Bioinformatics analyses of significant genes, related pathways and candidate prognostic biomarkers in Alzheimer's disease

Basavaraj Vastrad[1], Chanabasayya Vastrad*[2]

1. Department of Biochemistry, Basaveshwar College of Pharmacy, Gadag, Karnataka 582103, India.

2. Biostatistics and Bioinformatics, Chanabasava Nilaya, Bharthinagar, Dharwad 580001, Karnataka, India.

* Chanabasayya Vastrad

channu.vastrad@gmail.com

Ph: +919480073398

Chanabasava Nilaya, Bharthinagar,

Dharwad 580001 , Karanataka, India

Abstract

Alzheimer's disease (AD) is one of the most common causes of dementia and frailty. This study aimed to use bioinformatics analysis to identify differentially expressed genes (DEGs) in AD. The Expression profiling by high throughput sequencing dataset GSE125583 was downloaded from the Gene Expression Omnibus (GEO) database and DEGs were identified. After assessment of Gene Ontology (GO) terms and pathway enrichment for DEGs, a protein–protein interaction (PPI) network, module analysis, miRNA-hub gene regulatory network construction and TF-hub gene regulatory network were conducted via comprehensive target prediction and network analyses. Finally, we validated hub genes by receiver operating characteristic curve (ROC). In total, 956 DEGs were identified in the AD samples, including 479 up regulated genes and 477 down regulated genes. Functional enrichment analysis showed that these DEGs are mainly involved in the neuronal system, GPCR ligand binding, regulation of biological quality and cell communication. The hub genes of PAK1, ELAVL2, NSF, HTR2C, TERT, UBD, MKI67, HSPB1, PYHIN1 and TES might be associated with AD. The diagnostic value and expression levels of these hub genes in AD were further confirmed by ROC analysis. In conclusion, we identified pathways and crucial candidate genes that affect the outcomes of patients with AD, and these genes might serve as potential therapeutic targets.

Keywords: GEO database; bioinformatics analysis; Alzheimer's disease; pathways; differently expressed genes;

Introduction

Alzheimer's disease (AD) is a complex, dementia that mainly affects the memory, cognitive, and behavior functions [1]. Approximately over 45 million elderly people worldwide are affected with AD worldwide in 2020 which is expected to rise to 115 million by the year 2050 [2]. AD involves the degeneration of nervous tissues [3]. Numerous factors might affect AD progression, including genetic (70%) and environmental (30%) [4]; however, the cause and potential molecular mechanism of AD are still unclear. Therefore, there is a crucial commitment to establish new diagnostic strategies and therapeutic agents to develop the prognosis of patients with AD.

To find out novel genes and signaling pathways that is linked with AD and patient prognosis, which might not only help to elucidate the underlying molecular mechanisms involved, but also to discover new biomarkers and therapeutic targets. Apolipoprotein E epsilon 4 (APOE) [5], amyloid-β precursor protein (APP) [6], OPRM1 and OPRL1 [7], RAB10 [8], IL6 [9], Wnt/beta-catenin signaling pathway [10], glycogen synthase kinase-3 signaling pathway [11], insulin signaling pathway [12], CREB signaling pathway [13] and autotaxin-lysophosphatidic acid signaling pathway [14] are linked with development of AD. Therefore, identifying genes and the signal pathways, is essential for AD.

With the rapid advancement of bioinformatics such as RNA sequencing, some high throughput platforms for analysis of gene expression are frequently used to find the differentially expressed genes (DEGs) during disease progression. Now, through gene expression profiling studies using RNA sequencing, more and more DEGs linked with AD have been found.

Therefore, in the present study, we downloaded the original data (GSE125583), provided by Srinivasan et al [15], from the publically available Gene Expression Omnibus database (GEO, http://www.ncbi.nlm.nih.gov/geo/) [16] to identify DEGs and the associated biological processes between AD and healthy control using comprehensive bioinformatics analyses. The DEGs were subjected to gene ontology (GO) enrichment and pathway analyses; moreover, a protein-protein interaction (PPI) network, modules, miRNA-hub gene regulatory network construction and TF-hub gene regulatory network construction were

constructed and analyzed to screen for hub genes, miRNAs and TFs. Finely, hub genes were validated by receiver operating characteristic curve (ROC). The aim of this investigation was to find out hub genes and pathways in AD using bioinformatics methods and to then study the potential molecular mechanisms of AD.

Materials and methods

Data resources

Expression profiling by high throughput sequencing dataset GSE125583 [15] was downloaded from the GEO database. The data was produced using a GPL16791 Illumina HiSeq 2500 (Homo sapiens). The GSE125583 dataset contained data from 289 samples, including 219 AD samples and 70 normal control samples.

Identification of DEGs

The identification of DEGs between AD and normal control was performed in limma package in R software [17], an tool designed to compare different groups of samples. The P values were adjusted to correct for the occurrence of false positive results by using the Benjamini and Hochberg False Discovery Rate method [18]. An adjusted $P\Box<\Box.05$, and a $|\log_2 FC| > 0.731$ for up regulated genes and $|\log_2 FC| <$ -0.696 for down regulated genes were used as the cutoff values for identifying DEGs. Volcano plots of DEGs were provided using gplot package in R. The ggplot2 package in R was used to perform heatmap of up and down regulated genes in AD and healthy control.

GO and REACTOME pathway enrichment analysis of DEGs

GO (http://geneontology.org/) [19] and REACTOME (https://reactome.org/) [20] pathway enrichment analyses were executed using g:Profiler (http://biit.cs.ut.ee/gprofiler/) [21]. All DEG symbols were input as a list into the g:Profiler website. The results of GO and REACTOME pathway enrichment analyses were provided by bioinformatics tools in the website. There are processes in GO analysis involved biological processes (BP), cellular components (CC) and molecular functions (MF). The pathways of REACTOME involved metabolism, genetic information processing, environment information-related processes, cell physiological processes and drug research.

PPI network establishment and modules selection

Protein–protein interaction (PPI) analysis was performed using the Human Integrated Protein-Protein Interaction rEference (HIPPIE) interactome database (http://cbdm-01.zdv.uni-mainz.de/~mschaefer/hippie/network.php) [22], which is software used to explore interactions among proteins. All the symbols of DEGs were inputted. The network file among proteins was downloaded. Cytoscape software (version 3.8.2) (www.cytoscape.org) [23] is an excellent application for network visualization of proteins and was used to generate the PPI network plot constructed by nodes and edges. The hub genes were predicted by Network Analyzer, which is a plugin of Cytoscape to screen hub genes from numerous candidates. The ranks of the hub genes in the network were determined by the value of node degree [24], betweenness centrality [25], stress centrality [26] and closeness centrality [27], which are an algorithm provided by Network Analyzer. Because the node degree, betweenness centrality, stress centrality and closeness centrality values of genes are directly related to its importance, genes with a high node degree, betweenness centrality, stress centrality and closeness centrality value are more likely to be hub genes. The PEWCC1 (http://apps.cytoscape.org/apps/PEWCC1) [28], a plugin for Cytoscape, was used to screen the modules of the PPI network. The criteria were set as follows: degree cutoff=2, node score cutoff=0.2, k-core=2 and maximum depth=100. Moreover, the function and pathway enrichment analysis were performed for DEGs in the modules.

MiRNA-hub gene regulatory network construction

miRNet database (https://www.mirnet.ca/) is a web-based tool developed by Fan and Xia [29] that supplies the largest available collection of predicted and experimentally verified miRNA-hub gene interactions with various novel and unique features. In the current investigation, hub genes of the DEGs were identified using miRNet database. Furthermore, Cytoscape (version 3.8.2) software [23] was used to establish the miRNA-hub gene regulatory network.

TF-hub gene regulatory network construction

NetworkAnalyst database (https://www.networkanalyst.ca/) is a web-based tool developed by Zhou et al [30] that supplies the largest available collection of

predicted and experimentally verified TF-hub gene interactions with various novel and unique features. In the current investigation, hub genes of the DEGs were identified using NetworkAnalyst database. Furthermore, Cytoscape (version 3.8.2) software [23] was used to establish the miRNA-hub gene regulatory network.

Validation of hub genes by receiver operating characteristic curve (ROC) analysis

The ROC curves were used to explore the sensitivity and specificity of hub genes for AD diagnosis using R packages "pROC" [31].To further assess the predictive accuracy of the hub genes, ROC analysis was performed to discriminate AD from normal. The area under the ROC curve (AUC) was calculated and used to compare the diagnostic value of these genes.

Results

Identification of DEGs

Via limma package in R software, 956 DEGs (479 up regulated genes and 477 down regulated genes) (Table 1) in GSE125583 were extracted after gene expression profile data processing and standardization with the cutoff standard of adjusted P$\square$<$\square$.05, and a $|\log_2FC| > 0.731$ for up regulated genes and $|\log_2FC| < -0.696$. The volcano plot of all DEGs in dataset was shown in Fig. 1. The DEGs were clustered in the heatmap between patients with AD patients and healthy control (Fig. 2).

GO and REACTOME pathway enrichment analysis of DEGs

We performed GO and REACTOME pathway enrichment analysis to investigate the functions of DEGs using g:Profiler. The top GO (Table 2) and REACTOME pathway (Table 3) terms for DEGs were shown. For BP, DEGs were mainly enriched in regulation of biological quality, multicellular organismal process, cell communication and response to stimulus. The CC analysis indicated that proteins encoded by DEGs were mostly located in the cell junction, cell periphery, plasma membrane and extracellular region. DEGs in molecular function (MF) were significantly associated with channel activity, transmembranesignaling receptor activity, signaling receptor activity and G protein-coupled receptor activity. REACTOME pathway enrichment analysis showed that neuronal system,

neurotransmitter receptors and postsynaptic signal transmission, GPCR ligand binding and signal transduction were significantly enriched in DEGs.

PPI network establishment and modules selection

The PPI network of DEGs consisted of 6612 nodes and 13538 edges constructed in the HIPPIE interactome database and visualized using Cytoscape software (Fig.3). Based on the HIPPIE interactome database, the DEGs with the highest PPI scores identified by the four centrality methods are shown in Table 4. After repeated genes were removed, the hub genes (shown in Fig. 3, highlighted in green color for up regulated genes and red color for down regulated genes and shaped in round) were obtained using the four centrality methods, including PAK1, ELAVL2, NSF, HTR2C, TERT, UBD, MKI67, HSPB1, PYHIN1 and TES. A two significant modules were constructed from the PPI network of the DEGs using PEWCC1, including module 1 had 16 nodes and 38 edges (Fig. 4A) and module 2 had 47 nodes and 96 edges (Fig. 4B). GO and pathway enrichment analysis showed that genes in this module were markedly enriched in multicellular organismal process, neuronal system, regulation of biological quality, signal transduction, cell communication, plasma membrane, response to stimulus and cell communication.

MiRNA-hub gene regulatory network construction

As illustrated in Fig. 5, the miRNA-hub gene regulatory network consists of 2316 nodes (301 hub genes and 2015 miRNAs) and 11018 edges. Notably, NEFL targeted 78 miRNAs (ex; hsa-mir-378a-3p); NSF targeted 45 miRNAs (ex; hsa-mir-100-5p); ELAVL2 targeted 43 miRNAs (ex; hsa-mir-27a-3p); PRKCE targeted 42 miRNAs (ex; hsa-mir-513a-5p); MYB targeted 34 miRNAs (ex; hsa-mir-15b-5p); ANLN targeted 126 miRNAs (ex; hsa-mir-138-1-3p); MKI67 targeted 124 miRNAs (ex; hsa-mir-548d-5p); SERPINH1 targeted 83 miRNAs (ex; hsa-mir-4726-3p); LATS2 targeted 70 miRNAs (ex; hsa-mir-320d) and TES targeted 70 miRNAs (ex; hsa-mir-1202) and are listed in Table 5.

TF-hub gene regulatory network construction

As illustrated in Fig. 6, the TF-hub gene regulatory network consists of 386 (305 hub genes, 81 TFs) and 2380 edges. Notably, ELAVL2 targeted 15 TFs (ex; NRF1); MYB targeted 15 TFs (ex; STAT1); DCLK1 targeted 14 TFs (ex; YY1);

CD70 targeted 10 TFs (ex; PPARG); TERT targeted 10 TFs (ex; E2F6); TP63 targeted 17 TFs (ex; ZNF354C); TES targeted 11 TFs (ex; ARID3A); LCK targeted 10 TFs (ex; FOXL1); HSPB1 targeted 9 TFs (ex; RUNX2) and PYHIN1 targeted 8 TFs (ex; TP53) and are listed in Table 5.

Validation of hub genes by receiver operating characteristic curve (ROC) analysis

First of all, we performed the ROC curve analysis among 10 hub genes. The results showed that PAK1, ELAVL2, NSF, HTR2C, TERT, UBD, MKI67, HSPB1, PYHIN1 and TES achieved an AUC value of >0.9, demonstrating that these eight genes have high sensitivity and specificity for AD, suggesting they can be served as biomarkers for the diagnosis of AD (Fig. 7A-Fig. 7J).

Discussion

Genetic modification is widely accepted as a robust molecular event of AD. Unfortunately, little knowledge has focused on genetic modification in AD. In the present study, essential candidate genes and enriched pathways of AD were identified by bioinformatics analysis. We extracted the expression profiling by high throughput sequencing data from GSE125583 and obtained 479 up regulated and 477 down regulated genes in AD. A new study reported the CRH (corticotropin releasing hormone) [32], SST (somatostatin) [33] and GABRR2 [34] could be a biomarkers of AD. TAC1 has been shown to be prognostic biomarkers and therapeutic targets in multiple sclerosis [35], but this gene might be responsible for progression of AD. VGF (VGF nerve growth factor inducible) is a key regulator in patients with amyotrophic lateral sclerosis [36], but this gene might be linked with development of AD. A previous study indicated that the expression of MMP8 [37] and MMP7 [38] are associated with development of dementia.

Functional enrichment analysis was performed based on the GO database and the REACTOME database to screen the key pathways and genes to provide insights into the physiological functions and progress of AD. Neuronal system [39], neurotransmitter receptors and postsynaptic signal transmission [40], signaling by GPCR [41], signal transduction [42], GPCR ligand binding [43], immune system [44], hemostasis [45], cell surface interactions at the vascular wall

[46], cell periphery [47], channel activity [48], response to stimulus [49], plasma membrane [50], extracellular region [51], signaling receptor activity [52] and G protein-coupled receptor activity [53] were liable for progression of AD. Matsuzaki et al. [54], Shepard et al. [55], Lennertz et al. [56], Klemettilä et al. [57], Ullah et al. [58], Kim et al. [59], Sasayama et al. [60], Li et al. [61], Kowalczyk et al. [62] and Sun et al. [63] revealed that the expression of ADCYAP1, NPAS4, NPSR1, HTR2C, GABRB2, ALOX12B, ADRB3, EGR3, HSPA1A and IL3RA are associated with progression of schizophrenia, but these genes might be novel target for AD. GABRA6 [64], GABRA1 [65], GABRG2 [66], SLC4A10 [67], HCN1 [68], GABRA4 [69], KCNC2 [70], SCN2A [71], SYN2 [72], FGF12 [73], SCN8A [74], OLFM3 [75], PLCB1 [76], KCNQ5 [77], TUBB2A [78], SIK1 [79], ABCC2 [80], SLC6A12 [81] and COL6A2 [82] have been reported to be closely related to the occurrence and development of epilepsy, but these genes might be novel target for AD. Previous investigation demonstrates that RGS4 [83], CXCL11 [84], EGR1 [85], CALB1 [86], BDNF (brain derived neurotrophic factor) [87], TERT (telomerase reverse transcriptase) [88], NEFL (neurofilament light) [89], SNAP25 [90], RPH3A [91], NRN1 [92], SYT1 [93], GRIN2B [94], AVP (arginine vasopressin) [95], VSNL1 [96], HTR2A [97], PAK3 [98], STXBP5L [99], HCRTR2 [100], SYP (synaptophysin) [101], SYT10 [102], PRKCE (protein kinase C epsilon) [103], NRG1 [104], KISS1 [105], NRXN3 [106], RAB3A [107], IGF1 [108], PLK2 [109], CBLN4 [110], CAP2 [111], SV2B [112], CAMK4 [113], INA (internexin neuronal intermediate filament protein alpha) [114], GAP43 [115], TTR (transthyretin) [116], CXCR2 [117], IL1R2 [118], CXCR4 [119], CCR2 [120], MYOCD (myocardin) [121], S100A12 [122], CXCR3 [123], PROK2 [124], CXCL8 [125], RGS1 [126], NOTCH3 [127], P2RX7 [128], NGFR (nerve growth factor receptor) [129], GDF15 [130], CR1 [131], ADORA2A [132], GPER1 [133], FCGR2B [134], MMP9 [135], CNN2 [136], C5AR1 [137], CCL15 [138], RBPMS (RNA binding protein, mRNA processing factor) [139], TBX2 [140], FPR2 [141], PCK1 [142], ADH1B [143], TLR5 [144], C7 [145] and CD163 [146] are thought to contribute to AD development and it has been reported to act as a potential biomarkers for AD treatment. IL1RAPL2 [147], GAD1 [148], EPHA5 [149], HTR1A [150], CADPS (calcium dependent secretion activator) [151], GABRG3 [152], LRFN5 [153] and CXCR1 [154] are expressed in autism spectrum disorders, but these genes might be novel target for AD. GAD2 [155], TAC3 [156], NCR1 [157], IL7R [158], GATA3 [159], FCRL3 [160] and IL18R1

[161] have been reported as most promising biomarkers for early diagnosis and prognosis prediction of multiple sclerosis, but these genes might be novel target for AD. FLT3 [162], CHRNB4 [163], PAK1 [164], CHRNB3 [165], GRIN2A [166], CHRNA6 [167], PENK (proenkephalin) [168], CHRNB4 [169], IGF2 [170], TLR9 [171] and CACNG5 [172] were revealed to serve an important role in Parkinson's disease, but these genes might be novel target for AD. The expression of SLC30A3 [173], NEFH (neurofilament heavy) [174], SYNGR4 [175], S100A4 [176], HSPB1 [177] and KIF5A [178] are associated with amyotrophic lateral sclerosis, but these genes might be novel target for AD.

Based on the node degree, betweenness centrality, stress centrality and closeness centrality in PPI network and modules, the hub genes were ranked. These identified hub genes were functioned as a group, and might play a crucial role in AD. ELAVL2 has been identified in autism spectrum disorders [179], but this gene might be novel target for AD. NEFM (neurofilament medium) was revealed to be expressed in AD [180]. NSF (N-ethylmaleimide sensitive factor, vesicle fusing ATPase), UBD (ubiquitin D), MKI67, PYHIN1, TES (testin LIM domain protein), MYL9 and TGFB1I1 might be the novel biomarkers for AD.

By analyzing the miRNA-hub gene regulatory network construction and TF-hub gene regulatory network, a number of hub genes, miRNAs and TFs were identified that might provide novel approaches for therapeutic investigations of AD. CD70 has been shown as a promising biomarker in multiple sclerosis [181], but this gene might be novel target for AD. Hsa-mir-378a-3p [182], hsa-mir-100-5p [182], hsa-mir-27a-3p [183], hsa-mir-15b-5p [184], hsa-mir-320d [185], NRF1 [186], STAT1 [187], YY1 [188], PPARG (peroxisome proliferator-activated receptor gamma) [189] and TP53 [190] have been shown to be an important role in AD. MYB (MYB proto-oncogene, transcription factor), ANLN (anillin actin binding protein), SERPINH1, LATS2, DCLK1, TP63, LCK (LCK proto-oncogene, Src family tyrosine kinase), hsa-mir-513a-5p, hsa-mir-138-1-3p, hsa-mir-548d-5p, hsa-mir-4726-3p, hsa-mir-1202, E2F6, ZNF354C, ARID3A, FOXL1 and RUNX2 might be the novel biomarkers for AD.

In conclusion, integrated bioinformatics analysis of multiple datasets of newly diagnosed AD patients and healthy controls was performed. Common DEGs were identified that are significantly enriched in various pathways, followed by

evaluation of the prognostic value for patients with AD. Notably, most of the prognostic genes are neuron and immune related genes. The results of this investigation increase our understanding of the molecular drivers that underlie AD initiation and progression, and the identified key genes and pathways constitute potential therapeutic targets.

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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. [(GSE125583) (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE125583)]

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

Authors

Basavaraj Vastrad   ORCID ID: 0000-0003-2202-7637

Chanabasayya Vastrad   ORCID ID: 0000-0003-3615-4450

References

1. Blennow K, Zetterberg H. Biomarkers for Alzheimer's disease: current status and prospects for the future. J Intern Med. 2018;284(6):643-663. doi:10.1111/joim.12816

2. Qiu S, Joshi PS, Miller MI, Xue C, Zhou X, Karjadi C, Chang GH, Joshi AS, Dwyer B, Zhu S, et al. Development and validation of an interpretable deep learning framework for Alzheimer's disease classification. Brain. 2020;143(6):1920-1933. doi:10.1093/brain/awaa137

3. Nasrabady SE, Rizvi B, Goldman JE, Brickman AM. White matter changes in Alzheimer's disease: a focus on myelin and oligodendrocytes. Acta Neuropathol Commun. 2018;6(1):22. doi:10.1186/s40478-018-0515-3

4. Dorszewska J, Prendecki M, Oczkowska A, Dezor M, Kozubski W. Molecular Basis of Familial and Sporadic Alzheimer's Disease. Curr Alzheimer Res. 2016;13(9):952-963. doi:10.2174/1567205013666160314150501

5. Riedel BC, Thompson PM, Brinton RD. Age, APOE and sex: Triad of risk of Alzheimer's disease. J Steroid Biochem Mol Biol. 2016;160:134-147. doi:10.1016/j.jsbmb.2016.03.012

6. Jonsson T, Atwal JK, Steinberg S, Snaedal J, Jonsson PV, Bjornsson S, Stefansson H, Sulem P, Gudbjartsson D, Maloney J, et al. A mutation in APP protects against Alzheimer's disease and age-related cognitive decline. Nature. 2012;488(7409):96-99. doi:10.1038/nature11283

7. Xu C, Liu G, Ji H, Chen W, Dai D, Chen Z, Zhou D, Xu L, Hu H, Cui W, et al. Elevated methylation of OPRM1 and OPRL1 genes in Alzheimer's disease. Mol Med Rep. 2018;18(5):4297-4302. doi:10.3892/mmr.2018.9424

8. Tavana JP, Rosene M, Jensen NO, Ridge PG, Kauwe JS, Karch CM. RAB10: an Alzheimer's disease resilience locus and potential drug target. Clin Interv Aging. 2018;14:73-79. doi:10.2147/CIA.S159148

9. Sawkulycz X, Bradburn S, Robinson A, Payton A, Pendleton N, Murgatroyd C. Regulation of interleukin 6 by a polymorphic CpG within the frontal cortex in Alzheimer's disease. Neurobiol Aging. 2020;92:75-81. doi:10.1016/j.neurobiolaging.2020.04.008

10. Jia L, Piña-Crespo J, Li Y. Restoring Wnt/β-catenin signaling is a promising therapeutic strategy for Alzheimer's disease. Mol Brain. 2019;12(1):104. doi:10.1186/s13041-019-0525-5

11. Lauretti E, Dincer O, Praticò D. Glycogen synthase kinase-3 signaling in Alzheimer's disease. Biochim Biophys Acta Mol Cell Res. 2020;1867(5):118664. doi:10.1016/j.bbamcr.2020.118664

12. Akhtar A, Sah SP. Insulin signaling pathway and related molecules: Role in neurodegeneration and Alzheimer's disease. Neurochem Int. 2020;135:104707. doi:10.1016/j.neuint.2020.104707

13. Saura CA, Valero J. The role of CREB signaling in Alzheimer's disease and other cognitive disorders. Rev Neurosci. 2011;22(2):153-169. doi:10.1515/RNS.2011.018

14. Ramesh S, Govindarajulu M, Suppiramaniam V, Moore T, Dhanasekaran M. Autotaxin⬜Lysophosphatidic Acid Signaling in Alzheimer's Disease. Int J Mol Sci. 2018;19(7):1827. doi:10.3390/ijms19071827

15. Srinivasan K, Friedman BA, Etxeberria A, Huntley MA, van der Brug MP, Foreman O, Paw JS, Modrusan Z, Beach TG, Serrano GE, et al. Alzheimer's Patient Microglia Exhibit Enhanced Aging and Unique Transcriptional Activation. Cell Rep. 2020;31(13):107843. doi:10.1016/j.celrep.2020.107843

16. 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

17. Ritchie ME, Phipson B, Wu D, Hu Y, Law CW, Shi W, Smyth GK. limma powers differential expression analyses for RNA-sequencing and microarray studies. Nucleic Acids Res. 2015;43(7):e47. doi:10.1093/nar/gkv007

18. Hardcastle TJ. Generalized empirical Bayesian methods for discovery of differential data in high-throughput biology. Bioinformatics. 2016;32(2):195-202. doi:10.1093/bioinformatics/btv569

19. 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

20. 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

21. 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

22. 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

23. 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

24. Przulj N, Wigle DA, Jurisica I. Functional topology in a network of protein interactions. Bioinformatics. 2004;20(3):340–348. doi:10.1093/bioinformatics/btg415

25. Nguyen TP, Liu WC, Jordán F. Inferring pleiotropy by network analysis: linked diseases in the human PPI network. BMC Syst Biol. 2011;5:179. doi:10.1186/1752-0509-5-179

26. Shi Z, Zhang B. Fast network centrality analysis using GPUs. BMC Bioinformatics. 2011;12:149. doi:10.1186/1471-2105-12-149

