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 enrichmental 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 Cyctoscape (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). PEWCC1was 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), PLSCR1was 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. Kümpfel 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], NRGN (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], NRGN (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], TGFBR2 [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 NRGN (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], CHRNB2 [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 amd 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 amd 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 migt be regarded as an indicator of susceptibility to autism spectrum disorder. Kurzawski 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

References

1. Lotankar S, Prabhavalkar KS, Bhatt LK. Biomarkers for Parkinson's Disease: Recent Advancement. Neurosci Bull. 2017;33(5):585-597. doi:10.1007/s12264-017-0183-5
2. Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. J Neural Transm (Vienna). 2017;124(8):901-905. doi:10.1007/s00702-017-1686-y
3. Beitz JM. Parkinson's disease: a review. Front Biosci (Schol Ed). 2014;6:65-74. doi:10.2741/s415
4. Billingsley KJ, Bandres-Ciga S, Saez-Atienzar S, Singleton AB. Genetic risk factors in Parkinson's disease. Cell Tissue Res. 2018;373(1):9-20. doi:10.1007/s00441-018-2817-y
5. Jin H, Gu HY, Mao CJ, Chen J, Liu CF. Association of inflammatory factors and aging in Parkinson's disease. Neurosci Lett. 2020;736:135259. doi:10.1016/j.neulet.2020.135259
6. Yuan X, Tian Y, Liu C, Zhang Z. Environmental factors in Parkinson's disease: New insights into the molecular mechanisms. Toxicol Lett. 2022;356:1-10. doi:10.1016/j.toxlet.2021.12.003
7. Palasz E, Wysocka A, Gasiorowska A, Chalimoniuk M, Niewiadomski W, Niewiadomska G. BDNF as a Promising Therapeutic Agent in Parkinson's Disease. Int J Mol Sci. 2020;21(3):1170. doi:10.3390/ijms21031170

8. Lang C, Campbell KR, Ryan BJ, Carling P, Attar M, Vowles J, Perestenko OV, Bowden R, Baig F, Kasten M, et al. Single-Cell Sequencing of iPSC-Dopamine Neurons Reconstructs Disease Progression and Identifies HDAC4 as a Regulator of Parkinson Cell Phenotypes. Cell Stem Cell. 2019;24(1):93-106.e6. doi:10.1016/j.stem.2018.10.023
9. Sassone J, Reale C, Dati G, Regoni M, Pellecchia MT, Garavaglia B. The Role of VPS35 in the Pathobiology of Parkinson's Disease. Cell Mol Neurobiol. 2021;41(2):199-227. doi:10.1007/s10571-020-00849-8
10. Hur EM, Lee BD. LRRK2 at the Crossroad of Aging and Parkinson's Disease. Genes (Basel). 2021;12(4):505. doi:10.3390/genes12040505
11. Periñán MT, Macías-García D, Labrador-Espinosa MÁ, Jesús S, Buiza-Rueda D, Adarmes-Gómez AD, Muñoz-Delgado L, Gómez-Garre P, Mir P. Association of PICALM with Cognitive Impairment in Parkinson's Disease. Mov Disord. 2021;36(1):118-123. doi:10.1002/mds.28283
12. Iyer M, Subramaniam MD, Venkatesan D, Cho SG, Ryding M, Meyer M, Vellingiri B. Role of RhoA-ROCK signaling in Parkinson's disease. Eur J Pharmacol. 2021;894:173815. doi:10.1016/j.ejphar.2020.173815
13. Ammal Kaidery N, Ahuja M, Thomas B. Crosstalk between Nrf2 signaling and mitochondrial function in Parkinson's disease. Mol Cell Neurosci. 2019;101:103413. doi:10.1016/j.mcn.2019.103413
14. Obergasteiger J, Frapporti G, Pramstaller PP, Hicks AA, Volta M. A new hypothesis for Parkinson's disease pathogenesis: GTPase-p38 MAPK signaling and autophagy as convergence points of etiology and genomics. Mol Neurodegener. 2018;13(1):40. doi:10.1186/s13024-018-0273-5
15. Lashgari NA, Roudsari NM, Momtaz S, Sathyapalan T, Abdolghaffari AH, Sahebkar A. The involvement of JAK/STAT signaling pathway in the treatment of Parkinson's disease. J Neuroimmunol. 2021;361:577758. doi:10.1016/j.jneuroim.2021.577758
16. Ji Y, Wang D, Zhang B, Lu H. Bergenin Ameliorates MPTP-Induced Parkinson's Disease by Activating PI3K/Akt Signaling Pathway. J Alzheimers Dis. 2019;72(3):823-833. doi:10.3233/JAD-190870
17. Pant S, Weiner R, Marton MJ. Navigating the rapids: the development of regulated next-generation sequencing-based clinical trial assays and companion diagnostics. Front Oncol. 2014;4:78. doi:10.3389/fonc.2014.00078

18. Woollard PM, Mehta NA, Vamathevan JJ, Van Horn S, Bonde BK, Dow DJ. The application of next-generation sequencing technologies to drug discovery and development. Drug Discov Today. 2011;16(11-12):512-519. doi:10.1016/j.drudis.2011.03.006
19. Coenen-Stass AML, Magen I, Brooks T, Ben-Dov IZ, Greensmith L, Hornstein E, Fratta P. Evaluation of methodologies for microRNA biomarker detection by next generation sequencing. RNA Biol. 2018;15(8):1133-1145. doi:10.1080/15476286.2018.1514236
20. Gorostidi A, Martí-Massó JF, Bergareche A, Rodríguez-Oroz MC, López de Munain A, Ruiz-Martínez J. Genetic Mutation Analysis of Parkinson's Disease Patients Using Multigene Next-Generation Sequencing Panels. Mol Diagn Ther. 2016;20(5):481-491. doi:10.1007/s40291-016-0216-1
21. Li P, Ensink E, Lang S, Marshall L, Schilthuis M, Lamp J, Vega I, Labrie V. Hemispheric asymmetry in the human brain and in Parkinson's disease is linked to divergent epigenetic patterns in neurons. Genome Biol. 2020;21(1):61. doi:10.1186/s13059-020-01960-1
22. Clough E, Barrett T. The Gene Expression Omnibus Database. Methods Mol Biol. 2016;1418:93-110. doi:10.1007/978-1-4939-3578-9_5
23. Love MI, Huber W, Anders S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. Genome Biol. 2014;15(12):550. doi:10.1186/s13059-014-0550-8
24. Thomas PD. The Gene Ontology and the Meaning of Biological Function. Methods Mol Biol. 2017;1446:15□24. doi:10.1007/978-1-4939-3743-1_2
25. Fabregat A, Jupe S, Matthews L, Sidiropoulos K, Gillespie M, Garapati P, Haw R, Jassal B, Korninger F, May B et al The Reactome Pathway Knowledgebase. Nucleic Acids Res. 2018;46(D1):D649–D655. doi:10.1093/nar/gkx1132
26. Reimand J, Kull M, Peterson H, Hansen J, Vilo J. g:Profiler--a web-based toolset for functional profiling of gene lists from large-scale experiments. Nucleic Acids Res. 2007;35(Web Server issue):W193-W200. doi:10.1093/nar/gkm226
27. Alanis-Lobato G, Andrade-Navarro MA, Schaefer MH. HIPPIE v2.0: enhancing meaningfulness and reliability of protein-protein interaction networks. Nucleic Acids Res. 2017;45(D1):D408-D414. doi:10.1093/nar/gkw985

28. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, Amin N, Schwikowski B, Ideker T Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome Res 2003;13(11):2498-2504. doi:10.1101/gr.1239303
29. Luo X, Guo L, Dai XJ, Wang Q, Zhu W, Miao X, Gong H. Abnormal intrinsic functional hubs in alcohol dependence: evidence from a voxelwise degree centrality analysis. Neuropsychiatr Dis Treat. 2017;13:2011-2020. doi:10.2147/NDT.S142742
30. Li Y, Li W, Tan Y, Liu F, Cao Y, Lee KY. Hierarchical Decomposition for Betweenness Centrality Measure of Complex Networks. Sci Rep. 2017;7:46491.. doi:10.1038/srep46491
31. Gilbert M, Li Z, Wu XN, Rohr L, Gombos S, Harter K, Schulze WX. Comparison of path-based centrality measures in protein-protein interaction networks revealed proteins with phenotypic relevance during adaptation to changing nitrogen environments. J Proteomics. 2021;235:104114. doi:10.1016/j.jprot.2021.104114
32. Li G, Li M, Wang J, Li Y, Pan Y. United Neighborhood Closeness Centrality and Orthology for Predicting Essential Proteins. IEEE/ACM Trans Comput Biol Bioinform. 2020;17(4):1451-1458. doi:10.1109/TCBB.2018.2889978
33. Assenov Y, Ramírez F, Schelhorn SE, Lengauer T, Albrecht M. Computing topological parameters of biological networks. Bioinformatics. 2008;24(2):282-284. doi:10.1093/bioinformatics/btm554
34. Zaki N, Efimov D, Berengueres J. Protein complex detection using interaction reliability assessment and weighted clustering coefficient. BMC Bioinformatics. 2013;14:163. doi:10.1186/1471-2105-14
35. Fan Y, Xia J (2018) miRNet-Functional Analysis and Visual Exploration of miRNA-Target Interactions in a Network Context. Methods Mol Biol 1819:215-233. doi:10.1007/978-1-4939-8618-7_10
36. Zhou G, Soufan O, Ewald J, Hancock REW, Basu N, Xia J (2019) NetworkAnalyst 3.0: a visual analytics platform for comprehensive gene expression profiling and meta-analysis. Nucleic Acids Res 47:W234-W241. doi:10.1093/nar/gkz240

37. Robin X, Turck N, Hainard A, Tiberti N, Lisacek F, Sanchez JC, Müller M. pROC: an open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics 2011;12:77. doi:10.1186/1471-2105-12-77
38. Noda Y, Shimazawa M, Tanaka H, Tamura S, Inoue T, Tsuruma K, Hara H. VGF and striatal cell damage in in vitro and in vivo models of Huntington's disease. Pharmacol Res Perspect. 2015;3(3):e00140. doi:10.1002/prp2.140
39. Norris PJ, Waldvogel HJ, Faull RL, Love DR, Emson PC. Decreased neuronal nitric oxide synthase messenger RNA and somatostatin messenger RNA in the striatum of Huntington's disease. Neuroscience. 1996;72(4):1037-1047. doi:10.1016/0306-4522(95)00596-x
40. Noda Y, Tanaka M, Nakamura S, Ito J, Kakita A, Hara H, Shimazawa M. Identification of VGF nerve growth factor inducible-producing cells in human spinal cords and expression change in patients with amyotrophic lateral sclerosis. Int J Med Sci. 2020;17(4):480-489. doi:10.7150/ijms.39101
41. Prakash A, Kumar V, Banerjee A, Lynn AM, Prasad R. Structural heterogeneity in RNA recognition motif 2 (RRM2) of TAR DNA-binding protein 43 (TDP-43): clue to amyotrophic lateral sclerosis. J Biomol Struct Dyn. 2021;39(1):357-367. doi:10.1080/07391102.2020.1714481
42. Busse S, Bernstein HG, Busse M, Bielau H, Brisch R, Mawrin C, Müller S, Sarnyai Z, Gos T, Bogerts B, et al. Reduced density of hypothalamic VGF-immunoreactive neurons in schizophrenia: a potential link to impaired growth factor signaling and energy homeostasis. Eur Arch Psychiatry Clin Neurosci. 2012;262(5):365-374. doi:10.1007/s00406-011-0282-7
43. Bennett A O MR. Stress and anxiety in schizophrenia and depression: glucocorticoids, corticotropin-releasing hormone and synapse regression. Aust N Z J Psychiatry. 2008;42(12):995-1002. doi:10.1080/00048670802512073
44. Shepard R, Heslin K, Hagerdorn P, Coutellier L. Downregulation of Npas4 in parvalbumin interneurons and cognitive deficits after neonatal NMDA receptor blockade: relevance for schizophrenia. Transl Psychiatry. 2019;9(1):99. doi:10.1038/s41398-019-0436-3
45. Van Derveer AB, Bastos G, Ferrell AD, Gallimore CG, Greene ML, Holmes JT, Kubricka V, Ross JM, Hamm JP. A Role for Somatostatin-Positive Interneurons in Neuro-Oscillatory and Information Processing Deficits in

Schizophrenia. Schizophr Bull. 2021;47(5):1385-1398. doi:10.1093/schbul/sbaa184

46. Hoogendijk WJ, Purba JS, Hofman MA, de Vos RA, Jansen EN, Swaab DF. Depression in Parkinson's disease is not accompanied by more corticotropin-releasing hormone expressing neurons in the hypothalamic paraventricular nucleus. Biol Psychiatry. 1998;43(12):913-917. doi:10.1016/s0006-3223(97)00338-7
47. Shiraishi M, Kobayashi T, Watanabe H, Kamo T, Hasegawa Y. Serum somatostatin in early-stage Parkinson's disease. Acta Neurol Scand. 2010;121(4):225-229. doi:10.1111/j.1600-0404.2009.01178.x
48. Pedersen WA, McCullers D, Culmsee C, Haughey NJ, Herman JP, Mattson MP. Corticotropin-releasing hormone protects neurons against insults relevant to the pathogenesis of Alzheimer's disease. Neurobiol Dis. 2001;8(3):492-503. doi:10.1006/nbdi.2001.0395
49. Solarski M, Wang H, Wille H, Schmitt-Ulms G. Somatostatin in Alzheimer's disease: A new Role for an Old Player. Prion. 2018;12(1):1-8. doi:10.1080/19336896.2017.1405207
50. Kümpfel T, Then Bergh F, Friess E, Uhr M, Yassouridis A, Trenkwalder C, Holsboer F. Dehydroepiandrosterone response to the adrenocorticotropin test and the combined dexamethasone and corticotropin-releasing hormone test in patients with multiple sclerosis. Neuroendocrinology. 1999;70(6):431-438. doi:10.1159/000054505
51. Basivireddy J, Somvanshi RK, Romero IA, Weksler BB, Couraud PO, Oger J, Kumar U.Somatostatin preserved blood brain barrier against cytokine induced alterations: possible role in multiple sclerosis. Biochem Pharmacol. 2013;86(4):497-507. doi:10.1016/j.bcp.2013.06.001
52. Tsilioni I, Dodman N, Petra AI, Taliou A, Francis K, Moon-Fanelli A, Shuster L, Theoharides TC.Elevated serum neurotensin and CRH levels in children with autistic spectrum disorders and tail-chasing Bull Terriers with a phenotype similar to autism. Transl Psychiatry. 2014;4(10):e466. doi:10.1038/tp.2014.106
53. Shin S, Santi A, Huang S. Conditional Pten knockout in parvalbumin- or somatostatin-positive neurons sufficiently leads to autism-related behavioral phenotypes. Mol Brain. 2021;14(1):24. doi:10.1186/s13041-021-00731-8

54. Kirchner A, Bagla S, Dachet F, Loeb JA. DUSP4 appears to be a highly localized endogenous inhibitor of epileptic signaling in human neocortex. Neurobiol Dis. 2020;145:105073. doi:10.1016/j.nbd.2020.105073
55. Liu K, Zhang W, Li Y, Ding Q, Bai Y, Wang F, Xu G. Human peripheral blood-derived mesenchymal stem cells with NTRK1 over-expression enhance repairing capability in a rat model of Parkinson's disease. Cytotechnology. 2018;70(5):1291-1299. doi:10.1007/s10616-017-0175-3
56. Malek NM, Grosset KA, Stewart D, Macphee GJ, Grosset DG. Prescription of drugs with potential adverse effects on cardiac conduction in Parkinson's disease. Parkinsonism Relat Disord. 2013;19(6):586-589. doi:10.1016/j.parkreldis.2013.02.004
57. Guixa-Gonzalez R, Bruno A, Marti-Solano M, Selent J. Crosstalk within GPCR heteromers in schizophrenia and Parkinson's disease: physical or just functional?. Curr Med Chem. 2012;19(8):1119-1134. doi:10.2174/092986712799320574
58. Fleming SM, Davis A, Simons E. Targeting alpha-synuclein via the immune system in Parkinson's disease: Current vaccine therapies. Neuropharmacology. 2022;202:108870. doi:10.1016/j.neuropharm.2021.108870
59. Zhuang X, Chen Y, Zhuang X, Chen T, Xing T, Wang W, Yang X. Contribution of Pro-inflammatory Cytokine Signaling within Midbrain Periaqueductal Gray to Pain Sensitivity in Parkinson's Disease via GABAergic Pathway. Front Neurol. 2016;7:104. doi:10.3389/fneur.2016.00104
60. Ejlerskov P, Hultberg JG, Wang J, Carlsson R, Ambjørn M, Kuss M, Liu Y, Porcu G, Kolkova K, Friis Rundsten C, et al. Lack of Neuronal IFN-β-IFNAR Causes Lewy Body- and Parkinson's Disease-like Dementia. Cell. 2015;163(2):324-339. doi:10.1016/j.cell.2015.08.069
61. Caputi V, Giron MC. Microbiome-Gut-Brain Axis and Toll-Like Receptors in Parkinson's Disease. Int J Mol Sci. 2018;19(6):1689. doi:10.3390/ijms19061689
62. Swanberg SE, Nagarajan RP, Peddada S, Yasui DH, LaSalle JM. Reciprocal co-regulation of EGR2 and MECP2 is disrupted in Rett syndrome and autism. Hum Mol Genet. 2009;18(3):525-534. doi:10.1093/hmg/ddn380

63. Martin PM, Yang X, Robin N, Lam E, Rabinowitz JS, Erdman CA, Quinn J, Weiss LA, Hamilton SP, et al. A rare WNT1 missense variant overrepresented in ASD leads to increased Wnt signal pathway activation. Transl Psychiatry. 2013;3(9):e301. doi:10.1038/tp.2013.75
64. Alhowikan AM. Activity-Regulated Cytoskeleton-Associated Protein Dysfunction May Contribute to Memory Disorder and Earlier Detection of Autism Spectrum Disorders. Med Princ Pract. 2016;25(4):350-354. doi:10.1159/000445351
65. Bacchelli E, Battaglia A, Cameli C, Lomartire S, Tancredi R, Thomson S, Sutcliffe JS, Maestrini E. Analysis of CHRNA7 rare variants in autism spectrum disorder susceptibility. Am J Med Genet A. 2015;167A(4):715-723. doi:10.1002/ajmg.a.36847
66. Konyukh M, Delorme R, Chaste P, Leblond C, Lemière N, Nygren G, Anckarsäter H, Rastam M, Ståhlberg O, Amsellem F, et al. Variations of the candidate SEZ6L2 gene on Chromosome 16p11.2 in patients with autism spectrum disorders and in human populations. PLoS One. 2011;6(3):e17289. doi:10.1371/journal.pone.0017289
67. Kantojärvi K, Kotala I, Rehnström K, Ylisaukko-Oja T, Vanhala R, von Wendt TN, von Wendt L, Järvelä I. Fine mapping of Xq11.1-q21.33 and mutation screening of RPS6KA6, ZNF711, ACSL4, DLG3, and IL1RAPL2 for autism spectrum disorders (ASD). Autism Res. 2011;4(3):228-233. doi:10.1002/aur.187
68. Hoang N, Yuen RKC, Howe J, Drmic I, Ambrozewicz P, Russell C, Vorstman J, Weiss SK, Anagnostou E, Malow BA, et al. Sleep phenotype of individuals with autism spectrum disorder bearing mutations in the PER2 circadian rhythm gene. Am J Med Genet A. 2021;185(4):1120-1130. doi:10.1002/ajmg.a.62086
69. Breuillard D, Leunen D, Chemaly N, Auclair L, Pinard JM, Kaminska A, Desguerre I, Ouss L, Nabbout R. Autism spectrum disorder phenotype and intellectual disability in females with epilepsy and PCDH-19 mutations. Epilepsy Behav. 2016;60:75-80. doi:10.1016/j.yebeh.2016.04.009
70. de Jong JO, Llapashtica C, Genestine M, Strauss K, Provenzano F, Sun Y, Zhu H, Cortese GP, Brundu F, Brigatti KW, et al. Cortical overgrowth in a preclinical forebrain organoid model of CNTNAP2-associated autism

spectrum disorder. Nat Commun. 2021;12(1):4087. doi:10.1038/s41467-021-24358-4

71. Merner ND, Chandler MR, Bourassa C, Liang B, Khanna AR, Dion P, Rouleau GA, Kahle KT. Regulatory domain or CpG site variation in SLC12A5, encoding the chloride transporter KCC2, in human autism and schizophrenia. Front Cell Neurosci. 2015;9:386. doi:10.3389/fncel.2015.00386
72. Wang L, Li J, Jia M, Yue W, Ruan Y, Lu T, Zhang J, Liu J, Zhang D. No association of polymorphisms in the CDK5, NDEL1, and LIS1 with autism in Chinese Han population. Psychiatry Res. 2011;190(2-3):369-371. doi:10.1016/j.psychres.2011.08.004
73. Wenderski W, Wang L, Krokhotin A, Walsh JJ, Li H, Shoji H, Ghosh S, George RD, Miller EL, Elias L, et al. Loss of the neural-specific BAF subunit ACTL6B relieves repression of early response genes and causes recessive autism. Proc Natl Acad Sci U S A. 2020;117(18):10055-10066. doi:10.1073/pnas.1908238117
74. Fatemi SH, Reutiman TJ, Folsom TD, Rustan OG, Rooney RJ, Thuras PD. Downregulation of GABAA receptor protein subunits α6, β2, δ, ε, γ2, θ, and ρ2 in superior frontal cortex of subjects with autism. J Autism Dev Disord. 2014;44(8):1833-1845. doi:10.1007/s10803-014-2078-x
75. Strom SP, Stone JL, Ten Bosch JR, Merriman B, Cantor RM, Geschwind DH, Nelson SF.High-density SNP association study of the 17q21 chromosomal region linked to autism identifies CACNA1G as a novel candidate gene. Mol Psychiatry. 2010;15(10):996-1005. doi:10.1038/mp.2009.41
76. Orabona GM, Griesi-Oliveira K, Vadasz E, Bulcão VL, Takahashi VN, Moreira ES, Furia-Silva M, Ros-Melo AM, Dourado F, Matioli SR, et al. HTR1B and HTR2C in autism spectrum disorders in Brazilian families. Brain Res. 2009;1250:14-19. doi:10.1016/j.brainres.2008.11.007
77. Nakamura K, Iwata Y, Anitha A, Miyachi T, Toyota T, Yamada S, Tsujii M, Tsuchiya KJ, Iwayama Y, Yamada K, et al. Replication study of Japanese cohorts supports the role of STX1A in autism susceptibility. Prog Neuropsychopharmacol Biol Psychiatry. 2011;35(2):454-458. doi:10.1016/j.pnpbp.2010.11.033

78. Torres A, Brownstein CA, Tembulkar SK, Graber K, Genetti C, Kleiman RJ, Sweadner KJ, Mavros C, Liu KX, Smedemark-Margulies N, et al. De novo ATP1A3 and compound heterozygous NLRP3 mutations in a child with autism spectrum disorder, episodic fatigue and somnolence, and muckle-wells syndrome. Mol Genet Metab Rep. 2018;16:23-29. doi:10.1016/j.ymgmr.2018.06.001
79. Kumar RA, Sudi J, Babatz TD, Brune CW, Oswald D, Yen M, Nowak NJ, Cook EH, Christian SL, Dobyns WB. A de novo 1p34.2 microdeletion identifies the synaptic vesicle gene RIMS3 as a novel candidate for autism. J Med Genet. 2010;47(2):81-90. doi:10.1136/jmg.2008.065821
80. Dalla Vecchia E, Mortimer N, Palladino VS, Kittel-Schneider S, Lesch KP, Reif A, Schenck A, Norton WHJ. Cross-species models of attention-deficit/hyperactivity disorder and autism spectrum disorder: lessons from CNTNAP2, ADGRL3, and PARK2. Psychiatr Genet. 2019;29(1):1-17. doi:10.1097/YPG.0000000000000211
81. Weissberg O, Elliott E. The Mechanisms of CHD8 in Neurodevelopment and Autism Spectrum Disorders. Genes (Basel). 2021;12(8):1133. doi:10.3390/genes12081133
82. Hubert L, Cannata Serio M, Villoing-Gaudé L, Boddaert N, Kaminska A, Rio M, Lyonnet S, Munnich A, Poirier K, Simons M, et al. De novo SCAMP5 mutation causes a neurodevelopmental disorder with autistic features and seizures. J Med Genet. 2020;57(2):138-144. doi:10.1136/jmedgenet-2018-105927
83. Sriwimol W, Limprasert P. Significant Changes in Plasma Alpha-Synuclein and Beta-Synuclein Levels in Male Children with Autism Spectrum Disorder. Biomed Res Int. 2018;2018:4503871. doi:10.1155/2018/4503871
84. Scala M, Zonneveld-Huijssoon E, Brienza M, Mecarelli O, van der Hout AH, Zambrelli E, Turner K, Zara F, Peron A, Vignoli A, et al. De novo ARHGEF9 missense variants associated with neurodevelopmental disorder in females: expanding the genotypic and phenotypic spectrum of ARHGEF9 disease in females. Neurogenetics. 2021;22(1):87-94. doi:10.1007/s10048-020-00622-5
85. Kantojärvi K, Kotala I, Rehnström K, Ylisaukko-Oja T, Vanhala R, von Wendt TN, von Wendt L, Järvelä I. Fine mapping of Xq11.1-q21.33 and mutation screening of RPS6KA6, ZNF711, ACSL4, DLG3, and IL1RAPL2

for autism spectrum disorders (ASD). Autism Res. 2011;4(3):228-233. doi:10.1002/aur.187.

