2	-0.78962	7.38E-08	5.49E-05	-5.38165	Down	DNA replication helicase/nuclease 2
SHOC1	-0.78749	0.000455	0.013846	-3.506	Down	shortage in chiasmata 1
CTSS	-0.78733	0.001262	0.025427	-3.2244	Down	cathepsin S
SLC38A2	-0.78506	1.73E-06	0.000418	-4.78252	Down	solute carrier family 38 member 2
LPCAT2	-0.78354	0.002637	0.039477	-3.00715	Down	lysophosphatidylcholine acyltransferase 2
HELB	-0.78076	4.32E-06	0.000752	-4.59551	Down	DNA helicase B
BAZ1A	-0.77762	1.81E-05	0.001932	-4.28691	Down	bromodomain adjacent to zinc finger domain 1A

ARHGAP42	-0.77714	3.51E-07	0.000127	-5.0937	Down	Rho GTPase activating protein 42
HHEX	-0.77656	0.000203	0.008463	-3.71486	Down	hematopoietically expressed homeobox
PCOLCE2	-0.77646	0.002655	0.039638	-3.00509	Down	procollagen C-endopeptidase enhancer 2
CALD1	-0.77645	1.16E-08	2.12E-05	-5.706	Down	caldesmon 1
FLVCR1-DT	-0.77633	0.000419	0.013378	-3.52775	Down	FLVCR1 divergent transcript
ZIC2	-0.77456	0.000458	0.013911	-3.50416	Down	Zic family member 2
ACSS3	-0.77387	1.91E-06	0.000452	-4.76319	Down	acyl-CoA synthetase short chain family member 3
DIO1	-0.7722	0.000406	0.013127	-3.53616	Down	iodothyronine deiodinase 1
SP140L	-0.77187	6.42E-06	0.000982	-4.51201	Down	SP140 nuclear body protein like
ZNF813	-0.77179	6.36E-05	0.004086	-3.99918	Down	zinc finger protein 813
ITGA1	-0.77082	1.15E-05	0.001445	-4.38686	Down	integrin subunit alpha 1
LINC00472	-0.76778	6.27E-06	0.000963	-4.51721	Down	long intergenic non-protein coding RNA 472
RPS3AP22	-0.76742	0.000397	0.012973	-3.54212	Down	RPS3A pseudogene 22
LINC01561	-0.76472	0.001984	0.033274	-3.09255	Down	long intergenic non-protein coding RNA 1561
HK2	-0.76432	0.003666	0.047893	-2.90558	Down	hexokinase 2
ND4L	-0.76246	0.000324	0.011442	-3.59502	Down	NADH dehydrogenase subunit 4L
SQOR	-0.76222	0.001956	0.033063	-3.0969	Down	sulfide quinone oxidoreductase
GPR160	-0.76131	0.001944	0.032966	-3.09865	Down	G protein-coupled receptor 160
RNU6-759P	-0.76121	0.001994	0.033344	-3.0912	Down	RNA, U6 small nuclear 759, pseudogene poly(ADP-ribose) polymerase family member 14
PARP14	-0.75925	1.40E-06	0.000356	-4.82559	Down	
NABP1	-0.75911	7.98E-05	0.004625	-3.94499	Down	nucleic acid binding protein 1
MSTN	-0.75632	0.000875	0.020519	-3.32799	Down	myostatin
NRM	-0.75617	0.002475	0.037981	-3.02638	Down	nurim
RNF152	-0.75593	1.45E-07	7.50E-05	-5.2594	Down	ring finger protein 152
STAU2-AS1	-0.75549	0.00384	0.049281	-2.89101	Down	STAU2 antisense RNA 1
PSMB8-AS1	-0.75471	0.000435	0.013489	-3.5179	Down	PSMB8 antisense RNA 1 (head to head)
EVC2	-0.75384	0.003015	0.042459	-2.96618	Down	EvC ciliary complex subunit 2
CNTNAP3B	-0.75135	0.002515	0.038354	-3.02157	Down	contactin associated protein family member 3B
FBXO5	-0.75075	6.57E-06	0.000993	-4.50711	Down	F-box protein 5
OLFML1	-0.74907	0.001219	0.024894	-3.23446	Down	olfactomedin like 1
HEBP2	-0.74845	2.78E-06	0.000574	-4.68676	Down	heme binding protein 2
SAMD4A	-0.7477	1.41E-07	7.50E-05	-5.2645	Down	sterile alpha motif domain containing 4A
ZNF676	-0.74624	0.000538	0.015092	-3.46087	Down	zinc finger protein 676
LGR4-AS1	-0.74562	0.00208	0.034205	-3.07859	Down	LGR4 antisense RNA 1
FOXC1	-0.74331	0.00116	0.024117	-3.24842	Down	forkhead box C1
CD302	-0.74319	0.000153	0.007071	-3.78615	Down	CD302 molecule
IFITM3	-0.74225	0.00252	0.038417	-3.0209	Down	interferon induced transmembrane protein 3
DOCK2	-0.74156	0.001847	0.031874	-3.11374	Down	dedicator of cytokinesis 2
NEDD4	-0.74119	1.87E-07	9.01E-05	-5.2121	Down	NEDD4 E3 ubiquitin protein ligase
LOC105372321	-0.7407	2.00E-07	9.17E-05	-5.19929	Down	uncharacterized LOC105372321
DBI	-0.73676	1.11E-07	6.61E-05	-5.30846	Down	diazepam binding inhibitor, acyl-CoA binding protein
MEFV	-0.73627	0.003224	0.044246	-2.94554	Down	MEFV innate immunity regulator, pyrin

ROM1	-0.73574	0.000973	0.021872	-3.2982	Down	retinal outer segment membrane protein 1
FBXL19-AS1	-0.73573	3.63E-05	0.0029	-4.13016	Down	FBXL19 antisense RNA 1
IFIH1	-0.73571	2.09E-07	9.26E-05	-5.1914	Down	interferon induced with helicase C domain 1
ATP6	-0.73497	0.000158	0.007185	-3.77893	Down	ATP synthase F0 subunit 6 high mobility group nucleosome binding domain 5
HMG5	-0.73375	9.72E-05	0.005329	-3.89742	Down	small nucleolar RNA, H/ACA box 33
SNORA33	-0.73284	0.001137	0.02378	-3.25414	Down	discoidin domain receptor tyrosine kinase 2
DDR2	-0.73248	4.71E-08	4.05E-05	-5.46193	Down	NADH dehydrogenase subunit 4
ND4	-0.73217	5.40E-05	0.003754	-4.0375	Down	TPD52 like 1
TPD52L1	-0.73121	0.000604	0.015989	-3.42985	Down	BCL6 transcription repressor HECT and RLD domain containing E3 ubiquitin protein ligase 5
BCL6	-0.73109	4.32E-05	0.003272	-4.08959	Down	chromosome 4 open reading frame 19
HERC5	-0.73092	5.37E-05	0.003754	-4.03884	Down	2'-5'-oligoadenylate synthetase 2
C4orf19	-0.73007	0.002764	0.040567	-2.99287	Down	leucine rich repeat containing 1
OAS2	-0.72924	0.000443	0.013604	-3.51305	Down	coiled-coil domain containing 18
LRRC1	-0.72829	0.00123	0.025012	-3.23179	Down	cytochrome c oxidase subunit II
CCDC18	-0.72687	7.79E-06	0.001105	-4.47085	Down	ATPase phospholipid transporting 11C WW domain containing transcription regulator 1
COX2	-0.72549	0.000143	0.00676	-3.80295	Down	GALNT8 antisense upstream 1
ATP11C	-0.72387	5.94E-07	0.000192	-4.99332	Down	testin LIM domain protein
WWTR1	-0.72365	6.23E-07	0.000192	-4.98389	Down	raftlin family member 2
GAU1	-0.72061	0.000796	0.019294	-3.35422	Down	ribosomal protein L23a pseudogene 5
TES	-0.72036	0.002341	0.036779	-3.04323	Down	transmembrane protein 45B
RFTN2	-0.72016	0.000254	0.009732	-3.65824	Down	NADH dehydrogenase subunit 6
RPL23AP5	-0.71913	0.002909	0.041695	-2.97714	Down	ras homolog family member Q
TMEM45B	-0.7184	0.001649	0.029804	-3.14717	Down	solute carrier family 5 member 9
ND6	-0.71806	7.62E-05	0.004539	-3.95601	Down	centlein
RHOQ	-0.71729	1.01E-07	6.61E-05	-5.3249	Down	tripartite motif containing 22
SLC5A9	-0.71634	0.000228	0.009147	-3.68531	Down	NADH dehydrogenase subunit 2
CNTLN	-0.71557	1.14E-07	6.68E-05	-5.30262	Down	high mobility group box 3 pseudogene 4
TRIM22	-0.71401	5.49E-05	0.003806	-4.03366	Down	claudin 18
ND2	-0.71356	0.000101	0.005414	-3.88785	Down	dermatan sulfate epimerase
HMGB3P4	-0.71193	0.002276	0.036075	-3.05162	Down	NLR family CARD domain containing 5
CLDN18	-0.71128	0.001349	0.026519	-3.20527	Down	caspase 7
DSE	-0.70878	8.41E-08	5.93E-05	-5.35821	Down	multimerin 2
NLRC5	-0.70809	0.003005	0.042411	-2.96723	Down	leucine rich repeat containing 69
CASP7	-0.70804	0.000326	0.011469	-3.5934	Down	RELT like 1
MMRN2	-0.7073	0.001322	0.02615	-3.21117	Down	NOP2/Sun RNA methyltransferase family member 7
LRRC69	-0.70545	0.003532	0.046818	-2.91715	Down	Rho GDP dissociation inhibitor beta
RELL1	-0.7032	8.58E-05	0.00488	-3.9275	Down	complement factor H
NSUN7	-0.70027	0.001059	0.022812	-3.27443	Down	myosin light chain 12A
ARHGDIIB	-0.69836	0.002304	0.036366	-3.048	Down	erbb2 interacting protein
CFH	-0.69765	0.003441	0.046103	-2.92528	Down	
MYL12A	-0.69462	4.86E-06	0.000811	-4.57064	Down	
ERBIN	-0.69442	0.000715	0.017971	-3.38388	Down	