27. Fadhal E, Gamieldien J, Mwambene EC. Protein interaction networks as metric spaces: a novel perspective on distribution of hubs. BMC Syst Biol. 2014;8:6. doi:10.1186/1752-0509-8-6

28. 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

29. 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

30. 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

31. 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

32. Näsman B, Olsson T, Fagerlund M, Eriksson S, Viitanen M, Carlström K. Blunted adrenocorticotropin and increased adrenal steroid response to human corticotropin-releasing hormone in Alzheimer's disease. Biol Psychiatry. 1996;39(5):311-318. doi:10.1016/0006-3223(95)00173-5

33. 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

34. Ma Z, Niu B, Shi Z, Li J, Wang J, Zhang F, Gao X, Zhang K.Genetic Polymorphism of GABRR2 Modulates Individuals' General Cognitive Ability in Healthy Chinese Han People. Cell Mol Neurobiol. 2017;37(1):93-100. doi:10.1007/s10571-016-0347-2

35. 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

36. 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

37. Singh H, Samani D, Nambiar N, Ghate MV, Gangakhedkar RR. Prevalence of MMP-8 gene polymorphisms in HIV-infected individuals and its association with HIV-associated neurocognitive disorder. Gene. 2018;646:83-90. doi:10.1016/j.gene.2017.12.061

38. Singh H, Marathe SD, Nain S, Nema V, Angadi M, Bapat SS, Ghate MV, Gangakhedkar RR. Impact of variants of MMP-7(-181A>G) gene in susceptibility to the development of HIV-associated neurocognitive disorder and its severity. APMIS. 2016;124(11):966-972. doi:10.1111/apm.12594

39. Geula C, Nagykery N, Nicholas A, Wu CK. Cholinergic neuronal and axonal abnormalities are present early in aging and in Alzheimer disease. J Neuropathol Exp Neurol. 2008;67(4):309-318. doi:10.1097/NEN.0b013e31816a1df3

40. Xu Y, Yan J, Zhou P, Li J, Gao H, Xia Y, Wang Q. Neurotransmitter receptors and cognitive dysfunction in Alzheimer's disease and Parkinson's disease. Prog Neurobiol. 2012;97(1):1-13. doi:10.1016/j.pneurobio.2012.02.002

41. Sushma, Mondal AC. Role of GPCR signaling and calcium dysregulation in Alzheimer's disease. Mol Cell Neurosci. 2019;101:103414. doi:10.1016/j.mcn.2019.103414

42. Nguyen TV, Galvan V, Huang W, Banwait S, Tang H, Zhang J, Bredesen DE. Signal transduction in Alzheimer disease: p21-activated kinase signaling requires C-terminal cleavage of APP at Asp664. J Neurochem. 2008;104(4):1065-1080. doi:10.1111/j.1471-4159.2007.05031.x

43. Zhao J, Deng Y, Jiang Z, Qing H. G Protein-Coupled Receptors (GPCRs) in Alzheimer's Disease: A Focus on BACE1 Related GPCRs. Front Aging Neurosci. 2016;8:58. doi:10.3389/fnagi.2016.00058

44. Jevtic S, Sengar AS, Salter MW, McLaurin J. The role of the immune system in Alzheimer disease: Etiology and treatment. Ageing Res Rev. 2017;40:84-94. doi:10.1016/j.arr.2017.08.005

45. Cortes-Canteli M, Zamolodchikov D, Ahn HJ, Strickland S, Norris EH. Fibrinogen and altered hemostasis in Alzheimer's disease. J Alzheimers Dis. 2012;32(3):599-608. doi:10.3233/JAD-2012-120820

46. Rius-Pérez S, Tormos AM, Pérez S, Taléns-Visconti R. Vascular pathology: Cause or effect in Alzheimer disease?. Patología vascular: ¿causa o efecto en la enfermedad de Alzheimer?. Neurologia. 2018;33(2):112-120. doi:10.1016/j.nrl.2015.07.010

47. Chen SH, Bu XL, Jin WS, Shen LL, Wang J, Zhuang ZQ, Zhang T, Zeng F, Yao XQ, Zhou HD, et al. Altered peripheral profile of blood cells in Alzheimer disease: A hospital-based case-control study. Medicine (Baltimore). 2017;96(21):e6843. doi:10.1097/MD.0000000000006843

48. Arispe N, Pollard HB, Rojas E. beta-Amyloid Ca(2+)-channel hypothesis for neuronal death in Alzheimer disease. Mol Cell Biochem. 1994;140(2):119-125. doi:10.1007/BF00926750

49. Jensen-Dahm C, Werner MU, Jensen TS, Ballegaard M, Andersen BB, Høgh P, Waldemar G. Discrepancy between stimulus response and tolerance of pain in Alzheimer disease. Neurology. 2015;84(15):1575-1581. doi:10.1212/WNL.0000000000001465

50. Verdier Y, Zarándi M, Penke B. Amyloid beta-peptide interactions with neuronal and glial cell plasma membrane: binding sites and implications for Alzheimer's disease. J Pept Sci. 2004;10(5):229-248. doi:10.1002/psc.573

51. Avila J, Pallas N, Bolós M, Sayas CL, Hernandez F. Intracellular and extracellular microtubule associated protein tau as a therapeutic target in Alzheimer disease and other tauopathies. Expert Opin Ther Targets. 2016;20(6):653-661. doi:10.1517/14728222.2016.1131269

52. Berridge MJ. Dysregulation of neural calcium signaling in Alzheimer disease, bipolar disorder and schizophrenia. Prion. 2013;7(1):2-13. doi:10.4161/pri.21767

53. Qiu WQ. Amylin and its G-protein-coupled receptor: A probable pathological process and drug target for Alzheimer's disease. Neuroscience. 2017;356:44-51. doi:10.1016/j.neuroscience.2017.05.024

54. Matsuzaki S, Tohyama M. Regulation of pituitary adenylyl cyclase-activating polypeptide (PACAP, ADCYAP1: adenylyl cyclase-activating polypeptide 1) in the treatment of schizophrenia. Expert Opin Ther Targets. 2008;12(9):1097-1108. doi:10.1517/14728222.12.9.1097

55. 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

56. Lennertz L, Quednow BB, Schuhmacher A, Petrovsky N, Frommann I, Schulze-Rauschenbach S, Landsberg MW, Steinbrecher A, Höfels S, Pukrop R, et al. The functional coding variant Asn107Ile of the neuropeptide S receptor gene (NPSR1) is associated with schizophrenia and modulates verbal memory and the acoustic startle response. Int J Neuropsychopharmacol. 2012;15(9):1205-1215. doi:10.1017/S1461145711001623

57. Klemettilä JP, Kampman O, Seppälä N, Viikki M, Hämäläinen M, Moilanen E, Mononen N, Lehtimäki T, Leinonen E. Association study of the HTR2C, leptin and adiponectin genes and serum marker analyses in clozapine treated

long-term patients with schizophrenia. Eur Psychiatry. 2015;30(2):296-302. doi:10.1016/j.eurpsy.2014.08.006

58. Ullah A, Long X, Mat WK, Hu T, Khan MI, Hui L, Zhang X, Sun P, Gao M, Wang J, et al. Highly Recurrent Copy Number Variations in GABRB2 Associated With Schizophrenia and Premenstrual Dysphoric Disorder. Front Psychiatry. 2020;11:572. doi:10.3389/fpsyt.2020.00572

59. Kim T, Kim HJ, Park JK, Kim JW, Chung JH. Association between polymorphisms of arachidonate 12-lipoxygenase (ALOX12) and schizophrenia in a Korean population. Behav Brain Funct. 2010;6:44. doi:10.1186/1744-9081-6-44

60. Sasayama D, Hori H, Teraishi T, Hattori K, Ota M, Tatsumi M, Higuchi T, Amano N, Kunugi H. Possible impact of ADRB3 Trp64Arg polymorphism on BMI in patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2012;38(2):341-344. doi:10.1016/j.pnpbp.2012.05.007

61. Li G, Han X, Gao W, Song Z, Zhao S, Sun F, Ma H, Cui A, Tang X, Ma G. Influence of EGR3 Transfection on Imaging and Behavior in Rats and Therapeutic Effect of Risperidone in Schizophrenia Model. Front Psychiatry. 2020;11:00787. doi:10.3389/fpsyt.2020.00787

62. Kowalczyk M, Kucia K, Owczarek A, Suchanek-Raif R, Merk W, Paul-Samojedny M, Kowalski J. Association Studies of HSPA1A and HSPA1L Gene Polymorphisms With Schizophrenia. Arch Med Res. 2018;49(5):342-349. doi:10.1016/j.arcmed.2018.10.002

63. Sun S, Wei J, Li H, Jin S, Li P, Ju G, Liu Y, Zhang XY. A family-based study of the IL3RA gene on susceptibility to schizophrenia in a Chinese Han population. Brain Res. 2009;1268:13-16. doi:10.1016/j.brainres.2009.02.071

64. Prasad DK, Shaheen U, Satyanarayana U, Prabha TS, Jyothy A, Munshi A. Association of GABRA6 1519 T>C (rs3219151) and Synapsin II (rs37733634) gene polymorphisms with the development of idiopathic generalized epilepsy. Epilepsy Res. 2014;108(8):1267-1273. doi:10.1016/j.eplepsyres.2014.07.001

65. Hernandez CC, XiangWei W, Hu N, Shen D, Shen W, Lagrange AH, Zhang Y, Dai L, Ding C, Sun Z, et al. Altered inhibitory synapses in de novo GABRA5 and GABRA1 mutations associated with early onset epileptic encephalopathies. Brain. 2019;142(7):1938-1954. doi:10.1093/brain/awz123

66. 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

67. Gurnett CA, Veile R, Zempel J, Blackburn L, Lovett M, Bowcock A. Disruption of sodium bicarbonate transporter SLC4A10 in a patient with complex partial epilepsy and mental retardation. Arch Neurol. 2008;65(4):550-553. doi:10.1001/archneur.65.4.550

68. Marini C, Porro A, Rastetter A, Dalle C, Rivolta I, Bauer D, Oegema R, Nava C, Parrini E, Mei D, et al. HCN1 mutation spectrum: from neonatal epileptic encephalopathy to benign generalized epilepsy and beyond. Brain. 2018;141(11):3160-3178. doi:10.1093/brain/awy263

69. Fan C, Gao Y, Liang G, Huang L, Wang J, Yang X, Shi Y, Dräger UC, Zhong M, Gao TM, et al. Transcriptomics of Gabra4 knockout mice reveals common NMDAR pathways underlying autism, memory, and epilepsy. Mol Autism. 2020;11(1):13. doi:10.1186/s13229-020-0318-9

70. Vetri L, Calì F, Vinci M, Amato C, Roccella M, Granata T, Freri E, Solazzi R, Romano V, Elia M. A de novo heterozygous mutation in KCNC2 gene implicated in severe developmental and epileptic encephalopathy. Eur J Med Genet. 2020;63(4):103848. doi:10.1016/j.ejmg.2020.103848

71. Li X, Zhang J, Wu X, Yan H, Zhang Y, He RH, Tang YJ, He YJ, Tan D, Mao XY, et al. Polymorphisms of ABAT, SCN2A and ALDH5A1 may affect valproic acid responses in the treatment of epilepsy in Chinese. Pharmacogenomics. 2016;17(18):2007-2014. doi:10.2217/pgs-2016-0093

72. Haerian BS, Lim KS, Tan HJ, Wong CP, Wong SW, Tan CT, Raymond AA, Mohamed Z. Lack of association between synapsin II (SYN2) gene polymorphism and susceptibility epilepsy: a case-control study and meta-analysis. Synapse. 2011;65(10):1073-1079. doi:10.1002/syn.20939

73. Verheyen S, Speicher MR, Ramler B, Plecko B. Childhood-onset epileptic encephalopathy due to FGF12 exon 1-4 tandem duplication. Neurol Genet. 2020;6(5):e494. doi:10.1212/NXG.0000000000000494

74. Tidball AM, Lopez-Santiago LF, Yuan Y, Glenn TW, Margolis JL, Clayton Walker J, Kilbane EG, Miller CA, Martina Bebin E, Scott Perry M, et al. Variant-specific changes in persistent or resurgent sodium current in

SCN8A-related epilepsy patient-derived neurons. Brain. 2020;143(10):3025-3040. doi:10.1093/brain/awaa247

75. Tang S, Wang T, Zhang X, Guo Y, Xu P, Zeng J, Luo Z, Li D, Zheng Y, Luo Y, et al. Olfactomedin-3 Enhances Seizure Activity by Interacting With AMPA Receptors in Epilepsy Models. Front Cell Dev Biol. 2020;8:722. doi:10.3389/fcell.2020.00722

76. Desprairies C, Valence S, Maurey H, Helal SI, Weckhuysen S, Soliman H, Mefford HC, Spentchian M, Héron D, Leguern E, et al. Three novel patients with epileptic encephalopathy due to biallelic mutations in the PLCB1 gene. Clin Genet. 2020;97(3):477-482. doi:10.1111/cge.13696

77. Lehman A, Thouta S, Mancini GMS, Naidu S, van Slegtenhorst M, McWalter K, Person R, Mwenifumbo J, Salvarinova R. Loss-of-Function and Gain-of-Function Mutations in KCNQ5 Cause Intellectual Disability or Epileptic Encephalopathy. Am J Hum Genet. 2017;101(1):65-74. doi:10.1016/j.ajhg.2017.05.016

78. Cushion TD, Paciorkowski AR, Pilz DT, Mullins JG, Seltzer LE, Marion RW, Tuttle E, Ghoneim D, Christian SL, Chung SK, et al. De novo mutations in the beta-tubulin gene TUBB2A cause simplified gyral patterning and infantile-onset epilepsy. Am J Hum Genet. 2014;94(4):634-641. doi:10.1016/j.ajhg.2014.03.009

79. Hansen J, Snow C, Tuttle E, Ghoneim DH, Yang CS, Spencer A, Gunter SA, Smyser CD, Gurnett CA, Shinawi M, et al. De novo mutations in SIK1 cause a spectrum of developmental epilepsies. Am J Hum Genet. 2015;96(4):682-690. doi:10.1016/j.ajhg.2015.02.013

80. Al-Eitan LN, Al-Dalalah IM, Mustafa MM, Alghamdi MA, Elshammari AK, Khreisat WH, Aljamal HA. Effects of MTHFR and ABCC2 gene polymorphisms on antiepileptic drug responsiveness in Jordanian epileptic patients. Pharmgenomics Pers Med. 2019;12:87-95. doi:10.2147/PGPM.S211490

81. Li J, Lin H, Niu F, Zhu X, Shen N, Wang X, Li L, Liu A, Wu X, Sun W, et al. Combined effect between two functional polymorphisms of SLC6A12 gene is associated with temporal lobe epilepsy. J Genet. 2015;94(4):637-642. doi:10.1007/s12041-015-0567-0

82. Karkheiran S, Krebs CE, Makarov V, Nilipour Y, Hubert B, Darvish H, Frucht S, Shahidi GA, Buxbaum JD, Paisán-Ruiz C. Identification of

COL6A2 mutations in progressive myoclonus epilepsy syndrome. Hum Genet. 2013;132(3):275-283. doi:10.1007/s00439-012-1248-1

83. 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

84. Koper OM, Kamińska J, Sawicki K, Kemona H. CXCL9, CXCL10, CXCL11, and their receptor (CXCR3) in neuroinflammation and neurodegeneration. Adv Clin Exp Med. 2018;27(6):849-856. doi:10.17219/acem/68846

85. Bakalash S, Pham M, Koronyo Y, Salumbides BC, Kramerov A, Seidenberg H, Berel D, Black KL, Koronyo-Hamaoui M.Egr1 expression is induced following glatiramer acetate immunotherapy in rodent models of glaucoma and Alzheimer's disease. Invest Ophthalmol Vis Sci. 2011;52(12):9033-9046. doi:10.1167/iovs.11-7498

86. Sanfilippo C, Castrogiovanni P, Imbesi R, Di Rosa M. CHI3L2 Expression Levels Are Correlated with AIF1, PECAM1, and CALB1 in the Brains of Alzheimer's Disease Patients. J Mol Neurosci. 2020;70(10):1598-1610. doi:10.1007/s12031-020-01667-9

87. Borba EM, Duarte JA, Bristot G, Scotton E, Camozzato AL, Chaves ML. Brain-Derived Neurotrophic Factor Serum Levels and Hippocampal Volume in Mild Cognitive Impairment and Dementia due to Alzheimer Disease. Dement Geriatr Cogn Dis Extra. 2016;6(3):559-567. doi:10.1159/000450601

88. Scarabino D, Broggio E, Gambina G, Pelliccia F, Corbo RM. Common variants of human TERT and TERC genes and susceptibility to sporadic Alzheimers disease. Exp Gerontol. 2017;88:19-24. doi:10.1016/j.exger.2016.12.017

89. Moscoso A, Grothe MJ, Ashton NJ, Karikari TK, Lantero Rodríguez J, Snellman A, Suárez-Calvet M, Blennow K, Zetterberg H, Schöll M. Longitudinal Associations of Blood Phosphorylated Tau181 and Neurofilament Light Chain With Neurodegeneration in Alzheimer Disease. JAMA Neurol. 2021;78(4):396-406. doi:10.1001/jamaneurol.2020.4986

90. Agostini S, Mancuso R, Liuzzo G, Bolognesi E, Costa AS, Bianchi A, Clerici M. Serum miRNAs Expression and SNAP-25 Genotype in Alzheimer's Disease. Front Aging Neurosci. 2019;11:52. doi:10.3389/fnagi.2019.00052

91. 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

92. 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

93. Shi Z, Zhang K, Zhou H, Jiang L, Xie B, Wang R, Xia W, Yin Y, Gao Z, Cui D, et al. Increased miR-34c mediates synaptic deficits by targeting synaptotagmin 1 through ROS-JNK-p53 pathway in Alzheimer's Disease. Aging Cell. 2020;19(3):e13125. doi:10.1111/acel.13125

94. Andreoli V, De Marco EV, Trecroci F, Cittadella R, Di Palma G, Gambardella A. Potential involvement of GRIN2B encoding the NMDA receptor subunit NR2B in the spectrum of Alzheimer's disease. J Neural Transm (Vienna). 2014;121(5):533-542. doi:10.1007/s00702-013-1125-7

95. Peskind ER, Pascualy M, Edland SD, Wingerson D, Dobie DJ, Raskind MA. Plasma arginine vasopressin response to hypertonic saline infusion in Alzheimer disease. Alzheimer Dis Assoc Disord. 1995;9(4):238-242.

96. Lin CW, Chang LC, Tseng GC, Kirkwood CM, Sibille EL, Sweet RA. VSNL1 Co-Expression Networks in Aging Include Calcium Signaling, Synaptic Plasticity, and Alzheimer's Disease Pathways. Front Psychiatry. 2015;6:30. doi:10.3389/fpsyt.2015.00030

97. Wilkosz PA, Kodavali C, Weamer EA, Miyahara S, Lopez OL, Nimgaonkar VL, DeKosky ST, Sweet RA. Prediction of psychosis onset in Alzheimer disease: the role of depression symptom severity and the HTR2A T102C polymorphism. Am J Med Genet B Neuropsychiatr Genet. 2007;144B(8):1054-1062. doi:10.1002/ajmg.b.30549

98. McPhie DL, Coopersmith R, Hines-Peralta A, Chen Y, Ivins KJ, Manly SP, Kozlowski MR, Neve KA, Neve RL. DNA synthesis and neuronal apoptosis caused by familial Alzheimer disease mutants of the amyloid precursor protein are mediated by the p21 activated kinase PAK3. J Neurosci. 2003;23(17):6914-6927. doi:10.1523/JNEUROSCI.23-17-06914.2003

99. Kumar R, Corbett MA, Smith NJ, Jolly LA, Tan C, Keating DJ, Duffield MD, Utsumi T, Moriya K, Smith KR, et al. Homozygous mutation of STXBP5L explains an autosomal recessive infantile-onset neurodegenerative disorder. Hum Mol Genet. 2015;24(7):2000-2010. doi:10.1093/hmg/ddu614

100. Gallone S, Boschi S, Rubino E, De Martino P, Scarpini E, Galimberti D, Fenoglio C, Acutis PL, Maniaci MG, Pinessi L, et al. Is HCRTR2 a genetic risk factor for Alzheimer's disease?. Dement Geriatr Cogn Disord. 2014;38(3-4):245-253. doi:10.1159/000359964

101. Liu SJ, Yang C, Zhang Y, Su RY, Chen JL, Jiao MM, Chen HF, Zheng N, Luo S, Chen YB, 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

102. Woitecki AM, Müller JA, van Loo KM, Sowade RF, Becker AJ, Schoch S. Identification of Synaptotagmin 10 as Effector of NPAS4-Mediated Protection from Excitotoxic Neurodegeneration. J Neurosci. 2016;36(9):2561-2570. doi:10.1523/JNEUROSCI.2027-15.2016

103. de Barry J, Liégeois CM, Janoshazi A. Protein kinase C as a peripheral biomarker for Alzheimer's disease. Exp Gerontol. 2010;45(1):64-69. doi:10.1016/j.exger.2009.10.015

104. Mouton-Liger F, Dumurgier J, Cognat E, Hourregue C, Zetterberg H, Vanderstichele H, Vanmechelen E, Bouaziz-Amar E, Blennow K, Hugon J, et al.CSF levels of the BACE1 substrate NRG1 correlate with cognition in Alzheimer's disease. Alzheimers Res Ther. 2020;12(1):88. doi:10.1186/s13195-020-00655-w

105. Chilumuri A, Milton NG. The Role of Neurotransmitters in Protection against Amyloid- β Toxicity by KiSS-1 Overexpression in SH-SY5Y Neurons. ISRN Neurosci. 2013;2013:253210. doi:10.1155/2013/253210

106. Hishimoto A, Pletnikova O, Lang DL, Troncoso JC, Egan JM, Liu QR. Neurexin 3 transmembrane and soluble isoform expression and splicing haplotype are associated with neuron inflammasome and Alzheimer's disease. Alzheimers Res Ther. 2019;11(1):28. doi:10.1186/s13195-019-0475-2

107.   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

108.   Landel V, Millet P, Baranger K, Loriod B, Féron F. Vitamin D interacts with Esr1 and Igf1 to regulate molecular pathways relevant to Alzheimer's disease. Mol Neurodegener. 2016;11:22. doi:10.1186/s13024-016-0087-2

109.   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

110.   Chacón PJ, del Marco Á, Arévalo Á, Domínguez-Giménez P, García-Segura LM, Rodríguez-Tébar A. Cerebellin 4, a synaptic protein, enhances inhibitory activity and resistance of neurons to amyloid-β toxicity. Neurobiol Aging. 2015;36(2):1057-1071. doi:10.1016/j.neurobiolaging.2014.11.006

111.   Pelucchi S, Vandermeulen L, Pizzamiglio L, Aksan B, Yan J, Konietzny A, Bonomi E, Borroni B, Padovani A, Rust MB, et al. Cyclase-associated protein 2 dimerization regulates cofilin in synaptic plasticity and Alzheimer's disease. Brain Commun. 2020;2(2):fcaa086. doi:10.1093/braincomms/fcaa086

112.   Detrait E, Maurice T, Hanon E, Leclercq K, Lamberty Y. Lack of synaptic vesicle protein SV2B protects against amyloid-β□□□□□-induced oxidative stress, cholinergic deficit and cognitive impairment in mice. Behav Brain Res. 2014;271:277-285. doi:10.1016/j.bbr.2014.06.013

113.   Park D, Na M, Kim JA, Lee U, Cho E, Jang M, Chang S. Activation of CaMKIV by soluble amyloid-β1-42 impedes trafficking of axonal vesicles and impairs activity-dependent synaptogenesis. Sci Signal. 2017;10(487):eaam8661. doi:10.1126/scisignal.aam8661

114.   Cairns NJ, Uryu K, Bigio EH, Mackenzie IR, Gearing M, Duyckaerts C, Yokoo H, Nakazato Y, Jaros E, Perry RH, et al. alpha-Internexin aggregates are abundant in neuronal intermediate filament inclusion disease (NIFID) but rare in other neurodegenerative diseases. Acta Neuropathol. 2004;108(3):213-223. doi:10.1007/s00401-004-0882-7

115.   Sandelius Å, Portelius E, Källén Å, Zetterberg H, Rot U, Olsson B, Toledo JB, Shaw LM, Lee VMY, Irwin DJ, et al. Elevated CSF GAP-43 is Alzheimer's disease specific and associated with tau and amyloid pathology. Alzheimers Dement. 2019;15(1):55-64. doi:10.1016/j.jalz.2018.08.006

116.   Velayudhan L, Killick R, Hye A, Kinsey A, Güntert A, Lynham S, Ward M, Leung R, Lourdusamy A, To AW, et al. Plasma transthyretin as a candidate marker for Alzheimer's disease. J Alzheimers Dis. 2012;28(2):369-375. doi:10.3233/JAD-2011-110611

117.   Ryu JK, Cho T, Choi HB, Jantaratnotai N, McLarnon JG. Pharmacological antagonism of interleukin-8 receptor CXCR2 inhibits inflammatory reactivity and is neuroprotective in an animal model of Alzheimer's disease. J Neuroinflammation. 2015;12:144. doi:10.1186/s12974-015-0339-z

118.   Chen K, Tang Y, Zhao X, Hou C, Li G, Zhang B. Association of IL1R2 rs34043159 with sporadic Alzheimer's disease in southern Han Chinese. Eur J Neurol. 2020;27(10):1844-1847. doi:10.1111/ene.14319