86. Chen J, Chen J, Xu Y, Cheng P, Yu S, Fu Y, Du Y. Retinol-binding protein 4 in combination with lipids to predict the regression phenomenon of autism spectrum disorders. Lipids Health Dis. 2021;20(1):93. doi:10.1186/s12944-021-01522-9
87. Ahmad SF, Nadeem A, Ansari MA, Bakheet SA, Al-Ayadhi LY, Attia SM. Upregulation of IL-9 and JAK-STAT signaling pathway in children with autism. Prog Neuropsychopharmacol Biol Psychiatry. 2017;79(Pt B):472-480. doi:10.1016/j.pnpbp.2017.08.002
88. Boso M, Emanuele E, Minoretti P, Arra M, Politi P, Ucelli di Nemi S, Barale F. Alterations of circulating endogenous secretory RAGE and S100A9 levels indicating dysfunction of the AGE-RAGE axis in autism. Neurosci Lett. 2006;410(3):169-173. doi:10.1016/j.neulet.2006.08.092
89. Russo AJ. Increased Epidermal Growth Factor Receptor (EGFR) Associated with Hepatocyte Growth Factor (HGF) and Symptom Severity in Children with Autism Spectrum Disorders (ASDs). J Cent Nerv Syst Dis. 2014;6:79-83. doi:10.4137/JCNSD.S13767
90. Fagan K, Crider A, Ahmed AO, Pillai A. Complement C3 Expression Is Decreased in Autism Spectrum Disorder Subjects and Contributes to Behavioral Deficits in Rodents. Mol Neuropsychiatry. 2017;3(1):19-27. doi:10.1159/000465523
91. Patel N, Crider A, Pandya CD, Ahmed AO, Pillai A. Altered mRNA Levels of Glucocorticoid Receptor, Mineralocorticoid Receptor, and Co-Chaperones (FKBP5 and PTGES3) in the Middle Frontal Gyrus of Autism Spectrum Disorder Subjects. Mol Neurobiol. 2016;53(4):2090-2099. doi:10.1007/s12035-015-9178-2
92. Fatemi SH, Reutiman TJ, Folsom TD, Rustan OG, Rooney RJ, Thuras PD. Downregulation of GABAA receptor protein subunits α6, β2, δ, ε, γ2, θ, and ρ2 in superior frontal cortex of subjects with autism. J Autism Dev Disord. 2014;44(8):1833-1845. doi:10.1007/s10803-014-2078-x
93. Guo H, Zhang Q, Dai R, Yu B, Hoekzema K, Tan J, Tan S, Jia X, Chung WK, Hernan R, et al. NCKAP1 Disruptive Variants Lead to a Neurodevelopmental Disorder with Core Features of Autism. Am J Hum Genet. 2020;107(5):963-976. doi:10.1016/j.ajhg.2020.10.002

94. Serajee FJ, Nabi R, Zhong H, Mahbubul Huq AH. Association of INPP1, PIK3CG, and TSC2 gene variants with autistic disorder: implications for phosphatidylinositol signalling in autism. J Med Genet. 2003;40(11):e119. doi:10.1136/jmg.40.11.e119
95. Singh AS, Chandra R, Guhathakurta S, Sinha S, Chatterjee A, Ahmed S, Ghosh S, Rajamma U. Genetic association and gene-gene interaction analyses suggest likely involvement of ITGB3 and TPH2 with autism spectrum disorder (ASD) in the Indian population. Prog Neuropsychopharmacol Biol Psychiatry. 2013;45:131-143. doi:10.1016/j.pnpbp.2013.04.015
96. Correia CT, Conceição IC, Oliveira B, Coelho J, Sousa I, Sequeira AF, Almeida J, Café C, Duque F, Mouga S, et al. Recurrent duplications of the annexin A1 gene (ANXA1) in autism spectrum disorders. Mol Autism. 2014;5(1):28. doi:10.1186/2040-2392-5-28
97. Young N, Asif M, Jackson M, Fernández-Mayoralas DM, de la Peña MJ, Calleja-Pérez B, Álvarez S, Hunter-Featherstone E, Noegel AA, Höhne W, et al. Biallelic SYNE2 Missense Mutations Leading to Nesprin-2 Giant Hypo-Expression Are Associated with Intellectual Disability and Autism. Genes (Basel). 2021;12(9):1294. doi:10.3390/genes12091294
98. Pichitpunpong C, Thongkorn S, Kanlayaprasit S, Yuwattana W, Plaingam W, Sangsuthum S, Aizat WM, Baharum SN, Tencomnao T, Hu VW, et al. Phenotypic subgrouping and multi-omics analyses reveal reduced diazepam-binding inhibitor (DBI) protein levels in autism spectrum disorder with severe language impairment. PLoS One. 2019;14(3):e0214198. doi:10.1371/journal.pone.0214198
99. Balan S, Yamada K, Iwayama Y, Toyota T, Ohnishi T, Maekawa M, Toyoshima M, Iwata Y, Suzuki K, Kikuchi M, et al. Lack of association of EGR2 variants with bipolar disorder in Japanese population. Gene. 2013;526(2):246-250. doi:10.1016/j.gene.2013.05.055
100. Lohoff FW, Bloch PJ, Weller AE, Ferraro TN, Berrettini WH. Association analysis of the pituitary adenylate cyclase-activating polypeptide (PACAP/ADCYAP1) gene in bipolar disorder. Psychiatr Genet. 2008;18(2):53-58. doi:10.1097/YPG.0b013e3282f60320
101. Ancín I, Barabash A, Vázquez-Álvarez B, Santos JL, Sánchez-Morla E, Martínez JL, Aparicio A, Peláez JC, Díaz JA. Evidence for association of

the non-duplicated region of CHRNA7 gene with bipolar disorder but not with Schizophrenia. Psychiatr Genet. 2010;20(6):289-297. doi:10.1097/YPG.0b013e32833a9b7a

102. Fatjó-Vilas M, Prats C, Pomarol-Clotet E, Lázaro L, Moreno C, González-Ortega I, Lera-Miguel S, Miret S, Muñoz MJ, Ibáñez I, et al. Involvement of NRN1 gene in schizophrenia-spectrum and bipolar disorders and its impact on age at onset and cognitive functioning. World J Biol Psychiatry. 2016;17(2):129-139. doi:10.3109/15622975.2015.1093658

103. Williams MJ, Klockars A, Eriksson A, Voisin S, Dnyansagar R, Wiemerslage L, Kasagiannis A, Akram M, Kheder S, Ambrosi V, et al. The Drosophila ETV5 Homologue Ets96B: Molecular Link between Obesity and Bipolar Disorder. PLoS Genet. 2016;12(6):e1006104. doi:10.1371/journal.pgen.1006104

104. Behan AT, Byrne C, Dunn MJ, Cagney G, Cotter DR. Proteomic analysis of membrane microdomain-associated proteins in the dorsolateral prefrontal cortex in schizophrenia and bipolar disorder reveals alterations in LAMP, STXBP1 and BASP1 protein expression. Mol Psychiatry. 2009;14(6):601-613. doi:10.1038/mp.2008.7

105. Atakhorrami M, Rahimi-Aliabadi S, Jamshidi J, Moslemi E, Movafagh A, Ohadi M, Mirabzadeh A, Emamalizadeh B, Ghaedi H, Gholipour F, et al. A genetic variant in CAMKK2 gene is possibly associated with increased risk of bipolar disorder. J Neural Transm (Vienna). 2016;123(3):323-328. doi:10.1007/s00702-015-1456-7

106. Abou Jamra R, Gobina CM, Becker T, Georgi A, Schulze TG, Schmael C, Cichon S, Propping P, Rietschel M, Nöthen MM, et al. Association study between genetic variants at the VAMP2 and VAMP3 loci and bipolar affective disorder. Psychiatr Genet. 2008;18(4):199-203. doi:10.1097/YPG.0b013e3283050a83

107. Verma R, Kubendran S, Das SK, Jain S, Brahmachari SK. SYNGR1 is associated with schizophrenia and bipolar disorder in southern India. J Hum Genet. 2005;50(12):635-640. doi:10.1007/s10038-005-0307-z

108. Oliveira J, Hamdani N, Etain B, Bennabi M, Boukouaci W, Amokrane K, Fortier C, Marzais F, Bengoufa D, Bellivier F, et al. Genetic association between a 'standing' variant of NOD2 and bipolar disorder. Immunobiology. 2014;219(10):766-771. doi:10.1016/j.imbio.2014.06.003

109. Oliveira J, Kazma R, Le Floch E, Bennabi M, Hamdani N, Bengoufa D, Dahoun M, Manier C, Bellivier F, Krishnamoorthy R, et al. Toxoplasma gondii exposure may modulate the influence of TLR2 genetic variation on bipolar disorder: a gene-environment interaction study. Int J Bipolar Disord. 2016;4(1):11. doi:10.1186/s40345-016-0052-6

110. Tesli M, Athanasiu L, Mattingsdal M, Kähler AK, Gustafsson O, Andreassen BK, Werge T, Hansen T, Mors O, Mellerup E, et al. Association analysis of PALB2 and BRCA2 in bipolar disorder and schizophrenia in a scandinavian case-control sample. Am J Med Genet B Neuropsychiatr Genet. 2010;153B(7):1276-1282. doi:10.1002/ajmg.b.31098

111. Santos R, Linker SB, Stern S, Mendes APD, Shokhirev MN, Erikson G, Randolph-Moore L, Racha V, Kim Y, Kelsoe JR, et al. Deficient LEF1 expression is associated with lithium resistance and hyperexcitability in neurons derived from bipolar disorder patients. Mol Psychiatry. 2021;26(6):2440-2456. doi:10.1038/s41380-020-00981-3

112. Hu TM, Chen CH, Chuang YA, Hsu SH, Cheng MC. Resequencing of early growth response 2 (EGR2) gene revealed a recurrent patient-specific mutation in schizophrenia. Psychiatry Res. 2015;228(3):958-960. doi:10.1016/j.psychres.2015.05.035

113. Miyaoka T, Seno H, Ishino H. Increased expression of Wnt-1 in schizophrenic brains. Schizophr Res. 1999;38(1):1-6. doi:10.1016/s0920-9964(98)00179-0

114. Chuang YA, Hu TM, Chen CH, Hsu SH, Tsai HY, Cheng MC. Rare mutations and hypermethylation of the ARC gene associated with schizophrenia. Schizophr Res. 2016;176(2-3):106-113. doi:10.1016/j.schres.2016.07.019

115. Koga M, Ishiguro H, Horiuchi Y, Inada T, Ujike H, Itokawa M, Otowa T, Watanabe Y, Someya T, Arinami T. Replication study of association between ADCYAP1 gene polymorphisms and schizophrenia. Psychiatr Genet. 2010;20(3):123-125. doi:10.1097/YPG.0b013e32833a1f52

116. Roberts E. GABAergic malfunction in the limbic system resulting from an aboriginal genetic defect in voltage-gated Na+-channel SCN5A is proposed to give rise to susceptibility to schizophrenia. Adv Pharmacol. 2006;54:119-145. doi:10.1016/s1054-3589(06)54006-2

117. Kimura H, Fujita Y, Kawabata T, Ishizuka K, Wang C, Iwayama Y, Okahisa Y, Kushima I, Morikawa M, Uno Y, et al. A novel rare variant R292H in RTN4R affects growth cone formation and possibly contributes to schizophrenia susceptibility. Transl Psychiatry. 2017;7(8):e1214. doi:10.1038/tp.2017.170

118. Bakanidze G, Roinishvili M, Chkonia E, Kitzrow W, Richter S, Neumann K, Herzog MH, Brand A, Puls I. Association of the Nicotinic Receptor α7 Subunit Gene (CHRNA7) with Schizophrenia and Visual Backward Masking. Front Psychiatry. 2013;4:133. doi:10.3389/fpsyt.2013.00133

119. Hwang H, Szucs MJ, Ding LJ, Allen A, Ren X, Haensgen H, Gao F, Rhim H, Andrade A, Pan JQ, et al. Neurogranin, Encoded by the Schizophrenia Risk Gene NRGN, Bidirectionally Modulates Synaptic Plasticity via Calmodulin-Dependent Regulation of the Neuronal Phosphoproteome. Biol Psychiatry. 2021;89(3):256-269. doi:10.1016/j.biopsych.2020.07.014

120. Boiko AS, Ivanova SA, Pozhidaev IV, Freidin MB, Osmanova DZ, Fedorenko OY, Semke AV, Bokhan NA, Wilffert B, Loonen AJM. Pharmacogenetics of tardive dyskinesia in schizophrenia: The role of CHRM1 and CHRM2 muscarinic receptors. World J Biol Psychiatry. 2020;21(1):72-77. doi:10.1080/15622975.2018.1548780

121. Bourin M, Malinge M, Vasar E, Bradwejn J. Two faces of cholecystokinin: anxiety and schizophrenia. Fundam Clin Pharmacol. 1996;10(2):116-126. doi:10.1111/j.1472-8206.1996.tb00154.x

122. Xu FL, Yao J, Wu X, Xia X, Xing JX, Xuan JF, Liu YP, Wang BJ. Association Analysis Between SNPs in the Promoter Region of RGS4 and Schizophrenia in the Northern Chinese Han Population. Neuropsychiatr Dis Treat. 2020;16:985-992. doi:10.2147/NDT.S250282

123. Fernandez-Enright F, Andrews JL, Newell KA, Pantelis C, Huang XF. Novel implications of Lingo-1 and its signaling partners in schizophrenia. Transl Psychiatry. 2014;4(1):e348. doi:10.1038/tp.2013.121

124. Jiang J, Long J, Ling W, Huang G, Su L. Genetic variation in the 3'-untranslated region of PAK1 influences schizophrenia susceptibility. Exp Ther Med. 2017;13(3):1101-1108. doi:10.3892/etm.2017.4039

125. Vlaskamp DRM, Bassett AS, Sullivan JE, Robblee J, Sadleir LG, Scheffer IE, Andrade DM. Schizophrenia is a later-onset feature of PCDH19 Girls Clustering Epilepsy. Epilepsia. 2019;60(3):429-440. doi:10.1111/epi.14678

126. Chandler D, Dragović M, Cooper M, Badcock JC, Mullin BH, Faulkner D, Wilson SG, Hallmayer J, Howell S, Rock D, et al. Impact of Neuritin 1 (NRN1) polymorphisms on fluid intelligence in schizophrenia. Am J Med Genet B Neuropsychiatr Genet. 2010;153B(2):428-437. doi:10.1002/ajmg.b.30996

127. Chamera K, Kotarska K, Szuster-Głuszczak M, Trojan E, Skórkowska A, Pomierny B, Krzyżanowska W, Bryniarska N, Basta-Kaim A. The prenatal challenge with lipopolysaccharide and polyinosinic:polycytidylic acid disrupts CX3CL1-CX3CR1 and CD200-CD200R signalling in the brains of male rat offspring: a link to schizophrenia-like behaviours. J Neuroinflammation. 2020;17(1):247. doi:10.1186/s12974-020-01923-0

128. Ji W, Li T, Pan Y, Tao H, Ju K, Wen Z, Fu Y, An Z, Zhao Q, Wang T, et al. CNTNAP2 is significantly associated with schizophrenia and major depression in the Han Chinese population. Psychiatry Res. 2013;207(3):225-228. doi:10.1016/j.psychres.2012.09.024

129. Tao R, Li C, Newburn EN, Ye T, Lipska BK, Herman MM, Weinberger DR, Kleinman JE, Hyde TM. Transcript-specific associations of SLC12A5 (KCC2) in human prefrontal cortex with development, schizophrenia, and affective disorders. J Neurosci. 2012;32(15):5216-5222. doi:10.1523/JNEUROSCI.4626-11.2012

130. Meyer MA. Neuronal localization of GAS7 within human brain tissue: Implications for schizophrenia research. Neurol Int. 2018;10(4):7563. doi:10.4081/ni.2018.7563

131. Wilcox JA, Quadri S. Replication of NTNG1 association in schizophrenia. Psychiatr Genet. 2014;24(6):266-268. doi:10.1097/YPG.0000000000000061

132. Blennow K, Bogdanovic N, Heilig M, Grenfeldt B, Karlsson I, Davidsson P. Reduction of the synaptic protein rab3a in the thalamus and connecting brain regions in post-mortem schizophrenic brains. J Neural Transm (Vienna). 2000;107(8-9):1085-1097. doi:10.1007/s007020070054

133. Kishi T, Ikeda M, Kitajima T, Yamanouchi Y, Kinoshita Y, Kawashima K, Okochi T, Inada T, Ozaki N, Iwata N. Genetic association analysis of tagging SNPs in alpha4 and beta2 subunits of neuronal nicotinic acetylcholine receptor genes (CHRNA4 and CHRNB2) with schizophrenia in the Japanese population. J Neural Transm (Vienna). 2008;115(10):1457-1461. doi:10.1007/s00702-008-0114-8

134. Cantrup R, Sathanantham K, Rushlow WJ, Rajakumar N. Chronic hyperdopaminergic activity of schizophrenia is associated with increased ΔFosB levels and cdk-5 signaling in the nucleus accumbens. Neuroscience. 2012;222:124-135. doi:10.1016/j.neuroscience.2012.07.027

135. Guan F, Lin H, Chen G, Li L, Chen T, Liu X, Han J, Li T. Evaluation of association of common variants in HTR1A and HTR5A with schizophrenia and executive function. Sci Rep. 2016;6:38048. doi:10.1038/srep38048

136. Perez-Becerril C, Morris AG, Mortimer A, McKenna PJ, de Belleroche J. Common variants in the chromosome 2p23 region containing the SLC30A3 (ZnT3) gene are associated with schizophrenia in female but not male individuals in a large collection of European samples. Psychiatry Res. 2016;246:335-340. doi:10.1016/j.psychres.2016.09.052

137. Schuhmacher A, Mössner R, Quednow BB, Kühn KU, Wagner M, Cvetanovska G, Rujescu D, Zill P, Möller HJ, Rietschel M, et al. Influence of 5-HT3 receptor subunit genes HTR3A, HTR3B, HTR3C, HTR3D and HTR3E on treatment response to antipsychotics in schizophrenia. Pharmacogenet Genomics. 2009;19(11):843-851. doi:10.1097/FPC.0b013e3283313296

138. Grubor M, Zivkovic M, Sagud M, Nikolac Perkovic M, Mihaljevic-Peles A, Pivac N, Muck-Seler D, Svob Strac D. HTR1A, HTR1B, HTR2A, HTR2C and HTR6 Gene Polymorphisms and Extrapyramidal Side Effects in Haloperidol-Treated Patients with Schizophrenia. Int J Mol Sci. 2020;21(7):2345. doi:10.3390/ijms21072345

139. Matosin N, Fernandez-Enright F, Fung SJ, Lum JS, Engel M, Andrews JL, Huang XF, Weickert CS, Newell KA. Alterations of mGluR5 and its endogenous regulators Norbin, Tamalin and Preso1 in schizophrenia: towards a model of mGluR5 dysregulation. Acta Neuropathol. 2015;130(1):119-129. doi:10.1007/s00401-015-1411-6

140. Kawashima K, Kishi T, Ikeda M, Kitajima T, Yamanouchi Y, Kinoshita Y, Takahashi N, Saito S, Ohi K, Yasuda Y, et al. No association between tagging SNPs of SNARE complex genes (STX1A, VAMP2 and SNAP25) and schizophrenia in a Japanese population. Am J Med Genet B Neuropsychiatr Genet. 2008;147B(7):1327-1331. doi:10.1002/ajmg.b.30781

141. Tsunoka T, Kishi T, Kitajima T, Okochi T, Okumura T, Yamanouchi Y, Kinoshita Y, Kawashima K, Naitoh H, Inada T, et al. Association analysis of GRM2 and HTR2A with methamphetamine-induced psychosis and schizophrenia in the Japanese population. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34(4):639-644. doi:10.1016/j.pnpbp.2010.03.002

142. Wilmsdorff MV, Blaich C, Zink M, Treutlein J, Bauer M, Schulze T, Schneider-Axmann T, Gruber O, Rietschel M, Schmitt A, et al. Gene expression of glutamate transporters SLC1A1, SLC1A3 and SLC1A6 in the cerebellar subregions of elderly schizophrenia patients and effects of antipsychotic treatment. World J Biol Psychiatry. 2013;14(7):490-499. doi:10.3109/15622975.2011.645877

143. Xiao MF, Roh SE, Zhou J, Chien CC, Lucey BP, Craig MT, Hayes LN, Coughlin JM, Leweke FM, Jia M, et al. A biomarker-authenticated model of schizophrenia implicating NPTX2 loss of function. Sci Adv. 2021;7(48):eabf6935. doi:10.1126/sciadv.abf6935

144. Sayad A, Ranjbaran F, Ghafouri-Fard S, Arsang-Jang S, Taheri M. Expression Analysis of CYFIP1 and CAMKK2 Genes in the Blood of Epileptic and Schizophrenic Patients. J Mol Neurosci. 2018;65(3):336-342. doi:10.1007/s12031-018-1106-2

145. Zhang T, Tang Y, Yang X, Wang X, Ding S, Huang K, Liu Y, Lang B. Expression of GSK3β, PICK1, NEFL, C4, NKCC1 and Synaptophysin in peripheral blood mononuclear cells of the first-episode schizophrenia patients. Asian J Psychiatr. 2021;55:102520. doi:10.1016/j.ajp.2020.102520

146. Kawashima K, Kishi T, Ikeda M, Kitajima T, Yamanouchi Y, Kinoshita Y, Takahashi N, Saito S, Ohi K, Yasuda Y, et al. No association between tagging SNPs of SNARE complex genes (STX1A, VAMP2 and SNAP25) and schizophrenia in a Japanese population. Am J Med Genet B Neuropsychiatr Genet. 2008;147B(7):1327-1331. doi:10.1002/ajmg.b.30781

147. Chaumette B, Ferrafiat V, Ambalavanan A, Goldenberg A, Dionne-Laporte A, Spiegelman D, Dion PA, Gerardin P, Laurent C, Cohen D, et al.