EMX2	-0.69429	0.003395	0.045586	-2.92954	Down	empty spiracles homeobox 2
BTNL9	-0.69017	0.000942	0.021452	-3.30735	Down	butyrophilin like 9
YAP1	-0.68979	0.00042	0.013385	-3.52694	Down	Yes1 associated transcriptional regulator FXD domain containing ion transport regulator 3
FXD3	-0.68949	0.001038	0.02264	-3.27999	Down	
GIMAP5	-0.68807	0.00057	0.015579	-3.44569	Down	GTPase, IMA family member 5
CCDC146	-0.68789	4.59E-05	0.003402	-4.07572	Down	coiled-coil domain containing 146
CFAP53	-0.68727	5.83E-05	0.003929	-4.01977	Down	cilia and flagella associated protein 53
TGFBR2	-0.68671	3.19E-05	0.002706	-4.15973	Down	transforming growth factor beta receptor 2
DOK3	-0.68462	0.00173	0.030651	-3.13305	Down	docking protein 3
ZNF69	-0.68415	1.40E-05	0.001651	-4.34323	Down	zinc finger protein 69
ACTL6A	-0.68377	4.98E-05	0.003585	-4.05673	Down	actin like 6A
CASP6	-0.68288	8.88E-05	0.005029	-3.9192	Down	caspase 6
MTND5P14	-0.68088	0.00295	0.041993	-2.97287	Down	MT-ND5 pseudogene 14
PPP1R1C	-0.68049	0.001461	0.027926	-3.18222	Down	protein phosphatase 1 regulatory inhibitor subunit 1C
LCP2	-0.67819	0.000343	0.011874	-3.58048	Down	lymphocyte cytosolic protein 2
AKR1C3	-0.67594	1.11E-05	0.001414	-4.39461	Down	aldo-keto reductase family 1 member C3
SPATA13	-0.67468	0.003858	0.049465	-2.88955	Down	spermatogenesis associated 13
MYD88	-0.67369	0.002587	0.038945	-3.01293	Down	MYD88 innate immune signal transduction adaptor
CHEK2	-0.66927	0.00278	0.040598	-2.99109	Down	checkpoint kinase 2
RHOJ	-0.66873	6.48E-05	0.004108	-3.9946	Down	ras homolog family member J
COA6-AS1	-0.66868	0.000421	0.013385	-3.52638	Down	COA6 antisense RNA 1
MLKL	-0.666	0.003595	0.047364	-2.91165	Down	mixed lineage kinase domain like pseudokinase
MRPS6	-0.66587	0.001673	0.030016	-3.14293	Down	mitochondrial ribosomal protein S6
ST6GALNAC3	-0.66489	1.45E-05	0.001698	-4.33614	Down	ST6 N-acetylgalactosaminide alpha-2,6- sialyltransferase 3
PLIN2	-0.66475	0.002388	0.037204	-3.03717	Down	perilipin 2
NFKBIA	-0.66411	0.000812	0.019576	-3.34874	Down	NFKB inhibitor alpha
APOL1	-0.66315	0.001705	0.030405	-3.1373	Down	apolipoprotein L1
PLOD2	-0.66265	0.000314	0.011194	-3.60308	Down	procollagen-lysine,2-oxoglutarate 5- dioxygenase 2
ARHGAP11A	-0.66221	0.001076	0.023023	-3.26985	Down	Rho GTPase activating protein 11A
ANO6	-0.66169	2.28E-07	9.65E-05	-5.17488	Down	anoctamin 6
CYTB	-0.66104	0.001875	0.032169	-3.1093	Down	cytochrome b
IL13RA1	-0.65993	0.001574	0.029074	-3.1606	Down	interleukin 13 receptor subunit alpha 1
IQGAP1	-0.65637	9.92E-05	0.005384	-3.89251	Down	IQ motif containing GTPase activating protein 1
RGCC	-0.65607	0.003337	0.045254	-2.93485	Down	regulator of cell cycle
SLFN11	-0.65581	0.000121	0.006039	-3.8444	Down	schlafen family member 11
GIMAP8	-0.65478	0.002585	0.038945	-3.01324	Down	GTPase, IMA family member 8
ND1	-0.6541	0.000445	0.013652	-3.51179	Down	NADH dehydrogenase subunit 1
ITGB8	-0.6535	0.000246	0.009491	-3.66629	Down	integrin subunit beta 8
NEK7	-0.65261	2.51E-05	0.002324	-4.21401	Down	NIMA related kinase 7
LOC646870	-0.65136	0.000194	0.008201	-3.72666	Down	centrosomal protein 57kDa pseudogene
TP53INP1	-0.64796	0.000143	0.00676	-3.80349	Down	tumor protein p53 inducible nuclear protein 1

ITGB1	-0.64777	6.21E-07	0.000192	-4.98444	Down	integrin subunit beta 1
LPAR6	-0.64728	0.000596	0.015964	-3.4335	Down	lysophosphatidic acid receptor 6
ZNF761	-0.64725	1.93E-05	0.002007	-4.2733	Down	zinc finger protein 761
LOC100421091	-0.64546	0.000166	0.007394	-3.76532	Down	LSM14A, SCD6 homolog A (S. cerevisiae) pseudogene
CSF1	-0.64529	0.002899	0.04168	-2.97826	Down	colony stimulating factor 1
ANXA5	-0.64132	8.08E-06	0.001129	-4.46296	Down	annexin A5
IKZF2	-0.64039	0.001613	0.02946	-3.15346	Down	IKAROS family zinc finger 2
TBC1D8B	-0.6399	0.000598	0.015989	-3.43257	Down	TBC1 domain family member 8B
KIF5B	-0.63975	2.35E-05	0.002246	-4.2287	Down	kinesin family member 5B
ITPKB	-0.63935	0.000145	0.006837	-3.79929	Down	inositol-trisphosphate 3-kinase B
PLSCR1	-0.63878	0.00224	0.035881	-3.05639	Down	phospholipid scramblase 1
ANXA1	-0.63755	0.00078	0.019048	-3.35997	Down	annexin A1
SUMO4	-0.63589	0.001198	0.024671	-3.23938	Down	small ubiquitin like modifier 4
FAM241A	-0.63536	0.003158	0.043801	-2.95189	Down	family with sequence similarity 241 member A
NSRP1P1	-0.63413	0.000589	0.015912	-3.4366	Down	nuclear speckle splicing regulatory protein 1 pseudogene 1
PMP2	-0.63346	0.001478	0.028041	-3.17901	Down	peripheral myelin protein 2
KCNJ10	-0.63343	0.001796	0.031296	-3.12205	Down	potassium inwardly rectifying channel subfamily J member 10
SAMHD1	-0.63146	1.30E-06	0.000341	-4.83977	Down	SAM and HD domain containing deoxynucleoside triphosphate triphosphohydrolase 1
TMEM14EP	-0.63138	0.000121	0.006039	-3.84458	Down	transmembrane protein 14E, pseudogene
LEF1	-0.63073	8.44E-06	0.001155	-4.45382	Down	lymphoid enhancer binding factor 1
NOSTRIN	-0.62991	0.00105	0.022738	-3.27691	Down	nitric oxide synthase trafficking
ITGA8	-0.62808	0.000273	0.010246	-3.64006	Down	integrin subunit alpha 8
MAML2	-0.62779	7.54E-06	0.001091	-4.47797	Down	mastermind like transcriptional coactivator 2
MLANA	-0.62711	0.000748	0.018602	-3.37145	Down	melan-A
CLEC2D	-0.62491	0.002356	0.036894	-3.04126	Down	C-type lectin domain family 2 member D spectrin repeat containing nuclear envelope protein 2
SYNE2	-0.62484	7.58E-06	0.001092	-4.47673	Down	
CD2AP	-0.62425	1.01E-05	0.001309	-4.41534	Down	CD2 associated protein
REST	-0.62394	0.000525	0.014965	-3.46775	Down	RE1 silencing transcription factor
ELK3	-0.62299	4.03E-06	0.000738	-4.61006	Down	ETS transcription factor ELK3
PGR	-0.62281	0.001617	0.029482	-3.15285	Down	progesterone receptor
VIM	-0.62236	0.001679	0.030082	-3.14177	Down	vimentin
TSHR	-0.62199	0.000904	0.020993	-3.31878	Down	thyroid stimulating hormone receptor
XAF1	-0.62128	0.000121	0.006039	-3.84505	Down	XIAP associated factor 1
GIMAP6	-0.62121	0.000774	0.018941	-3.36196	Down	GTPase, IMAP family member 6
DDX58	-0.62027	1.67E-05	0.001876	-4.30478	Down	DEXD/H-box helicase 58
TGFB3	-0.61949	0.001004	0.022146	-3.2895	Down	transforming growth factor beta 3
MARCHF3	-0.61945	0.00136	0.026659	-3.20294	Down	membrane associated ring-CH-type finger 3
SASH1	-0.61737	4.39E-05	0.003291	-4.08595	Down	SAM and SH3 domain containing 1
AHNAK	-0.61676	0.000812	0.019576	-3.34851	Down	AHNAK nucleoprotein
SLC19A3	-0.61615	0.000237	0.009338	-3.67641	Down	solute carrier family 19 member 3
PPP1R3B	-0.61536	5.67E-05	0.003847	-4.02609	Down	protein phosphatase 1 regulatory subunit 3B