119.   Li H, Wang R. A focus on CXCR4 in Alzheimer's disease. Brain Circ. 2017;3(4):199-203. doi:10.4103/bc.bc_13_17

120.   Rivera-Escalera F, Matousek SB, Ghosh S, Olschowka JA, O'Banion MK. Interleukin-1β mediated amyloid plaque clearance is independent of CCR2 signaling in the APP/PS1 mouse model of Alzheimer's disease. Neurobiol Dis. 2014;69:124-133. doi:10.1016/j.nbd.2014.05.018

121.   Chow N, Bell RD, Deane R, Streb JW, Chen J, Brooks A, Van Nostrand W, Miano JM, Zlokovic BV. Serum response factor and myocardin mediate arterial hypercontractility and cerebral blood flow dysregulation in Alzheimer's phenotype. Proc Natl Acad Sci U S A. 2007;104(3):823-828. doi:10.1073/pnas.0608251104

122.   Shepherd CE, Goyette J, Utter V, Rahimi F, Yang Z, Geczy CL, Halliday GM. Inflammatory S100A9 and S100A12 proteins in Alzheimer's disease. Neurobiol Aging. 2006;27(11):1554-1563. doi:10.1016/j.neurobiolaging.2005.09.033

123.   Krauthausen M, Kummer MP, Zimmermann J, Reyes-Irisarri E, Terwel D, Bulic B, Heneka MT, Müller M. CXCR3 promotes plaque formation and behavioral deficits in an Alzheimer's disease model. J Clin Invest. 2015;125(1):365-378. doi:10.1172/JCI66771

124. Lattanzi R, Maftei D, Petrella C, Pieri M, Sancesario G, Schirinzi T, Bernardini S, Barbato C, Ralli M, Greco A, et al. Involvement of the Chemokine Prokineticin-2 (PROK2) in Alzheimer's Disease: From Animal Models to the Human Pathology. Cells. 2019;8(11):1430. doi:10.3390/cells8111430

125. Ashutosh, Kou W, Cotter R, Borgmann K, Wu L, Persidsky R, Sakhuja N, Ghorpade A. CXCL8 protects human neurons from amyloid-β-induced neurotoxicity: relevance to Alzheimer's disease. Biochem Biophys Res Commun. 2011;412(4):565-571. doi:10.1016/j.bbrc.2011.07.127

126. Lee JK, Bou Dagher J. Regulator of G-protein Signaling (RGS)1 and RGS10 Proteins as Potential Drug Targets for Neuroinflammatory and Neurodegenerative Diseases. AAPS J. 2016;18(3):545-549. doi:10.1208/s12248-016-9883-4

127. Sassi C, Nalls MA, Ridge PG, Gibbs JR, Lupton MK, Troakes C, Lunnon K, Al-Sarraj S, Brown KS, Medway C, et al. Mendelian adult-onset leukodystrophy genes in Alzheimer's disease: critical influence of CSF1R and NOTCH3. Neurobiol Aging. 2018;66:179.e17-179.e29. doi:10.1016/j.neurobiolaging.2018.01.015

128. Hu SJ, Calippe B, Lavalette S, Roubeix C, Montassar F, Housset M, Levy O, Delarasse C, Paques M, Sahel JA, et al. Upregulation of P2RX7 in Cx3cr1-Deficient Mononuclear Phagocytes Leads to Increased Interleukin-1β Secretion and Photoreceptor Neurodegeneration. J Neurosci. 2015;35(18):6987-6996. doi:10.1523/JNEUROSCI.3955-14.2015

129. Cheng HC, Sun Y, Lai LC, Chen SY, Lee WC, Chen JH, Chen TF, Chen HH, Wen LL, Yip PK, et al. Genetic polymorphisms of nerve growth factor receptor (NGFR) and the risk of Alzheimer's disease. J Negat Results Biomed. 2012;11:5. doi:10.1186/1477-5751-11-5

130. Conte M, Sabbatinelli J, Chiariello A, Martucci M, Santoro A, Monti D, Arcaro M, Galimberti D, Scarpini E, Bonfigli AR, et al. Disease-specific plasma levels of mitokines FGF21, GDF15, and Humanin in type II diabetes and Alzheimer's disease in comparison with healthy aging . Geroscience. 2020;10.1007/s11357-020-00287-w. doi:10.1007/s11357-020-00287-w

131. Mahmoudi R, Feldman S, Kisserli A, Duret V, Tabary T, Bertholon LA, Badr S, Nonnonhou V, Cesar A, Neuraz A, et al. Inherited and Acquired Decrease in Complement Receptor 1 (CR1) Density on Red Blood Cells

Associated with High Levels of Soluble CR1 in Alzheimer's Disease. Int J Mol Sci. 2018;19(8):2175. doi:10.3390/ijms19082175

132.   Horgusluoglu-Moloch E, Nho K, Risacher SL, Kim S, Foroud T, Shaw LM, Trojanowski JQ, Aisen PS, Petersen RC, Jack CR Jr, et al. Targeted neurogenesis pathway-based gene analysis identifies ADORA2A associated with hippocampal volume in mild cognitive impairment and Alzheimer's disease. Neurobiol Aging. 2017;60:92-103. doi:10.1016/j.neurobiolaging.2017.08.010

133.   Deng LJ, Cheng C, Wu J, Wang CH, Zhou HB, Huang J. Oxabicycloheptene Sulfonate Protects Against β-Amyloid-induced Toxicity by Activation of PI3K/Akt and ERK Signaling Pathways Via GPER1 in C6 Cells. Neurochem Res. 2017;42(8):2246-2256. doi:10.1007/s11064-017-2237-5

134.   Costa AS, Agostini S, Guerini FR, Mancuso R, Clerici M, Pandey JP. Relation between FCGRIIB rs1050501 and HSV-1 specific IgG antibodies in Alzheimer's disease. J Transl Med. 2020;18(1):325. doi:10.1186/s12967-020-02495-6

135.   Kaminari A, Tsilibary EC, Tzinia A. A New Perspective in Utilizing MMP-9 as a Therapeutic Target for Alzheimer's Disease and Type 2 Diabetes Mellitus. J Alzheimers Dis. 2018;64(1):1-16. doi:10.3233/JAD-180035

136.   Gonzalez D, Brandan E. CTGF/CCN2 from Skeletal Muscle to Nervous System: Impact on Neurodegenerative Diseases. Mol Neurobiol. 2019;56(8):5911-5916. doi:10.1007/s12035-019-1490-9

137.   Hernandez MX, Jiang S, Cole TA, Chu SH, Fonseca MI, Fang MJ, Hohsfield LA, Torres MD, Green KN, Wetsel RA, et al. Prevention of C5aR1 signaling delays microglial inflammatory polarization, favors clearance pathways and suppresses cognitive loss. Mol Neurodegener. 2017;12(1):66. doi:10.1186/s13024-017-0210-z

138.   Hochstrasser T, Marksteiner J, Defrancesco M, Deisenhammer EA, Kemmler G, Humpel C. Two Blood Monocytic Biomarkers (CCL15 and p21) Combined with the Mini-Mental State Examination Discriminate Alzheimer's Disease Patients from Healthy Subjects. Dement Geriatr Cogn Dis Extra. 2011;1(1):297-309. doi:10.1159/000330468

139.   Lim YW, James D, Huang J, Lee M. The Emerging Role of the RNA-Binding Protein SFPQ in Neuronal Function and Neurodegeneration. Int J Mol Sci. 2020;21(19):7151. doi:10.3390/ijms21197151

140.   Reinhardt S, Schuck F, Stoye N, Hartmann T, Grimm MOW, Pflugfelder G, Endres K. Transcriptional repression of the ectodomain sheddase ADAM10 by TBX2 and potential implication for Alzheimer's disease. Cell Mol Life Sci. 2019;76(5):1005-1025. doi:10.1007/s00018-018-2998-2

141.   Iribarren P, Zhou Y, Hu J, Le Y, Wang JM. Role of formyl peptide receptor-like 1 (FPRL1/FPR2) in mononuclear phagocyte responses in Alzheimer disease. Immunol Res. 2005;31(3):165-176. doi:10.1385/IR:31:3:165

142.   Xia Z, Chibnik LB, Glanz BI, Liguori M, Shulman JM, Tran D, Khoury SJ, Chitnis T, Holyoak T, Weiner HL, et al. A putative Alzheimer's disease risk allele in PCK1 influences brain atrophy in multiple sclerosis. PLoS One. 2010;5(11):e14169. doi:10.1371/journal.pone.0014169

143.   Ma L, Lu ZN. Role of ADH1B rs1229984 and ALDH2 rs671 gene polymorphisms in the development of Alzheimer's disease. Genet Mol Res. 2016;15(4):10.4238/gmr.15048740. doi:10.4238/gmr.15048740

144.   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

145.   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

146.   Pey P, Pearce RK, Kalaitzakis ME, Griffin WS, Gentleman SM. Phenotypic profile of alternative activation marker CD163 is different in Alzheimer's and Parkinson's disease. Acta Neuropathol Commun. 2014;2:21. doi:10.1186/2051-5960-2-21

147.   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

148.   Zhubi A, Chen Y, Guidotti A, Grayson DR. Epigenetic regulation of RELN and GAD1 in the frontal cortex (FC) of autism spectrum disorder (ASD) subjects. Int J Dev Neurosci. 2017;62:63-72. doi:10.1016/j.ijdevneu.2017.02.003

149.   Pascolini G, Majore S, Valiante M, Bottillo I, Laino L, Agolini E, Novelli A, Grammatico B, Calvani M, Grammatico P. Autism spectrum disorder in a patient with a genomic rearrangement that only involves the EPHA5 gene. Psychiatr Genet. 2019;29(3):86-90. doi:10.1097/YPG.0000000000000217

150.   Sener EF, Cıkılı Uytun M, Korkmaz Bayramov K, Zararsiz G, Oztop DB, Canatan H, Ozkul Y. The roles of CC2D1A and HTR1A gene expressions in autism spectrum disorders. Metab Brain Dis. 2016;31(3):613-619. doi:10.1007/s11011-016-9795-0

151.   Sadakata T, Furuichi T. Developmentally regulated Ca2+-dependent activator protein for secretion 2 (CAPS2) is involved in BDNF secretion and is associated with autism susceptibility. Cerebellum. 2009;8(3):312-322. doi:10.1007/s12311-009-0097-5

152.   Wang L, Li J, Shuang M, Lu T, Wang Z, Zhang T, Yue W, Jia M, Ruan Y, Liu J, et al. Association study and mutation sequencing of genes on chromosome 15q11-q13 identified GABRG3 as a susceptibility gene for autism in Chinese Han population. Transl Psychiatry. 2018;8(1):152. doi:10.1038/s41398-018-0197-4

153.   Cappuccio G, Attanasio S, Alagia M, Mutarelli M, Borzone R, Karali M, Genesio R, Mormile A, Nitsch L, Imperati F, et al. Microdeletion of pseudogene chr14.232.a affects LRFN5 expression in cells of a patient with autism spectrum disorder. Eur J Hum Genet. 2019;27(9):1475-1480. doi:10.1038/s41431-019-0430-5

154.   Ahmad SF, Ansari MA, Nadeem A, Bakheet SA, Al-Ayadhi LY, Alsaad AMS, Assiri MA, Al-Mazroua HA, Attia SM. Upregulation of interleukin (IL)-31, a cytokine producing CXCR1 peripheral immune cells, contributes to the immune abnormalities of autism spectrum disorder. J Neuroimmunol. 2020;349:577430. doi:10.1016/j.jneuroim.2020.577430

155.   Hughes AJ, Dunn KM, Chaffee T, Bhattarai JJ, Beier M. Diagnostic and Clinical Utility of the GAD-2 for Screening Anxiety Symptoms in Individuals With Multiple Sclerosis. Arch Phys Med Rehabil. 2018;99(10):2045-2049. doi:10.1016/j.apmr.2018.05.029

156.   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

157.   Galuppo M, Giacoppo S, Sessa E, Bramanti P, Mazzon E. Are natural killer cells involved in multiple sclerosis etiology? Evidences from NKp46/NCR1 receptor modulation in an observational study. J Neurol Sci. 2014;345(1-2):248-251. doi:10.1016/j.jns.2014.07.045

158.   Simsek H, Geckin H, Sensoz NP, List EO, Arman A. Association Between IL7R Promoter Polymorphisms and Multiple Sclerosis in Turkish Population. J Mol Neurosci. 2019;67(1):38-47. doi:10.1007/s12031-018-1205-0

159.   Scazzone C, Agnello L, Lo Sasso B, Salemi G, Gambino CM, Ragonese P, Candore G, Ciaccio AM, Giglio RV, Bivona G, et al. FOXP3 and GATA3 Polymorphisms, Vitamin D3 and Multiple Sclerosis. Brain Sci. 2021;11(4):415. doi:10.3390/brainsci11040415

160.   Yuan M, Wei L, Zhou R, Bai Q, Wei Y, Zhang W, Huang Y. Four FCRL3 Gene Polymorphisms (FCRL3_3, _5, _6, _8) Confer Susceptibility to Multiple Sclerosis: Results from a Case-Control Study. Mol Neurobiol. 2016;53(3):2029-2035. doi:10.1007/s12035-015-9149-7

161.   Gillett A, Thessen Hedreul M, Khademi M, Espinosa A, Beyeen AD, Jagodic M, Kockum I, Harris RA, Olsson T.Interleukin 18 receptor 1 expression distinguishes patients with multiple sclerosis. Mult Scler. 2010;16(9):1056-1065. doi:10.1177/1352458510364634

162.   Herbert MK, Aerts MB, Beenes M, Norgren N, Esselink RA, Bloem BR, Kuiperij HB, Verbeek MM. CSF Neurofilament Light Chain but not FLT3 Ligand Discriminates Parkinsonian Disorders. Front Neurol. 2015;6:91. doi:10.3389/fneur.2015.00091

163.   Gao J, Xu H, Weinberg C, Huang X, Park Y, Hollenbeck A, Blair A, Schatzkin A, Burch L, Chen H. An exploratory study on the CHRNA3-

CHRNA5-CHRNB4 cluster, smoking, and Parkinson's disease. Neurodegener Dis. 2011;8(5):296-299. doi:10.1159/000323190

164.   Wu DM, Wang S, Wen X, Han XR, Wang YJ, Shen M, Fan SH, Zhuang J, Zhang ZF, Shan Q, et al. Suppression of microRNA-342-3p increases glutamate transporters and prevents dopaminergic neuron loss through activating the Wnt signaling pathway via p21-activated kinase 1 in mice with Parkinson's disease. J Cell Physiol. 2019;234(6):9033-9044. doi:10.1002/jcp.27577

165.   Bar-Shira A, Gana-Weisz M, Gan-Or Z, Giladi E, Giladi N, Orr-Urtreger A. CHRNB3 c.-57A>G functional promoter change affects Parkinson's disease and smoking. Neurobiol Aging. 2014;35(9):2179.e1-2179.e21796. doi:10.1016/j.neurobiolaging.2014.03.014

166.   Kim IY, O'Reilly ÉJ, Hughes KC, Gao X, Schwarzschild MA, McCullough ML, Hannan MT, Betensky RA, Ascherio A. Interaction between caffeine and polymorphisms of glutamate ionotropic receptor NMDA type subunit 2A (GRIN2A) and cytochrome P450 1A2 (CYP1A2) on Parkinson's disease risk. Mov Disord. 2018;33(3):414-420. doi:10.1002/mds.27279

167.   Martinelli S, Cordeddu V, Galosi S, Lanzo A, Palma E, Pannone L, Ciolfi A, Di Nottia M, Rizza T, Bocchinfuso G, et al. Co-occurring WARS2 and CHRNA6 mutations in a child with a severe form of infantile parkinsonism. Parkinsonism Relat Disord. 2020;72:75-79. doi:10.1016/j.parkreldis.2020.02.003

168.   Bäckman CM, Shan L, Zhang Y, Hoffer BJ, Tomac AC. Alterations in prodynorphin, proenkephalin, and GAD67 mRNA levels in the aged human putamen: correlation with Parkinson's disease. J Neurosci Res. 2007;85(4):798-804. doi:10.1002/jnr.21164

169.   Gao J, Xu H, Weinberg C, Huang X, Park Y, Hollenbeck A, Blair A, Schatzkin A, Burch L, Chen H. An exploratory study on the CHRNA3-CHRNA5-CHRNB4 cluster, smoking, and Parkinson's disease. Neurodegener Dis. 2011;8(5):296-299. doi:10.1159/000323190

170.   Kaut O, Sharma A, Schmitt I, Wüllner U. DNA methylation of imprinted loci of autosomal chromosomes and IGF2 is not affected in Parkinson's disease patients' peripheral blood mononuclear cells. Neurol Res. 2017;39(3):281-284. doi:10.1080/01616412.2017.1279424

171.   Zhu K, Teng J, Zhao J, Liu H, Xie A. Association of TLR9 polymorphisms with sporadic Parkinson's disease in Chinese Han population. Int J Neurosci. 2016;126(7):612-616. doi:10.3109/00207454.2015.1050591

172.   Dong Y, Han LL, Xu ZX. Suppressed microRNA-96 inhibits iNOS expression and dopaminergic neuron apoptosis through inactivating the MAPK signaling pathway by targeting CACNG5 in mice with Parkinson's disease. Mol Med. 2018;24(1):61. doi:10.1186/s10020-018-0059-9

173.   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

174.   Figlewicz DA, Krizus A, Martinoli MG, Meininger V, Dib M, Rouleau GA, Julien JP. Variants of the heavy neurofilament subunit are associated with the development of amyotrophic lateral sclerosis. Hum Mol Genet. 1994;3(10):1757-1761. doi:10.1093/hmg/3.10.1757

175.   Marques RF, Engler JB, Küchler K, Jones RA, Lingner T, Salinas G, Gillingwater TH, Friese MA, Duncan KE. Motor neuron translatome reveals deregulation of SYNGR4 and PLEKHB1 in mutant TDP-43 amyotrophic lateral sclerosis models. Hum Mol Genet. 2020;29(16):2647-2661. doi:10.1093/hmg/ddaa140

176.   Serrano A, Apolloni S, Rossi S, Lattante S, Sabatelli M, Peric M, Andjus P, Michetti F, Carrì MT, Cozzolino M, et al. The S100A4 Transcriptional Inhibitor Niclosamide Reduces Pro-Inflammatory and Migratory Phenotypes of Microglia: Implications for Amyotrophic Lateral Sclerosis. Cells. 2019;8(10):1261. doi:10.3390/cells8101261

177.   Capponi S, Geuens T, Geroldi A, Origone P, Verdiani S, Cichero E, Adriaenssens E, De Winter V, Bandettini di Poggio M, et al. Molecular Chaperones in the Pathogenesis of Amyotrophic Lateral Sclerosis: The Role of HSPB1. Hum Mutat. 2016;37(11):1202-1208. doi:10.1002/humu.23062

178.   Nicolas A, Kenna KP, Renton AE, Ticozzi N, Faghri F, Chia R, Dominov JA, Kenna BJ, Nalls MA, Keagle P, et al. Genome-wide Analyses Identify KIF5A as a Novel ALS Gene. Neuron. 2018;97(6):1268-1283.e6. doi:10.1016/j.neuron.2018.02.027

179.   Berto S, Usui N, Konopka G, Fogel BL. ELAVL2-regulated transcriptional and splicing networks in human neurons link neurodevelopment and autism. Hum Mol Genet. 2016;25(12):2451-2464. doi:10.1093/hmg/ddw110

180.   Fernandez-Martos CM, King AE, Atkinson RA, Woodhouse A, Vickers JC. Neurofilament light gene deletion exacerbates amyloid, dystrophic neurite, and synaptic pathology in the APP/PS1 transgenic model of Alzheimer's disease. Neurobiol Aging. 2015;36(10):2757-2767. doi:10.1016/j.neurobiolaging.2015.07.003

181.   Dhaeze T, Tremblay L, Lachance C, Peelen E, Zandee S, Grasmuck C, Bourbonnière L, Larouche S, Ayrignac X, Rébillard RM, et al. CD70 defines a subset of proinflammatory and CNS-pathogenic TH1/TH17 lymphocytes and is overexpressed in multiple sclerosis. Cell Mol Immunol. 2019;16(7):652-665. doi:10.1038/s41423-018-0198-5

182.   Ye Z, Sun B, Mi X, Xiao Z. Gene co-expression network for analysis of plasma exosomal miRNAs in the elderly as markers of aging and cognitive decline. PeerJ. 2020;8:e8318. doi:10.7717/peerj.8318

183.   Sala Frigerio C, Lau P, Salta E, Tournoy J, Bossers K, Vandenberghe R, Wallin A, Bjerke M, Zetterberg H, Blennow K, et al. Reduced expression of hsa-miR-27a-3p in CSF of patients with Alzheimer disease. Neurology. 2013;81(24):2103-2106. doi:10.1212/01.wnl.0000437306.37850.22

184.   Wang Z, Shen L, Wang Y, Huang S. Integrated analysis of miRNA and mRNA expression in the blood of patients with Alzheimer's disease. Mol Med Rep. 2020;22(2):1053-1062. doi:10.3892/mmr.2020.11162

185.   Nagaraj S, Laskowska-Kaszub K, Dębski KJ, Wojsiat J, Dąbrowski M, Gabryelewicz T, Kuźnicki J, Wojda U. Profile of 6 microRNA in blood plasma distinguish early stage Alzheimer's disease patients from non-demented subjects. Oncotarget. 2017;8(10):16122-16143. doi:10.18632/oncotarget.15109

186.   Northrop A, Byers HA, Radhakrishnan SK. Regulation of NRF1, a master transcription factor of proteasome genes: implications for cancer and neurodegeneration. Mol Biol Cell. 2020;31(20):2158-2163. doi:10.1091/mbc.E20-04-0238

187.   Zhang Z, Li XG, Wang ZH, Song M, Yu SP, Kang SS, Liu X, Zhang Z, Xie M, Liu GP, et al. δ-Secretase-cleaved Tau stimulates Aβ production

via upregulating STAT1-BACE1 signaling in Alzheimer's disease. Mol Psychiatry. 2021;26(2):586-603. doi:10.1038/s41380-018-0286-z

188.   Lahiri DK, Ge YW, Rogers JT, Sambamurti K, Greig NH, Maloney B. Taking down the unindicted co-conspirators of amyloid beta-peptide-mediated neuronal death: shared gene regulation of BACE1 and APP genes interacting with CREB, Fe65 and YY1 transcription factors. Curr Alzheimer Res. 2006;3(5):475-483. doi:10.2174/156720506779025224

189.   Dong YT, Cao K, Xiang J, Shan L, Guan ZZ. Silent Mating-Type Information Regulation 2 Homolog 1 Attenuates the Neurotoxicity Associated with Alzheimer Disease via a Mechanism Which May Involve Regulation of Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-α.   Am   J   Pathol.   2020;190(7):1545-1564. doi:10.1016/j.ajpath.2020.03.015

190.   Rosas I, Martínez C, Coto E, Clarimón J, Lleó A, Illán-Gala I, Dols-Icardo O, Borroni B, Almeida MR, van der Zee J, et al. Genetic variation in APOE, GRN, and TP53 are phenotype modifiers in frontotemporal dementia. Neurobiol   Aging.   2021;99:99.e15-99.e22. doi:10.1016/j.neurobiolaging.2020.08.018

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 – A219= AD; B1 – B70 = healthy controls)

Fig. 3. PPI network of DEGs. The PPI network of DEGs was constructed using Cytoscap. 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 16 nodes and 38 edges for up regulated genes (B) The most significant module was obtained from PPI network with 47 nodes and 96 edges for down regulated genes. Up regulated genes are marked in green; down regulated genes are marked in red.

Fig. 5. MiRNA - hub gene regulatory network. The purple color diamond nodes represent the key miRNAs; up regulated genes are marked in green; down regulated genes are marked in red.