Missense variants in ATP1A3 and FXYD gene family are associated with childhood-onset schizophrenia. Mol Psychiatry. 2020;25(4):821-830. doi:10.1038/s41380-018-0103-8

148. Onwordi EC, Whitehurst T, Mansur A, Statton B, Berry A, Quinlan M, O'Regan DP, Rogdaki M, Marques TR, Rabiner EA, et al. The relationship between synaptic density marker SV2A, glutamate and N-acetyl aspartate levels in healthy volunteers and schizophrenia: a multimodal PET and magnetic resonance spectroscopy brain imaging study. Transl Psychiatry. 2021;11(1):393. doi:10.1038/s41398-021-01515-3

149. Ji W, Li T, Pan Y, Tao H, Ju K, Wen Z, Fu Y, An Z, Zhao Q, Wang T, et al. CNTNAP2 is significantly associated with schizophrenia and major depression in the Han Chinese population. Psychiatry Res. 2013;207(3):225-228. doi:10.1016/j.psychres.2012.09.024

150. Di Maio A, De Rosa A, Pelucchi S, Garofalo M, Marciano B, Nuzzo T, Gardoni F, Isidori AM, Di Luca M, Errico F, et al. Analysis of mRNA and Protein Levels of CAP2, DLG1 and ADAM10 Genes in Post-Mortem Brain of Schizophrenia, Parkinson's and Alzheimer's Disease Patients. Int J Mol Sci. 2022;23(3):1539. doi:10.3390/ijms23031539

151. Iatropoulos P, Gardella R, Valsecchi P, Magri C, Ratti C, Podavini D, Rossi G, Gennarelli M, Sacchetti E, Barlati S. et al. Association study and mutational screening of SYNGR1 as a candidate susceptibility gene for schizophrenia. Psychiatr Genet. 2009;19(5):237-243. doi:10.1097/YPG.0b013e32832cebf7

152. Noori-Daloii MR, Kheirollahi M, Mahbod P, Mohammadi F, Astaneh AN, Zarindast MR, Azimi C, Mohammadi MR. Alpha- and beta-synucleins mRNA expression in lymphocytes of schizophrenia patients. Genet Test Mol Biomarkers. 2010;14(5):725-729. doi:10.1089/gtmb.2010.0050.

153. Chen PY, Huang MC, Chiu CC, Liu HC, Lu ML, Chen CH. Association of plasma retinol-binding protein-4, adiponectin, and high molecular weight adiponectin with metabolic adversities in patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2011;35(8):1927-1932. doi:10.1016/j.pnpbp.2011.07.014

154. Ratta-Apha W, Mouri K, Boku S, Ishiguro H, Okazaki S, Otsuka I, Sora I, Arinami T, Shirakawa O, Hishimoto A. A decrease in protein level

and a missense polymorphism of KIF17 are associated with schizophrenia. Psychiatry Res. 2015;230(2):424-429. doi:10.1016/j.psychres.2015.09.031

155. Hill MJ, Kenny E, Roche S, Morris DW, Corvin A, Hawi Z, Gill M, Anney RJ. Allelic expression imbalance of the schizophrenia susceptibility gene CHI3L1: evidence of cis-acting variation and tissue specific regulation. Psychiatr Genet. 2011;21(6):281-286. doi:10.1097/YPG.0b013e328348045b

156. Rasmussen HB, Timm S, Wang AG, Søeby K, Lublin H, Fenger M, Hemmingsen R, Werge T. Association between the CCR5 32-bp deletion allele and late onset of schizophrenia. Am J Psychiatry. 2006;163(3):507-511. doi:10.1176/appi.ajp.163.3.507

157. Zakharyan R, Khoyetsyan A, Arakelyan A, Boyajyan A, Gevorgyan A, Stahelova A, Mrazek F, Petrek M. Association of C1QB gene polymorphism with schizophrenia in Armenian population. BMC Med Genet. 2011;12:126. doi:10.1186/1471-2350-12-126

158. Kwon J, Suessmilch M, McColl A, Cavanagh J, Morris BJ. Distinct trans-placental effects of maternal immune activation by TLR3 and TLR7 agonists: implications for schizophrenia risk. Sci Rep. 2021;11(1):23841. doi:10.1038/s41598-021-03216-9

159. Aflouk Y, Inoubli O, Saoud H, Zaafrane F, Gaha L, Bel Hadj Jrad B. Association between TLR2 polymorphisms (-□196-174 Ins/Del, R677W, R753Q, and P631H) and schizophrenia in a Tunisian population. Immunol Res. 2021;69(6):541-552. doi:10.1007/s12026-021-09238-9

160. Lahdelma L, Jee KJ, Joffe G, Tchoukhine E, Oksanen J, Kaur S, Knuutila S, Andersson LC. Altered expression of myeloperoxidase precursor, myeloid cell nuclear differentiation antigen, Fms-related tyrosine kinase 3 ligand, and antigen CD11A genes in leukocytes of clozapine-treated schizophrenic patients. J Clin Psychopharmacol. 2006;26(3):335-338. doi:10.1097/01.jcp.0000218984.99801.b6

161. Li H, Zhang Q, Li N, Wang F, Xiang H, Zhang Z, Su Y, Huang Y, Zhang S, Zhao G, et al. Plasma levels of Th17-related cytokines and complement C3 correlated with aggressive behavior in patients with schizophrenia. Psychiatry Res. 2016;246:700-706. doi:10.1016/j.psychres.2016.10.061

162. Ghazaryan H, Petrek M, Boyajyan A. Chronic schizophrenia is associated with over-expression of the interleukin-2 receptor gamma gene. Psychiatry Res. 2014;217(3):158-162. doi:10.1016/j.psychres.2014.03.020

163. Shirts BH, Kim JJ, Reich S, Dickerson FB, Yolken RH, Devlin B, Nimgaonkar VL. Polymorphisms in MICB are associated with human herpes virus seropositivity and schizophrenia risk. Schizophr Res. 2007;94(1-3):342-353. doi:10.1016/j.schres.2007.04.021

164. Daskalakis NP, Binder EB. Schizophrenia in the spectrum of gene-stress interactions: the FKBP5 example. Schizophr Bull. 2015;41(2):323-329. doi:10.1093/schbul/sbu189

165. Pinacho R, Villalmanzo N, Meana JJ, Ferrer I, Berengueras A, Haro JM, Villén J, Ramos B. Altered CSNK1E, FABP4 and NEFH protein levels in the dorsolateral prefrontal cortex in schizophrenia. Schizophr Res. 2016;177(1-3):88-97. doi:10.1016/j.schres.2016.04.050

166. Gross J, Grimm O, Ortega G, Teuber I, Lesch KP, Meyer J. Mutational analysis of the neuronal cadherin gene CELSR1 and exclusion as a candidate for catatonic schizophrenia in a large family. Psychiatr Genet. 2001;11(4):197-200. doi:10.1097/00041444-200112000-00003

167. Ashbrook DG, Cahill S, Hager R. A Cross-Species Systems Genetics Analysis Links APBB1IP as a Candidate for Schizophrenia and Prepulse Inhibition. Front Behav Neurosci. 2019;13:266. doi:10.3389/fnbeh.2019.00266

168. Löffler S, Klimke A, Kronenwett R, Kobbe G, Haas R, Fehsel K. Clozapine mobilizes CD34+ hematopoietic stem and progenitor cells and increases plasma concentration of interleukin 6 in patients with schizophrenia. J Clin Psychopharmacol. 2010;30(5):591-595. doi:10.1097/JCP.0b013e3181eeb7f7

169. Wang KS, Liu X, Arana TB, Thompson N, Weisman H, Devargas C, Mao C, Su BB, Camarillo C, Escamilla MA, et al. Genetic association analysis of ITGB3 polymorphisms with age at onset of schizophrenia. J Mol Neurosci. 2013;51(2):446-453. doi:10.1007/s12031-013-0059-8

170. Joaquim HPG, Costa AC, Serpa MH, Talib LL, Gattaz WF. Reduced Annexin A3 in schizophrenia. Eur Arch Psychiatry Clin Neurosci. 2020;270(4):489-494. doi:10.1007/s00406-019-01048-3

171. Lajin B, Alachkar A, Michati R, Alhaj Sakur A. Association between polymorphisms in the genes for tumor suppressor protein p53 and its regulator NAD(P)H: quinone oxidoreductase 1 (NQO1) and schizophrenia in a Syrian study cohort. Arch Med Res. 2013;44(2):121-126. doi:10.1016/j.arcmed.2012.12.009

172. Chittiprol S, Venkatasubramanian G, Neelakantachar N, Reddy NA, Shetty KT, Gangadhar BN. Longitudinal study of beta2-microglobulin abnormalities in schizophrenia. Int Immunopharmacol. 2009;9(10):1215-1217. doi:10.1016/j.intimp.2009.07.002

173. Scarr E, Udawela M, Greenough MA, Neo J, Suk Seo M, Money TT, Upadhyay A, Bush AI, Everall IP, Thomas EA, et al. Increased cortical expression of the zinc transporter SLC39A12 suggests a breakdown in zinc cellular homeostasis as part of the pathophysiology of schizophrenia. NPJ Schizophr. 2016;2:16002. doi:10.1038/npjschz.2016.2

174. Bi XJ, Hu L, Qiao DD, Han C, Sun MM, Cui KY, Wang LN, Yang LM, Liu LF, Chen ZY. Evidence for an Interaction Between NEDD4 and Childhood Trauma on Clinical Characters of Schizophrenia With Family History of Psychosis. Front Psychiatry. 2021;12:608231. doi:10.3389/fpsyt.2021.608231

175. Müller N, Schwarz MJ. COX-2 inhibition in schizophrenia and major depression. Curr Pharm Des. 2008;14(14):1452-1465. doi:10.2174/138161208784480243

176. Nursal AF, Aydin PC, Pehlivan M, Sever U, Pehlivan S. UCP2 and CFH Gene Variants with Genetic Susceptibility to Schizophrenia in Turkish Population. Endocr Metab Immune Disord Drug Targets. 2021;21(11):2084-2089. doi:10.2174/1871530320999201113103730

177. Numata S, Ueno S, Iga J, Yamauchi K, Hongwei S, Hashimoto R, Takeda M, Kunugi H, Itakura M, Ohmori T. TGFBR2 gene expression and genetic association with schizophrenia. J Psychiatr Res. 2008;42(6):425-432. doi:10.1016/j.jpsychires.2007.04.002

178. Chen CY, Liu HY, Hsueh YP. TLR3 downregulates expression of schizophrenia gene Disc1 via MYD88 to control neuronal morphology. EMBO Rep. 2017;18(1):169-183. doi:10.15252/embr.201642586

179. Supriyanto I, Watanabe Y, Mouri K, Shiroiwa K, Ratta-Apha W, Yoshida M, Tamiya G, Sasada T, Eguchi N, Okazaki K, et al. A missense

mutation in the ITGA8 gene, a cell adhesion molecule gene, is associated with schizophrenia in Japanese female patients. Prog Neuropsychopharmacol Biol Psychiatry. 2013;40:347-352. doi:10.1016/j.pnpbp.2012.11.002

180. Warburton A, Breen G, Rujescu D, Bubb VJ, Quinn JP. Characterization of a REST-Regulated Internal Promoter in the Schizophrenia Genome-Wide Associated Gene MIR137. Schizophr Bull. 2015;41(3):698-707. doi:10.1093/schbul/sbu117

181. Shen Q, Zhang J, Wang Y, Liu B, Li X, Zhao Q, Chen S, Ji J, Yang F, Wan C, et al. No association between the KCNH1, KCNJ10 and KCNN3 genes and schizophrenia in the Han Chinese population. Neurosci Lett. 2011;487(1):61-65. doi:10.1016/j.neulet.2010.09.074

182. Wei L, Chen C, Ding L, Mo M, Zou J, Lu Z, Li H, Wu H, Dai Y, Xu P, et al. Wnt1 Promotes EAAT2 Expression and Mediates the Protective Effects of Astrocytes on Dopaminergic Cells in Parkinson's Disease. Neural Plast. 2019;2019:1247276. doi:10.1155/2019/1247276

183. Koob AO, Shaked GM, Bender A, Bisquertt A, Rockenstein E, Masliah E. Neurogranin binds α-synuclein in the human superior temporal cortex and interaction is decreased in Parkinson's disease. Brain Res. 2014;1591:102-110. doi:10.1016/j.brainres.2014.10.013

184. Goldman JG, Marr D, Zhou L, Ouyang B, Leurgans SE, Berry-Kravis E, Goetz CG. Racial differences may influence the role of cholecystokinin polymorphisms in Parkinson's disease hallucinations. Mov Disord. 2011;26(9):1781-1782. doi:10.1002/mds.23655

185. Ko WK, Martin-Negrier ML, Bezard E, Crossman AR, Ravenscroft P. RGS4 is involved in the generation of abnormal involuntary movements in the unilateral 6-OHDA-lesioned rat model of Parkinson's disease. Neurobiol Dis. 2014;70:138-148. doi:10.1016/j.nbd.2014.06.013

186. Hong CT, Chen KY, Wang W, Chiu JY, Wu D, Chao TY, Hu CJ, Chau KD, Bamodu OA. Insulin Resistance Promotes Parkinson's Disease through Aberrant Expression of α-Synuclein, Mitochondrial Dysfunction, and Deregulation of the Polo-Like Kinase 2 Signaling. Cells. 2020;9(3):740. doi:10.3390/cells9030740

187. Deng H, Gu S, Jankovic J. LINGO1 variants in essential tremor and Parkinson's disease. Acta Neurol Scand. 2012;125(1):1-7. doi:10.1111/j.1600-0404.2011.01516.x

188. Ahn EH, Kang SS, Qi Q, Liu X, Ye K. Netrin1 deficiency activates MST1 via UNC5B receptor, promoting dopaminergic apoptosis in Parkinson's disease. Proc Natl Acad Sci U S A. 2020;117(39):24503-24513. doi:10.1073/pnas.2004087117

189. Dong Y, Xiong J, Ji L, Xue X. MiR-421 Aggravates Neurotoxicity and Promotes Cell Death in Parkinson's Disease Models by Directly Targeting MEF2D. Neurochem Res. 2021;46(2):299-308. doi:10.1007/s11064-020-03166-0

190. Angelopoulou E, Paudel YN, Shaikh MF, Piperi C. Fractalkine (CX3CL1) signaling and neuroinflammation in Parkinson's disease: Potential clinical and therapeutic implications. Pharmacol Res. 2020;158:104930. doi:10.1016/j.phrs.2020.104930

191. Ryo A, Togo T, Nakai T, Hirai A, Nishi M, Yamaguchi A, Suzuki K, Hirayasu Y, Kobayashi H, Perrem K, et al. Prolyl-isomerase Pin1 accumulates in lewy bodies of parkinson disease and facilitates formation of alpha-synuclein inclusions. J Biol Chem. 2006;281(7):4117-4125. doi:10.1074/jbc.M507026200

192. Walker DG, Beach TG, Xu R, Lile J, Beck KD, McGeer EG, McGeer PL. Expression of the proto-oncogene Ret, a component of the GDNF receptor complex, persists in human substantia nigra neurons in Parkinson's disease. Brain Res. 1998;792(2):207-217. doi:10.1016/s0006-8993(98)00131-0

193. Anantha J, Goulding SR, Tuboly E, O'Mahony AG, Moloney GM, Lomansey G, McCarthy CM, Collins LM, Sullivan AM, O'Keeffe GW. NME1 Protects Against Neurotoxin-, α-Synuclein- and LRRK2-Induced Neurite Degeneration in Cell Models of Parkinson's Disease. Mol Neurobiol. 2022;59(1):61-76. doi:10.1007/s12035-021-02569-6

194. Chang KH, Chen CM, Chen YC, Fung HC, Wu YR. Polymorphisms of ACMSD-TMEM163, MCCC1, and BCKDK-STX1B Are Not Associated with Parkinson's Disease in Taiwan. Parkinsons Dis. 2019;2019:3489638. doi:10.1155/2019/3489638

195. Cheng X, Xu S, Zhang C, Qin K, Yan J, Shao X. The BRCC3 regulated by Cdk5 promotes the activation of neuronal NLRP3 inflammasome in Parkinson's disease models. Biochem Biophys Res Commun. 2020;522(3):647-654. doi:10.1016/j.bbrc.2019.11.141

196. Lang Y, Li Y, Yu H, Lin L, Chen X, Wang S, Zhang H. HOTAIR drives autophagy in midbrain dopaminergic neurons in the substantia nigra compacta in a mouse model of Parkinson's disease by elevating NPTX2 via miR-221-3p binding. Aging (Albany NY). 2020;12(9):7660-7678. doi:10.18632/aging.103028

197. Kim K, Wi S, Seo JH, Pyo S, Cho SR. Reduced Interaction of Aggregated α-Synuclein and VAMP2 by Environmental Enrichment Alleviates Hyperactivity and Anxiety in a Model of Parkinson's Disease. Genes (Basel). 2021;12(3):392. doi:10.3390/genes12030392

198. Wong TH, Chiu WZ, Breedveld GJ, Li KW, Verkerk AJ, Hondius D, Hukema RK, Seelaar H, Frick P, Severijnen LA, et al. PRKAR1B mutation associated with a new neurodegenerative disorder with unique pathology. Brain. 2014;137(Pt 5):1361-1373. doi:10.1093/brain/awu067

199. Beyer K, Ispierto L, Latorre P, Tolosa E, Ariza A. Alpha- and beta-synuclein expression in Parkinson disease with and without dementia. J Neurol Sci. 2011;310(1-2):112-117. doi:10.1016/j.jns.2011.05.049

200. Liu Q, Bautista-Gomez J, Higgins DA, Yu J, Xiong Y. Dysregulation of the AP2M1 phosphorylation cycle by LRRK2 impairs endocytosis and leads to dopaminergic neurodegeneration. Sci Signal. 2021;14(693):eabg3555. doi:10.1126/scisignal.abg3555

201. Horvath I, Iashchishyn IA, Moskalenko RA, Wang C, Wärmländer SKTS, Wallin C, Gräslund A, Kovacs GG, Morozova-Roche LA. Co-aggregation of pro-inflammatory S100A9 with α-synuclein in Parkinson's disease: ex vivo and in vitro studies. J Neuroinflammation. 2018;15(1):172. doi:10.1186/s12974-018-1210-9

202. Campolo M, Filippone A, Biondo C, Mancuso G, Casili G, Lanza M, Cuzzocrea S, Esposito E, Paterniti I. TLR7/8 in the Pathogenesis of Parkinson's Disease. Int J Mol Sci. 2020;21(24):9384. doi:10.3390/ijms21249384

203. Halbgebauer S, Nagl M, Klafki H, Haußmann U, Steinacker P, Oeckl P, Kassubek J, Pinkhardt E, Ludolph AC, Soininen H, et al. Modified

serpinA1 as risk marker for Parkinson's disease dementia: Analysis of baseline data. Sci Rep. 2016;6:26145. doi:10.1038/srep26145

204. Subramanian N, Ramanathan S, Paul SFD, Venkatesan V, Koshy T. A case-control association of RANTES (-28C□>G) and CCR5-Delta32 polymorphisms with Parkinson's disease in Indians. Neurosci Lett. 2020;739:135404. doi:10.1016/j.neulet.2020.135404

205. Cheng L, Chen L, Wei X, Wang Y, Ren Z, Zeng S, Zhang X, Wen H, Gao C, Liu H. NOD2 promotes dopaminergic degeneration regulated by NADPH oxidase 2 in 6-hydroxydopamine model of Parkinson's disease. J Neuroinflammation. 2018;15(1):243. doi:10.1186/s12974-018-1289-z

206. Salehi Z, Rajaei F. Expression of hepatocyte growth factor in the serum and cerebrospinal fluid of patients with Parkinson's disease. J Clin Neurosci. 2010;17(12):1553-1556. doi:10.1016/j.jocn.2010.04.034

207. Nemutlu Samur D, Akçay G, Yıldırım S, Özkan A, Çeker T, Derin N, Tanrıöver G, Aslan M, Ağar A, Özbey G. Vortioxetine ameliorates motor and cognitive impairments in the rotenone-induced Parkinson's disease via targeting TLR-2 mediated neuroinflammation. Neuropharmacology. 2022;208:108977. doi:10.1016/j.neuropharm.2022.108977

208. Bottero V, Santiago JA, Potashkin JA. PTPRC Expression in Blood is Downregulated in Parkinson's and Progressive Supranuclear Palsy Disorders. J Parkinsons Dis. 2018;8(4):529-537. doi:10.3233/JPD-181391

209. Chen MM, Hu ZL, Ding JH, Du RH, Hu G. Astrocytic Kir6.1 deletion aggravates neurodegeneration in the lipopolysaccharide-induced mouse model of Parkinson's disease via astrocyte-neuron cross talk through complement C3-C3R signaling. Brain Behav Immun. 2021;95:310-320. doi:10.1016/j.bbi.2021.04.003

210. Lim JL, Ng EY, Lim SY, Tan AH, Abdul-Aziz Z, Ibrahim KA, Gopalai AA, Tay YW, Vijayanathan Y, Toh TS, et al. Association study of MCCC1/LAMP3 and DGKQ variants with Parkinson's disease in patients of Malay ancestry. Neurol Sci. 2021;42(10):4203-4207. doi:10.1007/s10072-021-05056-x

211. Suwelack D, Hurtado-Lorenzo A, Millan E, Gonzalez-Nicolini V, Wawrowsky K, Lowenstein PR, Castro MG. Neuronal expression of the transcription factor Gli1 using the Talpha1 alpha-tubulin promoter is

neuroprotective in an experimental model of Parkinson's disease. Gene Ther. 2004;11(24):1742-1752. doi:10.1038/sj.gt.3302377

212. Haque ME, Azam S, Akther M, Cho DY, Kim IS, Choi DK. The Neuroprotective Effects of GPR4 Inhibition through the Attenuation of Caspase Mediated Apoptotic Cell Death in an MPTP Induced Mouse Model of Parkinson's Disease. Int J Mol Sci. 2021;22(9):4674. doi:10.3390/ijms22094674

213. Daniele SG, Béraud D, Davenport C, Cheng K, Yin H, Maguire-Zeiss KA. Activation of MyD88-dependent TLR1/2 signaling by misfolded α-synuclein, a protein linked to neurodegenerative disorders. Sci Signal. 2015;8(376):ra45. doi:10.1126/scisignal.2005965

214. Gao JX, Li Y, Wang SN, Chen XC, Lin LL, Zhang H. Overexpression of microRNA-183 promotes apoptosis of substantia nigra neurons via the inhibition of OSMR in a mouse model of Parkinson's disease. Int J Mol Med. 2019;43(1):209-220. doi:10.3892/ijmm.2018.3982

215. Wang Y, Zhang X, Chen F, Chen L, Wang J, Xie J. LRRK2-NFATc2 Pathway Associated with Neuroinflammation May Be a Potential Therapeutic Target for Parkinson's Disease. J Inflamm Res. 2021;14:2583-2586. doi:10.2147/JIR.S301531

216. Moloney EB, Moskites A, Ferrari EJ, Isacson O, Hallett PJ. The glycoprotein GPNMB is selectively elevated in the substantia nigra of Parkinson's disease patients and increases after lysosomal stress. Neurobiol Dis. 2018;120:1-11. doi:10.1016/j.nbd.2018.08.013

217. Flores-Soto ME, Corona-Angeles JA, Tejeda-Martinez AR, Flores-Guzman PA, Luna-Mujica I, Chaparro-Huerta V, Viveros-Paredes JM. β-Caryophyllene exerts protective antioxidant effects through the activation of NQO1 in the MPTP model of Parkinson's disease. Neurosci Lett. 2021;742:135534. doi:10.1016/j.neulet.2020.135534

218. Mogi M, Harada M, Kondo T, Riederer P, Nagatsu T. Brain beta 2-microglobulin levels are elevated in the striatum in Parkinson's disease. J Neural Transm Park Dis Dement Sect. 1995;9(1):87-92. doi:10.1007/BF02252965