LRP4	-0.61454	0.002676	0.039743	-3.00264	Down	LDL receptor related protein 4
S1PR3	-0.61377	0.001065	0.022901	-3.27289	Down	sphingosine-1-phosphate receptor 3
ZBED6	-0.61217	1.05E-06	0.000296	-4.8821	Down	zinc finger BED-type containing 6
RP2	-0.61043	1.83E-05	0.001932	-4.28492	Down	RP2 activator of ARL3 GTPase

Table 2 The enriched GO terms of the up and down regulated differentially expressed genes

GO ID	CATEGORY	GO Name	Adjusted p value	negative log10 of adjusted p value	Gene Count	Gene
Up regulated genes						
GO:0007399	BP	nervous system development	5.45E-09	8.263687154	99	EGR2, ATOH7, WNT1, ARC, IGFN1, ADCYAP1, LRTM2, SCN5A, RTN4R, SLC32A1, NNAT, NEUROD6, C HRNA7, NRG, CHRM1, TUBB2A, OVOL2, SPINT2, EFNB3, CCK, HP CA, CDK5R2, ADAMTSL1, CPNE6, MAL2, KCNK3, SEZ6L2, IL1RAPL2, SLC6A17, INSM1, WNT10B, PCD HAC2, CDH22, RGS4, SEZ6, NGEF, DOC2A, PLK2, SCN3B, PER2, RNF165, ECRG4, LINGO1, TAGLN3, CLSTN3, LZTS1, PAK6, IGSF8, PAK1, SCN2B, SYNGR3, PCDH1, TRIM67, NRSN1, ADGRB2, STMN3, TENM2, PCDH19, NRN1, UNC5D, PRKCG, MEF2D, CX3CL1, NBL1, CA10, EN C1, VSTM5, NRSN2, CNTNAP2, CAMK1, ETV5, CALM3, SLC12A5, P1N1, NECTIN1, GAS7, NDN, NTNG1, RAB3A, KATNB1, STXBP1, SLC8A3, CHRN2, RND1, SLC17A7, NAPA, NELL1, RET, UNC13A, NME1, STX1B, CDK5, SNRPB, HTR5A, HPCAL4, ACTL6B, NRE P, GABRG2, CITED2
GO:0007154	BP	cell communication	1.42095E-05	4.847421834	191	NMBR, EGR2, PNOC, EGR1, ASB2, MYLK2, C1QTNF4, GNG3, IL11, WNT1, RGS8, NXPH2, CALY, CCKBR, DUSP2, HTR3B, ARC, NPBWR2, ADCYAP1, NCALD, RHEBL1, SPEF1, GABRD, MUC5B, CACNA1G, P CSK1, FCRLB, SCN5A, IGFBP2, RH OV, HTR2C, TAMALIN, SPRED3, RBP4, FFAR4, RTN4R, ADTRP, SLC32A1, NNAT, ADRA1D, PPEF1, CHRNA7, MCHR2, GJD2, PLPPR3, MAP1LC3A, HPX, REM2, STX1A, NRG N, RPH3A, CHRM4, CHRM1, MUC6, GRM2, SYT5, BAIAP3, OPRL1, OVOL2, LBH, EFNB3, CCK, DIRAS1, ERFE, HPCA, TRIM54, GNG13, SL C1A6, CPNE6, ARHGDI, RASL10A, KCNK3, SEZ6L2, IL1RAPL2, WNT10B, NPTX2, SYT13, SLC8A2, GPR88, NSG2, NPTXR, HIPK4, RGS4, SEZ6, CACNB1, NGEF, DOC2A, PLK2, SCN3B, PER2, EXTL1, RNF165, IL1RL2, NUA1, FAM83H, CAMKK2, RHBDD2, CLSTN3, LZTS1, SYT12, PAK6, DCTPP1, SPRYD3, KCNIP3, SYP, ATP6V0E2, PAK1, SCN2B, CORO1A, PCDH1, TRIM67, DLK2, ADGRB2, RHOB2, TMEM

						38A,VAMP2,STMN3,ATP1A3,NSG1,PTPN3,TENM2,RIMS3,SV2A,CAMK4,UNC5D,ATP6V0B,VIPR1,PPP2R1A,CACNG3,PRKCG,TRIB3,RAB40C,EMD,CX3CL1,PRKAR1B,NBL1,FNDC5,MN1,ADRA1B,ATP6V1B2,CDH13,GNNG4,CNTNAP2,CAMK1,STAT4,CALM3,SLC12A5,PIN1,CDH8,PTPRN,HINT1,PIM2,H4C3,NDN,TSPYL5,CAP2,SYNGR1,DMTN,NTNG1,CRY2,SNCB,RAB3A,STXBPI,SLC8A3,KLHDC3,CHRN2,RND1,AP2M1,ATP6A1,GABARAPL1,PSMB5,SLC17A7,NAPA,ARHGEF9,FBP,RET,NEURL1B,UNC13A,XK,STX1B,CDK5,HTR5A,HPCAL4,TSZH3,MAST3,NREP,TMEM9,GABRG2,DLG3,ADGRA1,CITED2
GO:0030054	CC	cell junction	7.04E-16	15.15260462	105	PNOC,MYLK2,GNNG3,SLC30A3,RGS8,CALY,HTR3B,ARC,IGFN1,ADCYAP1,GABRD,CACNA1G,SCN5A,HTR2C,TAMALIN,RTN4R,SLC32A1,SVOP,CHRNA7,GJD2,MAP1LC3A,SH2D5,STX1A,NRGN,RPH3A,CHRM4,CHRM1,GRM2,SYT5,BAIAP3,EFNB3,CCK,HPCA,SLC1A6,CPNE6,KCNK3,IL1RAPL2,SLC6A17,NPTX2,SYT13,CDH22,SLC8A2,NPTXR,SEZ6,CACNB1,DOC2A,CAMKV,CAMKK2,CLSTN3,LZTS1,SYT12,PAK6,KCNIP3,SYP,PAK1,SCN2B,CORO1A,SYNGR3,PCDH1,VAMP2,ATP1A3,NSG1,TENM2,NMNAT2,RIMS3,NRN1,SV2A,CAMK4,CACNG3,PRKCG,RAB40C,PRKAR1B,CDH13,CNTNAP2,CAMK1,CALM3,SLC12A5,NIPSNAP1,PIN1,CDH8,PTPRN,SCAMP5,NECTIN1,CAP2,SYNGR1,DMTN,NTNG1,SNCB,RAB3A,STXBPI,SLC8A3,CHRN2,RND1,AP2M1,PPL,SLC17A7,NAPA,ARHGEF9,UNC13A,STX1B,CDK5,HTR5A,GABRG2,DLG3,ADGRA1
GO:0016020	CC	membrane	2.74E-09	8.561706218	266	NMBR,KNCN,PNOC,GNNG3,SLC30A3,WNT1,TMEM200B,RGS8,CALY,CCKBR,DUSP2,HTR3B,KLHL14,ARC,ARL4D,NPBWR2,KCNF1,NCALD,RHEBL1,FAM241B,SEPEF1,GABRD,MUC5B,CACNA1G,NOXA1,LRTM2,PCSK1,FCRLB,SCN5A,IGFBP2,RHOV,HTR2C,SLC10A4,PRSS16,TAMALIN,SPRED3,CTXN1,SLC22A6,TPBGL,FAR4,TRBC2,RTN4R,ICAM5,ADTRP,SLC32A1,PCDHG5,NNAT,TMEM59L,SVOP,KCNH4,ADRA1D,CHRNA7,MCHR2,GJD2,PLPPR3,MAP1LC3A,BEST4,TMEM221,REM2,STX1A,NRGN,FLG,RPH3A,ABCC11,CHRM4,CHRM1,MUC6,GRM2,SYT5,BAIAP3,FAM163B,ABCC12,OPRL1,SPINT2,EFNB3,SLC22A17,HAS1,DIRAS1,HPCA,GNG13,CDK5R2,SLC1A6,GALNT17,ADAMTSL1,CPNE6,ARF5,ARHGDIG,MAL2,COX8A,RASL10A,CALHM1,SLC7A4,KCNK3,SE