Fig. 6. TF - hub gene regulatory network. The blue 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 validated the sensitivity, specificity of hub genes as a predictive biomarker for Alzheimer's disease diagnosis. A) PAK1 B) ELAVL2 C) NSF D) HTR2C E) TERT F) UBD G) MKI67 H) HSPB1 I) PYHIN1 J) TES

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

Gene Symbol	logFC	pValue	adj.P.Val	tvalue	Regulation	Gene name
RBBP8NL	1.792155	2.15E-10	4.28E-09	6.350402	Up	RBBP8 N-terminal like
CRH	1.723255	4.45E-15	4.89E-13	7.841503	Up	corticotropin releasing hormone
SPRR2G	1.564456	2.45E-12	9.42E-11	7.00588	Up	small proline rich protein 2G
REG1CP	1.513107	7.39E-06	3.69E-05	4.482086	Up	regenerating family member 1 gamma, pseudogene
TAC1	1.50299	3.07E-15	3.55E-13	7.888171	Up	tachykinin precursor 1
NMU	1.477089	2.32E-13	1.29E-11	7.328947	Up	neuromedin U

MAS1	1.466607	3.77E-05	0.000156	4.121265	Up	MAS1 proto-oncogene, G protein-coupled receptor
VGF	1.45949	1.47E-19	9.75E-17	9.046631	Up	VGF nerve growth factor inducible
PCSK1	1.421549	4.06E-11	1.02E-09	6.601835	Up	proproteinconvertasesubtilisin/kexin type 1
SST	1.404689	1.01E-15	1.45E-13	8.025125	Up	somatostatin
ADCYAP1	1.400453	2.56E-20	2.34E-17	9.236109	Up	adenylatecyclase activating polypeptide 1
PENK	1.360921	1.16E-13	7.07E-12	7.421705	Up	proenkephalin
OR7E47P	1.332921	8.23E-07	5.28E-06	4.929926	Up	olfactory receptor family 7 subfamily E member 47 pseudogene
GABRA6	1.326971	3.39E-10	6.24E-09	6.279742	Up	gamma-aminobutyric acid type A receptor subunit alpha6
HSPB3	1.300949	9.39E-19	4.58E-16	8.842146	Up	heat shock protein family B (small) member 3
SLN	1.283622	1.20E-13	7.33E-12	7.416601	Up	sarcolipin
SOWAHB	1.280945	1.03E-09	1.60E-08	6.10543	Up	sosondowahankyrin repeat domain family member B
DSG3	1.28065	0.002644	0.006733	3.006337	Up	desmoglein 3
C1QL3	1.275145	2.03E-07	1.52E-06	5.196433	Up	complement C1q like 3
PPEF1	1.274206	7.62E-19	3.96E-16	8.865398	Up	protein phosphatase with EF-hand domain 1
NPAS4	1.256782	1.24E-06	7.60E-06	4.84915	Up	neuronal PAS domain protein 4
OR52N2	1.24645	7.69E-05	0.000292	3.953898	Up	olfactory receptor family 52 subfamily N member 2
EGR4	1.245746	3.33E-15	3.78E-13	7.877942	Up	early growth response 4
SERTM1	1.240042	5.40E-13	2.63E-11	7.214786	Up	serine rich and transmembrane domain containing 1
SERTM2	1.236927	0.000444	0.001389	3.512644	Up	serine rich and transmembrane domain containing 2
CSN1S1	1.236875	0.002004	0.005264	3.089583	Up	casein alpha s1
MUC15	1.220349	4.35E-05	0.000176	4.088296	Up	mucin 15, cell surface associated
MOS	1.217979	6.69E-06	3.36E-05	4.503362	Up	MOS proto-oncogene, serine/threonine kinase
SI	1.216882	0.001498	0.004059	3.175165	Up	sucrase-isomaltase
GJD2	1.211457	1.62E-07	1.24E-06	5.23787	Up	gap junction protein delta 2
GSG1L2	1.210676	1.66E-06	9.77E-06	4.791418	Up	GSG1 like 2
NPSR1	1.207645	3.37E-06	1.83E-05	4.647064	Up	neuropeptide S receptor 1
KRT5	1.204534	2.37E-10	4.65E-09	6.335059	Up	keratin 5
CHGB	1.204116	3.65E-12	1.33E-10	6.949939	Up	chromogranin B
ADAD2	1.193409	2.50E-16	4.39E-14	8.195177	Up	adenosine deaminase domain containing 2
ABRA	1.190391	3.76E-07	2.63E-06	5.080655	Up	actin binding Rho activating protein
C4orf54	1.185335	3.31E-06	1.80E-05	4.650848	Up	chromosome 4 open reading frame 54
PNMA6A	1.181083	8.30E-05	0.000312	3.935645	Up	PNMA family member 6A
NEUROD6	1.172833	7.58E-11	1.75E-09	6.508686	Up	neuronal differentiation 6
RGS4	1.172806	1.06E-13	6.57E-12	7.433827	Up	regulator of G protein signaling 4
WFDC10A	1.165912	0.000749	0.002204	3.371031	Up	WAP four-disulfide core domain 10A
CWH43	1.165094	0.000615	0.001854	3.424724	Up	cell wall biogenesis 43 C-terminal homolog
KRT82	1.160963	8.82E-05	0.000329	3.921013	Up	keratin 82
SLC32A1	1.160424	1.71E-12	6.96E-11	7.056381	Up	solute carrier family 32 member 1
IL1RAPL2	1.159802	7.57E-05	0.000289	3.957525	Up	interleukin 1 receptor accessory protein like 2
GAD2	1.158021	3.98E-12	1.43E-10	6.937909	Up	glutamate decarboxylase 2
ANKRD18DP	1.152965	3.46E-12	1.28E-10	6.95756	Up	ankyrin repeat domain 18D, pseudogene
CAPZA3	1.151592	0.003936	0.009522	2.883259	Up	capping actin protein of muscle Z-line subunit alpha 3

GRP	1.141596	1.73E-12	7.04E-11	7.054306	Up	gastrin releasing peptide
CHRNA9	1.13746	3.87E-05	0.000159	4.114852	Up	cholinergic receptor nicotinic alpha 9 subunit
ACTL8	1.134624	1.38E-06	8.33E-06	4.827436	Up	actin like 8
NXPH2	1.131891	2.93E-09	3.96E-08	5.935607	Up	neurexophilin 2
C14orf39	1.124348	0.005002	0.011731	2.806924	Up	chromosome 14 open reading frame 39
EGR3	1.114913	1.21E-13	7.35E-12	7.415901	Up	early growth response 3
CRYM	1.114406	3.53E-11	9.10E-10	6.622406	Up	crystallin mu
SCHLAP1	1.114037	6.76E-05	0.000261	3.984639	Up	SWI/SNF complex antagonist associated with prostate cancer 1
CCNYL4	1.1091	3.62E-08	3.40E-07	5.508481	Up	cyclin Y like 4 (pseudogene)
PNOC	1.108493	7.24E-13	3.40E-11	7.174869	Up	prepronociceptin
GAD1	1.107448	1.07E-16	2.18E-14	8.297185	Up	glutamate decarboxylase 1
CXCL11	1.10341	9.47E-07	5.99E-06	4.90229	Up	C-X-C motif chemokine ligand 11
FREM3	1.102409	8.15E-08	6.85E-07	5.363685	Up	FRAS1 related extracellular matrix 3
C17orf102	1.101675	9.39E-13	4.22E-11	7.1392	Up	chromosome 17 open reading frame 102
DRGX	1.099711	0.005153	0.012039	2.797291	Up	dorsal root ganglia homeobox
CLEC4F	1.094546	2.56E-06	1.43E-05	4.703626	Up	C-type lectin domain family 4 member F
CTXN3	1.084705	1.52E-09	2.24E-08	6.042531	Up	cortexin 3
HDC	1.078277	2.54E-09	3.49E-08	5.959084	Up	histidine decarboxylase
GABRA1	1.070151	6.01E-09	7.22E-08	5.816533	Up	gamma-aminobutyric acid type A receptor subunit alpha1
EGR1	1.067688	3.11E-16	5.17E-14	8.168916	Up	early growth response 1
C3orf80	1.067379	4.87E-14	3.50E-12	7.535299	Up	chromosome 3 open reading frame 80
PCDH8	1.066795	2.50E-08	2.47E-07	5.573399	Up	protocadherin 8
PVALB	1.06419	4.39E-06	2.31E-05	4.592051	Up	parvalbumin
PLSCR5	1.06302	0.002759	0.006987	2.993373	Up	phospholipid scramblase family member 5
STAT4	1.061542	1.51E-12	6.32E-11	7.073489	Up	signal transducer and activator of transcription 4
OLFM3	1.05809	3.37E-08	3.19E-07	5.521089	Up	olfactomedin 3
FAM47C	1.054309	0.000879	0.002537	3.326739	Up	family with sequence similarity 47 member C
ATOH7	1.053408	4.33E-14	3.17E-12	7.550581	Up	atonal bHLH transcription factor 7
PRMT8	1.052567	1.17E-14	1.06E-12	7.71945	Up	protein arginine methyltransferase 8
KCNV1	1.05243	4.01E-09	5.17E-08	5.883803	Up	potassium voltage-gated channel modifier subfamily V member 1
TDO2	1.050395	2.03E-08	2.06E-07	5.609836	Up	tryptophan 2,3-dioxygenase
CALB1	1.050333	3.89E-09	5.04E-08	5.888779	Up	calbindin 1
OVOS2	1.048457	1.72E-08	1.80E-07	5.637677	Up	alpha-2-macroglobulin like 1 pseudogene
AMELX	1.048424	0.003178	0.007908	2.949998	Up	amelogenin X-linked
ANKRD62	1.044304	3.14E-05	0.000132	4.163275	Up	ankyrin repeat domain 62
WNT8A	1.042288	9.31E-10	1.48E-08	6.120858	Up	Wnt family member 8A
EFCAB3	1.042265	0.000303	0.000987	3.6127	Up	EF-hand calcium binding domain 3
CBLN4	1.040513	3.41E-08	3.22E-07	5.518871	Up	cerebellin 4 precursor
MYOG	1.037877	2.82E-07	2.04E-06	5.135063	Up	myogenin
C13orf42	1.035355	0.005916	0.013606	2.752395	Up	chromosome 13 open reading frame 42
CCDC196	1.035158	0.000916	0.002633	3.315008	Up	coiled-coil domain containing 196
MS4A8	1.033714	2.42E-06	1.36E-05	4.715149	Up	membrane spanning 4-domains A8

Gene	logFC	P.Value	adj.P.Val	AveExpr	Regulation	Description
KIRREL3-AS3	1.031608	0.000173	0.000598	3.756	Up	KIRREL3 antisense RNA 3
TEX26-AS1	1.029183	8.43E-08	7.05E-07	5.357708	Up	TEX26 antisense RNA 1
SYP-AS1	1.026727	4.49E-07	3.08E-06	5.046805	Up	SYP antisense RNA 1
DCTN1-AS1	1.023243	2.56E-13	1.40E-11	7.315949	Up	DCTN1 antisense RNA 1
BDNF	1.022065	4.31E-24	2.63E-20	10.12433	Up	brain derived neurotrophic factor
SPATA48	1.018411	0.000653	0.001951	3.408589	Up	spermatogenesis associated 48
ANKRD33	1.018068	8.75E-05	0.000327	3.92279	Up	ankyrin repeat domain 33
GABRG2	1.016224	6.43E-08	5.55E-07	5.406467	Up	gamma-aminobutyric acid type A receptor subunit gamma2
CD70	1.015253	2.55E-05	0.00011	4.210264	Up	CD70 molecule
ROBO2	1.008347	2.54E-10	4.92E-09	6.324275	Up	roundabout guidance receptor 2
TPH2	1.005576	7.25E-06	3.63E-05	4.486126	Up	tryptophan hydroxylase 2
ERICH3-AS1	1.00524	2.79E-05	0.00012	4.189763	Up	ERICH3 antisense RNA 1
FLT3	1.005056	1.10E-07	8.89E-07	5.308631	Up	fms related receptor tyrosine kinase 3
UBE2U	1.004904	0.000159	0.000557	3.776266	Up	ubiquitin conjugating enzyme E2 U
CHRNB4	1.004005	0.000529	0.001626	3.465596	Up	cholinergic receptor nicotinic beta 4 subunit
PART1	1.002783	3.50E-11	9.04E-10	6.62389	Up	prostate androgen-regulated transcript 1
SVOP	0.999571	1.91E-11	5.44E-10	6.712665	Up	SV2 related protein
SLC5A7	0.999569	0.014403	0.029714	2.447058	Up	solute carrier family 5 member 7
PIK3C2G	0.998847	2.44E-06	1.37E-05	4.713389	Up	phosphatidylinositol-4-phosphate 3-kinase catalytic subunit type 2 gamma
KCNK18	0.997672	0.012251	0.025798	2.504829	Up	potassium two pore domain channel subfamily K member 18
IQCJ	0.992878	2.42E-06	1.36E-05	4.714906	Up	IQ motif containing J
STYK1	0.992545	2.14E-08	2.17E-07	5.599941	Up	serine/threonine/tyrosine kinase 1
HTR2C	0.989166	5.69E-07	3.80E-06	5.001507	Up	5-hydroxytryptamine receptor 2C
ARL4D	0.988673	2.58E-20	2.34E-17	9.234915	Up	ADP ribosylation factor like GTPase 4D
NAP1L5	0.985169	2.87E-16	4.87E-14	8.178551	Up	nucleosome assembly protein 1 like 5
ADGRF2	0.984019	0.000289	0.000945	3.625412	Up	adhesion G protein-coupled receptor F2
CDH7	0.983533	3.61E-05	0.00015	4.130886	Up	cadherin 7
TCP11	0.981913	3.51E-08	3.30E-07	5.513967	Up	t-complex 11
PCP4	0.980196	7.90E-14	5.24E-12	7.471999	Up	Purkinje cell protein 4
TERT	0.980011	5.09E-06	2.63E-05	4.561017	Up	telomerase reverse transcriptase
BEX5	0.978943	2.45E-15	3.05E-13	7.915997	Up	brain expressed X-linked 5
NEFL	0.9786	1.83E-09	2.64E-08	6.012007	Up	neurofilament light
MLIP	0.978387	1.99E-11	5.62E-10	6.706744	Up	muscular LMNA interacting protein
SOSTDC1	0.97708	3.45E-07	2.44E-06	5.097088	Up	sclerostin domain containing 1
INTS6L-AS1	0.975855	1.68E-05	7.66E-05	4.303637	Up	INTS6L antisense RNA 1
SNAP25	0.97474	1.26E-09	1.90E-08	6.072715	Up	synaptosome associated protein 25
RAB3B	0.971743	3.59E-10	6.54E-09	6.271061	Up	RAB3B, member RAS oncogene family
TCF23	0.970766	0.020699	0.040846	2.313424	Up	transcription factor 23
SNTN	0.968452	0.001376	0.003768	3.199714	Up	sentan, cilia apical structure protein
NYAP2	0.968344	2.42E-05	0.000106	4.221754	Up	neuronal tyrosine-phosphorylated phosphoinositide-3-kinase adaptor 2
RAB27B	0.967279	9.16E-08	7.54E-07	5.342678	Up	RAB27B, member RAS oncogene family
OR1N1	0.96601	0.01512	0.030977	2.429486	Up	olfactory receptor family 1 subfamily N member 1

MUCL1	0.965921	1.75E-06	1.02E-05	4.780546	Up	mucin like 1
RXFP3	0.963798	0.014225	0.029419	2.451539	Up	relaxin family peptide receptor 3
SATB2-AS1	0.96374	1.65E-09	2.40E-08	6.02931	Up	SATB2 antisense RNA 1
MYPN	0.957798	0.000297	0.000969	3.618314	Up	myopalladin
CYP4A11	0.957237	9.73E-07	6.13E-06	4.897036	Up	cytochrome P450 family 4 subfamily A member 11
SUN3	0.95643	2.97E-07	2.14E-06	5.125412	Up	Sad1 and UNC84 domain containing 3
GDA	0.950478	1.53E-09	2.25E-08	6.041671	Up	guanine deaminase
GREM2	0.947377	5.17E-10	8.97E-09	6.213978	Up	gremlin 2, DAN family BMP antagonist
UNC5D	0.944438	3.29E-10	6.07E-09	6.284642	Up	unc-5 netrin receptor D
CREG2	0.944388	2.33E-07	1.71E-06	5.171094	Up	cellular repressor of E1A stimulated genes 2
ERICH6B	0.94413	0.004502	0.010706	2.840697	Up	glutamate rich 6B
RPH3A	0.943871	7.81E-13	3.60E-11	7.164518	Up	rabphilin 3A
CNTN5	0.942573	4.52E-07	3.10E-06	5.045602	Up	contactin 5
GABRB2	0.939695	1.42E-06	8.51E-06	4.822515	Up	gamma-aminobutyric acid type A receptor subunit beta2
MAL2	0.938674	2.03E-08	2.07E-07	5.609631	Up	mal, T cell differentiation protein 2
ZCCHC12	0.93839	8.18E-11	1.87E-09	6.497161	Up	zinc finger CCHC-type containing 12
NLRP2	0.937784	7.45E-08	6.33E-07	5.380024	Up	NLR family pyrin domain containing 2
FRMPD2B	0.937148	1.44E-10	3.04E-09	6.411959	Up	FERM and PDZ domain containing 2B, pseudogene
AGBL4	0.936178	2.62E-13	1.43E-11	7.31269	Up	ATP/GTP binding protein like 4
PTPRR	0.934759	5.28E-09	6.50E-08	5.838145	Up	protein tyrosine phosphatase receptor type R
RFX6	0.93464	4.62E-05	0.000186	4.074225	Up	regulatory factor X6
CDH18	0.934539	4.09E-10	7.32E-09	6.250537	Up	cadherin 18
TACR1	0.933255	2.05E-11	5.74E-10	6.702554	Up	tachykinin receptor 1
KCNG3	0.932517	1.14E-07	9.12E-07	5.302803	Up	potassium voltage-gated channel modifier subfamily G member 3
FBLN7	0.932076	1.46E-11	4.37E-10	6.751391	Up	fibulin 7
CARTPT	0.931108	1.00E-06	6.28E-06	4.891557	Up	CART prepropeptide
ALOX12B	0.930558	3.58E-10	6.53E-09	6.271334	Up	arachidonate 12-lipoxygenase, 12R type
CCDC105	0.929791	0.007671	0.017095	2.666235	Up	coiled-coil domain containing 105
SPTSSB	0.929526	1.66E-10	3.44E-09	6.389594	Up	serine palmitoyltransferase small subunit B
AMY2A	0.929227	4.13E-06	2.19E-05	4.604952	Up	amylase alpha 2A
MCHR1	0.924109	2.11E-10	4.21E-09	6.353393	Up	melanin concentrating hormone receptor 1
NRN1	0.923459	5.87E-19	3.11E-16	8.89451	Up	neuritin 1
KCNS2	0.92343	3.87E-09	5.02E-08	5.889649	Up	potassium voltage-gated channel modifier subfamily S member 2
YY1P2	0.922952	0.013143	0.027465	2.479877	Up	YY1 transcription factor pseudogene 2
SLC17A6	0.922759	1.03E-06	6.46E-06	4.885102	Up	solute carrier family 17 member 6
RAB3C	0.921229	1.49E-09	2.20E-08	6.045659	Up	RAB3C, member RAS oncogene family
SLC4A10	0.92009	1.86E-06	1.08E-05	4.768439	Up	solute carrier family 4 member 10
AFP	0.919009	2.07E-05	9.20E-05	4.256686	Up	alpha fetoprotein
HRG	0.918231	0.000358	0.001146	3.569348	Up	histidine rich glycoprotein
GPR22	0.918097	5.56E-07	3.73E-06	5.005804	Up	G protein-coupled receptor 22
NEFM	0.91801	3.36E-08	3.18E-07	5.52153	Up	neurofilament medium
SYT1	0.91656	5.76E-09	6.98E-08	5.823483	Up	synaptotagmin 1

Gene						Description
EPHA5	0.914525	2.17E-07	1.61E-06	5.183944	Up	EPH receptor A5
MSX2P1	0.913053	9.17E-07	5.82E-06	4.90863	Up	mshhomeobox 2 pseudogene 1
OR2AE1	0.912044	0.010487	0.022507	2.559343	Up	olfactory receptor family 2 subfamily AE member 1
PARM1	0.91119	6.57E-10	1.10E-08	6.176127	Up	prostate androgen-regulated mucin-like protein 1
GLP2R	0.910394	8.86E-07	5.65E-06	4.915458	Up	glucagon like peptide 2 receptor
CDH9	0.910322	6.71E-08	5.76E-07	5.398892	Up	cadherin 9
STARD6	0.907602	0.000134	0.000478	3.818379	Up	StAR related lipid transfer domain containing 6
CYP24A1	0.906744	1.35E-06	8.17E-06	4.83206	Up	cytochrome P450 family 24 subfamily A member 1
HTR3B	0.906486	8.43E-08	7.05E-07	5.357589	Up	5-hydroxytryptamine receptor 3B
C8orf89	0.90642	7.82E-05	0.000296	3.949981	Up	chromosome 8 open reading frame 89
GLRA3	0.906045	4.26E-05	0.000173	4.092805	Up	glycine receptor alpha 3
SCG2	0.905705	9.28E-15	8.96E-13	7.748698	Up	secretogranin II
HPRT1	0.904017	9.15E-12	2.92E-10	6.819211	Up	hypoxanthine phosphoribosyltransferase 1
SERPINA11	0.904017	0.013108	0.027399	2.480821	Up	serpin family A member 11
MEPE	0.902128	8.87E-07	5.65E-06	4.915184	Up	matrix extracellular phosphoglycoprotein
DEPDC1-AS1	0.90096	0.003069	0.007673	2.96077	Up	DEPDC1 antisense RNA 1
SYT4	0.900419	1.15E-08	1.26E-07	5.707159	Up	synaptotagmin 4
C5orf52	0.900038	0.006856	0.015497	2.703782	Up	chromosome 5 open reading frame 52
ST6GALNAC5	0.89952	3.01E-08	2.89E-07	5.540709	Up	ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 5
LAMP5-AS1	0.899431	3.77E-06	2.02E-05	4.623449	Up	LAMP5 antisense RNA 1
NMNAT2	0.899216	4.78E-11	1.18E-09	6.577507	Up	nicotinamide nucleotide adenylyltransferase 2
INHBA-AS1	0.896832	4.66E-13	2.32E-11	7.234822	Up	INHBA antisense RNA 1
SMIM21	0.896187	0.014305	0.029552	2.449511	Up	small integral membrane protein 21
PTER	0.895363	3.06E-09	4.12E-08	5.928114	Up	phosphotriesterase related
ENC1	0.893532	2.11E-08	2.14E-07	5.602776	Up	ectodermal-neural cortex 1
CCDC184	0.893363	2.03E-13	1.15E-11	7.346483	Up	coiled-coil domain containing 184
NELL1	0.891575	1.90E-08	1.96E-07	5.620431	Up	neural EGFL like 1
CALCB	0.889626	3.96E-05	0.000163	4.109638	Up	calcitonin related polypeptide beta
GPR158	0.888867	5.95E-10	1.01E-08	6.191769	Up	G protein-coupled receptor 158
GFRA4	0.888466	4.31E-08	3.94E-07	5.47784	Up	GDNF family receptor alpha 4
GRIN2B	0.885576	5.06E-08	4.53E-07	5.449014	Up	glutamate ionotropic receptor NMDA type subunit 2B
LAMP5	0.884614	2.89E-08	2.80E-07	5.547776	Up	lysosomal associated membrane protein family member 5
HCN1	0.884586	5.27E-08	4.69E-07	5.441852	Up	hyperpolarization activated cyclic nucleotide gated potassium channel 1
FBXL21P	0.883837	2.05E-05	9.11E-05	4.259079	Up	F-box and leucine rich repeat protein 21, pseudogene
ANKRD20A19P	0.882067	0.000222	0.000749	3.692125	Up	ankyrin repeat domain 20 family member A19, pseudogene
RHOV	0.881065	6.56E-10	1.10E-08	6.176433	Up	ras homolog family member V
JARID2-AS1	0.878863	3.34E-07	2.37E-06	5.10326	Up	JARID2 antisense RNA 1
KCNB2	0.87725	5.28E-08	4.69E-07	5.441764	Up	potassium voltage-gated channel subfamily B member 2
ENTPD3	0.876706	1.75E-10	3.60E-09	6.38155	Up	ectonucleoside triphosphate diphosphohydrolase 3
OTOL1	0.874487	0.000267	0.000879	3.645784	Up	otolin 1
DLGAP1	0.874408	2.22E-10	4.40E-09	6.344991	Up	DLG associated protein 1
PCP4L1	0.874291	8.62E-10	1.38E-08	6.133126	Up	Purkinje cell protein 4 like 1

FATE1	0.872197	9.00E-06	4.39E-05	4.440013	Up	fetal and adult testis expressed 1
GABRA4	0.871964	2.32E-07	1.71E-06	5.171299	Up	gamma-aminobutyric acid type A receptor subunit alpha4
AKAP5	0.871719	2.90E-09	3.93E-08	5.937232	Up	A-kinase anchoring protein 5
ADRA1D	0.870488	2.30E-10	4.53E-09	6.339877	Up	adrenoceptor alpha 1D
C11orf87	0.870409	2.83E-08	2.75E-07	5.551377	Up	chromosome 11 open reading frame 87
CDK6-AS1	0.867973	3.39E-08	3.20E-07	5.520107	Up	CDK6 antisense RNA 1
LGALS16	0.867257	0.00243	0.006243	3.031912	Up	galectin 16
CAP2	0.866391	1.34E-08	1.45E-07	5.680436	Up	cyclase associated actin cytoskeleton regulatory protein 2
KCNC2	0.86587	4.06E-09	5.23E-08	5.881548	Up	potassium voltage-gated channel subfamily C member 2
MGC12916	0.865719	4.90E-05	0.000196	4.060577	Up	uncharacterized protein MGC12916
PTPN3	0.865436	1.20E-10	2.60E-09	6.438716	Up	protein tyrosine phosphatase non-receptor type 3
DHRS7C	0.865012	6.22E-08	5.40E-07	5.412323	Up	dehydrogenase/reductase 7C
SERF1A	0.861415	0.02312	0.044943	2.271451	Up	small EDRK-rich factor 1A
GCNT4	0.859334	2.14E-05	9.45E-05	4.249654	Up	glucosaminyl (N-acetyl) transferase 4
TDRD5	0.859286	1.61E-07	1.23E-06	5.239612	Up	tudor domain containing 5
RGS7	0.859005	2.82E-10	5.33E-09	6.308637	Up	regulator of G protein signaling 7
KCNH5	0.858044	8.23E-06	4.05E-05	4.45907	Up	potassium voltage-gated channel subfamily H member 5
IL12RB2	0.856705	1.15E-08	1.26E-07	5.707141	Up	interleukin 12 receptor subunit beta 2
AVP	0.856049	0.005559	0.012881	2.772708	Up	arginine vasopressin
DYDC1	0.855875	0.000633	0.0019	3.417029	Up	DPY30 domain containing 1
DGKB	0.855847	5.27E-09	6.49E-08	5.838395	Up	diacylglycerol kinase beta
VSNL1	0.855091	2.13E-08	2.16E-07	5.601312	Up	visinin like 1
BNIP5	0.854939	4.47E-07	3.07E-06	5.047906	Up	BCL2 interacting protein 5
NAPB	0.853004	9.65E-12	3.04E-10	6.811636	Up	NSF attachment protein beta
FGF9	0.853004	1.18E-09	1.82E-08	6.082397	Up	fibroblast growth factor 9
FAM238B	0.851614	2.30E-07	1.70E-06	5.173432	Up	family with sequence similarity 238 member B
PAX5	0.851044	0.000141	0.000498	3.807051	Up	paired box 5
HTR2A	0.850773	5.59E-08	4.92E-07	5.431592	Up	5-hydroxytryptamine receptor 2A
NAP1L2	0.850242	2.61E-08	2.57E-07	5.56556	Up	nucleosome assembly protein 1 like 2
C6orf141	0.846646	3.50E-06	1.90E-05	4.638775	Up	chromosome 6 open reading frame 141
CLTRN	0.846631	1.29E-10	2.75E-09	6.428812	Up	collectrin, amino acid transport regulator
DLX1	0.845535	9.73E-10	1.53E-08	6.113723	Up	distal-less homeobox 1
PAK1	0.845205	9.72E-12	3.06E-10	6.810605	Up	p21 (RAC1) activated kinase 1
TESPA1	0.844983	6.79E-08	5.83E-07	5.396567	Up	thymocyte expressed, positive selection associated 1
DLX6	0.843311	6.63E-09	7.84E-08	5.800028	Up	distal-less homeobox 6
CACNA1C-IT2	0.842806	0.000864	0.002503	3.331345	Up	CACNA1C intronic transcript 2
NPSR1-AS1	0.841801	0.000674	0.002008	3.399907	Up	NPSR1 antisense RNA 1
PAK3	0.840507	7.34E-10	1.21E-08	6.158679	Up	p21 (RAC1) activated kinase 3
MCHR2-AS1	0.839539	0.013371	0.027878	2.473731	Up	MCHR2 antisense RNA 1
NAT16	0.838617	7.08E-13	3.34E-11	7.177972	Up	N-acetyltransferase 16 (putative)
LY86-AS1	0.83772	7.70E-09	8.92E-08	5.774911	Up	LY86 antisense RNA 1
SLC30A3	0.83743	1.41E-07	1.10E-06	5.263377	Up	solute carrier family 30 member 3
NCALD	0.837209	1.53E-12	6.38E-11	7.071777	Up	neurocalcin delta