219. Seo MH, Lim S, Yeo S. Association of decreased triadin expression level with apoptosis of dopaminergic cells in Parkinson's disease mouse model. BMC Neurosci. 2021;22(1):65. doi:10.1186/s12868-021-00668-7

220. Li J, Chen L, Qin Q, Wang D, Zhao J, Gao H, Yuan X, Zhang J, Zou Y, Mao Z, et al. Upregulated hexokinase 2 expression induces the apoptosis of dopaminergic neurons by promoting lactate production in Parkinson's disease. Neurobiol Dis. 2022;163:105605. doi:10.1016/j.nbd.2021.105605

221. Hatstat AK, Ahrendt HD, Foster MW, Mayne L, Moseley MA, Englander SW, McCafferty DG. Characterization of Small-Molecule-Induced Changes in Parkinson's-Related Trafficking via the Nedd4 Ubiquitin Signaling Cascade. Cell Chem Biol. 2021;28(1):14-25.e9. doi:10.1016/j.chembiol.2020.10.008

222. García S, López-Hernández L, Dávila-Maldonado L, Cuevas-García C, Gallegos-Arreola M, Alcaraz-Estrada S, Cortes-Espinosa L, Flores C, Canto P, Vázquez R. Association of mitochondrial variants A4336G of the tRNAGln gene and 8701G/A of the MT-ATP6 gene in Mexicans Mestizos with Parkinson disease. Folia Neuropathol. 2019;57(4):335-339. doi:10.5114/fn.2019.89859

223. Teismann P. COX-2 in the neurodegenerative process of Parkinson's disease. Biofactors. 2012;38(6):395-397. doi:10.1002/biof.1035

224. Giaime E, Sunyach C, Druon C, Scarzello S, Robert G, Grosso S, Auberger P, Goldberg MS, Shen J, Heutink P, et al. Loss of function of DJ-1 triggered by Parkinson's disease-associated mutation is due to proteolytic resistance to caspase-6. Cell Death Differ. 2010;17(1):158-169. doi:10.1038/cdd.2009.116

225. Li Q, Zhang P, Cai Y. Genkwanin suppresses MPP+-induced cytotoxicity by inhibiting TLR4/MyD88/NLRP3 inflammasome pathway in a cellular model of Parkinson's disease. Neurotoxicology. 2021;87:62-69. doi:10.1016/j.neuro.2021.08.018

226. Baltus THL, Morelli NR, de Farias CC, Trugilo KP, Okuyama NCM, de Oliveira KB, de Melo LB, Smaili SM, Barbosa DS. Association of -94 ATTG insertion/deletion NFkB1 and c.*126G>A NFkBIA genetic polymorphisms with oxidative and nitrosative stress biomarkers in Brazilian subjects with Parkinson's Disease. Neurosci Lett. 2021;740:135487. doi:10.1016/j.neulet.2020.135487

227. Aguirre CA, Concetta Morale M, Peng Q, Sanchez-Alavez M, Cintrón-Colón R, Feng K, Fazelpour S, Maher P, Conti B. Two single nucleotide polymorphisms in IL13 and IL13RA1 from individuals with

idiopathic Parkinson's disease increase cellular susceptibility to oxidative stress. Brain Behav Immun. 2020;88:920-924. doi:10.1016/j.bbi.2020.04.007

228. Zhang Y, Sun HM, He X, Wang YY, Gao YS, Wu HX, Xu H, Gong XG, Guo ZY. Da-Bu-Yin-Wan and Qian-Zheng-San, two traditional Chinese herbal formulas, up-regulate the expression of mitochondrial subunit NADH dehydrogenase 1 synergistically in the mice model of Parkinson's disease. J Ethnopharmacol. 2013;146(1):363-371. doi:10.1016/j.jep.2013.01.005

229. Dinh E, Rival T, Carrier A, Asfogo N, Corti O, Melon C, Salin P, Lortet S, Kerkerian-Le Goff L. TP53INP1 exerts neuroprotection under ageing and Parkinson's disease-related stress condition. Cell Death Dis. 2021;12(5):460. doi:10.1038/s41419-021-03742-4

230. Chang KH, Wu YR, Chen YC, Wu HC, Chen CM. Association between CSF1 and CSF1R Polymorphisms and Parkinson's Disease in Taiwan. J Clin Med. 2019;8(10):1529. doi:10.3390/jcm8101529

231. Fang HS, Wang CC, Chao CY, Fan WL, Su SC, Wu YR. Association of ITPKB, IL1R2 and COQ7 with Parkinson's disease in Taiwan. J Formos Med Assoc. 2021;S0929-6646(21)00296-5. doi:10.1016/j.jfma.2021.06.016

232. Darvish H, Azcona LJ, Taghavi S, Firouzabadi SG, Tafakhori A, Alehabib E, Mohajerani F, Zardadi S, Paisán-Ruiz C. ANXA1 with Anti-Inflammatory Properties Might Contribute to Parkinsonism. Ann Neurol. 2021;90(2):319-323. doi:10.1002/ana.26148

233. Küçükali CI, Salman B, Yüceer H, Ulusoy C, Abacı N, Ekmekci SS, Tüzün E, Bilgiç B, Hanağası HA. Small ubiquitin-related modifier (SUMO) 3 and SUMO4 gene polymorphisms in Parkinson's disease. Neurol Res. 2020;42(6):451-457. doi:10.1080/01616412.2020.1724464

234. Wu HC, Chen CM, Chen YC, Fung HC, Chang KH, Wu YR. DLG2, but not TMEM229B, GPNMB, and ITGA8 polymorphism, is associated with Parkinson's disease in a Taiwanese population. Neurobiol Aging. 2018;64:158.e1-158.e6. doi:10.1016/j.neurobiolaging.2017.11.016

235. Li H, Liu Z, Wu Y, Chen Y, Wang J, Wang Z, Huang D, Wang M, Yu M, Fei J, et al. The deficiency of NRSF/REST enhances the pro-inflammatory function of astrocytes in a model of Parkinson's disease.

Biochim Biophys Acta Mol Basis Dis. 2020;1866(1):165590. doi:10.1016/j.bbadis.2019.165590

236. Wang S, Guan Y, Chen Y, Li X, Zhang C, Yu L, Zhou F, Wang X. Role of Wnt1 and Fzd1 in the spinal cord pathogenesis of amyotrophic lateral sclerosis-transgenic mice. Biotechnol Lett. 2013;35(8):1199-1207. doi:10.1007/s10529-013-1199-1

237. Xu L, Li J, Tian D, Chen L, Tang L, Fan D. The rs696880 Polymorphism in the Nogo-A Receptor Gene (RTN4R) Is Associated With Susceptibility to Sporadic Amyotrophic Lateral Sclerosis in the Chinese Population. Front Aging Neurosci. 2018;10:108. doi:10.3389/fnagi.2018.00108

238. Arosio A, Sala G, Rodriguez-Menendez V, Grana D, Gerardi F, Lunetta C, Ferrarese C, Tremolizzo L.MEF2D and MEF2C pathways disruption in sporadic and familial ALS patients. Mol Cell Neurosci. 2016;74:10-17. doi:10.1016/j.mcn.2016.02.002

239. Liu C, Hong K, Chen H, Niu Y, Duan W, Liu Y, Ji Y, Deng B, Li Y, Li Z, et al. Evidence for a protective role of the CX3CL1/CX3CR1 axis in a model of amyotrophic lateral sclerosis. Biol Chem. 2019;400(5):651-661. doi:10.1515/hsz-2018-0204

240. Fagiani F, Govoni S, Racchi M, Lanni C. The Peptidyl-prolyl Isomerase Pin1 in Neuronal Signaling: from Neurodevelopment to Neurodegeneration. Mol Neurobiol. 2021;58(3):1062-1073. doi:10.1007/s12035-020-02179-8

241. Tan HHG, Westeneng HJ, van der Burgh HK, van Es MA, Bakker LA, van Veenhuijzen K, van Eijk KR, van Eijk RPA, Veldink JH, van den Berg LH. The Distinct Traits of the UNC13A Polymorphism in Amyotrophic Lateral Sclerosis. Ann Neurol. 2020;88(4):796-806. doi:10.1002/ana.25841

242. Bajaj NP. Cyclin-dependent kinase-5 (CDK5) and amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000;1(5):319-327. doi:10.1080/146608200300079563

243. Kurita H, Yabe S, Ueda T, Inden M, Kakita A, Hozumi I. MicroRNA-5572 Is a Novel MicroRNA-Regulating SLC30A3 in Sporadic Amyotrophic Lateral Sclerosis. Int J Mol Sci. 2020;21(12):4482. doi:10.3390/ijms21124482

244. Helferich AM, Brockmann SJ, Reinders J, Deshpande D, Holzmann K, Brenner D, Andersen PM, Petri S, Thal DR, Michaelis J, et al. Dysregulation of a novel miR-1825/TBCB/TUBA4A pathway in sporadic and familial ALS. Cell Mol Life Sci. 2018;75(23):4301-4319. doi:10.1007/s00018-018-2873-1

245. Iaccarino C, Mura ME, Esposito S, Carta F, Sanna G, Turrini F, Carrì MT, Crosio C. Bcl2-A1 interacts with pro-caspase-3: implications for amyotrophic lateral sclerosis. Neurobiol Dis. 2011;43(3):642-650. doi:10.1016/j.nbd.2011.05.013

246. Vu L, An J, Kovalik T, Gendron T, Petrucelli L, Bowser R. Cross-sectional and longitudinal measures of chitinase proteins in amyotrophic lateral sclerosis and expression of CHI3L1 in activated astrocytes. J Neurol Neurosurg Psychiatry. 2020;91(4):350-358. doi:10.1136/jnnp-2019-321916

247. Ebbert MTW, Ross CA, Pregent LJ, Lank RJ, Zhang C, Katzman RB, Jansen-West K, Song Y, da Rocha EL, Palmucci C, et al. Conserved DNA methylation combined with differential frontal cortex and cerebellar expression distinguishes C9orf72-associated and sporadic ALS, and implicates SERPINA1 in disease. Acta Neuropathol. 2017;134(5):715-728. doi:10.1007/s00401-017-1760-4

248. Wojta KJ, Ayer AH, Ramos EM, Nguyen PD, Karydas AM, Yokoyama JS, Kramer J, Lee SE, Boxer A, Miller BL, et al. Lack of Association Between the CCR5-delta32 Polymorphism and Neurodegenerative Disorders. Alzheimer Dis Assoc Disord. 2020;34(3):244-247. doi:10.1097/WAD.0000000000000367

249. He J, Fu J, Fan D. The complement C7 variant rs3792646 is associated with amyotrophic lateral sclerosis in a Han Chinese population. Neurobiol Aging. 2021;99:103.e1-103.e7. doi:10.1016/j.neurobiolaging.2020.10.012

250. Milani M, Mammarella E, Rossi S, Miele C, Lattante S, Sabatelli M, Cozzolino M, D'Ambrosi N, Apolloni S. Targeting S100A4 with niclosamide attenuates inflammatory and profibrotic pathways in models of amyotrophic lateral sclerosis. J Neuroinflammation. 2021;18(1):132. doi:10.1186/s12974-021-02184-1

251. Grewal RP, Morgan TE, Finch CE. C1qB and clusterin mRNA increase in association with neurodegeneration in sporadic amyotrophic

lateral sclerosis. Neurosci Lett. 1999;271(1):65-67. doi:10.1016/s0304-3940(99)00496-6

252. Yamamoto T, Murayama S, Takao M, Isa T, Higo N. Expression of secreted phosphoprotein 1 (osteopontin) in human sensorimotor cortex and spinal cord: Changes in patients with amyotrophic lateral sclerosis. Brain Res. 2017;1655:168-175. doi:10.1016/j.brainres.2016.10.030

253. Lehmann SM, Rosenberger K, Krüger C, Habbel P, Derkow K, Kaul D, Rybak A, Brandt C, Schott E, Wulczyn FG, et al. Extracellularly delivered single-stranded viral RNA causes neurodegeneration dependent on TLR7. J Immunol. 2012;189(3):1448-1458. doi:10.4049/jimmunol.1201078

254. Liu Y, Hao W, Dawson A, Liu S, Fassbender K. Expression of amyotrophic lateral sclerosis-linked SOD1 mutant increases the neurotoxic potential of microglia via TLR2. J Biol Chem. 2009;284(6):3691-3699. doi:10.1074/jbc.M804446200

255. Lin F, Lin W, Zhu C, Lin J, Zhu J, Li XY, Wang Z, Wang C, Huang H. Sequencing of neurofilament genes identified NEFH Ser787Arg as a novel risk variant of sporadic amyotrophic lateral sclerosis in Chinese subjects. BMC Med Genomics. 2021;14(1):222. doi:10.1186/s12920-021-01073-z

256. Oeckl P, Weydt P, Thal DR, Weishaupt JH, Ludolph AC, Otto M. Proteomics in cerebrospinal fluid and spinal cord suggests UCHL1, MAP2 and GPNMB as biomarkers and underpins importance of transcriptional pathways in amyotrophic lateral sclerosis. Acta Neuropathol. 2020;139(1):119-134. doi:10.1007/s00401-019-02093-x

257. Staats KA, Schönefeldt S, Van Rillaer M, Van Hoecke A, Van Damme P, Robberecht W, Liston A, Van Den Bosch L. Beta-2 microglobulin is important for disease progression in a murine model for amyotrophic lateral sclerosis. Front Cell Neurosci. 2013;7:249. doi:10.3389/fncel.2013.00249

258. Kiaei M, Kipiani K, Petri S, Choi DK, Chen J, Calingasan NY, Beal MF. Integrative role of cPLA with COX-2 and the effect of non-steriodal anti-inflammatory drugs in a transgenic mouse model of amyotrophic lateral sclerosis. J Neurochem. 2005;93(2):403-411. doi:10.1111/j.1471-4159.2005.03024.x

259. Liebl MP, Kaya AM, Tenzer S, Mittenzwei R, Koziollek-Drechsler I, Schild H, Moosmann B, Behl C, Clement AM. Dimerization of visinin-like protein 1 is regulated by oxidative stress and calcium and is a pathological hallmark of amyotrophic lateral sclerosis. Free Radic Biol Med. 2014;72:41-54. doi:10.1016/j.freeradbiomed.2014.04.008

260. Kang J, Rivest S. MyD88-deficient bone marrow cells accelerate onset and reduce survival in a mouse model of amyotrophic lateral sclerosis. J Cell Biol. 2007;179(6):1219-1230. doi:10.1083/jcb.200705046

261. Trias E, Kovacs M, King PH, Si Y, Kwon Y, Varela V, Ibarburu S, Moura IC, Hermine O, Beckman JS, et al. Schwann cells orchestrate peripheral nerve inflammation through the expression of CSF1, IL-34, and SCF in amyotrophic lateral sclerosis. Glia. 2020;68(6):1165-1181. doi:10.1002/glia.23768

262. Van Acker ZP, Declerck K, Luyckx E, Vanden Berghe W, Dewilde S. Non-Methylation-Linked Mechanism of REST-Induced Neuroglobin Expression Impacts Mitochondrial Phenotypes in a Mouse Model of Amyotrophic Lateral Sclerosis. Neuroscience. 2019;412:233-247. doi:10.1016/j.neuroscience.2019.05.039

263. MacNair L, Xiao S, Miletic D, Ghani M, Julien JP, Keith J, Zinman L, Rogaeva E, Robertson J. MTHFSD and DDX58 are novel RNA-binding proteins abnormally regulated in amyotrophic lateral sclerosis. Brain. 2016;139(Pt 1):86-100. doi:10.1093/brain/awv308

264. Lei L, Shen XM, Wang SY, Lu Y, Wang SB, Chen H, Liu Z, Ouyang YS, Duo JY, Da YW, et al. Presence of antibodies against low-density lipoprotein receptor-related protein 4 and impairment of neuromuscular junction in a Chinese cohort of amyotrophic lateral sclerosis. Chin Med J (Engl). 2019;132(12):1487-1489. doi:10.1097/CM9.0000000000000284

265. Kaiser M, Maletzki I, Hülsmann S, Holtmann B, Schulz-Schaeffer W, Kirchhoff F, Bähr M, Neusch C. Progressive loss of a glial potassium channel (KCNJ10) in the spinal cord of the SOD1 (G93A) transgenic mouse model of amyotrophic lateral sclerosis. J Neurochem. 2006;99(3):900-912. doi:10.1111/j.1471-4159.2006.04131.x

266. Cunningham S, O'Doherty C, Patterson C, McDonnell G, Hawkins S, Marrosu MG, Vandenbroeck K. The neuropeptide genes TAC1, TAC3, TAC4, VIP and PACAP(ADCYAP1), and susceptibility to multiple

sclerosis. J Neuroimmunol. 2007;183(1-2):208-213. doi:10.1016/j.jneuroim.2006.11.002

267. Bryld E, Zeeberg I, Gjerris A, Werdelin L, Rehfeld JF. Increased cerebrospinal fluid concentrations of C- but not N-terminal cholecystokinin fragments in multiple sclerosis. Brain Res. 1987;409(2):364-366. doi:10.1016/0006-8993(87)90723-2

268. García-Martín E, Lorenzo-Betancor O, Martínez C, Pastor P, Benito-León J, Millán-Pascual J, Calleja P, Díaz-Sánchez M, Pisa D, Turpín-Fenoll L, et al. LINGO1 rs9652490 and rs11856808 polymorphisms are not associated with risk for multiple sclerosis. BMC Neurol. 2013;13:34. doi:10.1186/1471-2377-13-34

269. Blauth K, Zhang X, Chopra M, Rogan S, Markovic-Plese S. The role of fractalkine (CX3CL1) in regulation of CD4(+) cell migration to the central nervous system in patients with relapsing-remitting multiple sclerosis. Clin Immunol. 2015;157(2):121-132. doi:10.1016/j.clim.2015.01.001

270. Castellanos KJ, Gagyi E, Kormos B, Valyi-Nagy K, Voros A, Shukla D, Horvath S, Slavin KV, Valyi-Nagy T. Increased axonal expression of nectin-1 in multiple sclerosis plaques. Neurol Sci. 2013;34(4):465-469. doi:10.1007/s10072-012-1026-9

271. Donninelli G, Saraf-Sinik I, Mazziotti V, Capone A, Grasso MG, Battistini L, Reynolds R, Magliozzi R, Volpe E.Interleukin-9 regulates macrophage activation in the progressive multiple sclerosis brain. J Neuroinflammation. 2020;17(1):149. doi:10.1186/s12974-020-01770-z

272. Johnson TP, Tyagi R, Patel K, Schiess N, Calabresi PA, Nath A. Impaired toll-like receptor 8 signaling in multiple sclerosis. J Neuroinflammation. 2013;10:74. doi:10.1186/1742-2094-10-74

273. van Veen T, Nielsen J, Berkhof J, Barkhof F, Kamphorst W, Bö L, Ravid R, Verweij CL, Huitinga I, Polman CH, et al. CCL5 and CCR5 genotypes modify clinical, radiological and pathological features of multiple sclerosis. J Neuroimmunol. 2007;190(1-2):157-164. doi:10.1016/j.jneuroim.2007.08.005

274. Fani Maleki A, Cisbani G, Laflamme N, Prefontaine P, Plante MM, Baillargeon J, Rangachari M, Gosselin J, Rivest S. Selective Immunomodulatory and Neuroprotective Effects of a NOD2 Receptor

Agonist on Mouse Models of Multiple Sclerosis. Neurotherapeutics. 2021;18(2):889-904. doi:10.1007/s13311-020-00998-0

275. Chataway J, Sawcer S, Sherman D, Hobart M, Fernie B, Coraddu F, Feakes R, Broadley S, Gray J, Jones HB, et al. No evidence for association of multiple sclerosis with the complement factors C6 and C7. J Neuroimmunol. 1999;99(1):150-156. doi:10.1016/s0165-5728(99)00054-5

276. Trend S, Leffler J, Cooper MN, Byrne SN, Kermode AG, French MA, Hart PH. Narrowband UVB phototherapy reduces TNF production by B-cell subsets stimulated via TLR7 from individuals with early multiple sclerosis. Clin Transl Immunology. 2020;9(10):e1197. doi:10.1002/cti2.1197

277. Moghadam S, Erfanmanesh M, Esmaeilzadeh A. Interleukin 35 and Hepatocyte Growth Factor; as a novel combined immune gene therapy for Multiple Sclerosis disease. Med Hypotheses. 2017;109:102-105. doi:10.1016/j.mehy.2017.09.017

278. Wasko NJ, Nichols F, Clark RB. Multiple sclerosis, the microbiome, TLR2, and the hygiene hypothesis. Autoimmun Rev. 2020;19(1):102430. doi:10.1016/j.autrev.2019.102430

279. Szvetko AL, Jones A, Mackenzie J, Tajouri L, Csurhes PA, Greer JM, Pender MP, Griffiths LR. An investigation of the C77G and C772T variations within the human protein tyrosine phosphatase receptor type C gene for association with multiple sclerosis in an Australian population. Brain Res. 2009;1255:148-152. doi:10.1016/j.brainres.2008.12.017

280. Bourel J, Planche V, Dubourdieu N, Oliveira A, Séré A, Ducourneau EG, Tible M, Maitre M, Lesté-Lasserre T, Nadjar A, et al. Complement C3 mediates early hippocampal neurodegeneration and memory impairment in experimental multiple sclerosis. Neurobiol Dis. 2021;160:105533. doi:10.1016/j.nbd.2021.105533

281. Guerini FR, Clerici M, Cagliani R, Malhotra S, Montalban X, Forni D, Agliardi C, Riva S, Caputo D, Galimberti D, et al. No association of IFI16 (interferon-inducible protein 16) variants with susceptibility to multiple sclerosis. J Neuroimmunol. 2014;271(1-2):49-52. doi:10.1016/j.jneuroim.2014.04.006

282. Wang Y, Imitola J, Rasmussen S, O'Connor KC, Khoury SJ. Paradoxical dysregulation of the neural stem cell pathway sonic hedgehog-

Gli1 in autoimmune encephalomyelitis and multiple sclerosis. Ann Neurol. 2008;64(4):417-427. doi:10.1002/ana.21457

283. Cardamone G, Paraboschi EM, Soldà G, Duga S, Saarela J, Asselta R. Genetic Association and Altered Gene Expression of CYBB in Multiple Sclerosis Patients. Biomedicines. 2018;6(4):117. doi:10.3390/biomedicines6040117

284. Enevold C, Oturai AB, Sørensen PS, Ryder LP, Koch-Henriksen N, Bendtzen K. Multiple sclerosis and polymorphisms of innate pattern recognition receptors TLR1-10, NOD1-2, DDX58, and IFIH1. J Neuroimmunol. 2009;212(1-2):125-131. doi:10.1016/j.jneuroim.2009.04.008

285. Håkansson I, Tisell A, Cassel P, Blennow K, Zetterberg H, Lundberg P, Dahle C, Vrethem M, Ernerudh J. Neurofilament levels, disease activity and brain volume during follow-up in multiple sclerosis. J Neuroinflammation. 2018;15(1):209. doi:10.1186/s12974-018-1249-7

286. Carlini V, Verduci I, Cianci F, Cannavale G, Fenoglio C, Galimberti D, Mazzanti M. CLIC1 Protein Accumulates in Circulating Monocyte Membrane during Neurodegeneration. Int J Mol Sci. 2020;21(4):1484. doi:10.3390/ijms21041484

287. Ghareghani M, Scavo L, Jand Y, Farhadi N, Sadeghi H, Ghanbari A, Mondello S, Arnoult D, Gharaghani S, Zibara K. Melatonin Therapy Modulates Cerebral Metabolism and Enhances Remyelination by Increasing PDK4 in a Mouse Model of Multiple Sclerosis. Front Pharmacol. 2019;10:147. doi:10.3389/fphar.2019.00147

288. Imani SZH, Hojati Z, Khalilian S, Dehghanian F, Kheirollahi M, Khorrami M, Shaygannejad V, Mirmosayyeb O. Expression and clinical significance of IL7R, NFATc2, and RNF213 in familial and sporadic multiple sclerosis. Sci Rep. 2021;11(1):19260. doi:10.1038/s41598-021-98691-5

289. Budge KM, Neal ML, Richardson JR, Safadi FF. Glycoprotein NMB: an Emerging Role in Neurodegenerative Disease. Mol Neurobiol. 2018;55(6):5167-5176. doi:10.1007/s12035-017-0707-z

290. Hecker M, Boxberger N, Illner N, Fitzner B, Schröder I, Winkelmann A, Dudesek A, Meister S, Koczan D, Lorenz P, et al. A genetic variant associated with multiple sclerosis inversely affects the expression of CD58

and microRNA-548ac from the same gene. PLoS Genet. 2019;15(2):e1007961. doi:10.1371/journal.pgen.1007961

291. Alexoudi A, Zachaki S, Stavropoulou C, Gavrili S, Spiliopoulou C, Papadodima S, Karageorgiou CE, Sambani C.Possible Implication of GSTP1 and NQO1 Polymorphisms on Natalizumab Response in Multiple Sclerosis. Ann Clin Lab Sci. 2016;46(6):586-591.