						Z6L2,GOLGA8B,MRPS12,IL1RA PL2,SLC6A17,SLC22A24,DNAJC 5G,SLC6A7,SYT13,PCDHAC2,C DH22,SLC45A1,SLC8A2,PRMT8, GPR88,IGSF3,TUBA1B,MARCHF 4,NSG2,NPTXR,STUM,RGS4,SE Z6,CACNB1,NGEF,DOC2A,INTS 5,SCN3B,CAMKV,PLD3,CYS1,E XTL1,ECRG4,IL1RL2,LINGO1,F XYD7,TIMM13,RHBDD2,CLSTN 3,LZTS1,SYT12,ENO2,KCNIP3,S YP,HPCAL1,ATP6V0E2,STOML1 ,IGSF8,PAK1,ST6GAL2,SCN2B,C ORO1A,SYNGR3,PCDH1,PPP1R1 4C,DLK2,PIGZ,NRSN1,NAT14,A DGRB2,TMIE,RHOBTB2,TMEM 38A,VAMP2,ATP1A3,NSG1,KCN B2,PTPN3,TENM2,PCDH19,NMN AT2,RIMS3,NRN1,SV2A,UNC5D, SHISAL1,ATP6V0B,C1ORF115,V IPR1,PPP2R1A,CACNG3,PRKCG, BFSP1,DNAL4,TRIB3,RAB40C,E MD,CX3CL1,PRKAR1B,VSTM5, NRSN2,PARM1,FNDC5,ADRA1B ,NDUFA4,MICOS13,ATP6V1B2, CDH13,GNG4,EFR3B,CNTNAP2, GGT7,FLRT1,KIF17,RAB36,CAL M3,SLC12A5,NIPSNAP1,ATP5M C1,C11ORF87,ARF3,ATP5F1B,C DH8,PTPRN,C3ORF80,PCDHGC4 ,SCAMP5,SYT16,HINT1,CYC1,Y IF1B,NECTIN1,PGAP3,GAS7,H4 C3,PODXL2,MELTF,CDIPT,CAP 2,SYNGR1,API51,DMTN,PIANP, PPOX,NTNG1,ASS1,RAB3A,B4G AT1,KATNB1,STXBPI,SLC8A3, CHRN2,RND1,AP2M1,PTPN5,A TP6AP1,GABARAPL1,PPL,SLC1 7A7,NAPA,APBB3,TIMM17B,CP NE7,FIBP,RET,UNC13A,CD200, XK,NME1,STX1B,CDK5,HTR5A, PEF1,RUSF1,TSHZ3,TMEM178B, FAM234B,TMEM9,GABRG2,DL G3,CYRIA,ADGRA1,KCNS2 SLC30A3,HTR3B,KCNF1,GABR D,CACNA1G,SCN5A,SLC10A4,A DAMTS8,RBP4,SLC22A6,SLC32 A1,SVOP,KCNH4,CHRNA7,GJD2 ,BEST4,HPX,ABCC11,ABCC12,S LC22A17,SLC1A6,CPNE6,COX8 A,CALHM1,SLC7A4,KCNK3,SL C6A17,SLC22A24,SLC6A7,SLC4 5A1,SLC8A2,CACNB1,SCN3B,K CNIP3,ATP6V0E2,SCN2B,TMEM 38A,ATP1A3,KCNB2,SV2A,ATP6 V0B,CACNG3,NDUFA4,ATP6V1 B2,SLC12A5,ATP5MC1,ATP5F1 B,SLC8A3,CHRN2,SLC17A7,TI MM17B,CPNE7,XK,CDK5,GABR G2,KCNS2
GO:0005215	MF	transporter activity	3.51636E-06	5.453906623	56	EGR2,PNOC,EGR1,ATOH7,ASB2 ,H1- 7,MYLK2,C1QTNF4,GNG3,IL11, SLC30A3,WNT1,RGS8,NXP2,S PATA2L,MPO,CALY,CCKBR,DU SP2,CCDC184,KLHL14,ARC,AR L4D,NPBWR2,IGFN1,ADCYAP1, CCNO,SPAG6,KCNF1,NCALD,R HEBL1,FAM241B,CRYM,PNMA 5,SPEF1,GABRD,MUC5B,OTOG
GO:0005515	MF	protein binding	0.03867521	1.412567324	331	

L,CACNA1G,NOXA1,LRTM2,PC
SK1,SCN5A,IGFBP2,RHOV,LOX
HD1,EMILIN3,HTR2C,SLC10A4,
ADAMTS8,TAMALIN,SPRED3,R
BP4,SLC22A6,TPBGL,FFAR4,RT
N4R,ICAM5,ADTRP,SVOP,NEU
ROD6,ADRA1D,PPEF1,CHRNA7,
SOWAHB,MAP1LC3A,SH2D5,H
PX,REM2,STX1A,NRGN,FLG,RP
H3A,CHRM1,MUC6,TUBB2A,GR
M2,SYT5,IQCN,DCAF12L2,BAIA
P3,FAM163B,OPRL1,OVOL2,LB
H,EFNB3,CCK,MYOZ3,HSPBP1,
SLC22A17,HAS1,DIRAS1,ERFE,
HPCA,TRIM54,LRRC73,GNG13,
CDK5R2,RCOR2,CPNE6,ARF5,A
RHGDIG,MAL2,COX8A,CALHM
1,KCNK3,GOLGA8B,MRPS12,IL
1RAPL2,SLC6A17,IQANK1,EXO
SC5,INSM1,WNT10B,NPTX2,SY
T13,CDH22,KLHL25,SLC8A2,PR
MT8,TUBA1B,PSMG3,NSG2,STU
M,HIPK4,RGS4,SEZ6,CACNB1,H
2AC21,NGEF,DOC2A,USP11,PL
K2,INTS5,SCN3B,CAMKV,PLD3,
CYS1,NPM3,PER2,EXTL1,RNF16
5,PYCR3,ECRG4,ZNF843,IL1RL2
,NUAK1,LINGO1,FXYP7,TIMM1
3,TAGLN3,FAM83H,CAMKK2,R
HBDD2,RTL8C,CLSTN3,LZTS1,
ASMTL,SYT12,PAK6,ENO2,DCT
PP1,RBM3,CHCHD2,SPRYD3,KC
NIP3,SYP,HPCAL1,STOML1,IGS
F8,PAK1,ST6GAL2,PNCK,CORO
1A,SYNGR3,POP7,TRIM67,DLK2
,NRSN1,CCNA1,ADGRB2,CIRBP
,TBCC,RHOB2,TMEM38A,VA
MP2,STMN3,ATP1A3,NSG1,KCN
B2,NLRP1,TUBA4A,PTPN3,TEN
M2,RIMS3,SV2A,CAMK4,COPS7
A,UNC5D,HR,SHISA1,ATP6V0
B,PNMA3,VIPR1,PPP2R1A,LAM
B3,CACNG3,PRKCG,BFSP1,MEF
2D,DNAL4,TRIB3,EMD,SULT4A
1,CX3CL1,PRKAR1B,NBL1,ENC
1,NRSN2,PARM1,FNDC5,KLHL2
6,MN1,ADRA1B,NDUFA4,MICO
S13,ATP6V1B2,CDH13,GNG4,EF
R3B,CNTNAP2,SPIN2B,GGT7,C
AMK1,ETV5,FLRT1,KIF17,RAB3
6,STAT4,CALM3,SLC12A5,NRIP
3,NIPSNAP1,PIN1,PHYHIP,ATP5
MC1,C11ORF87,ARF3,ATP5F1B,
CDH8,PTPRN,SCAMP5,SYT16,H
INT1,CYC1,NAA80,YIF1B,NECT
IN1,ACOT7,PGAP3,GAS7,PIM2,
H4C3,NDN,PODXL2,IER5,TSPY
L5,DMKN,MELTF,CDIPT,CAP2,
SYNGR1,DMTN,PIANP,NTNG1,
CRY2,SNCB,ASS1,RAB3A,B4GA
T1,KATNB1,STXBP1,SLC8A3,R
NF187,OTUB1,KLHDC3,CHRN3
2,RND1,AP2M1,SNU13,PTPN5,A
TP6AP1,GABARAPL1,PPL,PSMB
5,NAPA,APBB3,TIMM17B,ZNF7
10,NELL1,ZMYND12,TRIM66,A
RHGEF9,CPNE7,FIBP,RET,TRAP
PC1,NEURL1B,GPRASP2,UNC13
A,CD200,XK,NME1,CCDC113,ST
X1B,CDK5,SNRPB,HPCAL4,MB2

						1D2,PEF1,RUSF1,TSPYL4,TSHZ3, MAST3,NREP,TMEM9,GABRG2, DLG3,CYRIA,KCNS2,CITED2
Down regulated genes						
GO:0050896	BP	response to stimulus	1.02E-12	11.9923796	272	TOP2A,DLGAP5,CEP55,MELK,NDC80,VNN1,OR7A5,BCL2A1,CHI3L1,OR7C1,IL9,SHISA3,STC1,ANGPT2,MCM10,FPR2,S100A9,TLR8,MMRN1,SERPINA1,KIF14,MT1G,OR52B6,CDA,CCR5,TTK,NOD2,PLAC8,MT1F,GBP1,GBP5,GBP2,HPGD,C7,S100A4,OR51B5,MGAM,CD180,CDK1,C1QB,KLRC3,SPP1,FCGR3A,DDIT4L,SAMSN1,AZGP1,TLR7,TNFRSF10D,FYB1,SLFN13,HGF,TRIP10,PPEF2,TLR5,SULT1B1,TFPI,TLR2,MNDA,RUNX3,PTPRC,LVRN,C3,INSL6,IL2RG,MT1M,CLEC2B,CFL,NIBAN1,CENPF,PIK3AP1,TRIM5,JAML,NUPR1,E2F7,FCGR2A,CYSLTR2,HORMAD1,ALOX5AP,S100A11,ADAMDEC1,LAMP3,P2RY6,FER1G,MICB,IFI16,SELL,LAPTM5,FKBP5,CASP4,NMI,ALKAL2,IFNE,ADGRL4,SYK,CGAS,GLI1,LCP1,MT2A,LY75,MT1X,IL17RB,GPR4,SPN,DTX3L,CYBB,TLR1,NEFH,GABRE,SRGN,CELSR1,NCKAP1L,PARP9,GBP3,TRIM38,ASH3,SP100,CLIC1,IKBIP,APBB1IP,OSMR,SLA,MT1E,PK4,NFATC2,GNRH1,MAFF,CD34,CCNA2,BRCA2,HCLS1,RAB13,TFEC,PIK3CG,GBP4,CSF3R,GPNMB,ITGB3,ND3,ANXA3,MAP3K8,PERP,FAM111A,CDK2,PTAFR,ORC1,YES1,NCF2,CD58,NEXN,RASSF8,TNFSF10,ITGA10,BTK,PRKX,TRIM21,NQO1,FGF11,TEAD2,B2M,TRDN,MYOF,SLC39A12,ADGRE2,ANXA2,FLT1,MECOM,TGFBR1,IRAK3,GNG11,DNA2,CTSS,SLC38A2,HELB,ARHGAP42,HHEX,PCOLCE2,ITGA1,HK2,GPR160,PARP14,NABP1,MSTN,RNF152,EVC2,FBXO5,HEBP2,FOXC1,IFITM3,DOCK2,NEDD4,MEFV,ROM1,IFIH1,ATP6,DDR2,ND4,TPD52L1,BCL6,HERC5,OAS2,COX2,WTR1,RFTN2,ND6,RHOQ,TRIM22,CLDN18,NLRC5,CASP7,MMRN2,LRRC69,RELL1,ARHGDIB,CFH,MYL12A,ERBIN,EMX2,BTNL9,YAP1,TGFBR2,DOK3,ACTL6A,CASP6,PPP1R1C,LCP2,AKR1C3,MYD88,CHEK2,RHOJ,MLKL,PLIN2,NFKBIA,APOL1,PLD2,ARHGAP11A,ANO6,CYTB,IL13RA1,IQGAP1,RGCC,SLFN11,ND1,ITGB8,TP53INP1,ITGB1,LPAR6,CSF1,ANXA5,KIF5B,ITPKB,PLSCR1,ANXA1,SUMO4,SAMHD1,LEF1,NOSTRIN,ITGA8,MAML2,CLEC2D,CD2AP,REST,ELK3,PGR,VIAM,TSHR,XAF1,DDX58,TGFB3,ASH1,LRP4,S1PR3,ZBED6
GO:0007154	BP	cell communication	2.94E-09	8.53210726	208	DLGAP5,CEP55,MELK,NDC80,VNN1,OR7A5,BCL2A1,CHI3L1,OR7C1,IL9,SHISA3,STC1,ANGPT2,F