ANO3	0.836643	6.68E-08	5.74E-07	5.399576	Up	anoctamin 3
GLRA2	0.836266	1.39E-07	1.09E-06	5.266285	Up	glycine receptor alpha 2
SLC39A2	0.834221	0.000258	0.000853	3.654516	Up	solute carrier family 39 member 2
GUCA1C	0.833736	0.022726	0.044271	2.278005	Up	guanylatecyclase activator 1C
CFAP61-AS1	0.832953	0.001046	0.00296	3.27773	Up	CFAP61 antisense RNA 1
STXBP5L	0.83278	8.25E-09	9.48E-08	5.763243	Up	syntaxin binding protein 5 like
NELL2	0.832359	1.13E-07	9.08E-07	5.30379	Up	neural EGFL like 2
BHLHA9	0.832224	3.49E-05	0.000145	4.139005	Up	basic helix-loop-helix family member a9
TAFA1	0.83193	9.41E-10	1.49E-08	6.119151	Up	TAFA chemokine like family member 1
F7	0.831629	2.19E-10	4.35E-09	6.347394	Up	coagulation factor VII
PGM2L1	0.831592	1.46E-08	1.55E-07	5.666753	Up	phosphoglucomutase 2 like 1
RBFOX1	0.831543	1.07E-08	1.18E-07	5.719858	Up	RNA binding fox-1 homolog 1
CTSE	0.831448	0.014431	0.029756	2.446358	Up	cathepsin E
GADL1	0.830936	0.013697	0.028485	2.465104	Up	glutamate decarboxylase like 1
RTKN2	0.830778	3.81E-08	3.55E-07	5.49966	Up	rhotekin 2
ERICH3	0.830708	3.43E-07	2.43E-06	5.098109	Up	glutamate rich 3
ATP12A	0.830435	0.010676	0.022857	2.553118	Up	ATPase H+/K+ transporting non-gastric alpha2 subunit
SCN2A	0.830033	2.14E-08	2.16E-07	5.600563	Up	sodium voltage-gated channel alpha subunit 2
MCHR2	0.829027	0.000253	0.000838	3.659662	Up	melanin concentrating hormone receptor 2
NDST3	0.828983	4.21E-07	2.91E-06	5.059209	Up	N-deacetylase and N-sulfotransferase 3
SPRNP1	0.828608	1.83E-08	1.89E-07	5.627459	Up	shadow of prion protein pseudogene 1
HCRTR2	0.827387	1.72E-07	1.31E-06	5.227545	Up	hypocretin receptor 2
ADRB3	0.826858	1.72E-07	1.31E-06	5.226834	Up	adrenoceptor beta 3
FSTL5	0.826785	5.98E-08	5.22E-07	5.419258	Up	follistatin like 5
GPR88	0.824455	2.05E-11	5.74E-10	6.702157	Up	G protein-coupled receptor 88
NPBWR1	0.824374	0.0064	0.014591	2.726559	Up	neuropeptides B and W receptor 1
THCAT155	0.824154	6.82E-09	8.02E-08	5.795246	Up	thyroid cancer-associated transcript 155
SV2B	0.823749	2.17E-09	3.05E-08	5.984701	Up	synaptic vesicle glycoprotein 2B
SYT13	0.823406	2.61E-09	3.58E-08	5.954176	Up	synaptotagmin 13
GTF2IP7	0.823009	0.001843	0.004883	3.114385	Up	general transcription factor IIipseudogene 7
CDH12	0.822897	1.05E-06	6.52E-06	4.882926	Up	cadherin 12
NR1H4	0.821498	3.89E-05	0.00016	4.114001	Up	nuclear receptor subfamily 1 group H member 4
SYP	0.821434	3.78E-10	6.85E-09	6.262746	Up	synaptophysin
RSPO2	0.820785	5.58E-09	6.81E-08	5.828761	Up	R-spondin 2
PLCXD3	0.820371	5.10E-10	8.86E-09	6.216123	Up	phosphatidylinositol specific phospholipase C X domain containing 3
SYT2	0.81991	0.000194	0.000662	3.727284	Up	synaptotagmin 2
STMN2	0.81946	4.54E-09	5.73E-08	5.863345	Up	stathmin 2
SPATA31C1	0.819192	0.016741	0.033924	2.39235	Up	SPATA31 subfamily C member 1
RUNX1-IT1	0.816682	0.018606	0.037218	2.353329	Up	RUNX1 intronic transcript 1
CALY	0.816668	7.90E-10	1.29E-08	6.146997	Up	calcyon neuron specific vesicular protein
SLC12A1	0.815891	4.75E-06	2.47E-05	4.575638	Up	solute carrier family 12 member 1
FGF5	0.815253	5.48E-05	0.000217	4.034345	Up	fibroblast growth factor 5

Gene	Value	P-value	FDR	Log	Direction	Description
PRPH2	0.814442	6.03E-11	1.44E-09	6.542904	Up	peripherin 2
PRSS16	0.813423	2.27E-09	3.18E-08	5.976994	Up	serine protease 16
NSF	0.813317	4.16E-10	7.41E-09	6.248053	Up	N-ethylmaleimide sensitive factor, vesicle fusing ATPase
CYMP	0.812548	1.86E-05	8.35E-05	4.28113	Up	chymosin, pseudogene
GPR149	0.812373	0.001089	0.003064	3.266419	Up	G protein-coupled receptor 149
CHRNB3	0.811471	7.07E-07	4.61E-06	4.959386	Up	cholinergic receptor nicotinic beta 3 subunit
OR1F1	0.810384	0.000191	0.000654	3.731098	Up	olfactory receptor family 1 subfamily F member 1
LRTM2	0.809731	1.17E-09	1.80E-08	6.084398	Up	leucine rich repeats and transmembrane domains 2
RXFP1	0.809409	2.13E-06	1.22E-05	4.740566	Up	relaxin family peptide receptor 1
STYXL2	0.809064	1.89E-12	7.55E-11	7.042214	Up	serine/threonine/tyrosine interacting like 2
SYT10	0.808703	2.85E-05	0.000122	4.185372	Up	synaptotagmin 10
TAFA2	0.808593	8.31E-08	6.96E-07	5.360359	Up	TAFA chemokine like family member 2
GPR158-AS1	0.807864	8.35E-11	1.91E-09	6.494201	Up	GPR158 antisense RNA 1
NEURL1-AS1	0.807801	0.002609	0.006654	3.010454	Up	NEURL1 antisense RNA 1
PRKCE	0.807405	1.81E-10	3.70E-09	6.376777	Up	protein kinase C epsilon
PNMA2	0.806543	1.73E-10	3.56E-09	6.383802	Up	PNMA family member 2
LEXM	0.805554	0.000379	0.001207	3.554094	Up	lymphocyte expansion molecule
RASL11B	0.804277	1.33E-09	2.00E-08	6.063177	Up	RAS like family 11 member B
DCLK1	0.803629	1.59E-09	2.33E-08	6.035155	Up	doublecortin like kinase 1
PAX7	0.802991	5.33E-08	4.73E-07	5.439964	Up	paired box 7
GRIN2A	0.802863	1.94E-08	1.99E-07	5.617483	Up	glutamate ionotropic receptor NMDA type subunit 2A
VSIG1	0.802859	1.23E-08	1.33E-07	5.69593	Up	V-set and immunoglobulin domain containing 1
AKAIN1	0.801937	0.000446	0.001395	3.51131	Up	A-kinase anchor inhibitor 1
RFPL1	0.801552	1.58E-06	9.41E-06	4.800221	Up	ret finger protein like 1
DLX6-AS1	0.80028	0.000334	0.001078	3.587014	Up	DLX6 antisense RNA 1
KCNQ5	0.799723	4.12E-06	2.19E-05	4.605187	Up	potassium voltage-gated channel subfamily Q member 5
RHEX	0.799218	0.006464	0.01472	2.723255	Up	regulator of hemoglobinization and erythroid cell expansion
COL25A1	0.798211	1.03E-05	4.95E-05	4.411255	Up	collagen type XXV alpha 1 chain
CAMK4	0.798093	1.56E-07	1.20E-06	5.245789	Up	calcium/calmodulin dependent protein kinase IV
ATP2B1-AS1	0.798012	8.90E-13	4.04E-11	7.146452	Up	ATP2B1 antisense RNA 1
TUBB2A	0.796202	2.76E-12	1.04E-10	6.989311	Up	tubulin beta 2A class IIa
CDH8	0.796137	2.88E-10	5.44E-09	6.305043	Up	cadherin 8
VWC2L	0.795176	0.000152	0.000533	3.788101	Up	von Willebrand factor C domain containing 2 like
HUNK	0.791394	4.46E-11	1.11E-09	6.587934	Up	hormonally up-regulated Neu-associated kinase
MDH1	0.789285	2.31E-12	8.96E-11	7.014419	Up	malate dehydrogenase 1
HMGCLL1	0.788594	1.08E-11	3.33E-10	6.795805	Up	3-hydroxymethyl-3-methylglutaryl-CoA lyase like 1
HTR1A	0.788329	0.000357	0.001143	3.570135	Up	5-hydroxytryptamine receptor 1A
NWD2	0.788081	4.84E-06	2.52E-05	4.571641	Up	NACHT and WD repeat domain containing 2
SP9	0.788008	6.33E-05	0.000246	4.000026	Up	Sp9 transcription factor
RASSF6	0.787955	0.010396	0.02233	2.562355	Up	Ras association domain family member 6
C8orf86	0.787699	3.09E-05	0.000131	4.166672	Up	chromosome 8 open reading frame 86
SNX10	0.787314	2.14E-08	2.16E-07	5.600672	Up	sorting nexin 10
MAP7D2	0.787212	1.82E-09	2.62E-08	6.013113	Up	MAP7 domain containing 2

Gene	Value	p1	p2	FC	Dir	Description
SYN2	0.786693	2.37E-08	2.36E-07	5.582792	Up	synapsin II
UPK2	0.786654	6.21E-07	4.11E-06	4.984426	Up	uroplakin 2
LRRC38	0.786119	5.89E-06	3.00E-05	4.530286	Up	leucine rich repeat containing 38
PP12613	0.786114	3.42E-05	0.000143	4.143663	Up	uncharacterized LOC100192379
TRIM72	0.784408	2.17E-06	1.24E-05	4.737377	Up	tripartite motif containing 72
FBXO16	0.783954	2.66E-13	1.44E-11	7.310474	Up	F-box protein 16
TMEM200A	0.782944	6.78E-10	1.13E-08	6.171094	Up	transmembrane protein 200A
RIIAD1	0.782351	3.26E-11	8.49E-10	6.634452	Up	regulatory subunit of type II PKA R-subunit domain containing 1
GGNBP1	0.782076	4.25E-07	2.93E-06	5.057327	Up	gametogenetin binding protein 1 (pseudogene)
BEX1	0.781213	3.06E-12	1.14E-10	6.975154	Up	brain expressed X-linked 1
ELAVL2	0.780828	4.14E-07	2.87E-06	5.062446	Up	ELAV like RNA binding protein 2
ZNF98	0.780164	6.94E-05	0.000267	3.978392	Up	zinc finger protein 98
ELMOD1	0.779622	1.76E-08	1.83E-07	5.634133	Up	ELMO domain containing 1
IPCEF1	0.779195	2.68E-10	5.13E-09	6.316097	Up	interaction protein for cytohesin exchange factors 1
SIDT1	0.778754	1.19E-11	3.64E-10	6.781485	Up	SID1 transmembrane family member 1
CLEC2L	0.777808	3.00E-09	4.04E-08	5.931794	Up	C-type lectin domain family 2 member L
XK	0.777647	1.12E-08	1.24E-07	5.711239	Up	X-linked Kx blood group
WNT1	0.776704	1.24E-05	5.86E-05	4.370504	Up	Wnt family member 1
KRT222	0.776693	5.88E-08	5.15E-07	5.422283	Up	keratin 222
SULT4A1	0.776176	3.50E-09	4.62E-08	5.906184	Up	sulfotransferase family 4A member 1
NEFH	0.775778	6.14E-05	0.000239	4.007474	Up	neurofilament heavy
GABRD	0.775735	3.17E-08	3.02E-07	5.531769	Up	gamma-aminobutyric acid type A receptor subunit delta
TRPC7	0.775079	5.86E-05	0.00023	4.018197	Up	transient receptor potential cation channel subfamily C member 7
NRG1	0.774868	2.54E-07	1.86E-06	5.155013	Up	neuregulin 1
HS6ST3	0.774066	6.68E-09	7.88E-08	5.798765	Up	heparansulfate 6-O-sulfotransferase 3
RFPL1S	0.773705	1.41E-08	1.51E-07	5.671767	Up	RFPL1 antisense RNA 1
PTH2R	0.772967	6.01E-09	7.22E-08	5.816365	Up	parathyroid hormone 2 receptor
FAM81A	0.772769	6.58E-13	3.13E-11	7.187816	Up	family with sequence similarity 81 member A
HAO2-IT1	0.772461	0.011554	0.02452	2.525467	Up	HAO2 intronic transcript 1
NETO1	0.771691	2.54E-09	3.49E-08	5.959053	Up	neuropilin and tolloid like 1
INSYN1-AS1	0.770357	2.25E-06	1.28E-05	4.729212	Up	INSYN1 antisense RNA 1
FGF12	0.769374	6.08E-10	1.03E-08	6.188314	Up	fibroblast growth factor 12
PLPPR4	0.769269	1.24E-06	7.58E-06	4.849748	Up	phospholipid phosphatase related 4
LPA	0.769136	1.02E-08	1.14E-07	5.727883	Up	lipoprotein(a)
MACROD2	0.768905	2.52E-10	4.89E-09	6.325602	Up	mono-ADP ribosylhydrolase 2
SERPINB13	0.768716	0.006995	0.015776	2.69707	Up	serpin family B member 13
ZNF860	0.768457	8.12E-07	5.21E-06	4.932554	Up	zinc finger protein 860
PLCB1	0.767706	7.65E-08	6.48E-07	5.37509	Up	phospholipase C beta 1
SH3GL2	0.767358	1.37E-07	1.07E-06	5.269271	Up	SH3 domain containing GRB2 like 2, endophilin A1
MLLT11	0.767026	2.96E-10	5.57E-09	6.301095	Up	MLLT11 transcription factor 7 cofactor
KISS1	0.766693	0.000121	0.000437	3.843699	Up	KiSS-1 metastasis suppressor
FABP12	0.766559	0.009475	0.020563	2.59441	Up	fatty acid binding protein 12

PDP1	0.76636	2.99E-08	2.88E-07	5.541828	Up	pyruvate dehyrogenase phosphatase catalytic subunit 1
FUT3	0.766263	1.96E-05	8.73E-05	4.269365	Up	fucosyltransferase 3 (Lewis blood group)
REC114	0.765964	7.06E-08	6.02E-07	5.389706	Up	REC114 meiotic recombination protein
RFX8	0.765632	2.30E-07	1.70E-06	5.173009	Up	regulatory factor X8
SFTPA2	0.764227	2.53E-07	1.85E-06	5.155471	Up	surfactant protein A2
SMIM17	0.764165	3.86E-08	3.59E-07	5.497218	Up	small integral membrane protein 17
PCYOX1L	0.76389	8.74E-14	5.63E-12	7.458705	Up	prenylcysteine oxidase 1 like
TPBGL	0.76382	4.44E-09	5.64E-08	5.866783	Up	trophoblast glycoprotein like
TMEM210	0.7629	0.01941	0.038603	2.337553	Up	transmembrane protein 210
C2orf80	0.762762	4.75E-10	8.34E-09	6.227054	Up	chromosome 2 open reading frame 80
REEP1	0.762117	8.58E-12	2.76E-10	6.828519	Up	receptor accessory protein 1
UPK3A	0.760624	0.000286	0.000938	3.627529	Up	uroplakin 3A
CADPS	0.760332	2.95E-08	2.84E-07	5.544592	Up	calcium dependent secretion activator
MAJIN	0.760196	0.025221	0.048387	2.238008	Up	membrane anchored junction protein
OBSCN-AS1	0.759842	8.90E-11	2.01E-09	6.484617	Up	OBSCN antisense RNA 1
CHRNA6	0.758185	7.65E-05	0.000291	3.955065	Up	cholinergic receptor nicotinic alpha 6 subunit
OR13C5	0.757862	0.008411	0.018495	2.635112	Up	olfactory receptor family 13 subfamily C member 5
NRXN3	0.757322	2.45E-10	4.78E-09	6.329818	Up	neurexin 3
GSG1	0.757196	7.62E-10	1.25E-08	6.152657	Up	germ cell associated 1
INA	0.757189	3.87E-08	3.60E-07	5.496729	Up	internexin neuronal intermediate filament protein alpha
FBXW7-AS1	0.75659	2.31E-05	0.000101	4.232857	Up	FBXW7 antisense RNA 1
F2RL2	0.756403	9.35E-05	0.000347	3.906945	Up	coagulation factor II thrombin receptor like 2
VSX2	0.756098	1.11E-05	5.33E-05	4.393727	Up	visual system homeobox 2
SPINK9	0.75466	0.001462	0.003975	3.182099	Up	serine peptidase inhibitor Kazal type 9
SFTA3	0.753411	3.05E-05	0.00013	4.169403	Up	surfactant associated 3
FRMPD4	0.753395	4.22E-08	3.87E-07	5.481463	Up	FERM and PDZ domain containing 4
GPRASP2	0.753366	6.99E-12	2.33E-10	6.857949	Up	G protein-coupled receptor associated sorting protein 2
INSM2	0.753359	1.29E-07	1.01E-06	5.280938	Up	INSM transcriptional repressor 2
SERPINB2	0.752998	0.007622	0.016997	2.668386	Up	serpin family B member 2
CLSTN3	0.752866	7.63E-10	1.25E-08	6.152414	Up	calsyntenin 3
VSTM5	0.752664	0.000824	0.0024	3.344744	Up	V-set and transmembrane domain containing 5
P2RX2	0.75251	0.003585	0.008785	2.91252	Up	purinergic receptor P2X 2
SPRY3	0.751835	0.005222	0.012181	2.79298	Up	sprouty RTK signaling antagonist 3
GABRG3	0.751614	4.76E-05	0.000191	4.067112	Up	gamma-aminobutyric acid type A receptor subunit gamma3
LRRC3C	0.750568	0.008068	0.017857	2.649222	Up	leucine rich repeat containing 3C
MROH2A	0.750565	0.002065	0.005406	3.080709	Up	maestro heat like repeat family member 2A
CNGB1	0.750255	0.000123	0.000441	3.84077	Up	cyclic nucleotide gated channel subunit beta 1
FER1L6-AS2	0.749074	6.69E-07	4.39E-06	4.970062	Up	FER1L6 antisense RNA 2
MYH13	0.748804	2.76E-05	0.000119	4.192209	Up	myosin heavy chain 13
DYNC1I1	0.748414	5.49E-09	6.72E-08	5.831583	Up	dynein cytoplasmic 1 intermediate chain 1
SDR16C5	0.7482	1.59E-07	1.22E-06	5.241266	Up	short chain dehydrogenase/reductase family 16C member 5
CACNB4	0.7481	1.57E-08	1.66E-07	5.653746	Up	calcium voltage-gated channel auxiliary subunit beta 4
ATP8A2	0.747635	1.57E-09	2.31E-08	6.036654	Up	ATPase phospholipid transporting 8A2

RAB3A	0.746687	8.27E-09	9.50E-08	5.762897	Up	RAB3A, member RAS oncogene family
DIRAS2	0.745925	5.14E-07	3.48E-06	5.020932	Up	DIRAS family GTPase 2
IL1RL2	0.745482	3.83E-11	9.78E-10	6.610511	Up	interleukin 1 receptor like 2
ADTRP	0.745434	2.98E-10	5.60E-09	6.299984	Up	androgen dependent TFPI regulating protein
LDB2	0.745409	1.08E-08	1.19E-07	5.718067	Up	LIM domain binding 2
NUDT11	0.745215	7.96E-09	9.18E-08	5.769318	Up	nudix hydrolase 11
EID2B	0.745058	9.15E-22	1.60E-18	9.586027	Up	EP300 interacting inhibitor of differentiation 2B
SLC8A1-AS1	0.745008	0.009636	0.020876	2.58864	Up	SLC8A1 antisense RNA 1
PIWIL1	0.744685	0.004425	0.010547	2.846144	Up	piwi like RNA-mediated gene silencing 1
SLC7A4	0.743897	5.24E-07	3.53E-06	5.017316	Up	solute carrier family 7 member 4
ANKRD7	0.743718	4.30E-05	0.000174	4.090998	Up	ankyrin repeat domain 7
DSG1	0.743674	0.000363	0.001163	3.565281	Up	desmoglein 1
LMO7DN	0.743592	0.000191	0.000654	3.731036	Up	LMO7 downstream neighbor
GOLT1A	0.743087	2.01E-08	2.05E-07	5.610888	Up	golgi transport 1A
DNAJC5G	0.742717	4.41E-06	2.32E-05	4.591057	Up	DnaJ heat shock protein family (Hsp40) member C5 gamma
GALNTL6	0.742618	4.27E-07	2.94E-06	5.05662	Up	polypeptide N-acetylgalactosaminyltransferase like 6
CHML	0.74223	1.02E-08	1.14E-07	5.727261	Up	CHM like Rab escort protein
RHO	0.740772	3.28E-06	1.79E-05	4.652425	Up	rhodopsin
COPG2IT1	0.740493	1.99E-10	4.00E-09	6.362003	Up	COPG2 imprinted transcript 1
RTN1	0.740474	2.02E-09	2.88E-08	5.996057	Up	reticulon 1
MYB	0.740224	1.04E-05	5.01E-05	4.408437	Up	MYB proto-oncogene, transcription factor
CLPSL2	0.739861	3.45E-05	0.000144	4.141854	Up	colipase like 2
PPM1E	0.739682	5.59E-07	3.74E-06	5.004725	Up	protein phosphatase, Mg2+/Mn2+ dependent 1E
CCDC185	0.739573	0.007177	0.016129	2.688519	Up	coiled-coil domain containing 185
PYY	0.739488	2.95E-05	0.000125	4.177522	Up	peptide YY
CT45A10	0.739399	0.015067	0.030877	2.430774	Up	cancer/testis antigen family 45 member A10
CT45A9	0.738628	0.015619	0.031914	2.41769	Up	cancer/testis antigen family 45 member A9
B4GALT6	0.738589	3.22E-09	4.31E-08	5.91978	Up	beta-1,4-galactosyltransferase 6
NRIP3	0.738451	1.51E-10	3.17E-09	6.404415	Up	nuclear receptor interacting protein 3
ANKRD34B	0.738425	0.00056	0.001709	3.450278	Up	ankyrin repeat domain 34B
NECTIN3-AS1	0.738285	1.59E-08	1.68E-07	5.651105	Up	NECTIN3 antisense RNA 1
CHRM4	0.738258	0.000231	0.000774	3.682752	Up	cholinergic receptor muscarinic 4
ACTR3-AS1	0.737832	3.38E-08	3.19E-07	5.520441	Up	ACTR3 antisense RNA 1
PLK4	0.737252	2.13E-09	3.01E-08	5.987443	Up	polo like kinase 4
MSC-AS1	0.735383	4.88E-11	1.20E-09	6.574595	Up	MSC antisense RNA 1
FNDC9	0.734977	1.79E-10	3.66E-09	6.378465	Up	fibronectin type III domain containing 9
SYNGR4	0.734788	1.32E-06	7.99E-06	4.837367	Up	synaptogyrin 4
IGF1	0.734717	5.54E-08	4.89E-07	5.433202	Up	insulin like growth factor 1
PLK2	0.734232	1.84E-10	3.75E-09	6.37373	Up	polo like kinase 2
CT55	0.734099	0.005868	0.013503	2.755072	Up	cancer/testis antigen 55
TAC3	0.733809	9.94E-08	8.12E-07	5.327791	Up	tachykinin precursor 3
FSTL4	0.733439	6.59E-08	5.68E-07	5.402006	Up	follistatin like 4
LRFN5	0.733294	3.03E-08	2.91E-07	5.539536	Up	leucine rich repeat and fibronectin type III domain containing