292. Denic A, Pirko I, Wootla B, Bieber A, Macura S, Rodriguez M. Deletion of beta-2-microglobulin ameliorates spinal cord lesion load and promotes recovery of brainstem NAA levels in a murine model of multiple sclerosis. Brain Pathol. 2012;22(5):698-708. doi:10.1111/j.1750-3639.2012.00576.x

293. Iparraguirre L, Muñoz-Culla M, Prada-Luengo I, Castillo-Triviño T, Olascoaga J, Otaegui D. Circular RNA profiling reveals that circular RNAs from ANXA2 can be used as new biomarkers for multiple sclerosis. Hum Mol Genet. 2017;26(18):3564-3572. doi:10.1093/hmg/ddx243

294. Azimi G, Ranjbaran F, Arsang-Jang S, Ghafouri-Fard S, Mazdeh M, Sayad A, Taheri M.Upregulation of VEGF-A and correlation between VEGF-A and FLT-1 expressions in Iranian multiple sclerosis patients. Neurol Sci. 2020;41(6):1459-1465. doi:10.1007/s10072-019-04234-2

295. Bergamaschi L, Ban M, Leone MA, Sawcer SJ, D'Alfonso S. No evidence of association of the rare nsSNP rs35667974 in IFIH1 with multiple sclerosis. J Neuroimmunol. 2010;221(1-2):112-114. doi:10.1016/j.jneuroim.2010.01.005

296. Carlson NG, Hill KE, Tsunoda I, Fujinami RS, Rose JW. The pathologic role for COX-2 in apoptotic oligodendrocytes in virus induced demyelinating disease: implications for multiple sclerosis. J Neuroimmunol. 2006;174(1-2):21-31. doi:10.1016/j.jneuroim.2006.01.008

297. Torkamandi S, Bahrami S, Ghorashi T, Dehani M, Bayat H, Hoseini SM, Rezaei S, Soosanabadi M. Dysregulation of long noncoding RNA MEG3 and NLRC5 expressions in patients with relapsing-remitting multiple sclerosis: is there any correlation?. Genes Immun. 2021;22(7-8):322-326. doi:10.1038/s41435-021-00154-4

298. Abdel Rasol HA, Helmy H, Aziz MA. Serum complement factor H and Tyr402 His gene polymorphism among Egyptians with multiple

sclerosis. Neurol Res. 2015;37(10):845-852. doi:10.1179/1743132815Y.0000000075

299. Khalilian S, Hojati Z, Dehghanian F, Shaygannejad V, Imani SZH, Kheirollahi M, Khorrami M, Mirmosayyeb O. Gene expression profiles of YAP1, TAZ, CRB3, and VDR in familial and sporadic multiple sclerosis among an Iranian population. Sci Rep. 2021;11(1):7713. doi:10.1038/s41598-021-87131-z

300. Zheng C, Chen J, Chu F, Zhu J, Jin T. Inflammatory Role of TLR-MyD88 Signaling in Multiple Sclerosis. Front Mol Neurosci. 2020;12:314. doi:10.3389/fnmol.2019.00314

301. Keshari PK, Harbo HF, Myhr KM, Aarseth JH, Bos SD, Berge T. Allelic imbalance of multiple sclerosis susceptibility genes IKZF3 and IQGAP1 in human peripheral blood. BMC Genet. 2016;17:59. doi:10.1186/s12863-016-0367-4

302. Colamatteo A, Maggioli E, Azevedo Loiola R, Hamid Sheikh M, Calì G, Bruzzese D, Maniscalco GT, Centonze D, Buttari F, Lanzillo R, et al. Reduced Annexin A1 Expression Associates with Disease Severity and Inflammation in Multiple Sclerosis Patients. J Immunol. 2019;203(7):1753-1765. doi:10.4049/jimmunol.1801683

303. Enevold C, Oturai AB, Sørensen PS, Ryder LP, Koch-Henriksen N, Bendtzen K. Multiple sclerosis and polymorphisms of innate pattern recognition receptors TLR1-10, NOD1-2, DDX58, and IFIH1. J Neuroimmunol. 2009;212(1-2):125-131. doi:10.1016/j.jneuroim.2009.04.008

304. Satoh J, Yamamoto Y, Asahina N, Kitano S, Kino Y. RNA-Seq data mining: downregulation of NeuroD6 serves as a possible biomarker for alzheimer's disease brains. Dis Markers. 2014;2014:123165. doi:10.1155/2014/123165

305. Russo P, Kisialiou A, Moroni R, Prinzi G, Fini M. Effect of Genetic Polymorphisms (SNPs) in CHRNA7 Gene on Response to Acetylcholinesterase Inhibitors (AChEI) in Patients with Alzheimer's Disease. Curr Drug Targets. 2017;18(10):1179-1190. doi:10.2174/1389450116666151001111826

306. Sun X, Wang Q, Blennow K, Zetterberg H, McCarthy M, Loewenstein DA, Vontell R, Yue Z, Zhang B. Association of neurogranin

gene expression with Alzheimer's disease pathology in the perirhinal cortex. Alzheimers Dement (N Y). 2021;7(1):e12162. doi:10.1002/trc2.12162

307. Plagman A, Hoscheidt S, McLimans KE, Klinedinst B, Pappas C, Anantharam V, Kanthasamy A, Willette AA. Cholecystokinin and Alzheimer's disease: a biomarker of metabolic function, neural integrity, and cognitive performance. Neurobiol Aging. 2019;76:201-207. doi:10.1016/j.neurobiolaging.2019.01.002

308. Emilsson L, Saetre P, Jazin E. Low mRNA levels of RGS4 splice variants in Alzheimer's disease: association between a rare haplotype and decreased mRNA expression. Synapse. 2006;59(3):173-176. doi:10.1002/syn.20226

309. Paracchini L, Beltrame L, Boeri L, Fusco F, Caffarra P, Marchini S, Albani D, Forloni G. Exome sequencing in an Italian family with Alzheimer's disease points to a role for seizure-related gene 6 (SEZ6) rare variant R615H. Alzheimers Res Ther. 2018;10(1):106. doi:10.1186/s13195-018-0435-2

310. Lee JS, Lee Y, André EA, Lee KJ, Nguyen T, Feng Y, Jia N, Harris BT, Burns MP, Pak DTS. Inhibition of Polo-like kinase 2 ameliorates pathogenesis in Alzheimer's disease model mice. PLoS One. 2019;14(7):e0219691. doi:10.1371/journal.pone.0219691

311. Fernandez-Enright F, Andrews JL. Lingo-1: a novel target in therapy for Alzheimer's disease?. Neural Regen Res. 2016;11(1):88-89. doi:10.4103/1673-5374.175048

312. Piras IS, Krate J, Delvaux E, Nolz J, De Both MD, Mastroeni DF, Serrano GE, Sue LI, Beach TG, Coleman PD, et al. Association of AEBP1 and NRN1 RNA expression with Alzheimer's disease and neurofibrillary tangle density in middle temporal gyrus. Brain Res. 2019;1719:217-224. doi:10.1016/j.brainres.2019.06.004

313. Fan Q, He W, Gayen M, Benoit MR, Luo X, Hu X, Yan R. Activated CX3CL1/Smad2 Signals Prevent Neuronal Loss and Alzheimer's Tau Pathology-Mediated Cognitive Dysfunction. J Neurosci. 2020;40(5):1133-1144. doi:10.1523/JNEUROSCI.1333-19.2019

314. van Abel D, Michel O, Veerhuis R, Jacobs M, van Dijk M, Oudejans CB. Direct downregulation of CNTNAP2 by STOX1A is associated with

Alzheimer's disease. J Alzheimers Dis. 2012;31(4):793-800. doi:10.3233/JAD-2012-120472

315. Ibarreta D, Tao J, Parrilla R, Ayuso MS. Mutation analysis of chromosome 19 calmodulin (CALM3) gene in Alzheimer's disease patients. Neurosci Lett. 1997;229(3):157-160. doi:10.1016/s0304-3940(97)00453-9

316. Wang L, Zhou Y, Chen D, Lee TH. Peptidyl-Prolyl Cis/Trans Isomerase Pin1 and Alzheimer's Disease. Front Cell Dev Biol. 2020;8:355. doi:10.3389/fcell.2020.00355

317. Davidsson P, Bogdanovic N, Lannfelt L, Blennow K. Reduced expression of amyloid precursor protein, presenilin-1 and rab3a in cortical brain regions in Alzheimer's disease. Dement Geriatr Cogn Disord. 2001;12(4):243-250. doi:10.1159/000051266

318. Cook LJ, Ho LW, Taylor AE, Brayne C, Evans JG, Xuereb J, Cairns NJ, Pritchard A, Lemmon H, Mann D, et al. Candidate gene association studies of the alpha 4 (CHRNA4) and beta 2 (CHRNB2) neuronal nicotinic acetylcholine receptor subunit genes in Alzheimer's disease. Neurosci Lett. 2004;358(2):142-146. doi:10.1016/j.neulet.2004.01.016

319. Nikhil K, Viccaro K, Shah K. Multifaceted Regulation of ALDH1A1 by Cdk5 in Alzheimer's Disease Pathogenesis. Mol Neurobiol. 2019;56(2):1366-1390. doi:10.1007/s12035-018-1114-9

320. Tan MG, Lee C, Lee JH, Francis PT, Williams RJ, Ramírez MJ, Chen CP, Wong PT, Lai MK. Decreased rabphilin 3A immunoreactivity in Alzheimer's disease is associated with Aβ burden. Neurochem Int. 2014;64:29-36. doi:10.1016/j.neuint.2013.10.013

321. Libiger O, Shaw LM, Watson MH, Nairn AC, Umaña KL, Biarnes MC, Canet-Avilés RM, Jack CR Jr, Breton YA, Cortes L, et al. Longitudinal CSF proteomics identifies NPTX2 as a prognostic biomarker of Alzheimer's disease. Alzheimers Dement. 2021;17(12):1976-1987. doi:10.1002/alz.12353

322. Dulewicz M, Kulczyńska-Przybik A, Słowik A, Borawska R, Mroczko B. Neurogranin and Neuronal Pentraxin Receptor as Synaptic Dysfunction Biomarkers in Alzheimer's Disease. J Clin Med. 2021;10(19):4575. doi:10.3390/jcm10194575

323. Paracchini L, Beltrame L, Boeri L, Fusco F, Caffarra P, Marchini S, Albani D, Forloni G. Exome sequencing in an Italian family with

Alzheimer's disease points to a role for seizure-related gene 6 (SEZ6) rare variant R615H. Alzheimers Res Ther. 2018;10(1):106. doi:10.1186/s13195-018-0435-2

324. Gaff J, Jackaman C, Papadimitriou J, Waters S, McLean C, Price P. Immunohistochemical evidence of P2X7R, P2X4R and CaMKK2 in pyramidal neurons of frontal cortex does not align with Alzheimer's disease. Exp Mol Pathol. 2021;120:104636. doi:10.1016/j.yexmp.2021.104636

325. Liu SJ, Yang C, Zhang Y, Su RY, Chen JL, Jiao MM, Chen HF, Zheng N, Luo S, et al. Neuroprotective effect of β-asarone against Alzheimer's disease: regulation of synaptic plasticity by increased expression of SYP and GluR1. Drug Des Devel Ther. 2016;10:1461-1469. doi:10.2147/DDDT.S93559

326. Kong Y, Zhang S, Huang L, Zhang C, Xie F, Zhang Z, Huang Q, Jiang D, Li J, Zhou W, et al. Positron Emission Computed Tomography Imaging of Synaptic Vesicle Glycoprotein 2A in Alzheimer's Disease. Front Aging Neurosci. 2021;13:731114. doi:10.3389/fnagi.2021.731114

327. Liu FF, Zhang Z, Chen W, Gu HY, Yan QJ. Regulatory mechanism of microRNA-377 on CDH13 expression in the cell model of Alzheimer's disease. Eur Rev Med Pharmacol Sci. 2018;22(9):2801-2808. doi:10.26355/eurrev_201805_14979

328. van Abel D, Michel O, Veerhuis R, Jacobs M, van Dijk M, Oudejans CB. Direct downregulation of CNTNAP2 by STOX1A is associated with Alzheimer's disease. J Alzheimers Dis. 2012;31(4):793-800. doi:10.3233/JAD-2012-120472

329. Ibarreta D, Tao J, Parrilla R, Ayuso MS. Mutation analysis of chromosome 19 calmodulin (CALM3) gene in Alzheimer's disease patients. Neurosci Lett. 1997;229(3):157-160. doi:10.1016/s0304-3940(97)00453-9

330. Popova SN, Alafuzoff I. Distribution of SLC10A4, a synaptic vesicle protein in the human brain, and the association of this protein with Alzheimer's disease-related neuronal degeneration. J Alzheimers Dis. 2013;37(3):603-610. doi:10.3233/JAD-130548

331. Mody N, Agouni A, McIlroy GD, Platt B, Delibegovic M. Susceptibility to diet-induced obesity and glucose intolerance in the APP (SWE)/PSEN1 (A246E) mouse model of Alzheimer's disease is associated with increased brain levels of protein tyrosine phosphatase 1B (PTP1B) and

retinol-binding protein 4 (RBP4), and basal phosphorylation of S6 ribosomal protein. Diabetologia. 2011;54(8):2143-2151. doi:10.1007/s00125-011-2160-2

332. Ashraf A, Ashton NJ, Chatterjee P, Goozee K, Shen K, Fripp J, Ames D, Rowe C, Masters CL, Villemagne V, et al. Plasma transferrin and hemopexin are associated with altered Aβ uptake and cognitive decline in Alzheimer's disease pathology. Alzheimers Res Ther. 2020;12(1):72. doi:10.1186/s13195-020-00634-1

333. Koppel J, Campagne F, Vingtdeux V, Dreses-Werringloer U, Ewers M, Rujescu D, Hampel H, Gordon ML, Christen E, Chapuis J, et al. CALHM1 P86L polymorphism modulates CSF Aβ levels in cognitively healthy individuals at risk for Alzheimer's disease. Mol Med. 2011;17(9-10):974-979. doi:10.2119/molmed.2011.00154

334. Sanfilippo C, Musumeci G, Kazakova M, Mazzone V, Castrogiovanni P, Imbesi R, Di Rosa M. GNG13 Is a Potential Marker of the State of Health of Alzheimer's Disease Patients' Cerebellum. J Mol Neurosci. 2021;71(5):1046-1060. doi:10.1007/s12031-020-01726-1

335. Lananna BV, McKee CA, King MW, Del-Aguila JL, Dimitry JM, Farias FHG, Nadarajah CJ, Xiong DD, Guo C, Cammack AJ, et al. Chi3l1/YKL-40 is controlled by the astrocyte circadian clock and regulates neuroinflammation and Alzheimer's disease pathogenesis. Sci Transl Med. 2020;12(574):eaax3519. doi:10.1126/scitranslmed.aax3519

336. Wang P, Li XL, Cao ZH. STC1 ameliorates cognitive impairment and neuroinflammation of Alzheimer's disease mice via inhibition of ERK1/2 pathway. Immunobiology. 2021;226(3):152092. doi:10.1016/j.imbio.2021.152092

337. Trojan E, Tylek K, Schröder N, Kahl I, Brandenburg LO, Mastromarino M, Leopoldo M, Basta-Kaim A, Lacivita E. The N-Formyl Peptide Receptor 2 (FPR2) Agonist MR-39 Improves Ex Vivo and In Vivo Amyloid Beta (1-42)-Induced Neuroinflammation in Mouse Models of Alzheimer's Disease. Mol Neurobiol. 2021;58(12):6203-6221. doi:10.1007/s12035-021-02543-2

338. Leri M, Chaudhary H, Iashchishyn IA, Pansieri J, Svedružić ŽM, Gómez Alcalde S, Musteikyte G, Smirnovas V, Stefani M, Bucciantini M, et al. Natural Compound from Olive Oil Inhibits S100A9 Amyloid Formation

and Cytotoxicity: Implications for Preventing Alzheimer's Disease. ACS Chem Neurosci. 2021;12(11):1905-1918. doi:10.1021/acschemneuro.0c00828

339. Li T, Zhu J. Entanglement of CCR5 and Alzheimer's Disease. Front Aging Neurosci. 2019;11:209. doi:10.3389/fnagi.2019.00209

340. Zhang DF, Fan Y, Xu M, Wang G, Wang D, Li J, Kong LL, Zhou H, Luo R, Bi R, et al. Complement C7 is a novel risk gene for Alzheimer's disease in Han Chinese. Natl Sci Rev. 2019;6(2):257-274. doi:10.1093/nsr/nwy127

341. Hilgeroth A, Tell V, Kramer S, Totzke F, Schachtele C. Approaches to a multitargeting drug development: first profiled 3- ethoxycarbonyl-1-aza-9-oxafluorenes representing a perspective compound class targeting Alzheimer disease relevant kinases CDK1, CDK5 and GSK-3β. Med Chem. 2014;10(1):90-97. doi:10.2174/15734064100113122614160 6

342. Zhao LJ, Wang ZT, Ma YH, Zhang W, Dong Q, Yu JT, Tan L. Associations of the cerebrospinal fluid hepatocyte growth factor with Alzheimer's disease pathology and cognitive function. BMC Neurol. 2021;21(1):387. doi:10.1186/s12883-021-02356-9

343. Herrera-Rivero M, Santarelli F, Brosseron F, Kummer MP, Heneka MT. Dysregulation of TLR5 and TAM Ligands in the Alzheimer's Brain as Contributors to Disease Progression. Mol Neurobiol. 2019;56(9):6539-6550. doi:10.1007/s12035-019-1540-3

344. Piazza F, Galimberti G, Conti E, Isella V, Perlangeli MV, Speranza T, Borroni B, Pogliani EM, Padovani A, Ferrarese C. Increased tissue factor pathway inhibitor and homocysteine in Alzheimer's disease. Neurobiol Aging. 2012;33(2):226-233. doi:10.1016/j.neurobiolaging.2010.02.016

345. Zhang W, Wang LZ, Yu JT, Chi ZF, Tan L. Increased expressions of TLR2 and TLR4 on peripheral blood mononuclear cells from patients with Alzheimer's disease. J Neurol Sci. 2012;315(1-2):67-71. doi:10.1016/j.jns.2011.11.032

346. Rasmussen KL, Nordestgaard BG, Frikke-Schmidt R, Nielsen SF. An updated Alzheimer hypothesis: Complement C3 and risk of Alzheimer's disease-A cohort study of 95,442 individuals. Alzheimers Dement. 2018;14(12):1589-1601. doi:10.1016/j.jalz.2018.07.223

347. Lashkari K, Teague G, Chen H, Lin YQ, Kumar S, McLaughlin MM, López FJ. A monoclonal antibody targeting amyloid β (Aβ) restores complement factor I bioactivity: Potential implications in age-related macular degeneration and Alzheimer's disease. PLoS One. 2018;13(5):e0195751. doi:10.1371/journal.pone.0195751

348. Manev H, Manev R. 5-Lipoxygenase (ALOX5) and FLAP (ALOX5AP) gene polymorphisms as factors in vascular pathology and Alzheimer's disease. Med Hypotheses. 2006;66(3):501-503. doi:10.1016/j.mehy.2005.09.031

349. Corsi MM, Licastro F, Porcellini E, Dogliotti G, Galliera E, Lamont JL, Innocenzi PJ, Fitzgerald SP. Reduced plasma levels of P-selectin and L-selectin in a pilot study from Alzheimer disease: relationship with neuro-degeneration. Biogerontology. 2011;12(5):451-454. doi:10.1007/s10522-011-9335-6

350. Aminyavari S, Zahmatkesh M, Khodagholi F, Sanati M. Anxiolytic impact of Apelin-13 in a rat model of Alzheimer's disease: Involvement of glucocorticoid receptor and FKBP5. Peptides. 2019;118:170102. doi:10.1016/j.peptides.2019.170102

351. Kajiwara Y, McKenzie A, Dorr N, Gama Sosa MA, Elder G, Schmeidler J, Dickstein DL, Bozdagi O, Zhang B, Buxbaum JD. The human-specific CASP4 gene product contributes to Alzheimer-related synaptic and behavioural deficits. Hum Mol Genet. 2016;25(19):4315-4327. doi:10.1093/hmg/ddw265

352. Schweig JE, Yao H, Beaulieu-Abdelahad D, Ait-Ghezala G, Mouzon B, Crawford F, Mullan M, Paris D. Alzheimer's disease pathological lesions activate the spleen tyrosine kinase. Acta Neuropathol Commun. 2017;5(1):69. doi:10.1186/s40478-017-0472-2

353. Larrick JW, Mendelsohn AR. Modulation of cGAS-STING Pathway by Nicotinamide Riboside in Alzheimer's Disease. Rejuvenation Res. 2021;24(5):397-402. doi:10.1089/rej.2021.0062

354. Yamamoto A, Suzuki T, Sakaki Y. Isolation of hNap1BP which interacts with human Nap1 (NCKAP1) whose expression is down-regulated in Alzheimer's disease. Gene. 2001;271(2):159-169. doi:10.1016/s0378-1119(01)00521-2

355. Manocha GD, Ghatak A, Puig KL, Kraner SD, Norris CM, Combs CK. NFATc2 Modulates Microglial Activation in the AβPP/PS1 Mouse Model of Alzheimer's Disease. J Alzheimers Dis. 2017;58(3):775-787. doi:10.3233/JAD-151203

356. Bigalke B, Schreitmüller B, Sopova K, Paul A, Stransky E, Gawaz M, Stellos K, Laske C. Adipocytokines and CD34 progenitor cells in Alzheimer's disease. PLoS One. 2011;6(5):e20286. doi:10.1371/journal.pone.0020286

357. Aichholzer F, Klafki HW, Ogorek I, Vogelgsang J, Wiltfang J, Scherbaum N, Weggen S, Wirths O. Evaluation of cerebrospinal fluid glycoprotein NMB (GPNMB) as a potential biomarker for Alzheimer's disease. Alzheimers Res Ther. 2021;13(1):94. doi:10.1186/s13195-021-00828-1

358. Baumann K, Mandelkow EM, Biernat J, Piwnica-Worms H, Mandelkow E. Abnormal Alzheimer-like phosphorylation of tau-protein by cyclin-dependent kinases cdk2 and cdk5. FEBS Lett. 1993;336(3):417-424. doi:10.1016/0014-5793(93)80849-p

359. Burgaletto C, Platania CBM, Di Benedetto G, Munafò A, Giurdanella G, Federico C, Caltabiano R, Saccone S, Conti F, Bernardini R, et al. Targeting the miRNA-155/TNFSF10 network restrains inflammatory response in the retina in a mouse model of Alzheimer's disease. Cell Death Dis. 2021;12(10):905. doi:10.1038/s41419-021-04165-x

360. Keaney J, Gasser J, Gillet G, Scholz D, Kadiu I. Inhibition of Bruton's Tyrosine Kinase Modulates Microglial Phagocytosis: Therapeutic Implications for Alzheimer's Disease. J Neuroimmune Pharmacol. 2019;14(3):448-461. doi:10.1007/s11481-019-09839-0

361. Chhetri J, King AE, Gueven N. Alzheimer's Disease and NQO1: Is there a Link?. Curr Alzheimer Res. 2018;15(1):56-66. doi:10.2174/1567205014666170203095802

362. Lemere CA, Munger JS, Shi GP, Natkin L, Haass C, Chapman HA, Selkoe DJ. The lysosomal cysteine protease, cathepsin S, is increased in Alzheimer's disease and Down syndrome brain. An immunocytochemical study. Am J Pathol. 1995;146(4):848-860.