						<p>PR2,S100A9,TLR8,KIF14,OR52B 6,CDA,CCR5,TTK,NOD2,GBP1,G BP2,HPGD,S100A4,OR51B5,CD1 80,CDK1,SPP1,FCGR3A,DDIT4L, TFAP2C,TLR7,TNFRSF10D,FYB 1,SCN4A,HGF,TRIP10,PPEF2,TL R5,TLR2,MNDA,PTPRC,LVRN,C 3,INSL6,IL2RG,CENPF,PIK3AP1, TRIM5,NUPR1,E2F7,FCGR2A,C YSLTR2,HORMAD1,S100A11,P2 RY6,FCER1G,MICB,IFI16,LAPT M5,CASP4,NMI,ALKAL2,IFNE,A DGRL4,SYK,CGAS,GLI1,LCP1, MT2A,IL17RB,GPR4,SPN,DTX3L ,CYBB,TLR1,GABRE,SRGN,CEL SR1,NCKAP1L,PARP9,TRIM38,S P100,CLIC1,APBB1IP,OSMR,SL A,PDK4,NFATC2,GNRH1,CD34, CCNA2,BRCA2,HCLS1,RAB13,PI K3CG,CSF3R,GPNMB,ITGB3,M AP3K8,PERP,CDK2,PTAFR,ORC 1,YES1,NCF2,RASSF8,TNFSF10,I TGA10,BTK,PRKX,TRIM21,NQO 1,FGF11,TEAD2,B2M,TRDN,SLC 39A12,ADGRE2,ANXA2,FLT1,M ECOM,TGFBR1,IRAK3,GNG11,D NA2,CTSS,SLC38A2,ARHGAP42, HHEX,ITGA1,GPR160,PARP14,N ABP1,MSTN,RNF152,EVC2,FOX C1,IFITM3,DOCK2,NEDD4,MEF V,IFIH1,DDR2,TPD52L1,BCL6,O AS2,WVTR1,RHOQ,TRIM22,CL DN18,NLRC5,MMRN2,LRR69, RELL1,ARHGDIB,ERBIN,BTNL9 ,YAP1,TGFBR2,DOK3,ACTL6A, PPP1R1C,LCP2,AKR1C3,MYD88, CHEK2,RHOJ,MLKL,NFKBIA,A RHGAP11A,ANO6,IL13RA1,IQG AP1,RGCC,ITGB8,TP53INP1,ITG B1,LPAR6,CSF1,ANXA5,KIF5B,I TPKB,PLSCR1,ANXA1,SUMO4, KCNJ10,SAMHD1,LEF1,NOSTRI N,ITGA8,MAML2,CLEC2D,CD2 AP,REST,ELK3,PGR,VIM,TSHR, XAF1,DDX58,TGFB3,SASH1,LR P4,S1PR3,ZBED6 CEP55,MELK,VNN1,OR7A5,CHI 3L1,OR7C1,STC1,ANGPT2,FPR2, S100A9,TLR8,MMRN1,SERPINA 1,KIF14,KCNE4,OR52B6,CCR5,N OD2,VNN2,GBP1,SLC1A7,HPGD ,C7,S100A4,OR51B5,MGAM,CD1 80,KIF20A,BOLL,FCGR3A,LAM B4,KCNJ15,AZGP1,HMMR,TLR7 ,PRRG4,TNFRSF10D,FYB1,SCN4 A,TRIP10,TLR5,TFPI,TLR2,PTPR C,LVRN,C3,IL2RG,CLEC2B,NIB AN1,PIK3AP1,JAML,FCGR2A,C YSLTR2,ADAMDEC1,LAMP3,P2 RY6,FCER1G,MICB,SELL,LAPT M5,CASP4,STEAP4,ADGRL4,SY K,CGAS,LCP1,LY75,IL17RB,GP R4,SPN,CALHM5,CYBB,TLR1,B ACE2,GABRE,CELSR1,NCKAP1 L,CLIC1,APBB1IP,OSMR,SLA,K CNJ16,CD34,HCLS1,RAB13,PIK3 CG,GBP4,CSF3R,GPNMB,ITGB3, SLC7A2,ANXA3,PRELP,EMCN,P ERP,COL27A1,PTAFR,LIPH,YES 1,NCF2,CD58,NEXN,TNFSF10,IT</p>
GO:0071944	CC	cell periphery	9.0448E-06	5.043601216	178	

						GA10,BTK,B2M,TRDN,MYOF,S LC39A12,ADGRE2,ANXA2,ADA M28,FLT1,TGFB1,IRAK3,GNG1 1,CTSS,SLC38A2,LPCAT2,CALD 1,DIO1,ITGA1,HK2,GPR160,PAR P14,EVC2,CD302,IFITM3,NEDD4 ,ROM1,DDR2,ATP11C,WWTR1,T ES,RFTN2,RHOQ,SLC5A9,CLDN 18,MMRN2,RELL1,ERBIN,BTNL 9,TGFB2,DOK3,ACTL6A,LCP2, MYD88,RHOJ,MLKL,PLIN2,NFK BIA,ANO6,IL13RA1,IQGAP1,ITG B8,ITGB1,LPAR6,CSF1,ANXA5, PLSCR1,ANXA1,KCNJ10,SAMH D1,NOSTRIN,ITGA8,MLANA,CL EC2D,SYNE2,CD2AP,VIM,TSHR ,DDX58,TGFB3,AHNAK,SLC19A 3,LRP4,S1PR3,RP2
GO:0005737	CC	cytoplasm	0.003121618	2.505620241	280	TOP2A,DLGAP5,CEP55,RRM2,H JURP,MELK,NDC80,VNN1,BCL2 A1,CHI3L1,SHISA3,STC1,KNL1, FPR2,SGO1,S100A9,TLR8,MMR N1,SERPINA1,KIF14,MT1G,CDA ,CCR5,TTK,NOD2,PLAC8,MT1F, GBP1,MS4A6A,GBP5,GBP2,HPG D,S100A4,MGAM,PLA1A,KIF20 A,CDK1,BOLL,SPP1,DDIT4L,TM PRSS12,SAMSN1,TNFAIP8,TFAP 2C,HMMR,TLR7,PRRG4,REP15,F YB1,SLFN13,HGF,TRIP10,PPEF2 ,SULT1B1,TFPI,TLR2,MNDA,RU NX3,PTPRC,LVRN,C3,IL2RG,MT 1M,NIBAN1,GAS2L3,DNAH11,C ENPF,PIK3AP1,TRIM5,GIMAP4, NUPR1,NUSAP1,FCGR2A,ALOX 5AP,NEB,S100A11,LAMP3,HIGD 1B,FCER1G,SMTN,IFI16,SELL,L APTM5,FKBP5,DIAPH3,CASP4, NMI,STEAP4,ADGRL4,SYK,CG AS,GLI1,LCP1,MT2A,MT1X,ATP 8,RANBP3L,DTX3L,SAMD9,CY BB,TLR1,NEFH,BACE2,SRGN,N CKAP1L,PARP9,GBP3,TRIM38,S ASH3,CEP152,SP100,CLIC1,IKBI P,APBB1IP,SAMD9L,SLA,MT1E, PDK4,NFATC2,GNRH1,MAFF,C D34,CCNA2,BRCA2,HCLS1,RAB 13,PIK3CG,SLC25A48,GIMAP7,E HF,GBP4,GPNMB,ITGB3,ND3,A NXA3,MAP3K8,PRELP,PERP,FA M111A,COL27A1,CDK2,PTAFR, GIMAP2,ORC1,YES1,NCF2,CD58 ,NEXN,BTK,PRKX,TRIM21,NQO 1,FGF11,TEAD2,B2M,TRDN,MY OF,SLC39A12,ANXA2,ADAM28, FLT1,MECOM,TGFB1,IRAK3,G NG11,FLI1,DNA2,CTSS,SLC38A 2,LPCAT2,HELB,HHEX,CALD1, ZIC2,ACSS3,DIO1,ITGA1,HK2,N D4L,SQOR,PARP14,NABP1,MST N,RNF152,EVC2,FBXO5,HEBP2, SAMD4A,FOXC1,CD302,IFITM3, DOCK2,NEDD4,DBI,MEFV,IFIH 1,ATP6,HMGN5,ND4,TPD52L1,B CL6,HERC5,OAS2,LRR1,COX2, ATP11C,WWTR1,TES,ND6,RHO Q,CNTLN,TRIM22,ND2,DSE,NL RC5,CASP7,ARHGDIB,MYL12A, ERBIN,YAP1,GIMAP5,CCDC146, TGFB2,DOK3,CASP6,PPP1R1C,