ZNF441	0.732996	4.57E-12	1.61E-10	6.918248	Up	zinc finger protein 441
SCN8A	0.732736	1.62E-09	2.37E-08	6.03188	Up	sodium voltage-gated channel alpha subunit 8
TRHDE	0.732698	3.06E-05	0.00013	4.169187	Up	thyrotropin releasing hormone degrading enzyme
GAP43	0.732487	2.10E-09	2.98E-08	5.989608	Up	growth associated protein 43
ANKRD20A8P	0.731571	0.00292	0.00734	2.976044	Up	ankyrin repeat domain 20 family member A8, pseudogene
ALG1L2	0.731189	0.00366	0.008943	2.906099	Up	ALG1 chitobiosyldiphosphodolichol beta-mannosyltransferase like 2
PAQR9	0.731112	1.56E-07	1.20E-06	5.245276	Up	progestin and adipoQ receptor family member 9
MMP8	-1.87297	3.77E-06	2.02E-05	-4.62382	Down	matrix metallopeptidase 8
H4C4	-1.76756	2.85E-08	2.77E-07	-5.55021	Down	H4 clustered histone 4
MMP7	-1.62335	0.00384	0.009316	-2.89102	Down	matrix metallopeptidase 7
CRNN	-1.60805	0.000339	0.001093	-3.58316	Down	cornulin
SGO1-AS1	-1.56037	2.27E-16	4.07E-14	-8.20684	Down	SGO1 antisense RNA 1
PPBP	-1.55467	6.60E-10	1.11E-08	-6.17549	Down	pro-platelet basic protein
GABRR2	-1.52173	6.85E-15	7.00E-13	-7.78726	Down	gamma-aminobutyric acid type A receptor subunit rho2
CXCR6	-1.51769	7.75E-10	1.27E-08	-6.15003	Down	C-X-C motif chemokine receptor 6
MMP10	-1.48323	2.32E-05	0.000101	-4.23186	Down	matrix metallopeptidase 10
NTRK3-AS1	-1.4728	6.79E-11	1.59E-09	-6.52523	Down	NTRK3 antisense RNA 1
NMRAL2P	-1.46874	8.75E-07	5.58E-06	-4.91785	Down	NmrA like redox sensor 2, pseudogene
CD40LG	-1.46694	3.41E-05	0.000143	-4.14392	Down	CD40 ligand
TTR	-1.44982	1.69E-07	1.29E-06	-5.23065	Down	transthyretin
C11orf86	-1.4285	1.57E-08	1.66E-07	-5.6538	Down	chromosome 11 open reading frame 86
H3C6	-1.42644	1.22E-10	2.63E-09	-6.43685	Down	H3 clustered histone 6
FOXA3	-1.39254	1.41E-08	1.51E-07	-5.67182	Down	forkhead box A3
H1-6	-1.38752	3.88E-08	3.61E-07	-5.49626	Down	H1.6 linker histone, cluster member
NCR1	-1.38367	3.00E-05	0.000128	-4.17317	Down	natural cytotoxicity triggering receptor 1
CXCR1	-1.37112	4.34E-09	5.54E-08	-5.87056	Down	C-X-C motif chemokine receptor 1
CXCR2	-1.35865	4.88E-09	6.08E-08	-5.85111	Down	C-X-C motif chemokine receptor 2
OR7C1	-1.35682	1.42E-10	3.01E-09	-6.41342	Down	olfactory receptor family 7 subfamily C member 1
RIPOR3	-1.34988	3.00E-24	2.44E-20	-10.1596	Down	RIPOR family member 3
NPC1L1	-1.34313	2.14E-09	3.02E-08	-5.98674	Down	NPC1 like intracellular cholesterol transporter 1
SLC22A2	-1.33872	2.66E-05	0.000115	-4.20053	Down	solute carrier family 22 member 2
SLAMF1	-1.29934	7.02E-05	0.00027	-3.97572	Down	signaling lymphocytic activation molecule family member 1
PRR33	-1.29322	7.50E-13	3.50E-11	-7.16998	Down	proline rich 33
IRX5	-1.28506	2.32E-05	0.000101	-4.23169	Down	iroquoishomeobox 5
GZMK	-1.27079	4.93E-08	4.42E-07	-5.45395	Down	granzyme K
HSPA6	-1.26101	2.52E-07	1.85E-06	-5.15606	Down	heat shock protein family A (Hsp70) member 6
GPR174	-1.25999	0.000597	0.001805	-3.43277	Down	G protein-coupled receptor 174
GPR20	-1.25517	4.24E-10	7.55E-09	-6.24483	Down	G protein-coupled receptor 20
SRPX2	-1.24021	1.00E-21	1.63E-18	-9.57659	Down	sushi repeat containing protein X-linked 2
PIGR	-1.24014	2.72E-05	0.000117	-4.19549	Down	polymeric immunoglobulin receptor
SERPINA5	-1.23944	4.11E-11	1.03E-09	-6.6002	Down	serpin family A member 5

Gene	logFC	P.Value	adj.P.Val	t	Regulation	Description
RAB42	-1.23573	1.34E-10	2.86E-09	-6.42264	Down	RAB42, member RAS oncogene family
OR2B11	-1.21985	0.000677	0.002015	-3.39876	Down	olfactory receptor family 2 subfamily B member 11
VHLL	-1.21725	1.37E-05	6.41E-05	-4.34826	Down	VHL like
CDC42BPG	-1.20827	3.29E-16	5.39E-14	-8.16222	Down	CDC42 binding protein kinase gamma
PF4	-1.20232	9.11E-06	4.44E-05	-4.43736	Down	platelet factor 4
FCRL1	-1.20214	0.000217	0.000732	-3.69837	Down	Fc receptor like 1
IL1R2	-1.20129	3.69E-06	1.99E-05	-4.62798	Down	interleukin 1 receptor type 2
P2RY10	-1.19993	0.000181	0.000624	-3.74418	Down	P2Y receptor family member 10
CXCR4	-1.19848	3.47E-16	5.61E-14	-8.15568	Down	C-X-C motif chemokine receptor 4
GFI1B	-1.19277	6.41E-08	5.54E-07	-5.40696	Down	growth factor independent 1B transcriptional repressor
LBX2	-1.19273	2.61E-15	3.19E-13	-7.9082	Down	ladybird homeobox 2
OGFRP1	-1.19216	1.83E-05	8.24E-05	-4.28468	Down	opioid growth factor receptor pseudogene 1
MFAP2	-1.18848	5.58E-08	4.92E-07	-5.43177	Down	microfibril associated protein 2
C9orf152	-1.18027	3.53E-07	2.49E-06	-5.09287	Down	chromosome 9 open reading frame 152
HMGA2-AS1	-1.17619	5.66E-09	6.88E-08	-5.82655	Down	HMGA2 antisense RNA 1
BNC1	-1.17603	1.69E-06	9.96E-06	-4.78696	Down	basonuclin 1
ETV4	-1.17116	1.12E-15	1.56E-13	-8.01319	Down	ETS variant transcription factor 4
SLC35G6	-1.16741	0.000452	0.001414	-3.5076	Down	solute carrier family 35 member G6
ASCL3	-1.15897	0.000491	0.00152	-3.48569	Down	achaete-scute family bHLH transcription factor 3
H2AC11	-1.15382	2.30E-06	1.30E-05	-4.72535	Down	H2A clustered histone 11
S100A4	-1.15246	6.15E-17	1.39E-14	-8.36228	Down	S100 calcium binding protein A4
MGC34796	-1.15202	0.004248	0.010177	-2.85911	Down	sepiapterinreductase (7,8-dihydrobiopterin:NADP+ oxidoreductase) pseudogene
IGF2-AS	-1.15093	2.75E-12	1.03E-10	-6.99008	Down	IGF2 antisense RNA
SGO1	-1.14519	8.98E-12	2.87E-10	-6.82197	Down	shugoshin 1
NKX6-1	-1.13969	7.81E-13	3.60E-11	-7.1645	Down	NK6 homeobox 1
MS4A1	-1.12463	0.000135	0.000481	-3.81645	Down	membrane spanning 4-domains A1
CASP12	-1.12382	1.39E-10	2.96E-09	-6.41649	Down	caspase 12 (gene/pseudogene)
VNN3	-1.12378	3.92E-06	2.09E-05	-4.6157	Down	vanin 3
OBP2B	-1.11759	0.001125	0.003153	-3.25733	Down	odorant binding protein 2B
MCEMP1	-1.11703	1.08E-06	6.70E-06	-4.87659	Down	mast cell expressed membrane protein 1
CCR2	-1.11595	1.14E-07	9.09E-07	-5.30366	Down	C-C motif chemokine receptor 2
OR7A5	-1.11498	5.76E-07	3.84E-06	-4.99921	Down	olfactory receptor family 7 subfamily A member 5
OTX2	-1.11472	0.006137	0.014054	-2.74036	Down	orthodenticlehomeobox 2
NLRP4	-1.11124	4.24E-05	0.000172	-4.09387	Down	NLR family pyrin domain containing 4
FAM167B	-1.10988	4.63E-12	1.63E-10	-6.91644	Down	family with sequence similarity 167 member B
TREML4	-1.10858	0.00863	0.018926	-2.62636	Down	triggering receptor expressed on myeloid cells like 4
KCNJ15	-1.10673	1.41E-07	1.10E-06	-5.26341	Down	potassium inwardly rectifying channel subfamily J member 15
TBX10	-1.1034	5.87E-07	3.91E-06	-4.99532	Down	T-box transcription factor 10
CSAG4	-1.10161	0.000364	0.001163	-3.56517	Down	CSAG family member 4 (pseudogene)
SIT1	-1.10067	1.36E-05	6.36E-05	-4.35041	Down	signaling threshold regulating transmembrane adaptor 1
KCNE4	-1.09597	2.57E-14	2.04E-12	-7.61825	Down	potassium voltage-gated channel subfamily E regulatory subunit 4
IL7R	-1.09393	4.43E-09	5.64E-08	-5.86717	Down	interleukin 7 receptor

MIA	-1.08897	1.06E-08	1.18E-07	-5.72106	Down	MIA SH3 domain containing
CR1L	-1.08683	4.83E-05	0.000193	-4.06387	Down	complement C3b/C4b receptor 1 like
MRGPRF	-1.08673	2.31E-21	2.97E-18	-9.48981	Down	MAS related GPR family member F
HERC2P3	-1.08534	5.78E-09	6.99E-08	-5.82311	Down	hect domain and RLD 2 pseudogene 3
KCNE1	-1.07928	3.48E-05	0.000145	-4.13936	Down	potassium voltage-gated channel subfamily E regulatory subunit 1
MYOCD	-1.07852	4.63E-15	5.07E-13	-7.8365	Down	myocardin
NANOS2	-1.07812	1.01E-07	8.27E-07	-5.32428	Down	nanos C2HC-type zinc finger 2
S100A12	-1.07697	4.64E-05	0.000186	-4.0732	Down	S100 calcium binding protein A12
CCL26	-1.07567	0.000178	0.000614	-3.74856	Down	C-C motif chemokine ligand 26
CLDN18	-1.07505	7.55E-12	2.47E-10	-6.84684	Down	claudin 18
HP	-1.07397	4.95E-07	3.36E-06	-5.02833	Down	haptoglobin
ARHGAP11B	-1.07397	2.60E-07	1.90E-06	-5.15061	Down	Rho GTPase activating protein 11B
MIOX	-1.07318	0.001638	0.004392	-3.1491	Down	myo-inositol oxygenase
ORM1	-1.0723	0.005072	0.011876	-2.80245	Down	orosomucoid 1
ITGA10	-1.07112	4.12E-21	4.57E-18	-9.42952	Down	integrin subunit alpha 10
SLC16A12	-1.06927	1.10E-07	8.83E-07	-5.31011	Down	solute carrier family 16 member 12
LBX2-AS1	-1.06837	1.15E-14	1.05E-12	-7.7214	Down	LBX2 antisense RNA 1
INSRR	-1.06702	1.52E-06	9.03E-06	-4.80912	Down	insulin receptor related receptor
ESPNL	-1.06388	2.79E-10	5.29E-09	-6.31023	Down	espin like
CXCR3	-1.06066	0.001008	0.002864	-3.28824	Down	C-X-C motif chemokine receptor 3
SLC6A12	-1.05294	7.94E-26	1.94E-21	-10.5079	Down	solute carrier family 6 member 12
UBD	-1.05052	3.43E-06	1.86E-05	-4.64337	Down	ubiquitin D
SLC22A8	-1.04807	0.000734	0.002165	-3.37659	Down	solute carrier family 22 member 8
PROK2	-1.04774	3.45E-09	4.57E-08	-5.90839	Down	prokineticin 2
BCAR4	-1.04744	8.90E-05	0.000332	-3.91876	Down	breast cancer anti-estrogen resistance 4
F2RL3	-1.0461	5.42E-06	2.79E-05	-4.54797	Down	F2R like thrombin or trypsin receptor 3
DIO3OS	-1.03974	2.55E-10	4.93E-09	-6.32373	Down	DIO3 opposite strand upstream RNA
SNORA51	-1.03814	0.000115	0.000416	-3.85711	Down	small nucleolar RNA, H/ACA box 51
SLC16A12-AS1	-1.03812	0.016377	0.033273	-2.40039	Down	SLC16A12 antisense RNA 1
FOXD1	-1.03811	9.48E-17	1.98E-14	-8.3111	Down	forkhead box D1
SLC23A3	-1.03762	3.70E-14	2.78E-12	-7.57109	Down	solute carrier family 23 member 3
CLEC18A	-1.02711	0.000212	0.000717	-3.70419	Down	C-type lectin domain family 18 member A
LUCAT1	-1.02365	1.05E-06	6.56E-06	-4.88175	Down	lung cancer associated transcript 1
C1QTNF1-AS1	-1.02237	0.000624	0.001878	-3.42083	Down	C1QTNF1 antisense RNA 1
NXPE4	-1.02124	0.002617	0.006672	-3.00947	Down	neurexophilin and PC-esterase domain family member 4
GATA3	-1.02116	0.000132	0.000471	-3.82287	Down	GATA binding protein 3
FAM205A	-1.01575	6.74E-05	0.000261	-3.9852	Down	family with sequence similarity 205 member A
SHISA3	-1.01357	6.85E-10	1.14E-08	-6.16941	Down	shisa family member 3
TBX15	-1.01045	2.80E-15	3.39E-13	-7.89934	Down	T-box transcription factor 15
MYRF-AS1	-1.01028	2.42E-09	3.35E-08	-5.96703	Down	MYRF antisense RNA 1
CXCL8	-1.00794	2.95E-08	2.84E-07	-5.5442	Down	C-X-C motif chemokine ligand 8
CKM	-1.00756	1.03E-07	8.41E-07	-5.32076	Down	creatine kinase, M-type

FOXC2	-1.00696	9.44E-12	2.99E-10	-6.81474	Down	forkhead box C2
C7orf61	-1.0067	6.47E-10	1.09E-08	-6.17844	Down	chromosome 7 open reading frame 61
MKI67	-1.00097	1.84E-05	8.28E-05	-4.28356	Down	marker of proliferation Ki-67
PYHIN1	-0.99769	2.99E-06	1.65E-05	-4.67144	Down	pyrin and HIN domain family member 1
COL1A2	-0.99733	2.92E-17	7.32E-15	-8.44981	Down	collagen type I alpha 2 chain
GIPR	-0.98922	1.74E-10	3.58E-09	-6.38237	Down	gastric inhibitory polypeptide receptor
SLCO4A1-AS1	-0.98892	1.46E-09	2.17E-08	-6.0484	Down	SLCO4A1 antisense RNA 1
FOXD2	-0.98832	6.68E-12	2.25E-10	-6.86432	Down	forkhead box D2
CD2	-0.98199	5.68E-07	3.80E-06	-5.0017	Down	CD2 molecule
LCK	-0.98101	4.01E-08	3.72E-07	-5.49042	Down	LCK proto-oncogene, Src family tyrosine kinase
SNORD16	-0.97848	4.87E-06	2.53E-05	-4.57029	Down	small nucleolar RNA, C/D box 16
TNFRSF10D	-0.97444	3.42E-13	1.76E-11	-7.27681	Down	TNF receptor superfamily member 10d
NUP210L	-0.97332	7.43E-12	2.45E-10	-6.84906	Down	nucleoporin 210 like
ALOX15B	-0.97229	8.31E-09	9.54E-08	-5.76196	Down	arachidonate 15-lipoxygenase type B
FOXD2-AS1	-0.97193	6.73E-14	4.55E-12	-7.49305	Down	FOXD2 adjacent opposite strand RNA 1
RGS1	-0.96924	1.88E-05	8.43E-05	-4.27843	Down	regulator of G protein signaling 1
FMO1	-0.96835	1.67E-06	9.80E-06	-4.7903	Down	flavin containing dimethylanilinemonoxygenase 1
OLFM5P	-0.96282	2.55E-06	1.43E-05	-4.70399	Down	olfactomedin family member 5, pseudogene
HOXB3	-0.9627	6.99E-07	4.56E-06	-4.96172	Down	homeobox B3
ARHGEF35	-0.96261	0.006737	0.015254	-2.70958	Down	Rho guanine nucleotide exchange factor 35
SIK1	-0.9609	0.000179	0.000618	-3.74665	Down	salt inducible kinase 1
H2AC12	-0.95989	0.009466	0.02055	-2.59477	Down	H2A clustered histone 12
LCN10	-0.95972	1.75E-07	1.33E-06	-5.22385	Down	lipocalin 10
UHRF1	-0.95876	5.57E-15	5.94E-13	-7.8133	Down	ubiquitin like with PHD and ring finger domains 1
FOXD3	-0.9583	0.0021	0.005487	-3.07569	Down	forkhead box D3
UBASH3A	-0.95823	0.000975	0.002779	-3.29761	Down	ubiquitin associated and SH3 domain containing A
HSPB7	-0.95559	8.47E-20	6.46E-17	-9.10693	Down	heat shock protein family B (small) member 7
ABCA6	-0.95498	3.37E-07	2.39E-06	-5.10137	Down	ATP binding cassette subfamily A member 6
SMTN	-0.95308	1.83E-19	1.17E-16	-9.02322	Down	smoothelin
SNORD124	-0.953	8.74E-08	7.25E-07	-5.35122	Down	small nucleolar RNA, C/D box 124
GHRHR	-0.95292	0.011363	0.024151	-2.53133	Down	growth hormone releasing hormone receptor
FFAR2	-0.951	7.32E-05	0.00028	-3.9655	Down	free fatty acid receptor 2
SERPINH1	-0.95047	8.73E-08	7.24E-07	-5.35139	Down	serpin family H member 1
IL24	-0.94784	7.32E-05	0.00028	-3.96574	Down	interleukin 24
HCAR3	-0.94742	2.61E-05	0.000113	-4.20512	Down	hydroxycarboxylic acid receptor 3
OR2B6	-0.94698	0.007691	0.017131	-2.66534	Down	olfactory receptor family 2 subfamily B member 6
SNORA28	-0.94565	0.000891	0.002568	-3.32281	Down	small nucleolar RNA, H/ACA box 28
HIGD1B	-0.94489	2.52E-15	3.09E-13	-7.91262	Down	HIG1 hypoxia inducible domain family member 1B
CCDC102A	-0.94457	4.60E-18	1.67E-15	-8.66292	Down	coiled-coil domain containing 102A
GPR15	-0.94455	0.003696	0.009017	-2.90299	Down	G protein-coupled receptor 15
FAM106B	-0.94409	3.48E-05	0.000145	-4.13966	Down	family with sequence similarity 106 member B
GJA4	-0.9434	9.38E-13	4.22E-11	-7.13928	Down	gap junction protein alpha 4
MMRN1	-0.93931	1.22E-07	9.72E-07	-5.29	Down	multimerin 1

Gene						Description
CLEC4D	-0.93808	0.000134	0.000478	-3.81828	Down	C-type lectin domain family 4 member D
MT1JP	-0.93667	1.01E-06	6.31E-06	-4.89064	Down	metallothionein 1J, pseudogene
REM1	-0.93542	1.03E-08	1.15E-07	-5.7253	Down	RRAD and GEM like GTPase 1
CST7	-0.93518	7.52E-08	6.38E-07	-5.37832	Down	cystatin F
HCCAT5	-0.93436	0.000302	0.000986	-3.61319	Down	hepatocellular carcinoma associated transcript 5
COL8A1	-0.93122	1.65E-06	9.72E-06	-4.79271	Down	collagen type VIII alpha 1 chain
WNT6	-0.93084	9.58E-12	3.02E-10	-6.81274	Down	Wnt family member 6
SH2D3A	-0.92951	1.98E-11	5.60E-10	-6.70758	Down	SH2 domain containing 3A
TRNE	-0.92948	1.56E-06	9.28E-06	-4.8032	Down	tRNA
TRNQ	-0.92916	1.74E-06	1.02E-05	-4.78105	Down	tRNA
FMO3	-0.92748	9.98E-13	4.44E-11	-7.13084	Down	flavin containing dimethylanilinemonooxygenase 3
TEX43	-0.92694	1.88E-05	8.42E-05	-4.2788	Down	testis expressed 43
HSPB1	-0.92535	5.06E-08	4.53E-07	-5.44915	Down	heat shock protein family B (small) member 1
ECM2	-0.9229	8.93E-08	7.38E-07	-5.34718	Down	extracellular matrix protein 2
HRH4	-0.91793	7.52E-06	3.75E-05	-4.47835	Down	histamine receptor H4
HOXB-AS1	-0.9143	5.79E-05	0.000228	-4.02113	Down	HOXB cluster antisense RNA 1
HSPA1A	-0.914	5.81E-05	0.000228	-4.02048	Down	heat shock protein family A (Hsp70) member 1A
FOXC2-AS1	-0.91312	1.33E-06	8.04E-06	-4.83577	Down	FOXC2 antisense RNA 1
CD177	-0.91302	0.000313	0.001016	-3.6044	Down	CD177 molecule
ADAM33	-0.91131	1.91E-19	1.19E-16	-9.01836	Down	ADAM metallopeptidase domain 33
PEAR1	-0.91122	1.53E-12	6.38E-11	-7.07184	Down	platelet endothelial aggregation receptor 1
TBX3	-0.90827	1.14E-14	1.04E-12	-7.72295	Down	T-box transcription factor 3
TCN1	-0.90727	0.003681	0.008986	-2.90427	Down	transcobalamin 1
OIT3	-0.90614	0.000955	0.002732	-3.30348	Down	oncoprotein induced transcript 3
MAFF	-0.90563	2.04E-11	5.73E-10	-6.70312	Down	MAF bZIP transcription factor F
LY9	-0.90486	3.09E-05	0.000131	-4.16704	Down	lymphocyte antigen 9
SLCO4A1	-0.90466	2.61E-10	5.03E-09	-6.32022	Down	solute carrier organic anion transporter family member 4A1
FAM170B-AS1	-0.90431	0.002954	0.007419	-2.97251	Down	FAM170B antisense RNA 1
UBQLNL	-0.90192	2.32E-08	2.32E-07	-5.5859	Down	ubiquilin like
SNORD15A	-0.90159	0.001077	0.003037	-3.26956	Down	small nucleolar RNA, C/D box 15A
FHL5	-0.89902	2.41E-09	3.35E-08	-5.96714	Down	four and a half LIM domains 5
ABCC2	-0.89852	3.06E-13	1.61E-11	-7.29184	Down	ATP binding cassette subfamily C member 2
VAV3-AS1	-0.8985	0.007239	0.016248	-2.68564	Down	VAV3 antisense RNA 1
OR2A7	-0.89701	0.002863	0.007216	-2.98206	Down	olfactory receptor family 2 subfamily A member 7
LILRA4	-0.89674	4.10E-10	7.34E-09	-6.25006	Down	leukocyte immunoglobulin like receptor A4
FRG1EP	-0.89265	0.010903	0.023299	-2.54579	Down	FSHD region gene 1 family member E, pseudogene
TRNI	-0.89223	3.35E-06	1.82E-05	-4.64808	Down	tRNA
FOXJ1	-0.89173	2.00E-07	1.50E-06	-5.19969	Down	forkhead box J1
NOTCH3	-0.8893	2.17E-16	3.98E-14	-8.21232	Down	notch receptor 3
ITGA11	-0.8888	2.30E-22	6.25E-19	-9.7274	Down	integrin subunit alpha 11
TEAD2	-0.88575	1.44E-17	4.08E-15	-8.53197	Down	TEA domain transcription factor 2
DDX12P	-0.88421	1.95E-09	2.79E-08	-6.00189	Down	DEAD/H-box helicase 12, pseudogene
GATA2-AS1	-0.88359	2.77E-12	1.04E-10	-6.98902	Down	GATA2 antisense RNA 1