363. Lin YS, Lin FY, Hsiao YH. Myostatin Is Associated With Cognitive Decline in an Animal Model of Alzheimer's Disease. Mol Neurobiol. 2019;56(3):1984-1991. doi:10.1007/s12035-018-1201-y

364. Hur JY. Innate Immunity Protein IFITM3 in Alzheimer's Disease. DNA Cell Biol. 2021;40(11):1351-1355. doi:10.1089/dna.2021.0585

365. Cimino PJ, Yang Y, Li X, Hemingway JF, Cherne MK, Khademi SB, Fukui Y, Montine KS, Montine TJ, Keene CD. Ablation of the microglial protein DOCK2 reduces amyloid burden in a mouse model of Alzheimer's disease. Exp Mol Pathol. 2013;94(2):366-371. doi:10.1016/j.yexmp.2013.01.002

366. Baron BW, Pytel P. Expression Pattern of the BCL6 and ITM2B Proteins in Normal Human Brains and in Alzheimer Disease. Appl Immunohistochem Mol Morphol. 2017;25(7):489-496. doi:10.1097/PAI.0000000000000329

367. Lee JY, Han SH, Park MH, Baek B, Song IS, Choi MK, Takuwa Y, Ryu H, Kim SH, He X, et al. Neuronal SphK1 acetylates COX2 and contributes to pathogenesis in a model of Alzheimer's Disease. Nat Commun. 2018;9(1):1479. doi:10.1038/s41467-018-03674-2

368. Zhang X, Zhu C, Beecham G, Vardarajan BN, Ma Y, Lancour D, Farrell JJ, Chung J. A rare missense variant of CASP7 is associated with familial late-onset Alzheimer's disease. Alzheimers Dement. 2019;15(3):441-452. doi:10.1016/j.jalz.2018.10.005

369. Lu G, Liu W, Huang X, Zhao Y. Complement factor H levels are decreased and correlated with serum C-reactive protein in late-onset Alzheimer's disease. Arq Neuropsiquiatr. 2020;78(2):76-80. doi:10.1590/0004-282X20190151

370. Xu M, Zhang DF, Luo R, Wu Y, Zhou H, Kong LL, Bi R, Yao YG.A systematic integrated analysis of brain expression profiles reveals YAP1 and other prioritized hub genes as important upstream regulators in Alzheimer's disease. Alzheimers Dement. 2018;14(2):215-229. doi:10.1016/j.jalz.2017.08.012

371. Fessel J. If ineffective levels of transforming growth factors and their receptor account for old age being a risk factor for Alzheimer's disease, then increasing TGFBR2 might be therapeutic. Alzheimers Dement (N Y). 2020;6(1):e12019. doi:10.1002/trc2.12019

372. Islam MI, Nagakannan P, Ogungbola O, Djordjevic J, Albensi BC, Eftekharpour E. Thioredoxin system as a gatekeeper in caspase-6 activation and nuclear lamina integrity: Implications for Alzheimer's disease. Free Radic Biol Med. 2019;134:567-580. doi:10.1016/j.freeradbiomed.2019.02.010

373. Rangasamy SB, Jana M, Roy A, Corbett GT, Kundu M, Chandra S, Mondal S, Dasarathi S, Mufson EJ, Mishra RK, et al. Selective disruption of TLR2-MyD88 interaction inhibits inflammation and attenuates Alzheimer's pathology. J Clin Invest. 2018;128(10):4297-4312. doi:10.1172/JCI96209

374. Xu Y, Cheng L, Sun J, Li F, Liu X, Wei Y, Han M, Zhu Z, Bi J, Lai C, et al. Hypermethylation of Mitochondrial Cytochrome b and Cytochrome c Oxidase II Genes with Decreased Mitochondrial DNA Copy Numbers in the APP/PS1 Transgenic Mouse Model of Alzheimer's Disease. Neurochem Res. 2021;46(3):564-572. doi:10.1007/s11064-020-03192-y

375. Counts SE, Mufson EJ. Regulator of Cell Cycle (RGCC) Expression During the Progression of Alzheimer's Disease. Cell Transplant. 2017;26(4):693-702. doi:10.3727/096368916X694184

376. Pons V, Lévesque P, Plante MM, Rivest S. Conditional genetic deletion of CSF1 receptor in microglia ameliorates the physiopathology of Alzheimer's disease. Alzheimers Res Ther. 2021;13(1):8. doi:10.1186/s13195-020-00747-7

377. Zhang Y, Xu C, Nan Y, Nan S. Microglia-Derived Extracellular Vesicles Carrying miR-711 Alleviate Neurodegeneration in a Murine Alzheimer's Disease Model by Binding to Itpkb. Front Cell Dev Biol. 2020;8:566530. doi:10.3389/fcell.2020.566530

378. Camacho J, Rábano A, Marazuela P, Bonaterra-Pastra A, Serna G, Moliné T, Ramón Y Cajal S, Martínez-Sáez E, Hernández-Guillamon M. Association of CD2AP neuronal deposits with Braak neurofibrillary stage in Alzheimer's disease. Brain Pathol. 2022;32(1):e13016. doi:10.1111/bpa.13016

379. González-Mundo I, Pérez-Vielma NM, Gómez-López M, Fleury A, Correa-Basurto J, Rosales-Hernández MC, Sixto-López Y, Martínez-Godinez MLÁ, Domínguez-López A, Miliar-García A. DNA methylation of the RE-1 silencing transcription factor in peripheral blood mononuclear cells and gene expression of antioxidant enzyme in patients with late-onset

Alzheimer disease. Exp Gerontol. 2020;136:110951. doi:10.1016/j.exger.2020.110951

380. Wang Z, Xu Q, Cai F, Liu X, Wu Y, Song W. BACE2, a conditional β-secretase, contributes to Alzheimer's disease pathogenesis. JCI Insight. 2019;4(1):e123431. doi:10.1172/jci.insight.123431

381. Byrne LM, Rodrigues FB, Johnson EB, De Vita E, Blennow K, Scahill R, Zetterberg H, Heslegrave A, Wild EJ. Cerebrospinal fluid neurogranin and TREM2 in Huntington's disease. Sci Rep. 2018;8(1):4260. doi:10.1038/s41598-018-21788-x

382. Lee J, Hwang YJ, Shin JY, Lee WC, Wie J, Kim KY, Lee MY, Hwang D, Ratan RR, Pae AN, et al. Epigenetic regulation of cholinergic receptor M1 (CHRM1) by histone H3K9me3 impairs Ca(2+) signaling in Huntington's disease. Acta Neuropathol. 2013;125(5):727-739. doi:10.1007/s00401-013-1103-z

383. Hays SE, Goodwin FK, Paul SM. Cholecystokinin receptors are decreased in basal ganglia and cerebral cortex of Huntington's disease. Brain Res. 1981;225(2):452-456. doi:10.1016/0006-8993(81)90853-2

384. Rudinskiy N, Kaneko YA, Beesen AA, Gokce O, Régulier E, Déglon N, Luthi-Carter R. Diminished hippocalcin expression in Huntington's disease brain does not account for increased striatal neuron vulnerability as assessed in primary neurons. J Neurochem. 2009;111(2):460-472. doi:10.1111/j.1471-4159.2009.06344.x

385. Subbarayan MS, Joly-Amado A, Bickford PC, Nash KR. CX3CL1/CX3CR1 signaling targets for the treatment of neurodegenerative diseases. Pharmacol Ther. 2021;107989. doi:10.1016/j.pharmthera.2021.107989

386. Carnemolla A, Michelazzi S, Agostoni E. PIN1 Modulates Huntingtin Levels and Aggregate Accumulation: An In vitro Model. Front Cell Neurosci. 2017;11:121. doi:10.3389/fncel.2017.00121

387. Cherubini M, Puigdellívol M, Alberch J, Ginés S. Cdk5-mediated mitochondrial fission: A key player in dopaminergic toxicity in Huntington's disease. Biochim Biophys Acta. 2015;1852(10 Pt A):2145-2160. doi:10.1016/j.bbadis.2015.06.025

388. Wang H, Del Mar N, Deng Y, Reiner A. Rescue of BDNF expression by the thalamic parafascicular nucleus with chronic treatment with the

mGluR2/3 agonist LY379268 may contribute to the LY379268 rescue of enkephalinergic striatal projection neurons in R6/2 Huntington's disease mice. Neurosci Lett. 2021;763:136180. doi:10.1016/j.neulet.2021.136180

389. Goto S, Hirano A. Synaptophysin expression in the striatum in Huntington's disease. Acta Neuropathol. 1990;80(1):88-91. doi:10.1007/BF00294227

390. Bertoglio D, Verhaeghe J, Wyffels L, Miranda A, Stroobants S, Mrzljak L, Dominguez C, Skinbjerg M, Bard J, Liu L, et al. Synaptic vesicle glycoprotein 2A is affected in the CNS of Huntington's Disease mice and post-mortem human HD brain. J Nucl Med. 2021;jnumed.121.262709. doi:10.2967/jnumed.121.262709

391. Griffioen K, Mattson MP, Okun E. Deficiency of Toll-like receptors 2, 3 or 4 extends life expectancy in Huntington's disease mice. Heliyon. 2018;4(1):e00508. doi:10.1016/j.heliyon.2018.e00508

392. Larkin PB, Muchowski PJ. Genetic Deficiency of Complement Component 3 Does Not Alter Disease Progression in a Mouse Model of Huntington's Disease. J Huntingtons Dis. 2012;1(1):107-118. doi:10.3233/JHD-2012-120021

393. Bailus BJ, Scheeler SM, Simons J, Sanchez MA, Tshilenge KT, Creus-Muncunill J, Naphade S, Lopez-Ramirez A, Zhang N, Lakshika Madushani K, et al. Modulating FKBP5/FKBP51 and autophagy lowers HTT (huntingtin) levels. Autophagy. 2021;17(12):4119-4140. doi:10.1080/15548627.2021.1904489

394. Sharma M, Rajendrarao S, Shahani N, Ramírez-Jarquín UN, Subramaniam S. Cyclic GMP-AMP synthase promotes the inflammatory and autophagy responses in Huntington disease. Proc Natl Acad Sci U S A. 2020;117(27):15989-15999. doi:10.1073/pnas.2002144117

395. Bondulich MK, Jolinon N, Osborne GF, Smith EJ, Rattray I, Neueder A, Sathasivam K, Ahmed M, Ali N, Benjamin AC, et al. Myostatin inhibition prevents skeletal muscle pathophysiology in Huntington's disease mice. Sci Rep. 2017;7(1):14275. Published 2017 Oct 27. doi:10.1038/s41598-017-14290-3

396. Wong BKY, Ehrnhoefer DE, Graham RK, Martin DDO, Ladha S, Uribe V, Stanek LM, Franciosi S, Qiu X, Deng Y, et al. Partial rescue of some features of Huntington Disease in the genetic absence of caspase-6 in

YAC128 mice. Neurobiol Dis. 2015;76:24-36. doi:10.1016/j.nbd.2014.12.030

397. Orozco-Díaz R, Sánchez-Álvarez A, Hernández-Hernández JM, Tapia-Ramírez J. The interaction between RE1-silencing transcription factor (REST) and heat shock protein 90 as new therapeutic target against Huntington's disease. PLoS One. 2019;14(7):e0220393. doi:10.1371/journal.pone.0220393

398. Picó S, Parras A, Santos-Galindo M, Pose-Utrilla J, Castro M, Fraga E, Hernández IH, Elorza A, Anta H, Wang N, et al. CPEB alteration and aberrant transcriptome-polyadenylation lead to a treatable SLC19A3 deficiency in Huntington's disease. Sci Transl Med. 2021;13(613):eabe7104. doi:10.1126/scitranslmed.abe7104

399. Sferra A, Fattori F, Rizza T, Flex E, Bellacchio E, Bruselles A, Petrini S, Cecchetti S, Teson M, Restaldi F, et al. Defective kinesin binding of TUBB2A causes progressive spastic ataxia syndrome resembling sacsinopathy. Hum Mol Genet. 2018;27(11):1892-1904. doi:10.1093/hmg/ddy096

400. Cheng C, Hou Y, Zhang Z, Wang Y, Lu L, Zhang L, Jiang P, Gao S, Fang Q, Zhu C, et al. Disruption of the autism-related gene Pak1 causes stereocilia disorganization, hair cell loss, and deafness in mice. J Genet Genomics. 2021;48(4):324-332. doi:10.1016/j.jgg.2021.03.010

401. Verbeek DS, Knight MA, Harmison GG, Fischbeck KH, Howell BW. Protein kinase C gamma mutations in spinocerebellar ataxia 14 increase kinase activity and alter membrane targeting. Brain. 2005;128(Pt 2):436-442. doi:10.1093/brain/awh378

402. Coutelier M, Blesneac I, Monteil A, Monin ML, Ando K, Mundwiller E, Brusco A, Le Ber I, Anheim M, Castrioto A, A Recurrent Mutation in CACNA1G Alters Cav3.1 T-Type Calcium-Channel Conduction and Causes Autosomal-Dominant Cerebellar Ataxia. Am J Hum Genet. 2015;97(5):726-737. doi:10.1016/j.ajhg.2015.09.007

403. Garcez D, Marques J, Fernandes M, Coimbra MF, Lourenço MC, Machado D, Freire J. ATP1A3: an unusual antigen to consider in patients with subacute ataxia and vertical gaze palsy. Mult Scler Relat Disord. 2020;43:102160. doi:10.1016/j.msard.2020.102160

404. Al Dhaibani MA, El-Hattab AW, Holroyd KB, Orthmann-Murphy J, Larson VA, Siddiqui KA, Szolics M, Schiess N.Novel mutation in the KCNJ10 gene in three siblings with seizures, ataxia and no electrolyte abnormalities. J Neurogenet. 2018;32(1):1-5. doi:10.1080/01677063.2017.1404057

405. Al-Eitan LN, Al-Dalalah IM, Aljamal HA. Effects of GRM4, SCN2A and SCN3B polymorphisms on antiepileptic drugs responsiveness and epilepsy susceptibility. Saudi Pharm J. 2019;27(5):731-737. doi:10.1016/j.jsps.2019.04.009

406. Gecz J, Thomas PQ. Disentangling the paradox of the PCDH19 clustering epilepsy, a disorder of cellular mosaics. Curr Opin Genet Dev. 2020;65:169-175. doi:10.1016/j.gde.2020.06.012

407. Friedman JI, Vrijenhoek T, Markx S, Janssen IM, van der Vliet WA, Faas BH, Knoers NV, Cahn W, Kahn RS, Edelmann L, et al. CNTNAP2 gene dosage variation is associated with schizophrenia and epilepsy. Mol Psychiatry. 2008;13(3):261-266. doi:10.1038/sj.mp.4002049

408. Stamberger H, Nikanorova M, Willemsen MH, Accorsi P, Angriman M, Baier H, Benkel-Herrenbrueck I, Benoit V, Budetta M, Caliebe A, et al. STXBP1 encephalopathy: A neurodevelopmental disorder including epilepsy. Neurology. 2016;86(10):954-962. doi:10.1212/WNL.0000000000002457

409. Cadieux-Dion M, Meneghini S, Villa C, Toffa DH, Wickstrom R, Bouthillier A, Sandvik U, Gustavsson B, Mohamed I, Cossette P, et al. Variants in CHRNB2 and CHRNA4 Identified in Patients with Insular Epilepsy. Can J Neurol Sci. 2020;47(6):800-809. doi:10.1017/cjn.2020.126

410. Xi Z, Deng W, Wang L, Xiao F, Li J, Wang Z, Wang X, Mi X, Wang N, Wang X. Association of Alpha-Soluble NSF Attachment Protein with Epileptic Seizure. J Mol Neurosci. 2015;57(3):417-425. doi:10.1007/s12031-015-0596-4

411. Wang S, Zhou L, He C, Wang D, Cai X, Yu Y, Chen L, Lu D, Bian L, Du S, et al. The Association Between STX1B Polymorphisms and Treatment Response in Patients With Epilepsy. Front Pharmacol. 2021;12:701575.doi:10.3389/fphar.2021.701575

412. Kang JQ, Macdonald RL. Molecular Pathogenic Basis for GABRG2 Mutations Associated With a Spectrum of Epilepsy Syndromes, From

Generalized Absence Epilepsy to Dravet Syndrome. JAMA Neurol. 2016;73(8):1009-1016. doi:10.1001/jamaneurol.2016.0449

413. Friedman JI, Vrijenhoek T, Markx S, Janssen IM, van der Vliet WA, Faas BH, Knoers NV, Cahn W, Kahn RS, Edelmann L, et al. CNTNAP2 gene dosage variation is associated with schizophrenia and epilepsy. Mol Psychiatry. 2008;13(3):261-266. doi:10.1038/sj.mp.4002049

414. Kalscheuer VM, Musante L, Fang C, Hoffmann K, Fuchs C, Carta E, Deas E, Venkateswarlu K, Menzel C, Ullmann R, et al. A balanced chromosomal translocation disrupting ARHGEF9 is associated with epilepsy, anxiety, aggression, and mental retardation. Hum Mutat. 2009;30(1):61-68. doi:10.1002/humu.20814

415. Hallmann K, Kudin AP, Zsurka G, Kornblum C, Reimann J, Stüve B, Waltz S, Hattingen E, Thiele H, Nürnberg P, et al. Loss of the smallest subunit of cytochrome c oxidase, COX8A, causes Leigh-like syndrome and epilepsy. Brain. 2016;139(Pt 2):338-345. doi:10.1093/brain/awv357

416. Lv RJ, He JS, Fu YH, Shao XQ, Wu LW, Lu Q, Jin LR, Liu H.A polymorphism in CALHM1 is associated with temporal lobe epilepsy. Epilepsy Behav. 2011;20(4):681-685. doi:10.1016/j.yebeh.2011.02.007

417. Srour M, Shimokawa N, Hamdan FF, Nassif C, Poulin C, Al Gazali L, Rosenfeld JA, Koibuchi N, Rouleau GA, Al Shamsi A, et al. Dysfunction of the Cerebral Glucose Transporter SLC45A1 in Individuals with Intellectual Disability and Epilepsy. Am J Hum Genet. 2017;100(5):824-830. doi:10.1016/j.ajhg.2017.03.009

418. Zhao MW, Qiu WJ, Yang P. SP1 activated-lncRNA SNHG1 mediates the development of epilepsy via miR-154-5p/TLR5 axis. Epilepsy Res. 2020;168:106476. doi:10.1016/j.eplepsyres.2020.106476

419. Jiang C, Li L, Wu M, Hao M, Feng J. Association of KCNJ10 variants and the susceptibility to clinical epilepsy. Clin Neurol Neurosurg. 2021;200:106340. doi:10.1016/j.clineuro.2020.106340

420. Shao K, Shan S, Ru W, Ma C. Association between serum NPTX2 and cognitive function in patients with vascular dementia. Brain Behav. 2020;10(10):e01779. doi:10.1002/brb3.1779

421. Vallortigara J, Whitfield D, Quelch W, Alghamdi A, Howlett D, Hortobágyi T, Johnson M, Attems J, O'Brien JT, Thomas A, et al. Decreased Levels of VAMP2 and Monomeric Alpha-Synuclein Correlate with Duration

of Dementia. J Alzheimers Dis. 2016;50(1):101-110. doi:10.3233/JAD-150707

422. Cohn-Hokke PE, Wong TH, Rizzu P, Breedveld G, van der Flier WM, Scheltens P, Baas F, Heutink P, Meijers-Heijboer EJ, van Swieten JC, et al. Mutation frequency of PRKAR1B and the major familial dementia genes in a Dutch early onset dementia cohort. J Neurol. 2014;261(11):2085-2092. doi:10.1007/s00415-014-7456-y

423. Helbig I, Lopez-Hernandez T, Shor O, Galer P, Ganesan S, Pendziwiat M, Rademacher A, Ellis CA, Hümpfer N, Schwarz N, et al. A Recurrent Missense Variant in AP2M1 Impairs Clathrin-Mediated Endocytosis and Causes Developmental and Epileptic Encephalopathy. Am J Hum Genet. 2019;104(6):1060-1072. doi:10.1016/j.ajhg.2019.04.001

424. Mol MO, Wong TH, Melhem S, Basu S, Viscusi R, Galjart N, Rozemuller AJM, Fallini C, Landers JE, Kaat LD, et al. Novel TUBA4A Variant Associated With Familial Frontotemporal Dementia. Neurol Genet. 2021;7(3):e596. doi:10.1212/NXG.0000000000000596

425. Goldstein O, Gana-Weisz M, Shiner T, Attar R, Mordechai Y, Waldman YY, Bar-Shira A, Thaler A, Gurevich T, Mirelman A, et al. R869C mutation in molecular motor KIF17 gene is involved in dementia with Lewy bodies. Alzheimers Dement (Amst). 2021;13(1):e12143. doi:10.1002/dad2.12143

426. Kim Y, Kong M, Lee C. Association of intronic sequence variant in the gene encoding spleen tyrosine kinase with susceptibility to vascular dementia. World J Biol Psychiatry. 2013;14(3):220-226. doi:10.3109/15622975.2011.559272

427. Kumari R, Kumar R, Kumar S, Singh AK, Hanpude P, Jangir D, Maiti TK. Amyloid aggregates of the deubiquitinase OTUB1 are neurotoxic, suggesting that they contribute to the development of Parkinson's disease. J Biol Chem. 2020;295(11):3466-3484. doi:10.1074/jbc.RA119.009546

428. Miron J, Picard C, Labonté A, Auld D, Breitner J, Poirier J. Association of PPP2R1A with Alzheimer's disease and specific cognitive domains. Neurobiol Aging. 2019;81:234-243. doi:10.1016/j.neurobiolaging.2019.06.008

429. Groen K, Maltby VE, Scott RJ, Tajouri L, Lechner-Scott J. Erythrocyte microRNAs show biomarker potential and implicate multiple

sclerosis susceptibility genes. Clin Transl Med. 2020;10(1):74-90. doi:10.1002/ctm2.22

430. Wu YE, Parikshak NN, Belgard TG, Geschwind DH. Genome-wide, integrative analysis implicates microRNA dysregulation in autism spectrum disorder. Nat Neurosci. 2016;19(11):1463-1476. doi:10.1038/nn.4373

431. Kurzawski M, Białecka M, Sławek J, Kłodowska-Duda G, Droździk M. Association study of GATA-2 transcription factor gene (GATA2) polymorphism and Parkinson's disease. Parkinsonism Relat Disord. 2010;16(4):284-287. doi:10.1016/j.parkreldis.2009.10.006

432. Lou F, Li M, Liu N, Li X, Ren Y, Luo X. The polymorphism of SREBF1 gene rs11868035□G/A is associated with susceptibility to Parkinson's disease in a Chinese population. Int J Neurosci. 2019;129(7):660-665. doi:10.1080/00207454.2018.1526796

433. Yuan X, Cao B, Wu Y, Chen Y, Wei Q, Ou R, Yang J, Chen X, Zhao B, Song W, et al. Association analysis of SNP rs11868035 in SREBF1 with sporadic Parkinson's disease, sporadic amyotrophic lateral sclerosis and multiple system atrophy in a Chinese population. Neurosci Lett. 2018;664:128-132. doi:10.1016/j.neulet.2017.11.015