						LCP2,AKR1C3,MYD88,CHEK2,RHOJ,MLKL,MRPS6,ST6GALNAC3,PLIN2,NFKBIA,APOL1,PLOD2,ARHGAP11A,ANO6,CYTB,IQGA P1,RGCC,SLFN11,GIMAP8,ND1,NEK7,TP53INP1,ITGB1,CSF1,ANXA5,TBC1D8B,KIF5B,ITPKB,PLSCR1,ANXA1,FAM241A,PMP2,LEF1,NOSTRIN,ITGA8,MLANA,CLEC2D,SYNE2,CD2AP,REST,ELK3,PGR,VIM,XAF1,GIMAP6,DDX58,TGFB3,MARCHF3,SASH1,AHNAK,PPP1R3B,S1PR3,ZBED6,RP2
GO:0042802	MF	identical protein binding	3.95963E-05	4.40234582	80	TOP2A,CEP55,RRM2,HJURP,ND C80,BCL2A1,STC1,MCM10,TLR8,SERPINA1,CDA,CCR5,GBP1,GBP5,GBP2,HPGD,S100A4,HGF,TRIP10,TLR2,TBX15,CLEC2B,CENPF,PIK3AP1,TRIM5,JAML,E2F7,ALOX5AP,S100A11,FCER1G,IFI16,NM1,LCP1,TLR1,GBP3,TRIM38,SP100,BRCA2,PIK3CG,GIMAP7,GBP4,ITGB3,GIMAP2,TNFSF10,BTK,TRIM21,NQO1,B2M,ANXA2,MECOM,IRAK3,HHEX,MSTN,DBI,MEFV,ROM1,IFIH1,TPD52L1,BCL6,WWTR1,TRIM22,CLDN18,CFH,ZNF69,CASP6,MYD88,CH EK2,MLKL,NFKBIA,CSF1,KIF5B,ANXA1,SAMHD1,CD2AP,PGR,VIM,DDX58,TGFB3,AHNAK,LRP4
GO:0060089	MF	molecular transducer activity	0.005140349	2.289007434	55	MELK,OR7A5,OR7C1,FPR2,TLR8,OR52B6,CCR5,TTK,NOD2,HPGD,OR51B5,KLRC3,FCGR3A,TLR7,TNFRSF10D,TLR5,TLR2,PTPRC,IL2RG,TRIM5,FCGR2A,CYSLTR2,P2RY6,FCER1G,ADGRL4,SYK,LY75,IL17RB,GPR4,SPN,TLR1,GABRE,CELSR1,OSMR,CSF3R,ITGB3,PTAFR,YES1,BTK,ADGRE2,FLT1,TGFB1,GPR160,CD302,DDR2,TGFB2,IL13RA1,ITGB8,ITGB1,LPAR6,LEF1,CLEC2D,PGR,TSHR,S1PR3

Table 3 The enriched pathway terms of the up and down regulated differentially expressed genes

Pathway ID	Pathway Name	Adjusted p value	Negative log10 of adjusted p value	Gene Count	Gene
Up regulated genes					
REAC:R-HSA-112316	Neuronal System	1.02E-11	10.98934789	37	GNG3,HTR3B,KCNF1,NCALD,SLC32A1,KCNH4,CHRNA7,GJD2,STX1A,NRGN,TUBB2A,GNG13,SLC1A6,KCNK3,IL1RAPL2,TUBA1B,CACNB1,CAMKK2,SYT12,VAMP2,KCNB2,TUBA4A,CAMK4,CACNG3,PRKCG,PRKAR1B,NG4,CAMK1,KIF17,RAB3A,STXBP1,CHRNA2,SLC17A7,ARHGEF9,GABRG2,DLG3,KCNS2
REAC:R-HSA-112315	Transmission across Chemical Synapses	2.64E-10	9.578744597	28	GNG3,HTR3B,NCALD,SLC32A1,CHRNA7,STX1A,NRGN,TUBB2

REAC:R-HSA-187037	Signaling by NTRK1 (TRKA)	0.008665023	2.062230269	10	A,GNG13,SLC1A6,TUBA1B,CACNB1,CAMKK2,VAMP2,TUBA4A,CAMK4,CACNG3,PRKCG,PRKAR1B,GNG4,CAMK1,KIF17,RAB3A,CHRNA2,SLC17A7,ARHGEF9,GABRG2,DLG3
REAC:R-HSA-5576891	Cardiac conduction	0.016791344	1.774914548	10	EGR2,EGR1,ARC,ADCYAP1,CDK5R2,PPP2R1A,MEF2D,DNAL4,AP2M1,CDK5
REAC:R-HSA-372790	Signaling by GPCR	0.022140035	1.654821703	40	SCN5A,KCNK3,SLC8A2,CACNB1,SCN3B,FXR1,SCN3B,ATP1A3,SLC8A3
REAC:R-HSA-9006934	Signaling by Receptor Tyrosine Kinases	0.058821515	1.230463795	20	NMBR,PNOC,GNG3,WNT1,RGS8,CCKBR,NPBWR2,ADCYAP1,HTR2C,RBP4,FFAR4,SDR9C7,ADRA1D,PPEF1,MCHR2,PLPPR3,CHRM4,CHRM1,GRM2,OPRL1,CCKA,GNG13,WNT10B,RGS4,NGEF,CAMKK2,PAK1,CAMK4,VIPR1,PPP2R1A,PRKCG,CX3CL1,PRKAR1B,ADRA1B,GNG4,RBP2,ARHGEF9,XK,CDK5,HTR5A
Down regulated genes					EGR2,EGR1,ARC,ADCYAP1,SPIR1,CDK5R2,ATP6V0E2,PAK1,PTPN3,ATP6V0B,PPP2R1A,LAMB3,MEF2D,DNAL4,TRIB3,ATP6V1B2,AP2M1,ATP6A1,CDK5,GABRG2
REAC:R-HSA-168256	Immune System	1.91E-09	8.718362079	97	VNN1,CHI3L1,IL9,FPR2,S100A9,TLR8,SERPINA1,CDA,CCR5,NOD2,PLAC8,GBP1,GBP5,GBP2,C7,MGAM,CD180,KIF20A,FCGR3A,TLR7,FYB1,HGF,TLR5,TLR2,MNDA,PTPRC,C3,IL2RG,CLEC2B,CFL,PIK3AP1,TRIM5,JAML,FCGR2A,S100A11,FCER1G,MICB,IFI16,SELL,CASP4,SYK,CGAS,LCP1,MT2A,IL17RB,DTX3L,CYBB,TLR1,NCKAP1L,GBP3,TRIM38,SP100,OSMR,SLA,NFATC2,GBP4,CSF3R,MAP3K8,PTAFR,YES1,NCF2,CD58,BTK,TRIM21,B2M,ANXA2,IRAK3,CTSS,HEBP2,IFITM3,DOCK2,NEDD4,MEFV,IFIH1,BCL6,HERC5,OAS2,TRIM22,NLRP5,CFH,BTNL9,DOK3,LCP2,MYD88,NFKBIA,ANO6,IL13RA1,IQGAP1,ITGB1,CSF1,KIF5B,ANXA1,SAMHD1,CLEC2D,VIM,XAF1,DDX58
REAC:R-HSA-1280215	Cytokine Signaling in Immune system	3.8871E-06	5.410373893	43	IL9,CCR5,NOD2,GBP1,GBP5,GBP2,HGF,IL2RG,TRIM5,SYK,LCP1,MT2A,IL17RB,GBP3,TRIM38,SP100,OSMR,SLA,GBP4,CSF3R,MAP3K8,PTAFR,YES1,TRIM21,B2M,ANXA2,IRAK3,IFITM3,NEDD4,BCL6,HERC5,OAS2,TRIM22,MYD88,NFKBIA,IL13RA1,ITGB1,CSF1,ANXA1,SAMHD1,VIM,XAF1,DDX58
REAC:R-HSA-913531	Interferon Signaling	7.42255E-06	5.129446658	20	GBP1,GBP5,GBP2,TRIM5,MT2A,GBP3,TRIM38,SP100,GBP4,PTAFR,TRIM21,B2M,IFITM3,NEDD4,HERC5,OAS2,TRIM22,SAMHD1,XAF1,DDX58
REAC:R-HSA-168898	Toll-like Receptor Cascades	0.0014753	2.831119584	14	S100A9,TLR8,NOD2,CD180,TLR7,TLR5,TLR2,TLR1,MAP3K8,BTK,IRAK3,CTSS,MYD88,NFKBIA,ANGPT2,MMRN1,SERPINA1,KI
REAC:R-HSA-109582	Hemostasis	0.038318795	1.416588151	30	

REAC:R-HSA-397014	Muscle contraction	0.071675415	1.144629782	12	F20A,TNFRSF10D,HGF,TFPI,JA ML,FCER1G,SELL,SYK,SPN,SR GN,APBB1IP,MAFF,PIK3CG,ITG B3,CDK2,YES1,CD58,ITGA10,A NXA2,GNG11,ITGA1,DOCK2,LC P2,ITGB1,ANXA5,KIF5B,TGFB3 KCNE4,SCN4A,NEB,FGF11,TRD N,ANXA2,CALD1,ITGA1,WWTR 1,MYL12A,ANXA1,VIM
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Table 4 Topology table for up and down regulated genes.