SLC13A4	-0.88239	1.41E-09	2.10E-08	-6.05486	Down	solute carrier family 13 member 4
FNDC11	-0.88215	1.34E-07	1.05E-06	-5.27392	Down	fibronectin type III domain containing 11
NUTM2G	-0.8813	0.000307	0.000999	-3.60931	Down	NUT family member 2G
PCDH18	-0.88027	1.85E-12	7.44E-11	-7.04513	Down	protocadherin 18
LEF1-AS1	-0.88016	6.85E-11	1.60E-09	-6.52381	Down	LEF1 antisense RNA 1
C6	-0.87705	0.000701	0.002078	-3.38906	Down	complement C6
PITX1	-0.87501	0.01508	0.030899	-2.43046	Down	paired like homeodomain 1
LYZ	-0.87431	3.97E-06	2.12E-05	-4.61275	Down	lysozyme
TGFB1I1	-0.8728	4.64E-18	1.67E-15	-8.6619	Down	transforming growth factor beta 1 induced transcript 1
TMCC2-AS1	-0.87275	2.52E-05	0.000109	-4.21269	Down	TMCC2 antisense RNA 1
P2RX7	-0.87155	3.63E-10	6.60E-09	-6.26933	Down	purinergic receptor P2X 7
OTP	-0.871	0.008237	0.018173	-2.6422	Down	orthopediahomeobox
HIC1	-0.86948	9.95E-14	6.26E-12	-7.4416	Down	HIC ZBTB transcriptional repressor 1
CLDN15	-0.86829	1.83E-18	8.11E-16	-8.76738	Down	claudin 15
SCT	-0.86732	5.42E-06	2.79E-05	-4.54771	Down	secretin
ABCC3	-0.86614	1.08E-12	4.80E-11	-7.11931	Down	ATP binding cassette subfamily C member 3
ZBED6	-0.86609	0.00011	0.0004	-3.86804	Down	zinc finger BED-type containing 6
RNU4-2	-0.86535	0.001127	0.00316	-3.25671	Down	RNA, U4 small nuclear 2
IL3RA	-0.86507	6.76E-10	1.13E-08	-6.17157	Down	interleukin 3 receptor subunit alpha
SNORD14C	-0.86393	2.24E-06	1.27E-05	-4.73022	Down	small nucleolar RNA, C/D box 14C
TRNM	-0.86364	5.16E-07	3.49E-06	-5.02016	Down	tRNA
NCKAP5-AS1	-0.86291	0.008386	0.018445	-2.63613	Down	NCKAP5 antisense RNA 1
CD3E	-0.86258	1.65E-06	9.74E-06	-4.79232	Down	CD3e molecule
LCN6	-0.86132	3.45E-08	3.25E-07	-5.51715	Down	lipocalin 6
NGFR	-0.86118	1.24E-09	1.88E-08	-6.07518	Down	nerve growth factor receptor
FLJ20712	-0.85686	0.003125	0.0078	-2.95516	Down	uncharacterized FLJ20712
TBX2-AS1	-0.8554	1.64E-12	6.75E-11	-7.06215	Down	TBX2 antisense RNA 1
MLANA	-0.85393	3.97E-11	1.01E-09	-6.6052	Down	melan-A
SNORD14E	-0.8531	9.23E-06	4.49E-05	-4.43455	Down	small nucleolar RNA, C/D box 14E
CSNK1G2-AS1	-0.85278	0.001135	0.003178	-3.25481	Down	CSNK1G2 antisense RNA 1
REP15	-0.85245	6.91E-12	2.31E-10	-6.85953	Down	RAB15 effector protein
C10orf126	-0.85236	0.022573	0.044018	-2.28058	Down	chromosome 10 open reading frame 126
DDX11L2	-0.852	5.75E-06	2.94E-05	-4.53535	Down	DEAD/H-box helicase 11 like 2 (pseudogene)
THRB-AS2	-0.85098	6.08E-06	3.09E-05	-4.52373	Down	THRB antisense RNA 2
ANPEP	-0.85061	1.33E-12	5.62E-11	-7.09111	Down	alanylaminopeptidase, membrane
ZBTB46-AS1	-0.85052	0.002039	0.005346	-3.08444	Down	ZBTB46 antisense RNA 1
MYBPH	-0.84995	4.80E-06	2.49E-05	-4.57354	Down	myosin binding protein H
KANK2	-0.84932	1.28E-24	1.56E-20	-10.2424	Down	KN motif and ankyrin repeat domains 2
RUNX3	-0.84762	1.45E-12	6.08E-11	-7.07924	Down	RUNX family transcription factor 3
GDF15	-0.8465	1.71E-08	1.78E-07	-5.63934	Down	growth differentiation factor 15
GZMM	-0.84577	3.20E-10	5.94E-09	-6.28887	Down	granzyme M
CR1	-0.84522	2.00E-08	2.05E-07	-5.61182	Down	complement C3b/C4b receptor 1 (Knops blood group)
CCDC168	-0.84361	5.92E-08	5.18E-07	-5.42109	Down	coiled-coil domain containing 168

ANGPT2	-0.84323	1.09E-07	8.82E-07	-5.31047	Down	angiopoietin 2
GMNC	-0.84319	0.000345	0.001108	-3.57902	Down	geminin coiled-coil domain containing
JAML	-0.8413	1.06E-08	1.18E-07	-5.72075	Down	junction adhesion molecule like
TBX18	-0.84089	2.55E-11	6.90E-10	-6.67049	Down	T-box transcription factor 18
BOK-AS1	-0.84085	1.62E-06	9.60E-06	-4.7956	Down	BOK antisense RNA 1
IL2RB	-0.83988	1.71E-06	1.00E-05	-4.7855	Down	interleukin 2 receptor subunit beta
MGAM	-0.83938	1.01E-08	1.13E-07	-5.72883	Down	maltase-glucoamylase
MS4A14	-0.83869	5.46E-10	9.41E-09	-6.20536	Down	membrane spanning 4-domains A14
TRIP10	-0.83791	2.56E-16	4.46E-14	-8.19256	Down	thyroid hormone receptor interactor 10
SPACA6P-AS	-0.83566	6.61E-16	9.78E-14	-8.07749	Down	SPACA6P antisense RNA
SLAMF6	-0.83513	4.60E-05	0.000185	-4.0753	Down	SLAM family member 6
PLN	-0.83484	7.09E-06	3.55E-05	-4.4909	Down	phospholamban
LYG2	-0.83453	1.02E-07	8.34E-07	-5.32258	Down	lysozyme g2
TNFSF14	-0.83408	7.32E-07	4.76E-06	-4.95272	Down	TNF superfamily member 14
TBX6	-0.83237	1.40E-18	6.46E-16	-8.79725	Down	T-box transcription factor 6
RNR1	-0.83128	5.94E-06	3.03E-05	-4.52837	Down	s-rRNA
SIX1	-0.83066	2.94E-08	2.84E-07	-5.54475	Down	SIX homeobox 1
HOXB6	-0.83022	0.017776	0.035771	-2.37026	Down	homeobox B6
ONECUT1	-0.82866	0.000437	0.001371	-3.51653	Down	one cut homeobox 1
CEACAM1	-0.82649	7.18E-09	8.38E-08	-5.78676	Down	CEA cell adhesion molecule 1
PRELP	-0.82459	1.09E-16	2.19E-14	-8.2943	Down	proline and arginine rich end leucine rich repeat protein
C21orf62	-0.82451	2.49E-08	2.46E-07	-5.5741	Down	chromosome 21 open reading frame 62
SYNE3	-0.82438	4.71E-12	1.65E-10	-6.91416	Down	spectrin repeat containing nuclear envelope family member 3
DKKL1	-0.82313	7.75E-06	3.85E-05	-4.47209	Down	dickkopf like acrosomal protein 1
ZNF683	-0.82275	0.000993	0.002823	-3.29263	Down	zinc finger protein 683
CCL14	-0.82228	0.000116	0.00042	-3.85432	Down	C-C motif chemokine ligand 14
AEBP1	-0.82205	1.70E-11	4.95E-10	-6.72939	Down	AE binding protein 1
PACRG-AS3	-0.822	3.81E-10	6.89E-09	-6.26174	Down	PACRG antisense RNA 3
RRAD	-0.82142	9.02E-08	7.44E-07	-5.34544	Down	RRAD, Ras related glycolysis inhibitor and calcium channel regulator
TLR8	-0.8185	4.25E-05	0.000172	-4.09368	Down	toll like receptor 8
GPRC5A	-0.81821	3.75E-06	2.01E-05	-4.62484	Down	G protein-coupled receptor class C group 5 member A
IL18RAP	-0.81741	2.83E-06	1.57E-05	-4.68265	Down	interleukin 18 receptor accessory protein
P2RY14	-0.81545	4.12E-09	5.29E-08	-5.87928	Down	purinergic receptor P2Y14
BLK	-0.81529	0.008186	0.018073	-2.64431	Down	BLK proto-oncogene, Src family tyrosine kinase
ADH1B	-0.81442	7.71E-09	8.93E-08	-5.77461	Down	alcohol dehydrogenase 1B (class I), beta polypeptide
HSPB9	-0.81341	2.38E-06	1.34E-05	-4.71838	Down	heat shock protein family B (small) member 9
VNN1	-0.81265	5.93E-05	0.000232	-4.01575	Down	vanin 1
LILRP2	-0.81264	0.025542	0.048927	-2.2331	Down	leukocyte immunoglobulin-like receptor pseudogene 2
SH2D6	-0.81251	5.74E-12	1.98E-10	-6.88598	Down	SH2 domain containing 6
LILRB5	-0.81118	4.60E-07	3.15E-06	-5.04219	Down	leukocyte immunoglobulin like receptor B5
OR51E1	-0.80785	0.000353	0.001132	-3.5728	Down	olfactory receptor family 51 subfamily E member 1
AOC1	-0.80766	0.023396	0.045401	-2.26691	Down	amine oxidase copper containing 1

GPR4	-0.80745	5.78E-09	7.00E-08	-5.82288	Down	G protein-coupled receptor 4
ADORA2A	-0.80735	1.74E-14	1.46E-12	-7.66847	Down	adenosine A2a receptor
FSCN3	-0.80712	0.00035	0.001124	-3.57488	Down	fascin actin-bundling protein 3
AZGP1	-0.80586	1.40E-07	1.10E-06	-5.26492	Down	alpha-2-glycoprotein 1, zinc-binding
MRGPRF-AS1	-0.80565	0.000112	0.000407	-3.86317	Down	MRGPRF antisense RNA 1
ITGA5	-0.80399	1.21E-12	5.21E-11	-7.10459	Down	integrin subunit alpha 5
FOXF1	-0.80311	2.48E-11	6.71E-10	-6.67463	Down	forkhead box F1
ADGRG3	-0.80191	3.22E-05	0.000135	-4.15719	Down	adhesion G protein-coupled receptor G3
TNIP2P1	-0.80145	0.002166	0.005639	-3.06642	Down	TNIP2 pseudogene 1
E2F2	-0.79846	0.000575	0.001748	-3.44334	Down	E2F transcription factor 2
FAM41C	-0.79713	0.004294	0.010268	-2.8557	Down	family with sequence similarity 41 member C
LNCAROD	-0.79532	0.018256	0.036595	-2.36039	Down	lncRNA activating regulator of DKK1
SLC4A11	-0.79416	3.00E-13	1.58E-11	-7.29432	Down	solute carrier family 4 member 11
COL1A1	-0.79324	4.12E-09	5.29E-08	-5.87915	Down	collagen type I alpha 1 chain
SNRPD2P2	-0.79316	0.000911	0.002619	-3.31666	Down	small nuclear ribonucleoprotein D2 pseudogene 2
IQGAP2	-0.7923	2.87E-08	2.78E-07	-5.549	Down	IQ motif containing GTPase activating protein 2
WFDC21P	-0.79198	0.000829	0.002413	-3.34309	Down	WAP four-disulfide core domain 21, pseudogene
PLEKHA4	-0.79029	2.69E-11	7.23E-10	-6.66277	Down	pleckstrin homology domain containing A4
TM4SF18	-0.78902	3.83E-09	4.98E-08	-5.8913	Down	transmembrane 4 L six family member 18
FOLR3	-0.78898	0.004717	0.011152	-2.82573	Down	folate receptor gamma
CTB-41I6.1	-0.78862	4.18E-07	2.89E-06	-5.06079	Down	uncharacterized CTB-41I6.1
PSORS1C3	-0.78843	0.009943	0.021458	-2.5778	Down	psoriasis susceptibility 1 candidate 3
ADM2	-0.78809	3.01E-05	0.000128	-4.17262	Down	adrenomedullin 2
BCL6B	-0.78762	4.45E-09	5.64E-08	-5.86647	Down	BCL6B transcription repressor
H4C5	-0.78754	3.89E-08	3.62E-07	-5.49557	Down	H4 clustered histone 5
NFE2	-0.78705	5.21E-08	4.64E-07	-5.44409	Down	nuclear factor, erythroid 2
ADRA2B	-0.78637	5.44E-11	1.31E-09	-6.55848	Down	adrenoceptor alpha 2B
LDLRAD4-AS1	-0.78437	2.14E-06	1.22E-05	-4.73956	Down	LDLRAD4 antisense RNA 1
FCRLA	-0.78113	1.02E-06	6.40E-06	-4.88715	Down	Fc receptor like A
COL3A1	-0.78106	2.55E-07	1.87E-06	-5.15363	Down	collagen type III alpha 1 chain
C22orf34	-0.78074	4.39E-08	4.00E-07	-5.47456	Down	chromosome 22 putative open reading frame 34
C11orf52	-0.78057	2.73E-10	5.20E-09	-6.31337	Down	chromosome 11 open reading frame 52
IFNA2	-0.77921	1.29E-05	6.07E-05	-4.36211	Down	interferon alpha 2
RCVRN	-0.77891	1.12E-05	5.37E-05	-4.3918	Down	recoverin
ND6	-0.77825	8.04E-06	3.97E-05	-4.46422	Down	NADH dehydrogenase subunit 6
CHRNG	-0.77788	0.004243	0.010168	-2.85949	Down	cholinergic receptor nicotinic gamma subunit
ZNF750	-0.77642	5.52E-06	2.84E-05	-4.54382	Down	zinc finger protein 750
COL8A2	-0.77525	4.61E-11	1.14E-09	-6.58293	Down	collagen type VIII alpha 2 chain
PSG8-AS1	-0.77385	1.01E-08	1.13E-07	-5.72902	Down	PSG8 antisense RNA 1
OLAH	-0.77126	3.61E-10	6.58E-09	-6.26994	Down	oleoyl-ACP hydrolase
KLHL30	-0.77107	5.60E-06	2.87E-05	-4.54114	Down	kelch like family member 30
FCRL3	-0.77106	0.010255	0.022058	-2.56711	Down	Fc receptor like 3
COL27A1	-0.77091	2.08E-22	6.25E-19	-9.73797	Down	collagen type XXVII alpha 1 chain

Gene	Value 1	Value 2	Value 3	Value 4	Direction	Description
GPER1	-0.77045	7.81E-13	3.60E-11	-7.16447	Down	G protein-coupled estrogen receptor 1
LGSN	-0.76926	0.012727	0.026688	-2.49132	Down	lengsin, lens protein with glutamine synthetase domain
OR5K2	-0.76715	0.000448	0.001401	-3.51007	Down	olfactory receptor family 5 subfamily K member 2
ACAN	-0.76684	1.23E-09	1.87E-08	-6.07691	Down	aggrecan
KLRB1	-0.76667	0.000101	0.00037	-3.88921	Down	killer cell lectin like receptor B1
IGF2	-0.76347	6.22E-11	1.48E-09	-6.53834	Down	insulin like growth factor 2
SNORD56	-0.763	2.79E-05	0.00012	-4.18991	Down	small nucleolar RNA, C/D box 56
FRRS1	-0.76197	0.000342	0.0011	-3.5811	Down	ferric chelate reductase 1
CRYBG2	-0.76179	0.002757	0.006982	-2.99362	Down	crystallin beta-gamma domain containing 2
PRLR	-0.76159	2.19E-07	1.63E-06	-5.18203	Down	prolactin receptor
H2AC6	-0.75997	1.43E-09	2.13E-08	-6.05157	Down	H2A clustered histone 6
BTN1A1	-0.75982	0.000458	0.00143	-3.50395	Down	butyrophilin subfamily 1 member A1
S1PR4	-0.75956	3.24E-11	8.46E-10	-6.63535	Down	sphingosine-1-phosphate receptor 4
TGM4	-0.75775	0.003586	0.008785	-2.91249	Down	transglutaminase 4
INS-IGF2	-0.75742	8.98E-11	2.03E-09	-6.4832	Down	INS-IGF2 readthrough
FCGR2B	-0.7568	5.08E-05	0.000202	-4.05171	Down	Fc fragment of IgG receptor IIb
DNAJB1	-0.75597	1.59E-05	7.28E-05	-4.31622	Down	DnaJ heat shock protein family (Hsp40) member B1
NFE4	-0.75363	0.016524	0.033546	-2.39713	Down	nuclear factor, erythroid 4
CFHR3	-0.7536	0.000541	0.001658	-3.45958	Down	complement factor H related 3
MID1IP1	-0.75357	2.44E-14	1.95E-12	-7.62489	Down	MID1 interacting protein 1
CLYBL-AS2	-0.75322	0.014747	0.030308	-2.43854	Down	CLYBL antisense RNA 2
MMP9	-0.75305	0.000106	0.000387	-3.8772	Down	matrix metallopeptidase 9
FANCC	-0.75292	8.78E-23	3.06E-19	-9.82506	Down	FA complementation group C
VNN2	-0.75244	0.000124	0.000444	-3.83887	Down	vanin 2
PRKX	-0.7511	3.52E-14	2.69E-12	-7.57766	Down	protein kinase X-linked
TNFRSF10A	-0.75101	2.30E-06	1.30E-05	-4.72524	Down	TNF receptor superfamily member 10a
MAGEA12	-0.74908	1.65E-07	1.26E-06	-5.23469	Down	MAGE family member A12
ZNF878	-0.74846	1.15E-07	9.22E-07	-5.30076	Down	zinc finger protein 878
SLC12A7	-0.74703	6.97E-16	1.03E-13	-8.07099	Down	solute carrier family 12 member 7
SYDE1	-0.74675	4.47E-18	1.65E-15	-8.66627	Down	synapse defective Rho GTPase homolog 1
TGFBI	-0.74625	5.99E-07	3.98E-06	-4.99161	Down	transforming growth factor beta induced
LPEQ6126	-0.74623	0.000247	0.000822	-3.66551	Down	uncharacterized LOC100128818
TLR5	-0.74528	2.11E-09	2.98E-08	-5.98924	Down	toll like receptor 5
IL18R1	-0.74465	1.69E-05	7.69E-05	-4.30259	Down	interleukin 18 receptor 1
H2AC7	-0.74437	0.000902	0.002597	-3.31949	Down	H2A clustered histone 7
SNORA29	-0.74408	0.000271	0.000892	-3.64165	Down	small nucleolar RNA, H/ACA box 29
IHH	-0.74353	1.70E-05	7.73E-05	-4.30134	Down	Indian hedgehog signaling molecule
FOXO4	-0.74326	5.85E-13	2.82E-11	-7.20388	Down	forkhead box O4
APOBEC3A	-0.74309	0.000422	0.001329	-3.52596	Down	apolipoprotein B mRNA editing enzyme catalytic subunit 3A
ANLN	-0.74182	2.97E-08	2.86E-07	-5.5434	Down	anillin actin binding protein
SERPINF2	-0.74097	1.36E-10	2.90E-09	-6.42022	Down	serpin family F member 2
CNN2	-0.7406	2.15E-09	3.03E-08	-5.98642	Down	calponin 2
ATAD3C	-0.7406	5.72E-10	9.80E-09	-6.19805	Down	ATPase family AAA domain containing 3C

C7	-0.74021	6.00E-07	3.98E-06	-4.99135	Down	complement C7
PTX4	-0.74004	0.000402	0.001273	-3.53852	Down	pentraxin 4
IL2RG	-0.73974	4.53E-11	1.12E-09	-6.5856	Down	interleukin 2 receptor subunit gamma
PFN1P2	-0.73956	0.000752	0.002213	-3.36975	Down	profilin 1 pseudogene 2
SAP25	-0.7384	1.15E-09	1.78E-08	-6.08717	Down	Sin3A associated protein 25
YBX3P1	-0.73798	5.88E-07	3.91E-06	-4.99513	Down	Y-box binding protein 3 pseudogene 1
SCARNA12	-0.73773	7.84E-12	2.55E-10	-6.84136	Down	small Cajal body-specific RNA 12
COX8C	-0.73767	1.73E-06	1.01E-05	-4.78306	Down	cytochrome c oxidase subunit 8C
SNX31	-0.73747	1.12E-05	5.36E-05	-4.39198	Down	sorting nexin 31
DLL4	-0.73642	5.23E-10	9.06E-09	-6.21219	Down	delta like canonical Notch ligand 4
TES	-0.73604	4.81E-09	6.01E-08	-5.85352	Down	testin LIM domain protein
A4GALT	-0.7357	3.85E-13	1.96E-11	-7.26086	Down	alpha 1,4-galactosyltransferase (P blood group)
GAGE10	-0.73511	0.000201	0.000683	-3.7181	Down	G antigen 10
COL4A4	-0.73496	9.66E-13	4.32E-11	-7.13526	Down	collagen type IV alpha 4 chain
APOC4	-0.73494	2.10E-06	1.20E-05	-4.74403	Down	apolipoprotein C4
TNFRSF12A	-0.73494	1.84E-09	2.65E-08	-6.01092	Down	TNF receptor superfamily member 12A
TLR9	-0.73488	1.85E-10	3.75E-09	-6.3734	Down	toll like receptor 9
HOXB2	-0.73477	0.000166	0.000576	-3.76636	Down	homeobox B2
ZC3H12A	-0.73424	2.27E-12	8.83E-11	-7.01691	Down	zinc finger CCCH-type containing 12A
ADAMTS2	-0.73179	4.20E-14	3.09E-12	-7.55475	Down	ADAM metallopeptidase with thrombospondin type 1 motif 2
TP63	-0.73136	1.81E-06	1.05E-05	-4.77338	Down	tumor protein p63
FBXL19-AS1	-0.73036	9.08E-14	5.80E-12	-7.45361	Down	FBXL19 antisense RNA 1
ALX4	-0.73029	1.60E-05	7.34E-05	-4.31412	Down	ALX homeobox 4
OLFML1	-0.73009	2.65E-10	5.08E-09	-6.31809	Down	olfactomedin like 1
ADGRD1	-0.72973	6.42E-09	7.63E-08	-5.80545	Down	adhesion G protein-coupled receptor D1
DOK2	-0.72963	1.77E-05	8.02E-05	-4.29187	Down	docking protein 2
KRT15	-0.72909	0.000889	0.002563	-3.32343	Down	keratin 15
SNORD17	-0.72896	7.32E-05	0.00028	-3.96572	Down	small nucleolar RNA, C/D box 17
GUSBP2	-0.72854	0.00062	0.001865	-3.42292	Down	GUSB pseudogene 2
CLMN	-0.72849	1.75E-11	5.06E-10	-6.72537	Down	calmin
EPHA2	-0.72775	1.22E-11	3.72E-10	-6.77824	Down	EPH receptor A2
KIF1C-AS1	-0.72742	8.57E-10	1.38E-08	-6.13394	Down	KIF1C antisense RNA 1
GFRA3	-0.72704	0.000129	0.00046	-3.82927	Down	GDNF family receptor alpha 3
CERNA2	-0.72654	0.000912	0.002622	-3.31623	Down	competing endogenous lncRNA 2 for microRNA let-7b
H2BC11	-0.72645	0.000135	0.00048	-3.81752	Down	H2B clustered histone 11
KIF1C	-0.72556	5.68E-10	9.75E-09	-6.19907	Down	kinesin family member 1C
ADORA2A-AS1	-0.72547	1.53E-11	4.53E-10	-6.74495	Down	ADORA2A antisense RNA 1
SLC1A7	-0.7233	0.000198	0.000676	-3.72108	Down	solute carrier family 1 member 7
KRT19	-0.72322	5.13E-08	4.58E-07	-5.44682	Down	keratin 19
ELMO1-AS1	-0.72198	4.46E-08	4.05E-07	-5.4716	Down	ELMO1 antisense RNA 1
ITPRIP	-0.7218	1.03E-14	9.74E-13	-7.73549	Down	inositol 1,4,5-trisphosphate receptor interacting protein
SNORD117	-0.72147	0.016271	0.033087	-2.40278	Down	small nucleolar RNA, C/D box 117