434. Yang L, Chen J, Li Y, Wang Y, Liang S, Shi Y, Shi S, Xu Y. ssociation between SCAP and SREBF1 gene polymorphisms and metabolic syndrome in schizophrenia patients treated with atypical antipsychotics. World J Biol Psychiatry. 2016;17(6):467-474. doi:10.3109/15622975.2016.1165865

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
LINC01164	1.333661	7.57E-05	0.004516	3.957733	Up	long intergenic non-protein coding RNA 1164
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
LINC01007	1.295971	0.000109	0.005643	3.870309	Up	long intergenic non-protein coding RNA 1007
LINC01844	1.21576	0.001892	0.032354	3.106686	Up	long intergenic non-protein coding RNA 1844
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
FAM163A	1.157978	0.000989	0.022033	3.293654	Up	family with sequence similarity 163 member A
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
LINC01511	1.12459	2.43E-05	0.002285	4.220911	Up	long intergenic non-protein coding RNA 1511
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
LINC02395	1.103745	0.001607	0.029425	3.154692	Up	long intergenic non-protein coding RNA 2395
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
LINC01166	1.089345	3.45E-06	0.000671	4.64193	Up	long intergenic non-protein coding RNA 1166
LINCR-0003	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	lipoxygenase 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 metallopeptidase 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	0.692895	0.000182	0.007858	3.742894	Up	stum, mechanosensory transduction mediator homolog
HIPK4	0.692477	0.003623	0.047557	2.90922	Up	homeodomain interacting protein kinase 4
RGS4	0.69105	0.00061	0.016083	3.42694	Up	regulator of G protein signaling 4
SEZ6	0.688386	3.64E-07	0.00013	5.086728	Up	seizure related 6 homolog
GUSBP5	0.687454	0.003388	0.045578	2.930135	Up	GUSB pseudogene 5
CACNB1	0.686313	8.13E-06	0.00113	4.461619	Up	calcium voltage-gated channel auxiliary subunit beta 1
H2AC21	0.685202	0.000306	0.011024	3.610526	Up	H2A clustered histone 21
NGEF	0.68419	4.76E-06	0.000799	4.575213	Up	neuronal guanine nucleotide exchange factor
DOC2A	0.684045	8.18E-05	0.004711	3.939051	Up	double C2 domain alpha
USP11	0.682506	2.28E-08	2.73E-05	5.58935	Up	ubiquitin specific peptidase 11
PLK2	0.679706	3.21E-05	0.002719	4.157774	Up	polo like kinase 2
TMEM121B	0.679167	8.25E-07	0.000244	4.929298	Up	transmembrane protein 121B
INTS5	0.677933	0.00138	0.026881	3.19882	Up	integrator complex subunit 5
SCN3B	0.676599	2.57E-06	0.000545	4.702124	Up	sodium voltage-gated channel beta subunit 3
CAMKV	0.676166	1.51E-06	0.000374	4.810257	Up	CaM kinase like vesicle associated
PLD3	0.675655	0.000307	0.011054	3.609378	Up	phospholipase D family member 3
CYS1	0.674066	0.001363	0.026672	3.202387	Up	cystin 1
NPM3	0.673765	0.000204	0.008482	3.713911	Up	nucleophosmin/nucleoplasmin 3
PER2	0.673499	3.02E-05	0.002625	4.171985	Up	period circadian regulator 2
EXTL1	0.672999	0.000845	0.020033	3.337759	Up	exostosin like glycosyltransferase 1
SMIM10L2A	0.672892	2.30E-05	0.002224	4.233981	Up	small integral membrane protein 10 like 2A
RNF165	0.672744	1.61E-09	6.14E-06	6.03323	Up	ring finger protein 165
SLC26A10	0.670661	0.001998	0.033378	3.090535	Up	solute carrier family 26 member 10
PYCR3	0.670446	0.001408	0.027164	3.193042	Up	pyrroline-5-carboxylate reductase 3
ECRG4	0.669705	0.001477	0.028041	3.179068	Up	ECRG4 augurin precursor
ZNF843	0.669329	0.002869	0.041444	2.9814	Up	zinc finger protein 843
IL1RL2	0.667346	0.002248	0.035946	3.055298	Up	interleukin 1 receptor like 2
NUAK1	0.666452	1.96E-07	9.17E-05	5.203046	Up	NUAK family kinase 1
LINGO1	0.665604	0.000345	0.011881	3.578594	Up	leucine rich repeat and Ig domain containing 1
OPN3	0.665526	0.000696	0.017674	3.391285	Up	opsin 3
FXYD7	0.664062	0.000433	0.013489	3.518977	Up	FXYD domain containing ion transport regulator 7
TIMM13	0.66333	0.001988	0.03328	3.091952	Up	translocase of inner mitochondrial membrane 13
TAGLN3	0.66322	0.000158	0.007185	3.778598	Up	transgelin 3
FAM83H	0.66238	0.002036	0.033747	3.084998	Up	family with sequence similarity 83 member H

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
SYP	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
KCNB2	0.6271	2.21E-05	0.002185	4.24216	Up	potassium voltage-gated channel subfamily B member 2
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 adenylyltransferase 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	neuritin 1
SV2A	0.623085	1.68E-05	0.001876	4.303091	Up	synaptic vesicle glycoprotein 2A
CAMK4	0.622566	0.000412	0.013274	3.532277	Up	calcium/calmodulin dependent protein kinase IV
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
PPP2R1A	0.613768	0.000244	0.009491	3.668319	Up	protein phosphatase 2 scaffold subunit Aalpha
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
CACNG3	0.611001	1.50E-05	0.001737	4.329255	Up	calcium voltage-gated channel auxiliary subunit gamma 3
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
FAM131A	0.600311	2.56E-05	0.002346	4.209238	Up	family with sequence similarity 131 member A
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
STAT4	0.575097	0.00093	0.021351	3.310765	Up	signal transducer and activator of 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
CHRNB2	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
AP2M1	0.540869	5.38E-05	0.003754	4.038527	Up	adaptor related protein complex 2 subunit mu 1
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
GABARAPL1	0.539014	0.000143	0.00676	3.803709	Up	GABA type A receptor associated protein like 1
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
FHIP1B	0.536474	5.91E-05	0.003973	4.016568	Up	FHF complex subunit HOOK interacting protein 1B
NAPA	0.536199	0.000601	0.015989	3.431062	Up	NSF attachment protein alpha
APBB3	0.536081	0.000835	0.019852	3.341	Up	amyloid beta precursor protein binding family B member 3
TIMM17B	0.53556	0.001665	0.029949	3.144235	Up	translocase of inner mitochondrial membrane 17B
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
TRAPPC1	0.528748	0.000639	0.016635	3.414474	Up	trafficking protein particle complex subunit 1
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
GPRASP2	0.527069	0.000166	0.007373	3.766433	Up	G protein-coupled receptor associated sorting protein 2
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, IMAP family member 4
NUPR1	-1.0891	1.52E-05	0.001755	-4.32604	Down	nuclear protein 1, transcriptional regulator
PI15	-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	ovochymase 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 metalloreductase
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
RNU4ATAC18P	-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
FAM89A	-0.87651	0.000121	0.006039	-3.8438	Down	family with sequence similarity 89 member A
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
GPNMB	-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 metallopeptidase 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
PARP14	-0.75925	1.40E-06	0.000356	-4.82559	Down	poly(ADP-ribose) polymerase family member 14
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 immuity 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
HMGN5	-0.73375	9.72E-05	0.005329	-3.89742	Down	high mobility group nucleosome binding domain 5
SNORA33	-0.73284	0.001137	0.02378	-3.25414	Down	small nucleolar RNA, H/ACA box 33
DDR2	-0.73248	4.71E-08	4.05E-05	-5.46193	Down	discoidin domain receptor tyrosine kinase 2
ND4	-0.73217	5.40E-05	0.003754	-4.0375	Down	NADH dehydrogenase subunit 4
TPD52L1	-0.73121	0.000604	0.015989	-3.42985	Down	TPD52 like 1
BCL6	-0.73109	4.32E-05	0.003272	-4.08959	Down	BCL6 transcription repressor
HERC5	-0.73092	5.37E-05	0.003754	-4.03884	Down	HECT and RLD domain containing E3 ubiquitin protein ligase 5
C4orf19	-0.73007	0.002764	0.040567	-2.99287	Down	chromosome 4 open reading frame 19
OAS2	-0.72924	0.000443	0.013604	-3.51305	Down	2'-5'-oligoadenylate synthetase 2
LRRC1	-0.72829	0.00123	0.025012	-3.23179	Down	leucine rich repeat containing 1
CCDC18	-0.72687	7.79E-06	0.001105	-4.47085	Down	coiled-coil domain containing 18
COX2	-0.72549	0.000143	0.00676	-3.80295	Down	cytochrome c oxidase subunit II
ATP11C	-0.72387	5.94E-07	0.000192	-4.99332	Down	ATPase phospholipid transporting 11C
WWTR1	-0.72365	6.23E-07	0.000192	-4.98389	Down	WW domain containing transcription regulator 1
GAU1	-0.72061	0.000796	0.019294	-3.35422	Down	GALNT8 antisense upstream 1
TES	-0.72036	0.002341	0.036779	-3.04323	Down	testin LIM domain protein
RFTN2	-0.72016	0.000254	0.009732	-3.65824	Down	raftlin family member 2
RPL23AP5	-0.71913	0.002909	0.041695	-2.97714	Down	ribosomal protein L23a pseudogene 5
TMEM45B	-0.7184	0.001649	0.029804	-3.14717	Down	transmembrane protein 45B
ND6	-0.71806	7.62E-05	0.004539	-3.95601	Down	NADH dehydrogenase subunit 6
RHOQ	-0.71729	1.01E-07	6.61E-05	-5.3249	Down	ras homolog family member Q
SLC5A9	-0.71634	0.000228	0.009147	-3.68531	Down	solute carrier family 5 member 9
CNTLN	-0.71557	1.14E-07	6.68E-05	-5.30262	Down	centlein
TRIM22	-0.71401	5.49E-05	0.003806	-4.03366	Down	tripartite motif containing 22
ND2	-0.71356	0.000101	0.005414	-3.88785	Down	NADH dehydrogenase subunit 2
HMGB3P4	-0.71193	0.002276	0.036075	-3.05162	Down	high mobility group box 3 pseudogene 4
CLDN18	-0.71128	0.001349	0.026519	-3.20527	Down	claudin 18
DSE	-0.70878	8.41E-08	5.93E-05	-5.35821	Down	dermatan sulfate epimerase
NLRC5	-0.70809	0.003005	0.042411	-2.96723	Down	NLR family CARD domain containing 5
CASP7	-0.70804	0.000326	0.011469	-3.5934	Down	caspase 7
MMRN2	-0.7073	0.001322	0.02615	-3.21117	Down	multimerin 2
LRRC69	-0.70545	0.003532	0.046818	-2.91715	Down	leucine rich repeat containing 69
RELL1	-0.7032	8.58E-05	0.00488	-3.9275	Down	RELT like 1
NSUN7	-0.70027	0.001059	0.022812	-3.27443	Down	NOP2/Sun RNA methyltransferase family member 7
ARHGDIB	-0.69836	0.002304	0.036366	-3.048	Down	Rho GDP dissociation inhibitor beta
CFH	-0.69765	0.003441	0.046103	-2.92528	Down	complement factor H
MYL12A	-0.69462	4.86E-06	0.000811	-4.57064	Down	myosin light chain 12A
ERBIN	-0.69442	0.000715	0.017971	-3.38388	Down	erbb2 interacting protein

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
FXYD3	-0.68949	0.001038	0.02264	-3.27999	Down	FXYD domain containing ion transport regulator 3
GIMAP5	-0.68807	0.00057	0.015579	-3.44569	Down	GTPase, IMAP 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, IMAP 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
SYNE2	-0.62484	7.58E-06	0.001092	-4.47673	Down	spectrin repeat containing nuclear envelope protein 2
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,CHRNA7,NRGN,CHRM1,TUBB2A,OVOL2,SPINT2,EFNB3,CCK,HPCA,CDK5R2,ADAMTSL1,CPNE6,MAL2,KCNK3,SEZ6L2,IL1RAPL2,SLC6A17,INSM1,WNT10B,PCDHAC2,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,ENC1,VSTM5,NRSN2,CNTNAP2,CAMK1,ETV5,CALM3,SLC12A5,PIN1,NECTIN1,GAS7,NDN,NTNG1,RAB3A,KATNB1,STXBP1,SLC8A3,CHRNB2,RND1,SLC17A7,NAPA,NELL1,RET,UNC13A,NME1,STX1B,CDK5,SNRPB,HTR5A,HPCAL4,ACTL6B,NREP,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,PCSK1,FCRLB,SCN5A,IGFBP2,RHOV,HTR2C,TAMALIN,SPRED3,RBP4,FFAR4,RTN4R,ADTRP,SLC32A1,NNAT,ADRA1D,PPEF1,CHRNA7,MCHR2,GJD2,PLPPR3,MAP1LC3A,HPX,REM2,STX1A,NRGN,RPH3A,CHRM4,CHRM1,MUC6,GRM2,SYT5,BAIAP3,OPRL1,OVOL2,LBH,EFNB3,CCK,DIRAS1,ERFE,HPCA,TRIM54,GNG13,SLC1A6,CPNE6,ARHGDIG,RASL10A,KCNK3,SEZ6L2,IL1RAPL2,WNT10B,NPTX2,SYT13,SLC8A2,GPR88,NSG2,NPTXR,HIPK4,RGS4,SEZ6,CACNB1,NGEF,DOC2A,PLK2,SCN3B,PER2,EXTL1,RNF165,IL1RL2,NUAK1,FAM83H,CAMKK2,RHBDD2,CLSTN3,LZTS1,SYT12,PAK6,DCTPP1,SPRYD3,KCNIP3,SYP,ATP6V0E2,PAK1,SCN2B,CORO1A,PCDH1,TRIM67,DLK2,ADGRB2,RHOBTB2,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,GNG4,CNTNAP2,CAMK1,STAT4,CALM3,SLC12A5,PIN1,CDH8,PTPRN,HINT1,PIM2,H4C3,NDN,TSPYL5,CAP2,SYNGR1,DMTN,NTNG1,CRY2,SNCB,RAB3A,STXBP1,SLC8A3,KLHDC3,CHRNB2,RND1,AP2M1,ATP6AP1,GABARAPL1,PSMB5,SLC17A7,NAPA,ARHGEF9,FIBP,RET,NEURL1B,UNC13A,XK,STX1B,CDK5,HTR5A,HPCAL4,TSHZ3,MAST3,NREP,TMEM9,GABRG2,DLG3,ADGRA1,CITED2
GO:0030054	CC	cell junction	7.04E-16	15.15260462	105	PNOC,MYLK2,GNG3,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,STXBP1,SLC8A3,CHRNB2,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,GNG3,SLC30A3,WNT1,TMEM200B,RGS8,CALY,CCKBR,DUSP2,HTR3B,KLHL14,ARC,ARL4D,NPBWR2,KCNF1,NCALD,RHEBL1,FAM241B,SPEF1,GABRD,MUC5B,CACNA1G,NOXA1,LRTM2,PCSK1,FCRLB,SCN5A,IGFBP2,RHOV,HTR2C,SLC10A4,PRSS16,TAMALIN,SPRED3,CTXN1,SLC22A6,TPBGL,FFAR4,TRBC2,RTN4R,ICAM5,ADTRP,SLC32A1,PCDHGC5,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,IL1RAPL2,SLC6A17,SLC22A24,DNAJC5G,SLC6A7,SYT13,PCDHAC2,CDH22,SLC45A1,SLC8A2,PRMT8,GPR88,IGSF3,TUBA1B,MARCHF4,NSG2,NPTXR,STUM,RGS4,SEZ6,CACNB1,NGEF,DOC2A,INTS5,SCN3B,CAMKV,PLD3,CYS1,EXTL1,ECRG4,IL1RL2,LINGO1,FXYD7,TIMM13,RHBDD2,CLSTN3,LZTS1,SYT12,ENO2,KCNIP3,SYP,HPCAL1,ATP6V0E2,STOML1,IGSF8,PAK1,ST6GAL2,SCN2B,CORO1A,SYNGR3,PCDH1,PPP1R14C,DLK2,PIGZ,NRSN1,NAT14,ADGRB2,TMIE,RHOBTB2,TMEM38A,VAMP2,ATP1A3,NSG1,KCNB2,PTPN3,TENM2,PCDH19,NMNAT2,RIMS3,NRN1,SV2A,UNC5D,SHISAL1,ATP6V0B,C1ORF115,VIPR1,PPP2R1A,CACNG3,PRKCG,BFSP1,DNAL4,TRIB3,RAB40C,EMD,CX3CL1,PRKAR1B,VSTM5,NRSN2,PARM1,FNDC5,ADRA1B,NDUFA4,MICOS13,ATP6V1B2,CDH13,GNG4,EFR3B,CNTNAP2,GGT7,FLRT1,KIF17,RAB36,CALM3,SLC12A5,NIPSNAP1,ATP5MC1,C11ORF87,ARF3,ATP5F1B,CDH8,PTPRN,C3ORF80,PCDHGC4,SCAMP5,SYT16,HINT1,CYC1,YIF1B,NECTIN1,PGAP3,GAS7,H4C3,PODXL2,MELTF,CDIPT,CAP2,SYNGR1,AP1S1,DMTN,PIANP,PPOX,NTNG1,ASS1,RAB3A,B4GAT1,KATNB1,STXBP1,SLC8A3,CHRNB2,RND1,AP2M1,PTPN5,ATP6AP1,GABARAPL1,PPL,SLC17A7,NAPA,APBB3,TIMM17B,CPNE7,FIBP,RET,UNC13A,CD200,XK,NME1,STX1B,CDK5,HTR5A,PEF1,RUSF1,TSHZ3,TMEM178B,FAM234B,TMEM9,GABRG2,DLG3,CYRIA,ADGRA1,KCNS2
GO:0005215	MF	transporter activity	3.51636E-06	5.453906623	56	SLC30A3,HTR3B,KCNF1,GABRD,CACNA1G,SCN5A,SLC10A4,ADAMTS8,RBP4,SLC22A6,SLC32A1,SVOP,KCNH4,CHRNA7,GJD2,BEST4,HPX,ABCC11,ABCC12,SLC22A17,SLC1A6,CPNE6,COX8A,CALHM1,SLC7A4,KCNK3,SLC6A17,SLC22A24,SLC6A7,SLC45A1,SLC8A2,CACNB1,SCN3B,KCNIP3,ATP6V0E2,SCN2B,TMEM38A,ATP1A3,KCNB2,SV2A,ATP6V0B,CACNG3,NDUFA4,ATP6V1B2,SLC12A5,ATP5MC1,ATP5F1B,SLC8A3,CHRNB2,SLC17A7,TIMM17B,CPNE7,XK,CDK5,GABRG2,KCNS2
GO:0005515	MF	protein binding	0.03867521	1.412567324	331	EGR2,PNOC,EGR1,ATOH7,ASB2,H1-7,MYLK2,C1QTNF4,GNG3,IL11,SLC30A3,WNT1,RGS8,NXPH2,SPATA2L,MPO,CALY,CCKBR,DUSP2,CCDC184,KLHL14,ARC,ARL4D,NPBWR2,IGFN1,ADCYAP1,CCNO,SPAG6,KCNF1,NCALD,RHEBL1,FAM241B,CRYM,PNMA5,SPEF1,GABRD,MUC5B,OTOG

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,FXYD7,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,RHOBTB2,TMEM38A,VA
MP2,STMN3,ATP1A3,NSG1,KCN
B2,NLRP1,TUBA4A,PTPN3,TEN
M2,RIMS3,SV2A,CAMK4,COPS7
A,UNC5D,HR,SHISAL1,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,CHRNB
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,CFI,NIBAN1,CENPF,PIK3AP1,TRIM5,JAML,NUPR1,E2F7,FCGR2A,CYSLTR2,HORMAD1,ALOX5AP,S100A11,ADAMDEC1,LAMP3,P2RY6,FCER1G,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,SASH3,SP100,CLIC1,IKBIP,APBB1IP,OSMR,SLA,MT1E,PDK4,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,WWTR1,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,PLOD2,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,VIM,TSHR,XAF1,DDX58,TGFB3,SASH1,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

						PR2,S100A9,TLR8,KIF14,OR52B6,CDA,CCR5,TTK,NOD2,GBP1,GBP2,HPGD,S100A4,OR51B5,CD180,CDK1,SPP1,FCGR3A,DDIT4L,TFAP2C,TLR7,TNFRSF10D,FYB1,SCN4A,HGF,TRIP10,PPEF2,TLR5,TLR2,MNDA,PTPRC,LVRN,C3,INSL6,IL2RG,CENPF,PIK3AP1,TRIM5,NUPR1,E2F7,FCGR2A,CYSLTR2,HORMAD1,S100A11,P2RY6,FCER1G,MICB,IFI16,LAPTM5,CASP4,NMI,ALKAL2,IFNE,ADGRL4,SYK,CGAS,GLI1,LCP1,MT2A,IL17RB,GPR4,SPN,DTX3L,CYBB,TLR1,GABRE,SRGN,CELSR1,NCKAP1L,PARP9,TRIM38,SP100,CLIC1,APBB1IP,OSMR,SLA,PDK4,NFATC2,GNRH1,CD34,CCNA2,BRCA2,HCLS1,RAB13,PIK3CG,CSF3R,GPNMB,ITGB3,MAP3K8,PERP,CDK2,PTAFR,ORC1,YES1,NCF2,RASSF8,TNFSF10,ITGA10,BTK,PRKX,TRIM21,NQO1,FGF11,TEAD2,B2M,TRDN,SLC39A12,ADGRE2,ANXA2,FLT1,MECOM,TGFBR1,IRAK3,GNG11,DNA2,CTSS,SLC38A2,ARHGAP42,HHEX,ITGA1,GPR160,PARP14,NABP1,MSTN,RNF152,EVC2,FOXC1,IFITM3,DOCK2,NEDD4,MEFV,IFIH1,DDR2,TPD52L1,BCL6,OAS2,WWTR1,RHOQ,TRIM22,CLDN18,NLRC5,MMRN2,LRRC69,RELL1,ARHGDIB,ERBIN,BTNL9,YAP1,TGFBR2,DOK3,ACTL6A,PPP1R1C,LCP2,AKR1C3,MYD88,CHEK2,RHOJ,MLKL,NFKBIA,ARHGAP11A,ANO6,IL13RA1,IQGAP1,RGCC,ITGB8,TP53INP1,ITGB1,LPAR6,CSF1,ANXA5,KIF5B,ITPKB,PLSCR1,ANXA1,SUMO4,KCNJ10,SAMHD1,LEF1,NOSTRIN,ITGA8,MAML2,CLEC2D,CD2AP,REST,ELK3,PGR,VIM,TSHR,XAF1,DDX58,TGFB3,SASH1,LRP4,S1PR3,ZBED6
GO:0071944	CC	cell periphery	9.0448E-06	5.043601216	178	CEP55,MELK,VNN1,OR7A5,CHI3L1,OR7C1,STC1,ANGPT2,FPR2,S100A9,TLR8,MMRN1,SERPINA1,KIF14,KCNE4,OR52B6,CCR5,NOD2,VNN2,GBP1,SLC1A7,HPGD,C7,S100A4,OR51B5,MGAM,CD180,KIF20A,BOLL,FCGR3A,LAMB4,KCNJ15,AZGP1,HMMR,TLR7,PRRG4,TNFRSF10D,FYB1,SCN4A,TRIP10,TLR5,TFPI,TLR2,PTPRC,LVRN,C3,IL2RG,CLEC2B,NIBAN1,PIK3AP1,JAML,FCGR2A,CYSLTR2,ADAMDEC1,LAMP3,P2RY6,FCER1G,MICB,SELL,LAPTM5,CASP4,STEAP4,ADGRL4,SYK,CGAS,LCP1,LY75,IL17RB,GPR4,SPN,CALHM5,CYBB,TLR1,BACE2,GABRE,CELSR1,NCKAP1L,CLIC1,APBB1IP,OSMR,SLA,KCNJ16,CD34,HCLS1,RAB13,PIK3CG,GBP4,CSF3R,GPNMB,ITGB3,SLC7A2,ANXA3,PRELP,EMCN,PERP,COL27A1,PTAFR,LIPH,YES1,NCF2,CD58,NEXN,TNFSF10,IT