Regulation	Node	Degree	Betweenness	Stress	Closeness
Up	OTUB1	168	0.07141	9945498	0.319279
Up	PPP2R1A	167	0.082265	13013540	0.330066
Up	AP2M1	124	0.042956	12345552	0.301153
Up	PIN1	121	0.055885	9510528	0.322668
Up	USP11	98	0.036757	7849042	0.298812
Up	MAP1LC3A	84	0.02886	3940580	0.301354
Up	SPINT2	70	0.029283	4295274	0.270554
Up	CDK5	65	0.019983	3668464	0.300842
Up	TUBA4A	64	0.027425	4267060	0.315814
Up	GABARAPL1	61	0.013241	1769776	0.278602
Up	SCN2B	57	0.020358	2474674	0.244552
Up	DLG3	54	0.022883	2212964	0.269017
Up	PAK1	54	0.015822	2630050	0.302383
Up	EMD	54	0.017582	3156228	0.296205
Up	COPS7A	52	0.015587	4080222	0.267621
Up	STX1A	50	0.015161	1961900	0.269534
Up	PSMB5	50	0.016229	3697432	0.280733
Up	ATP5F1B	50	0.020934	3474666	0.294641
Up	SNRPB	48	0.017132	3542636	0.265788
Up	RET	47	0.014483	2395004	0.294556
Up	PPEF1	46	0.01187	1436250	0.281062
Up	NDN	45	0.014736	3118374	0.280385
Up	NIPSNAP1	43	0.012181	2808016	0.273606
Up	CCNA1	40	0.005324	731796	0.291
Up	MAST3	39	0.012072	2038396	0.266396
Up	STXBP1	37	0.012163	1488860	0.277086
Up	TIMM13	37	0.010596	2545900	0.27414
Up	EXOSC5	35	0.010651	2802368	0.244362
Up	TUBB2A	35	0.011719	1761072	0.297503
Up	PTPN3	34	0.010358	2507486	0.272072
Up	ATP6V1B2	32	0.008845	1266236	0.272527
Up	PRMT8	30	0.008639	981910	0.270356
Up	PLK2	30	0.011608	1925362	0.24667
Up	EGR1	29	0.006593	1374190	0.280443
Up	TUBA1B	29	0.007247	1515320	0.295925
Up	VAMP2	27	0.004698	582590	0.239915
Up	RAB3A	27	0.010134	2372496	0.245644
Up	NME1	27	0.007847	1040722	0.264907
Up	CHCHD2	27	0.008993	1710698	0.232747
Up	TRIB3	23	0.008231	938710	0.282211
Up	NAPA	22	0.006186	1166566	0.252839
Up	FAM83H	22	0.005418	1210472	0.259987
Up	CAMKK2	22	0.005092	971692	0.265234
Up	KLHDC3	22	0.006703	648526	0.23858
Up	PTPN5	21	0.00367	504710	0.259259
Up	LAMB3	21	0.004804	1502760	0.23686
Up	GAS7	20	0.004451	848144	0.246252
Up	CORO1A	20	0.006302	1121082	0.231136
Up	HIPK4	20	0.004399	996272	0.237967
Up	PTPRN	19	0.004817	912066	0.214998
Up	PPL	18	0.006724	426754	0.263485
Up	ADCYAP1	18	0.005602	1085272	0.212886
Up	SLC4A1	18	0.005619	445156	0.255151
Up	MYLK2	17	0.00398	664800	0.269498
Up	SNU13	16	0.003591	1087894	0.251466

Up	MEF2D	16	0.002058	614922	0.266728
Up	ASS1	16	0.003131	560618	0.261405
Up	SCN5A	15	0.004508	390980	0.23952
Up	PRKCG	15	0.004037	332602	0.267621
Up	HSPBP1	15	0.00325	742384	0.237551
Up	INTS5	15	0.003351	241056	0.26398
Up	HINT1	14	0.002383	290694	0.258453
Up	PAK6	14	0.001919	553154	0.269373
Up	CRY2	14	0.003031	307230	0.246252
Up	CYC1	14	0.004055	978962	0.243573
Up	CAMK1	14	0.002831	379528	0.251917
Up	GPRASP2	14	0.002978	563876	0.243792
Up	NDUFA4	14	0.003771	399940	0.266658
Up	PRKAR1B	13	0.0022	523610	0.24667
Up	KRT5	13	0.003521	627862	0.27656
Up	PHYHIP	13	0.00362	561040	0.216944
Up	ARF5	12	0.003859	494656	0.212975
Up	POP7	12	0.002996	432912	0.227204
Up	STX1B	12	3.31E-04	66908	0.224389
Up	CIRBP	12	0.002706	467172	0.250986
Up	NELL1	12	0.002712	581170	0.246044
Up	TRAPPC1	11	0.00397	882746	0.184086
Up	SYP	11	0.001445	234918	0.243864
Up	PEF1	11	0.001809	383856	0.228005
Up	PSMG3	10	0.001161	238338	0.213187
Up	TARBP1	10	0.003381	362168	0.238287
Up	CDIPT	10	0.0014	237860	0.259292
Up	KATNB1	9	0.002492	275332	0.205529
Up	IGSF8	9	0.002966	701636	0.191736
Up	ACTL6B	9	6.02E-04	101388	0.211241
Up	HPCAL1	9	0.00147	350022	0.241394
Up	TRIM54	8	0.00155	305518	0.214162
Up	RBM3	8	7.73E-04	171472	0.2309
Up	ENO2	8	9.07E-04	131346	0.2548
Up	KLHL26	8	0.002463	371158	0.207592
Up	HTR2C	7	6.15E-04	114798	0.210488
Up	EFNB3	7	1	20	1
Up	PYCR3	7	0.001488	198522	0.202798
Up	ATP6AP1	7	8.04E-04	199204	0.239028
Up	DDX28	7	0.001597	287238	0.218821
Up	DCTPP1	7	6.56E-04	103376	0.229456
Up	ACOT7	7	0.001071	297560	0.220789
Up	MICOS13	7	7.84E-04	158776	0.234259
Up	NPM3	6	0.001048	226888	0.248581
Up	ASB2	6	2.67E-04	49820	0.238455
Up	VIPR1	6	0.00197	151914	0.194435
Up	FLG	6	0.001573	242370	0.208645
Up	IQCN	6	0.001674	106818	0.23819
Up	DUSP4	5	5.50E-04	156260	0.223588
Up	CHRM4	5	9.82E-04	193118	0.177919
Up	ARL4D	4	0.001007	128230	0.209331
Up	GGT7	4	0.001472	214566	0.186427
Up	CAMKV	4	6.47E-06	1848	0.194788
Up	UNC13A	3	5.10E-04	106484	0.181204
Up	PLD3	3	7.67E-05	14284	0.219138
Up	CA10	3	2.18E-04	48066	0.212664
Up	CDH13	3	1.17E-06	470	0.190891
Up	DLK2	3	1.46E-04	4934	0.224043
Up	CX3CL1	2	1.54E-05	7966	0.227103
Up	FAM234B	2	1.14E-05	1280	0.183571
Up	CPNE7	2	4.91E-04	50828	0.242053
Up	RPH3A	1	0	0	0.197212
Up	CITED2	1	0	0	0.207624
Up	FIBP	1	0	0	0.23128
Up	ADRA1B	1	0	0	0.231464
Up	BFSP1	1	0	0	0.240666
Up	B4GAT1	1	0	0	1
Up	API51	1	0	0	0.231464
Up	NUAK1	1	0	0	0.222101
Up	PER2	1	0	0	0.197604

Up	SPRYD3	1	0	0	0.230079
Up	SULT4A1	1	0	0	0.243967
Up	KLHL14	1	0	0	0.171913
Up	NAT14	1	0	0	0.206498
Up	FAM241B	1	0	0	0.150493
Up	VWA5B2	1	0	0	0.197212
Up	SV2A	1	0	0	0.231464
Up	TAGLN3	1	0	0	0.20301
Up	SDR9C7	1	0	0	0.197873
Up	ATP1A3	1	0	0	1
Up	TSPYL4	1	0	0	0.192633
Up	STOML1	1	0	0	0.254673
Up	PIM2	1	0	0	0.215168
Up	STAT4	1	0	0	0.212188
Up	IER5	1	0	0	0.248173
Up	DOC2A	1	0	0	0.216979
Down	CDK2	266	0.112091	26621858	0.341664
Down	IQGAP1	187	0.071324	17647666	0.327387
Down	NEDD4	142	0.055443	10650202	0.320434
Down	VIM	128	0.054878	9003984	0.316919
Down	CDK1	102	0.033728	5868324	0.326364
Down	YAP1	100	0.037372	6470746	0.31601
Down	TEAD2	97	0.035043	4388736	0.301644
Down	NFKBIA	95	0.033392	7173334	0.310731
Down	IFI16	93	0.034793	7989162	0.280193
Down	BCL6	92	0.033786	2993878	0.290088
Down	FKBP5	80	0.024037	5754610	0.298418
Down	CCNA2	79	0.021411	3068314	0.31365
Down	BTX	77	0.027655	3871414	0.306546
Down	SYK	77	0.025076	4962946	0.297916
Down	PLSCR1	74	0.028772	5643644	0.275979
Down	ITGB1	72	0.030542	6994814	0.289244
Down	SUMO4	72	0.027092	4105944	0.300797
Down	ACTL6A	68	0.022131	4165820	0.270034
Down	TGFBR2	60	0.016685	2909000	0.290212
Down	CHEK2	59	0.017851	2485420	0.30782
Down	BRCA2	57	0.018747	2368156	0.308636
Down	TGFBR1	55	0.015763	2209422	0.299361
Down	KIF5B	54	0.016013	4350456	0.278907
Down	TOP2A	54	0.017858	4289336	0.313505
Down	ANXA2	54	0.016436	4806976	0.311135
Down	B2M	51	0.012509	2444652	0.242039
Down	YES1	51	0.01526	4218212	0.290626
Down	ORC1	43	0.011657	1207704	0.286619
Down	ERBIN	43	0.011431	3883630	0.281024
Down	PGR	43	0.011693	1392800	0.300111
Down	TRIM21	43	0.013054	2650410	0.296917
Down	MYD88	41	0.011462	1404158	0.27735
Down	SGO1	40	0.012421	1088650	0.279962
Down	FOXC1	40	0.011349	1155294	0.28674
Down	PTPRC	38	0.008059	2799532	0.266449
Down	S100A4	37	0.011593	1114180	0.299009
Down	MCM10	36	0.004682	1557502	0.269998
Down	CD2AP	35	0.006407	910094	0.279328
Down	NDC80	35	0.006414	2318512	0.264528
Down	GLI1	35	0.009183	2015686	0.271184
Down	NMI	35	0.010002	2515616	0.26932
Down	ANXA1	33	0.016364	2992794	0.294194
Down	ITGB3	32	0.005582	1573674	0.271256
Down	CASP7	32	0.006895	828298	0.274862
Down	MKI67	32	0.010358	1696668	0.287104
Down	NOD2	31	0.009377	882872	0.264031
Down	CEP55	31	0.017614	4100306	0.261422
Down	LEF1	30	0.007168	2170294	0.26727
Down	LCP2	30	0.006378	1286260	0.271293
Down	DDX58	30	0.006811	1896598	0.249281
Down	HGF	30	0.005518	1003412	0.279692
Down	CASP4	30	0.008429	688954	0.279328
Down	RASSF8	29	0.007814	1008256	0.270824
Down	TRIP10	28	0.00737	2156390	0.251621