						GA10,BTK,B2M,TRDN,MYOF,SLC39A12,ADGRE2,ANXA2,ADAM28,FLT1,TGFBR1,IRAK3,GNG11,CTSS,SLC38A2,LPCAT2,CALD1,DIO1,ITGA1,HK2,GPR160,PARP14,EVC2,CD302,IFITM3,NEDD4,ROM1,DDR2,ATP11C,WWTR1,TES,RFTN2,RHOQ,SLC5A9,CLDN18,MMRN2,RELL1,ERBIN,BTNL9,TGFBR2,DOK3,ACTL6A,LCP2,MYD88,RHOJ,MLKL,PLIN2,NFKBIA,ANO6,IL13RA1,IQGAP1,ITGB8,ITGB1,LPAR6,CSF1,ANXA5,PLSCR1,ANXA1,KCNJ10,SAMHD1,NOSTRIN,ITGA8,MLANA,CLEC2D,SYNE2,CD2AP,VIM,TSHR,DDX58,TGFB3,AHNAK,SLC19A3,LRP4,S1PR3,RP2
GO:0005737	CC	cytoplasm	0.003121618	2.505620241	280	TOP2A,DLGAP5,CEP55,RRM2,HJURP,MELK,NDC80,VNN1,BCL2A1,CHI3L1,SHISA3,STC1,KNL1,FPR2,SGO1,S100A9,TLR8,MMRN1,SERPINA1,KIF14,MT1G,CDA,CCR5,TTK,NOD2,PLAC8,MT1F,GBP1,MS4A6A,GBP5,GBP2,HPGD,S100A4,MGAM,PLA1A,KIF20A,CDK1,BOLL,SPP1,DDIT4L,TMPRSS12,SAMSN1,TNFAIP8,TFAP2C,HMMR,TLR7,PRRG4,REP15,FYB1,SLFN13,HGF,TRIP10,PPEF2,SULT1B1,TFPI,TLR2,MNDA,RUNX3,PTPRC,LVRN,C3,IL2RG,MT1M,NIBAN1,GAS2L3,DNAH11,CENPF,PIK3AP1,TRIM5,GIMAP4,NUPR1,NUSAP1,FCGR2A,ALOX5AP,NEB,S100A11,LAMP3,HIGD1B,FCER1G,SMTN,IFI16,SELL,LAPTM5,FKBP5,DIAPH3,CASP4,NMI,STEAP4,ADGRL4,SYK,CGAS,GLI1,LCP1,MT2A,MT1X,ATP8,RANBP3L,DTX3L,SAMD9,CYBB,TLR1,NEFH,BACE2,SRGN,NCKAP1L,PARP9,GBP3,TRIM38,SASH3,CEP152,SP100,CLIC1,IKBIP,APBB1IP,SAMD9L,SLA,MT1E,PDK4,NFATC2,GNRH1,MAFF,CD34,CCNA2,BRCA2,HCLS1,RAB13,PIK3CG,SLC25A48,GIMAP7,EHF,GBP4,GPNMB,ITGB3,ND3,ANXA3,MAP3K8,PRELP,PERP,FAM111A,COL27A1,CDK2,PTAFR,GIMAP2,ORC1,YES1,NCF2,CD58,NEXN,BTK,PRKX,TRIM21,NQO1,FGF11,TEAD2,B2M,TRDN,MYOF,SLC39A12,ANXA2,ADAM28,FLT1,MECOM,TGFBR1,IRAK3,GNG11,FLI1,DNA2,CTSS,SLC38A2,LPCAT2,HELB,HHEX,CALD1,ZIC2,ACSS3,DIO1,ITGA1,HK2,ND4L,SQOR,PARP14,NABP1,MSTN,RNF152,EVC2,FBXO5,HEBP2,SAMD4A,FOXC1,CD302,IFITM3,DOCK2,NEDD4,DBI,MEFV,IFIH1,ATP6,HMGN5,ND4,TPD52L1,BCL6,HERC5,OAS2,LRRC1,COX2,ATP11C,WWTR1,TES,ND6,RHOQ,CNTLN,TRIM22,ND2,DSE,NLRC5,CASP7,ARHGDIB,MYL12A,ERBIN,YAP1,GIMAP5,CCDC146,TGFBR2,DOK3,CASP6,PPP1R1C,

						LCP2,AKR1C3,MYD88,CHEK2,RHOJ,MLKL,MRPS6,ST6GALNAC3,PLIN2,NFKBIA,APOL1,PLOD2,ARHGAP11A,ANO6,CYTB,IQGAP1,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,NDC80,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,NMI,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,CHEK2,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,TGFBR1,GPR160,CD302,DDR2,TGFBR2,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,GNG4,CAMK1,KIF17,RAB3A,STXBP1,CHRNB2,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

					A,GNG13,SLC1A6,TUBA1B,CACNB1,CAMKK2,VAMP2,TUBA4A,CAMK4,CACNG3,PRKCG,PRKAR1B,GNG4,CAMK1,KIF17,RAB3A,CHRNB2,SLC17A7,ARHGEF9,GABRG2,DLG3
REAC:R-HSA-187037	Signaling by NTRK1 (TRKA)	0.008665023	2.062230269	10	EGR2,EGR1,ARC,ADCYAP1,CDK5R2,PPP2R1A,MEF2D,DNAL4,AP2M1,CDK5
REAC:R-HSA-5576891	Cardiac conduction	0.016791344	1.774914548	10	SCN5A,KCNK3,SLC8A2,CACNB1,SCN3B,FXYD7,KCNIP3,SCN2B,ATP1A3,SLC8A3
REAC:R-HSA-372790	Signaling by GPCR	0.022140035	1.654821703	40	NMBR,PNOC,GNG3,WNT1,RGS8,CCKBR,NPBWR2,ADCYAP1,HTR2C,RBP4,FFAR4,SDR9C7,ADRA1D,PPEF1,MCHR2,PLPPR3,CHRM4,CHRM1,GRM2,OPRL1,CCK,GNG13,WNT10B,RGS4,NGEF,CAMKK2,PAK1,CAMK4,VIPR1,PPP2R1A,PRKCG,CX3CL1,PRKAR1B,ADRA1B,GNG4,RBP2,ARHGEF9,XK,CDK5,HTR5A
REAC:R-HSA-9006934	Signaling by Receptor Tyrosine Kinases	0.058821515	1.230463795	20	EGR2,EGR1,ARC,ADCYAP1,SPINT2,CDK5R2,ATP6V0E2,PAK1,PTPN3,ATP6V0B,PPP2R1A,LAMB3,MEF2D,DNAL4,TRIB3,ATP6V1B2,AP2M1,ATP6AP1,CDK5,GABRG2
		Down regulated genes			
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,CFI,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,NLRC5,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
REAC:R-HSA-109582	Hemostasis	0.038318795	1.416588151	30	ANGPT2,MMRN1,SERPINA1,KI

REAC:R-HSA-397014	Muscle contraction	0.071675415	1.144629782	12	F20A,TNFRSF10D,HGF,TFPI,JAML,FCER1G,SELL,SYK,SPN,SRGN,APBB1IP,MAFF,PIK3CG,ITGB3,CDK2,YES1,CD58,ITGA10,ANXA2,GNG11,ITGA1,DOCK2,LCP2,ITGB1,ANXA5,KIF5B,TGFB3 KCNE4,SCN4A,NEB,FGF11,TRDN,ANXA2,CALD1,ITGA1,WWTR1,MYL12A,ANXA1,VIM

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	AP1S1	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	BTK	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

Down	IFI16	6	hsa-mir-136-5p	Down	NFKBIA	8	RUNX2
Down	BTK	6	hsa-mir-425-5p	Down	IQGAP1	7	HINFP
Down	NEDD4	4	hsa-mir-30c-5p	Down	PLSCR1	5	E2F1
Down	TEAD2	3	hsa-mir-193b-3p	Down	BTK	2	SOX5

Figures

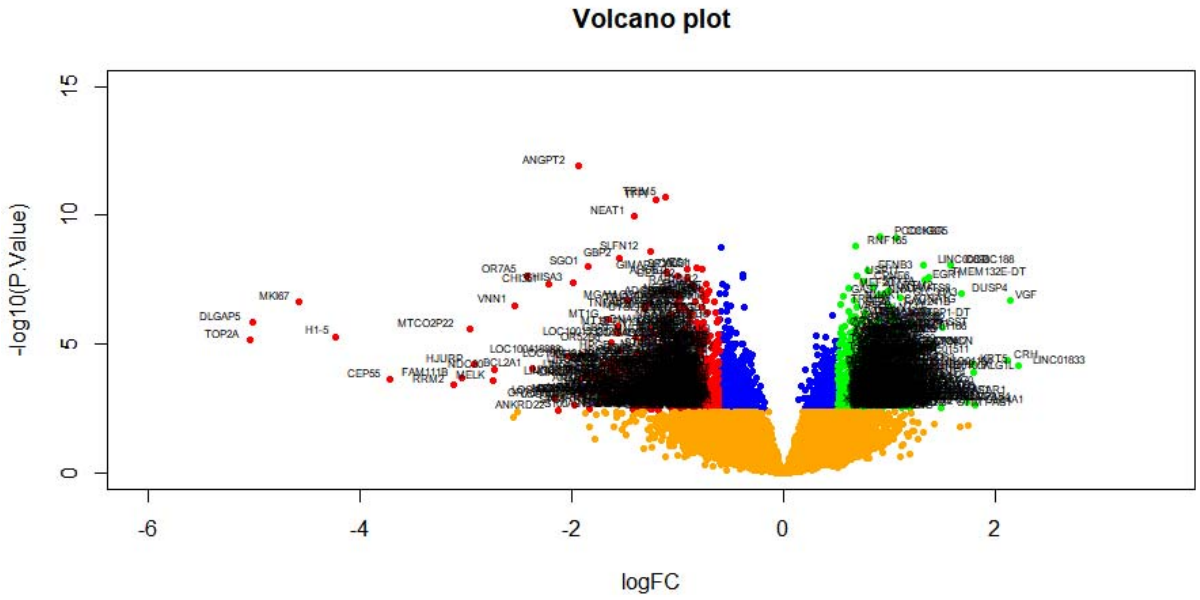

Fig. 1. Volcano plot of differentially expressed genes. Genes with a significant change of more than two-fold were selected. Green dot represented up regulated significant genes and red dot represented down regulated significant genes.

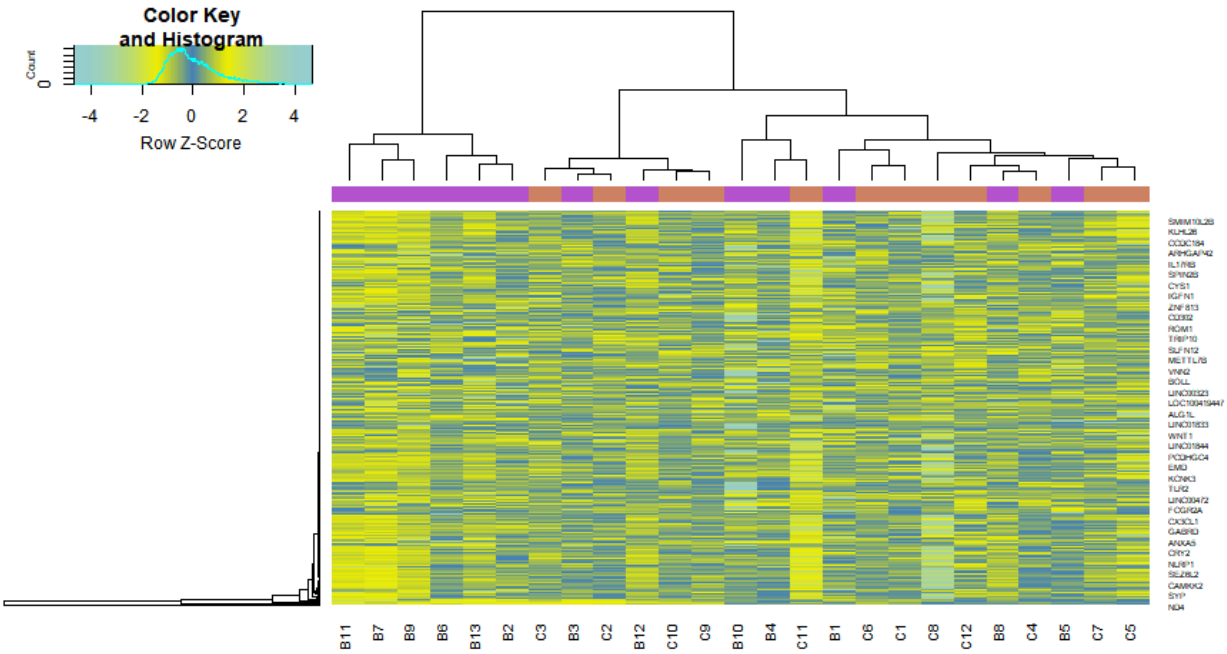

Fig. 2. Heat map of differentially expressed genes. Legend on the top left indicate log fold change of genes. (A1 – A37 = normal control samples; B1 – B47 = HF samples)

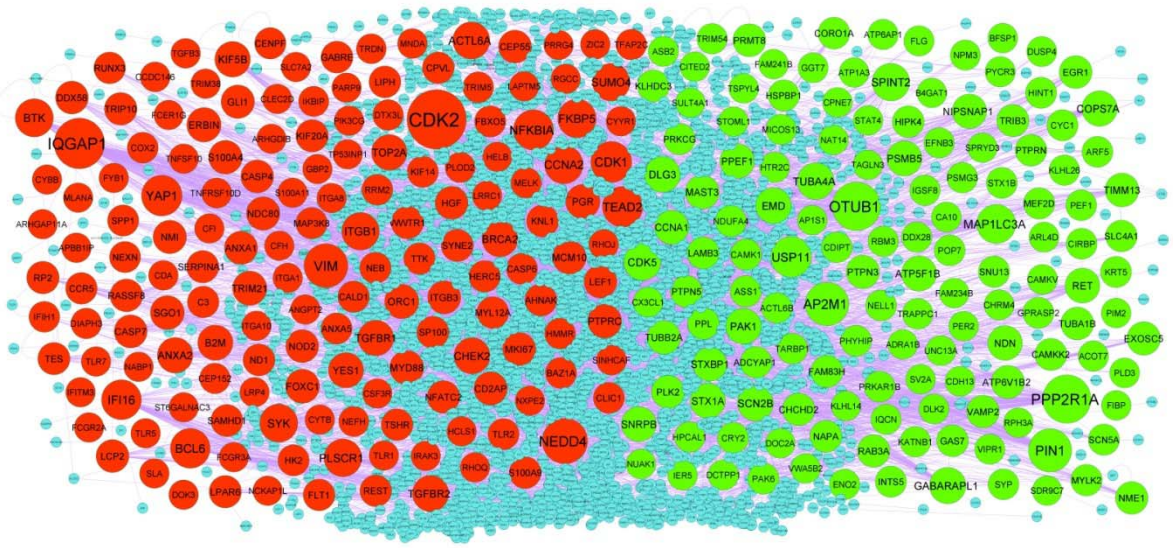

Fig. 3. PPI network of DEGs. Up regulated genes are marked in green; down regulated genes are marked in red

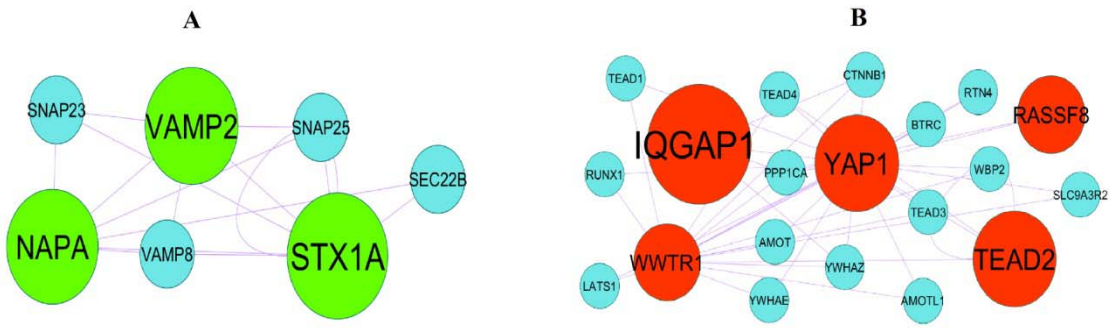

Fig. 4. Modules of isolated form PPI of DEGs. (A) The most significant module was obtained from PPI network with 7 nodes and 15 edges for up regulated genes (B) The most significant module was obtained from PPI network with 20 nodes and 41 edges for down regulated genes. Up regulated genes are marked in green; down regulated genes are marked in red

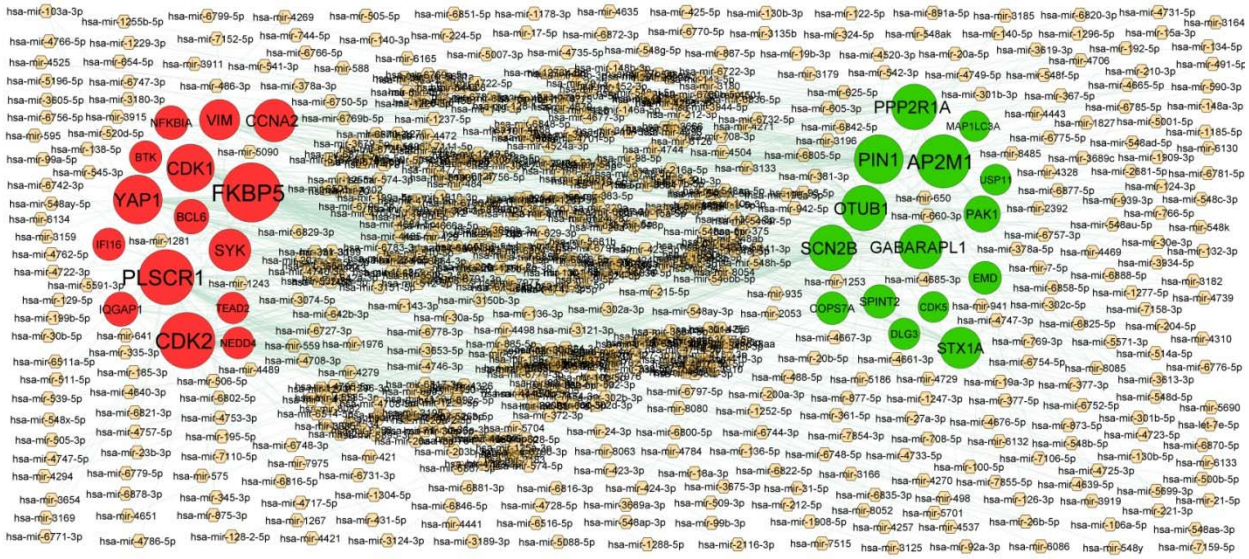

Fig. 5. Target gene - miRNA regulatory network between target genes. The orange color diamond nodes represent the key miRNAs; up regulated genes are marked in green; down regulated genes are marked in red.

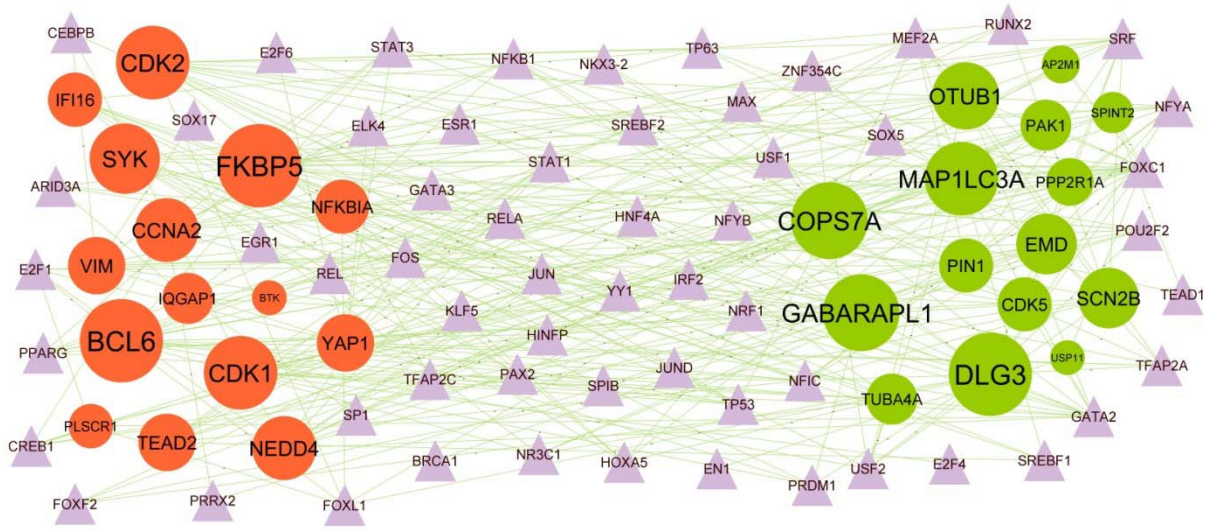

Fig. 6. Target gene - TF regulatory network between target genes. The purple color triangle nodes represent the key TFs; up regulated genes are marked in green; down regulated genes are marked in red.

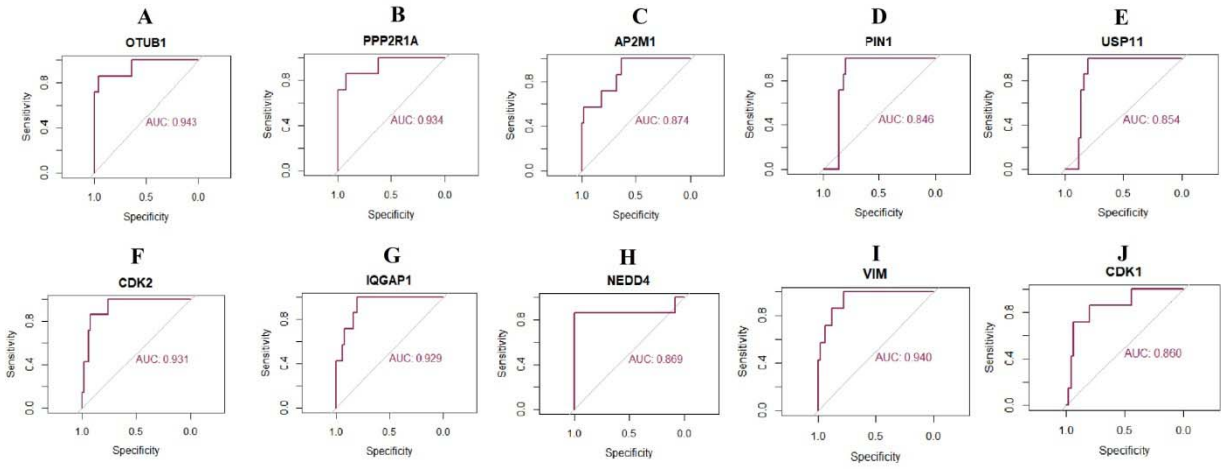

Fig. 7. ROC curve analyses of hub genes. A) OTUB1 B) PPP2R1A C) AP2M1 D) PIN1 E) USP11 F) CDK2 G) IQGAP1 H) NEDD4 I) VIM J) CDK1