Down	NFATC2	28	0.007579	920916	0.295389
Down	RP2	27	0.008128	1628202	0.227496
Down	KIF20A	26	0.008819	2742112	0.25173
Down	WWTR1	26	0.004113	721282	0.283724
Down	LPAR6	26	0.011845	2466340	0.220264
Down	TES	25	0.004245	598836	0.278336
Down	SERPINA1	25	0.009865	1353946	0.247119
Down	SYNE2	24	0.006627	675844	0.27501
Down	KNL1	24	0.004511	1066872	0.268167
Down	SP100	23	0.005003	1130392	0.261691
Down	SAMHD1	23	0.005744	833346	0.281276
Down	AHNAK	22	0.00364	1474678	0.287428
Down	GABRE	22	0.009836	2200408	0.177146
Down	S100A9	21	0.004273	605884	0.285494
Down	MYL12A	21	0.002684	1025554	0.260419
Down	ND1	21	0.006153	965560	0.218433
Down	LIPH	21	0.009326	1429872	0.216299
Down	REST	20	0.004416	1144470	0.253043
Down	FLT1	20	0.004803	683518	0.260736
Down	RUNX3	20	0.002903	501702	0.274917
Down	TSHR	20	0.006063	955592	0.270428
Down	CPVL	20	0.005358	573972	0.26022
Down	CCR5	19	0.004161	975644	0.24318
Down	C3	19	0.007227	1504884	0.20903
Down	HERC5	19	0.003223	625504	0.273331
Down	MAP3K8	18	0.002347	347442	0.274048
Down	CALD1	18	0.004685	677158	0.281743
Down	TTK	18	0.003774	597730	0.275661
Down	FBXO5	17	0.003569	1006980	0.248339
Down	CENPF	17	0.003746	374014	0.265062
Down	NEB	16	0.003044	834378	0.238776
Down	CASP6	16	0.002255	210662	0.258765
Down	SPP1	16	0.003428	363174	0.254022
Down	KIF14	16	0.00576	601548	0.233307
Down	HK2	16	0.004074	729230	0.249007
Down	BAZ1A	15	0.003258	421200	0.255023
Down	TLR2	15	0.003171	337512	0.257815
Down	ANXA5	15	0.003129	753934	0.252808
Down	NEXN	15	8.37E-04	178902	0.264322
Down	CLIC1	15	0.002321	309010	0.279846
Down	RRM2	13	0.003003	323748	0.264391
Down	COX2	13	0.003251	687014	0.263741
Down	IFIH1	12	0.001826	370462	0.208613
Down	TRIM5	12	0.002144	1016118	0.230209
Down	HMMR	12	0.002047	362910	0.257538
Down	DTX3L	11	0.001543	464720	0.228684
Down	TFAP2C	10	0.002285	556108	0.26201
Down	DIAPH3	10	0.005234	680428	0.251249
Down	CEP152	9	0.001965	408206	0.225033
Down	MELK	9	0.004174	1114356	0.232773
Down	PLOD2	7	0.001043	178040	0.204827
Down	IKBIP	7	0.002459	394590	0.220622
Down	TNFRSF10D	6	0.00149	186350	0.202848
Down	NEFH	6	0.001017	308984	0.222757
Down	SINHCAF	5	0.001187	271076	0.216208
Down	TRDN	4	1	12	1
Down	CCDC146	4	8.82E-04	173322	0.214477
Down	MNDA	3	5.08E-04	61158	0.192488
Down	TGFB3	2	0	0	0.23627
Down	ZIC2	2	1.04E-04	21644	0.236723
Down	CDA	2	4.91E-04	55536	0.195358
Down	APBB1IP	2	6.83E-05	18040	0.222113
Down	RHOJ	1	0	0	0.23219
Down	CFH	1	0	0	0.172898
Down	FCGR2A	1	0	0	0.229547
Down	CFI	1	0	0	0.172898
Down	S100A11	1	0	0	0.227331
Down	FYB1	1	0	0	0.21341
Down	TNFSF10	1	0	0	0.168647
Down	PARP9	1	0	0	0.186129

Down	TLR1	1	0	0	0.204981
Down	FCER1G	1	0	0	0.229547
Down	RGCC	1	0	0	0.246074
Down	CLEC2D	1	0	0	1
Down	LAPTM5	1	0	0	0.242688
Down	ITGA8	1	0	0	0.224364
Down	ITGA10	1	0	0	0.224364
Down	TLR5	1	0	0	0.217141
Down	SLA	1	0	0	0.229547
Down	GBP2	1	0	0	0.191673
Down	RHOQ	1	0	0	0.201046
Down	MLANA	1	0	0	0.242688
Down	LRRC1	1	0	0	0.219386
Down	ITGA1	1	0	0	0.224364
Down	ANGPT2	1	0	0	0.224364
Down	IRAK3	1	0	0	0.217141
Down	HELB	1	0	0	0.238776
Down	SLC7A2	1	0	0	0.150493
Down	PRRG4	1	0	0	0.240141
Down	CYYR1	1	0	0	0.240141
Down	TP53INP1	1	0	0	0.231583
Down	TRIM38	1	0	0	0.216979
Down	CSF3R	1	0	0	0.229547
Down	TLR7	1	0	0	0.217141
Down	ST6GALNAC3	1	0	0	0.201235
Down	PIK3CG	1	0	0	0.217908
Down	LRP4	1	0	0	0.196385
Down	NABP1	1	0	0	0.248173
Down	ARHGAP11A	1	0	0	0.246655
Down	CYTB	1	0	0	0.195875
Down	DOK3	1	0	0	0.227547
Down	NCKAP1L	1	0	0	0.197604
Down	ARHGDIB	1	0	0	0.215613
Down	CYBB	1	0	0	0.246655
Down	IFITM3	1	0	0	0.242688
Down	FCGR3A	1	0	0	0.229547
Down	NXPE2	1	0	0	0.219386
Down	HCLS1	1	0	0	0.229547

Table 5 miRNA - target gene and TF - target gene interaction

Regulation	Target Genes	Degree	MicroRNA	Regulation	Target Genes	Degree	TF
Up	AP2M1	69	hsa-mir-3911	UP	DLG3	17	FOXC1
Up	PIN1	56	hsa-mir-199b-5p	UP	COPS7A	15	IRF2
Up	PPP2R1A	46	hsa-mir-6779-5p	UP	GABARAPL1	15	PPARG
Up	SCN2B	46	hsa-mir-4722-3p	UP	MAP1LC3A	14	GATA2
Up	OTUB1	45	hsa-mir-1908-5p	UP	OTUB1	12	ARID3A
Up	GABARAPL1	41	hsa-mir-545-3p	UP	EMD	10	BRCA1
Up	STX1A	33	hsa-mir-6846-5p	UP	SCN2B	10	CREB1
Up	PAK1	18	hsa-mir-7-5p	UP	CDK5	8	RELA
Up	SPINT2	9	hsa-mir-421	UP	PIN1	8	SRF
Up	COPS7A	7	hsa-mir-215-5p	UP	PAK1	7	HOXA5
Up	EMD	7	hsa-mir-124-3p	UP	TUBA4A	7	JUN
Up	DLG3	3	hsa-mir-615-3p	UP	PPP2R1A	6	STAT3
Up	USP11	1	hsa-mir-10a-5p	UP	SPINT2	4	TFAP2C
Up	CDK5	1	hsa-mir-155-5p	UP	AP2M1	3	YY1
Up	MAP1LC3A	1	hsa-mir-335-5p	UP	USP11	2	EN1
Down	FKBP5	88	hsa-mir-3654	Down	BCL6	17	FOXL1
Down	CDK2	78	hsa-mir-1296-5p	Down	FKBP5	17	SREBF1
Down	PLSCR1	75	hsa-mir-1304-5p	Down	CDK1	14	NFIC
Down	YAP1	56	hsa-mir-548d-5p	Down	CDK2	14	POU2F2
Down	CDK1	52	hsa-mir-103a-3p	Down	SYK	13	PRDM1
Down	CCNA2	37	hsa-mir-19b-3p	Down	CCNA2	11	MEF2A
Down	SYK	35	hsa-mir-486-3p	Down	NEDD4	11	FOS
Down	VIM	30	hsa-mir-4328	Down	TEAD2	9	STAT1
Down	BCL6	13	hsa-mir-30b-5p	Down	VIM	9	SOX17
Down	IQGAP1	12	hsa-mir-136-3p	Down	YAP1	9	ELK4
Down	NFKBIA	10	hsa-mir-381-3p	Down	IFI16	8	JUND

Volcano plot

Fig. 2. Heat map of differentially expressed genes. Legend on the top left indicate log fold change of genes. (A1 – A37 = normal control samples; B1 – B47 = HF samples)

Fig. 5. Target gene - miRNA regulatory network between target genes. The orange color diamond nodes represent the key miRNAs; up regulated genes are marked in green; down regulated genes are marked in red.