MARVELD2	-0.72144	4.02E-07	2.79E-06	-5.06813	Down	MARVEL domain containing 2
SEMA3F	-0.72138	4.10E-08	3.78E-07	-5.48666	Down	semaphorin 3F
GEM	-0.72116	9.80E-09	1.10E-07	-5.73424	Down	GTP binding protein overexpressed in skeletal muscle
C5AR1	-0.72096	9.87E-07	6.21E-06	-4.89413	Down	complement C5a receptor 1
TMC8	-0.72075	1.45E-14	1.25E-12	-7.69226	Down	transmembrane channel like 8
CD163	-0.72075	0.001616	0.00434	-3.153	Down	CD163 molecule
FLT4	-0.72062	2.10E-11	5.86E-10	-6.69871	Down	fms related receptor tyrosine kinase 4
STON1-GTF2A1L	-0.72018	3.44E-06	1.87E-05	-4.6424	Down	STON1-GTF2A1L readthrough
PLA2G12B	-0.72004	0.024139	0.046668	-2.25491	Down	phospholipase A2 group XIIB
SAMD4A	-0.72002	1.25E-13	7.59E-12	-7.41101	Down	sterile alpha motif domain containing 4A
CYSLTR2	-0.71962	9.23E-05	0.000343	-3.90998	Down	cysteinyl leukotriene receptor 2
CCL15-CCL14	-0.7196	0.000364	0.001165	-3.56467	Down	CCL15-CCL14 readthrough (NMD candidate)
PIK3R5	-0.71896	6.08E-10	1.03E-08	-6.18823	Down	phosphoinositide-3-kinase regulatory subunit 5
SELENOP	-0.71781	3.71E-08	3.46E-07	-5.50428	Down	selenoprotein P
NEK5	-0.71776	3.48E-06	1.88E-05	-4.64038	Down	NIMA related kinase 5
PMAIP1	-0.71767	1.36E-06	8.24E-06	-4.83016	Down	phorbol-12-myristate-13-acetate-induced protein 1
ST13P4	-0.7176	0.010946	0.023383	-2.54441	Down	ST13, Hsp70 interacting protein pseudogene 4
S100P	-0.71743	3.95E-05	0.000162	-4.11045	Down	S100 calcium binding protein P
PGF	-0.71684	8.08E-10	1.31E-08	-6.14343	Down	placental growth factor
COL4A2-AS2	-0.71666	0.000699	0.002073	-3.3898	Down	COL4A2 antisense 2
HAL	-0.71612	0.000171	0.000592	-3.75909	Down	histidine ammonia-lyase
CACNG5	-0.71594	0.000107	0.000393	-3.87319	Down	calcium voltage-gated channel auxiliary subunit gamma 5
KIF5A	-0.7159	6.79E-07	4.45E-06	-4.9673	Down	kinesin family member 5A
TRNC	-0.71548	8.58E-05	0.000322	-3.92758	Down	tRNA
RBPMS	-0.71508	4.90E-15	5.29E-13	-7.82948	Down	RNA binding protein, mRNA processing factor
ARRDC2	-0.71507	5.87E-13	2.82E-11	-7.20357	Down	arrestin domain containing 2
PCAT19	-0.71482	2.01E-07	1.51E-06	-5.19797	Down	prostate cancer associated transcript 19
DIO3	-0.71478	8.43E-10	1.36E-08	-6.13659	Down	iodothyroninedeiodinase 3
HSPA1B	-0.71442	0.000745	0.002194	-3.37244	Down	heat shock protein family A (Hsp70) member 1B
TOR4A	-0.71359	2.00E-11	5.64E-10	-6.70575	Down	torsin family 4 member A
PTH1R	-0.71357	6.77E-11	1.59E-09	-6.52571	Down	parathyroid hormone 1 receptor
ERI3-IT1	-0.71251	9.16E-20	6.78E-17	-9.09844	Down	ERI3 intronic transcript 1
RBPMS2	-0.71222	2.34E-17	6.36E-15	-8.47534	Down	RNA binding protein, mRNA processing factor 2
PDE9A-AS1	-0.71188	9.37E-06	4.55E-05	-4.43119	Down	PDE9A antisense RNA 1
CEL	-0.71029	6.45E-10	1.08E-08	-6.17912	Down	carboxyl ester lipase
SNORD23	-0.70985	8.36E-05	0.000315	-3.93373	Down	small nucleolar RNA, C/D box 23
TRNK	-0.70982	2.59E-06	1.45E-05	-4.7006	Down	tRNA
RNF152	-0.70953	1.26E-15	1.71E-13	-7.99826	Down	ring finger protein 152
SLC38A2	-0.70903	1.47E-10	3.09E-09	-6.40886	Down	solute carrier family 38 member 2
IP6K3	-0.70897	8.05E-07	5.17E-06	-4.93426	Down	inositol hexakisphosphate kinase 3
JADE3	-0.70818	5.85E-14	4.09E-12	-7.51142	Down	jade family PHD finger 3
COL6A2	-0.70817	1.37E-13	8.20E-12	-7.39907	Down	collagen type VI alpha 2 chain

CD180	-0.70801	1.99E-06	1.14E-05	-4.75486	Down	CD180 molecule
FZD9	-0.70692	1.92E-13	1.10E-11	-7.35447	Down	frizzled class receptor 9
UICLM	-0.7065	0.000525	0.001614	-3.46772	Down	up-regulated in colorectal cancer liver metastasis
AJUBA	-0.70641	6.94E-11	1.62E-09	-6.52193	Down	ajuba LIM protein
LEF1	-0.70621	3.62E-11	9.29E-10	-6.61891	Down	lymphoid enhancer binding factor 1
MYH11	-0.70454	4.22E-08	3.87E-07	-5.48136	Down	myosin heavy chain 11
TBX2	-0.70408	2.25E-12	8.80E-11	-7.01787	Down	T-box transcription factor 2
CARD6	-0.70348	6.85E-11	1.60E-09	-6.5239	Down	caspase recruitment domain family member 6
FMO2	-0.70308	3.30E-08	3.12E-07	-5.52493	Down	flavin containing dimethylanilinemonooxygenase 2
SLC37A2	-0.70204	1.76E-12	7.12E-11	-7.05248	Down	solute carrier family 37 member 2
H2BC9	-0.70203	0.006488	0.014763	-2.72204	Down	H2B clustered histone 9
LATS2	-0.70054	6.37E-13	3.03E-11	-7.19235	Down	large tumor suppressor kinase 2
TRIM63	-0.70027	0.004002	0.009655	-2.878	Down	tripartite motif containing 63
MYL9	-0.69999	4.27E-09	5.46E-08	-5.87322	Down	myosin light chain 9
TNS1	-0.69928	1.28E-17	3.75E-15	-8.54591	Down	tensin 1
FPR2	-0.69884	0.004147	0.009962	-2.86678	Down	formyl peptide receptor 2
CBX2	-0.69857	1.06E-14	9.96E-13	-7.73175	Down	chromobox 2
PCK1	-0.69648	0.000372	0.001187	-3.55916	Down	phosphoenolpyruvatecarboxykinase 1

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

GO ID	CATEGORY	GO Name	Adj.P.Val	Negative_log 10_of_adjusted_p_value	Gene Count	Gene
			Up regulated genes			
GO:0065008	BP	regulation of biological quality	1.51E-08	7.821012262	142	CRH,TAC1,NMU,VGF,PCSK1,ADCYAP1,GABRA6,SLN,C1QL3,NPAS4,GJD2,NPSR1,RGS4,SLC32A1,IL1RAPL2,GAD2,CAPZA3,CHRNA9,CRYM,GAD1,CXCL11,GABRA1,EGR1,PCDH8,PLSCR5,CALB1,BDNF,GABRG2,ROBO2,FLT3,CHRNB4,SLC5A7,KCNK18,HTR2C,TERT,NEFL,SNAP25,RAB3B,CYP4A11,RPH3A,GABRB2,RFX6,TACR1,CARTPT,ALOX12B,MCHR1,NRN1,SLC17A6,SLC4A10,AFP,HRG,SYT1,EPHA5,HTR3B,GLRA3,SYT4,CALCB,GRIN2B,HCN1,FATE1,GABRA4,AKAP5,ADRA1D,KCNC2,PTPN3,DHRS7C,GCNT4,KCNH5,AVP,DGKB,

VSNL1,NAPB,HTR2A,CLTRN,PAK1,PAK3,SLC30A3,NCALD,ANO3,GLRA2,STXBP5L,NELL2,F7,ATP12A,SCN2A,HCRTR2,ADRB3,GPR88,NR1H4,SYP,SYT2,CALY,SLC12A1,CHRNB3,LRTM2,SYT10,PRKCE,GRIN2A,VSIG1,RHEX,CDH8,HTR1A,SNX10,SYN2,XK,GABRD,TRPC7,NRG1,PTH2R,NETO1,FGF12,SH3GL2,MLLT11,KISS1,UPK3A,CADPS,CHRNA6,NRXN3,F2RL2,FRMPD4,GPRASP2,SERPINB2,CLSTN3,VSTM5,P2RX2,GABRG3,CNGB1,SDR16C5,ATP8A2,RAB3A,ADTRP,LDB2,DSG1,RHO,MYB,IGF1,PLK2,TAC3,FSTL4,LRFN5,SCN8A,TRHDE

| GO:0032501 | BP | multicellular organismal process | 1.37284E-06 | 5.862378621 | 220 | CRH,SPRR2G,TAC1,NMU,MAS1,VGF,SST,ADCYAP1,PENK,GABRA6,SLN,DSG3,PPEF1,NPAS4,OR52N2,SI,GJD2,KRT5,NEUROD6,RGS4,KRT82,SLC32A1,IL1RAPL2,CAPZA3,CHRNA9,C14ORF39,EGR3,CRYM,PNOC,DRGX,GABRA1,EGR1,PCDH8,PVALB,OLFM3,ATOH7,CALB1,AMELX,WNT8A,CBLN4,MYOG,BDNF,ANKRD33,GABRG2,ROBO2,FLT3,CHRNB4,SLC5A7,HTR2C,CDH7,TCP11,PCP4,TERT,NEFL,MLIP,SOSTDC1,SNAP25,TCF23,NYAP2,OR1N1,MYPN,CYP4A11,GDA,GREM2,UNC5D,CNTN5,GABRB2,MAL2,NLRP2,AGBL4,PTPRR,RFX6,CDH18,TACR1,CARTPT,ALOX12B,AMY2A,NRN1,SLC17A6,SLC4A10,AFP,HRG,SYT1,EPHA5,OR2AE1,CDH9,CYP24A1,HTR3B,GLRA3,SCG2,HPRT1,MEPE,SYT4,ENC1,NELL1,GFRA4,GRIN2B,HCN1,KCNB2,OTOL1,DLGAP1,GABRA4,ADRA1D,KCNC2,PTPN3,GCNT4,TDRD5,IL12RB2,AVP,DGKB,FGF9,PAX5,HTR2A,NAP1L2,C6ORF141,DLX1,PAK1,TESPA1,DLX6,PAK3,NCALD,GLRA2,GUCA1C,BHLHA9,TAFA1,F7,RBFOX1,RTKN2,SCN2A,HCRTR2,ADRB3,FSTL5,GPR88,CDH12,NR1H4,RSPO2,SYT2,STMN2,FGF5,PRPH2,GPR149,CHRNB3,LRTM2,RXFP1,SYT10,TAFA2,PRKCE,DCLK1,PAX7,GRIN2A,VSIG1,RHEX,COL25A1,CAMK4,TUBB2A,CDH8,VWC2L,HUNK,HTR1A,SP9,SNX10,UPK2,TRIM72,B |

						EX1,XK,WNT1,NEFH,GABRD,TRPC7,NRG1,PTH2R,NETO1,FGF12,PLPPR4,LPA,MACROD2,SERPINB13,PLCB1,SH3GL2,SFTPA2,UPK3A,CHRNA6,OR13C5,NRXN3,INA,F2RL2,VSX2,SPINK9,INSM2,SERPINB2,CLSTN3,VSTM5,P2RX2,SPRY3,GABRG3,CNGB1,MYH13,ATP8A2,RAB3A,IL1RL2,ADTRP,LDB2,EID2B,PIWIL1,DSG1,RHO,RTN1,MYB,CLPSL2,PYY,B4GALT6,PLK4,IGF1,PLK2,TAC3,FSTL4,LRFN5,SCN8A,TRHDE,GAP43
GO:0030054	CC	cell junction	9.36E-19	18.02890974	110	CRH,TAC1,NMU,SST,ADCYAP1,PENK,GABRA6,DSG3,NPAS4,GJD2,SLC32A1,IL1RAPL2,GAD2,CHRNA9,EGR3,PNOC,GAD1,GABRA1,PCDH8,OLFM3,CALB1,CBLN4,BDNF,GABRG2,CHRNB4,SVOP,SLC5A7,HTR2C,CDH7,NEFL,SNAP25,RAB3B,RAB27B,RPH3A,CNTN5,GABRB2,PTPRR,CDH18,FBLN7,CARTPT,NRN1,SLC17A6,RAB3C,SLC4A10,SYT1,EPHA5,CDH9,HTR3B,GLRA3,SYT4,NMNAT2,GRIN2B,LAMP5,DLGAP1,GABRA4,AKAP5,CAP2,KCNC2,DGKB,NAPB,HTR2A,PAK1,PAK3,SLC30A3,GLRA2,STXBP5L,SCN2A,HCRTR2,NPBWR1,SV2B,SYT13,CDH12,SYP,SYT2,CALY,NSF,CHRNB3,SYT10,DCLK1,GRIN2A,CAMK4,CDH8,VWC2L,HTR1A,SYN2,NEFH,GABRD,NRG1,NETO1,FGF12,PLPPR4,PLCB1,SH3GL2,CADPS,CHRNA6,NRXN3,INA,FRMPD4,CLSTN3,P2RX2,GABRG3,CNGB1,RAB3A,DSG1,RHO,CHRM4,SYNGR4,LRFN5,SCN8A,GAP43
GO:0071944	CC	cell periphery	9.72E-11	10.01230888	184	SPRR2G,TAC1,MAS1,PENK,GABRA6,DSG3,OR52N2,MUC15,SI,GJD2,GSG1L2,NPSR1,KRT5,ABRA,RGS4,SLC32A1,IL1RAPL2,GAD2,CAPZA3,CHRNA9,PNOC,GAD1,GABRA1,PCDH8,PVALB,PLSCR5,OLFM3,PRMT8,KCNV1,CALB1,MS4A8,GABRG2,CD70,ROBO2,FLT3,CHRNB4,SLC5A7,PIK3C2G,KCNK18,STYK1,HTR2C,ARL4D,CDH7,TERT,MLIP,SNAP25,RAB3B,RAB27B,OR1N1,MUCL1,RXFP3,MYPN,CYP4A11,UNC5D,RPH3A,CNTN5,GABRB2,MAL2,PTPRR,CDH18,TACR1,KCNG3,MCHR1,NRN1,KCNS2,RAB3C,SLC4A

						10,HRG,GPR22,SYT1,EPHA5,OR2AE1,PARM1,GLP2R,CDH9,CYP24A1,HTR3B,GLRA3,SYT4,GPR158,GFRA4,GRIN2B,LAMP5,HCN1,RHOV,KCNB2,ENTPD3,DLGAP1,GABRA4,AKAP5,ADRA1D,CAP2,KCNC2,PTPN3,RGS7,KCNH5,IL12RB2,DGKB,HTR2A,CLTRN,PAK1,PAK3,SLC30A3,ANO3,GLRA2,SLC39A2,STXBP5L,F7,RTKN2,ATP12A,SCN2A,MCHR2,HCRTR2,ADRB3,GPR88,NPBWR1,SV2B,SYT13,CDH12,SYP,SYT2,CALY,SLC12A1,PRPH2,NSF,GPR149,CHRNB3,RXFP1,SYT10,PRKCE,DCLK1,GRIN2A,VSIG1,KCNQ5,RHEX,COL25A1,CDH8,VWC2L,HTR1A,SYN2,UPK2,LRRC38,TRIM72,IPCEF1,SIDT1,XK,WNT1,GABRD,TRPC7,NRG1,PTH2R,NETO1,PLPPR4,SH3GL2,UPK3A,CHRNA6,OR13C5,NRXN3,GSG1,F2RL2,SERPINB2,CLSTN3,VSTM5,P2RX2,GABRG3,CNGB1,SDR16C5,ATP8A2,RAB3A,DIRAS2,IL1RL2,ADTRP,LDB2,SLC7A4,DSG1,RHO,CHRM4,PLK4,IGF1,LRFN5,SCN8A,TRHDE,GAP43,PAQR9
GO:0015267	MF	channel activity	3.82E-07	6.418007209	34	GABRA6,GJD2,CHRNA9,GABRA1,KCNV1,GABRG2,CHRNB4,KCNK18,SNAP25,GABRB2,KCNG3,KCNS2,HTR3B,GLRA3,GRIN2B,HCN1,KCNB2,GABRA4,KCNC2,KCNH5,ANO3,GLRA2,SCN2A,CHRNB3,GRIN2A,KCNQ5,LRRC38,GABRD,TRPC7,CHRNA6,P2RX2,GABRG3,CNGB1,SCN8A
GO:0004888	MF	transmembranesignaling receptor activity	9.96545E-06	5.001503151	57	MAS1,GABRA6,OR52N2,NPSR1,IL1RAPL2,CHRNA9,GABRA1,GABRG2,ROBO2,FLT3,CHRNB4,HTR2C,ADGRF2,SOSTDC1,OR1N1,RXFP3,UNC5D,GABRB2,PTPRR,TACR1,MCHR1,GPR22,EPHA5,OR2AE1,GLP2R,HTR3B,GLRA3,GPR158,GFRA4,GRIN2B,GABRA4,ADRA1D,IL12RB2,HTR2A,GLRA2,MCHR2,HCRTR2,ADRB3,GPR88,NPBWR1,GPR149,CHRNB3,RXFP1,GRIN2A,HTR1A,GABRD,PTH2R,CHRNA6,OR13C5,NRXN3,F2RL2,P2RX2,GABRG3,IL1RL2,CHML,RHO,CHRM4
Down regulated genes						
GO:0007154	BP	cell communication	4.63E-09	8.334588565	199	MMP8,CRNN,PPBP,GABRR2,CXCR6,CD40LG,TTR,H3C6,FOXA3,NCR1,CXCR

						1,CXCR2,OR7C1,SLC22A2,SLAMF1,GPR174,GPR20,PIGR,RAB42,OR2B11,CDC42BPG,PF4,FCRL1,IL1R2,P2RY10,CXCR4,LBX2,S100A4,NKX6-1,MS4A1,CASP12,CCR2,OR7A5,OTX2,TREML4,SIT1,IL7R,MIA,MRGPRF,MYOCD,S100A12,CCL26,CLDN18,ITGA10,INSRR,CXCR3,UBD,PROK2,F2RL3,FOXD1,GATA3,CXCL8,FOXC2,PYHIN1,COL1A2,GIPR,CD2,LCK,TNFRSF10D,ALOX15B,RGS1,SIK1,UBASH3A,GHRHR,FFAR2,IL24,HCAR3,OR2B6,GPR15,GJA4,CLEC4D,REM1,WNT6,SH2D3A,HSPB1,HRH4,HSPA1A,CD177,PEAR1,TBX3,ABCC2,OR2A7,LILRA4,NOTCH3,ITGA11,TEAD2,TGFB1I1,P2RX7,HIC1,SCT,ZBED6,IL3RA,CD3E,NGFR,ANPEP,KANK2,GDF15,CR1,ANGPT2,TBX18,IL2RB,TRIP10,PLN,TNFSF14,TBX6,ONECUT1,CEACAM1,DKKL1,ZNF683,CCL14,RRAD,TLR8,GPRC5A,IL18RAP,P2RY14,BLK,VNN1,SH2D6,LILRB5,OR51E1,AOC1,GPR4,ADORA2A,ITGA5,FOXF1,ADGRG3,E2F2,COL1A1,IQGAP2,PLEKHA4,ADM2,ADRA2B,FCRLA,COL3A1,IFNA2,RCVRN,CHRNG,FCRL3,GPER1,OR5K2,KLRB1,IGF2,PRLR,BTN1A1,S1PR4,INS-IGF2,FCGR2B,MMP9,PRKX,TNFRSF10A,SLC12A7,SYDE1,TLR5,IL18R1,IHH,FOXO4,SERPINF2,CNN2,IL2RG,DLL4,TNFRSF12A,TLR9,ZC3H12A,TP63,ADGRD1,DOK2,EPHA2,GFRA3,H2BC11,KRT19,ITPRIP,SEMA3F,GEM,C5AR1,TMC8,FLT4,CYSLTR2,CCL15-CCL14,PIK3R5,PMAIP1,PGF,CACNG5,KIF5A,RBPMS,PTH1R,RBPMS2,CEL,RNF152,SLC38A2,CD180,FZD9,AJUBA,LEF1,TBX2,LATS2,TRIM63,TNS1,FPR2,PCK1
GO:0050896	BP	response to stimulus	5.62E-09	8.250628776	249	MMP8,H4C4,MMP7,CRNN,PPBP,GABRR2,CXCR6,CD40LG,TTR,H3C6,FOXA3,NCR1,CXCR1,CXCR2,OR7C1,NPC1L1,SLC22A2,SLAMF1,IRX5,HSPA6,GPR174,GPR20,PIGR,SERPINA5,RAB42,OR2B11,CDC42BPG,PF4,FCRL1,IL1R2,P2RY10,CXCR4,LBX2,S100A4,NKX6-1,MS4A1,CASP12,OBP2B,

MCEMP1,CCR2,OR7A5,OTX2,NLRP4,TREML4,SIT1,IL7R,MIA,CR1L,MRGPRF,KCNE1,MYOCD,S100A12,CCL26,CLDN18,HP,ORM1,ITGA10,INSRR,CXCR3,UBD,SLC22A8,PROK2,F2RL3,FOXD1,GATA3,CXCL8,FOXC2,PYHIN1,COL1A2,GIPR,CD2,LCK,TNFRSF10D,ALOX15B,RGS1,FMO1,SIK1,UHRF1,UBASH3A,HSPB7,GHRHR,FFAR2,SERPINH1,IL24,HCAR3,OR2B6,GPR15,GJA4,MMRN1,CLEC4D,REM1,CST7,WNT6,SH2D3A,FMO3,HSPB1,HRH4,HSPA1A,CD177,PEAR1,TBX3,TCN1,MAFF,LY9,ABCC2,OR2A7,LILRA4,FOXJ1,NOTCH3,ITGA11,TEAD2,C6,LYZ,TGFB1I1,P2RX7,HIC1,SCT,ABCC3,ZBED6,IL3RA,CD3E,NGFR,ANPEP,KANK2,RUNX3,GDF15,GZMM,CR1,ANGPT2,JAML,TBX18,IL2RB,MGAM,TRIP10,SLAMF6,PLN,LYG2,TNFSF14,TBX6,SIX1,ONECUT1,CEACAM1,DKKL1,ZNF683,CCL14,RRAD,TLR8,GPRC5A,IL18RAP,P2RY14,BLK,VNN1,SH2D6,LILRB5,OR51E1,AOC1,GPR4,ADORA2A,AZGP1,ITGA5,FOXF1,ADGRG3,E2F2,COL1A1,IQGAP2,PLEKHA4,FOLR3,ADM2,BCL6B,H4C5,NFE2,ADRA2B,FCRLA,COL3A1,IFNA2,RCVRN,ND6,CHRNG,FCRL3,GPER1,OR5K2,KLRB1,IGF2,PRLR,BTN1A1,S1PR4,INS-IGF2,FCGR2B,DNAJB1,MMP9,FANCC,PRKX,TNFRSF10A,SYDE1,TGFBI,TLR5,IL18R1,IHH,FOXO4,APOBEC3A,SERPINF2,CNN2,C7,IL2RG,DLL4,TNFRSF12A,TLR9,ZC3H12A,TP63,ADGRD1,DOK2,EPHA2,GFRA3,H2BC11,KRT19,ITPRIP,SEMA3F,GEM,C5AR1,TMC8,CD163,FLT4,CYSLTR2,CCL15-CCL14,PIK3R5,SELENOP,PMAIP1,S100P,PGF,CACNG5,KIF5A,RBPMS,PTH1R,RBPMS2,RNF152,SLC38A2,COL6A2,CD180,FZD9,AJUBA,LEF1,TBX2,FMO2,LATS2,TRIM63,MYL9,TNS1,FPR2,PCK1

GO:0005886	CC	plasma membrane	5.05E-08	7.296828963	166	GABRR2,CXCR6,CD40LG,NCR1,CXCR1,CXCR2,OR7C1,NPC1L1,SLC22A2,SLAMF1,HSPA6,GPR174,GPR20,SRPX2,PIGR,SERPINA5,RAB42,OR2B11,FCRL1,IL1R2,P2RY10,CXCR4,GFI1

						B,MS4A1,VNN3,MCEMP1,CCR2,OR7A5,TREML4,KCNJ15,SIT1,KCNE4,IL7R,MRGPRF,KCNE1,S100A12,CLDN18,ITGA10,SLC16A12,INSRR,CXCR3,SLC6A12,SLC22A8,F2RL3,GIPR,CD2,LCK,TNFRSF10D,ALOX15B,RGS1,ABCA6,GHRHR,FFAR2,HCAR3,OR2B6,GPR15,GJA4,CLEC4D,REM1,WNT6,HSPB1,HRH4,HSPA1A,CD177,PEAR1,LY9,SLCO4A1,ABCC2,OR2A7,LILRA4,NOTCH3,ITGA11,SLC13A4,PCDH18,C6,TGFB1I1,P2RX7,CLDN15,ABCC3,IL3RA,CD3E,NGFR,MLANA,ANPEP,CR1,ANGPT2,JAML,IL2RB,MGAM,TRIP10,SLAMF6,TNFSF14,CEACAM1,RRAD,TLR8,GPRC5A,IL18RAP,P2RY14,BLK,ADH1B,VNN1,OR51E1,AOC1,GPR4,ADORA2A,FSCN3,AZGP1,ITGA5,ADGRG3,SLC4A11,IQGAP2,PLEKHA4,FOLR3,ADRA2B,FCRLA,CHRNG,FCRL3,GPER1,LGSN,OR5K2,KLRB1,PRLR,BTN1A1,S1PR4,FCGR2B,VNN2,TNFRSF10A,SLC12A7,TGFBI,TLR5,IL18R1,IHH,C7,IL2RG,DLL4,TES,TNFRSF12A,TLR9,ADGRD1,EPHA2,GFRA3,H2BC11,SLC1A7,KRT19,ITPRIP,MARVELD2,SEMA3F,GEM,C5AR1,TMC8,CD163,FLT4,CYSLTR2,PIK3R5,S100P,CACNG5,ARRDC2,DIO3,PTH1R,CEL,SLC38A2,COL6A2,CD180,FZD9,AJUBA,FPR2
GO:0005576	CC	extracellular region	7.33E-07	6.134830394	139	MMP8,H4C4,MMP7,CRNN,PPBP,MMP10,CD40LG,TTR,H3C6,SLC22A2,SLAMF1,GZMK,HSPA6,SRPX2,PIGR,SERPINA5,PF4,IL1R2,CXCR4,MFAP2,S100A4,NKX6-1,MS4A1,VNN3,OBP2B,TREML4,SIT1,IL7R,MIA,CR1L,S100A12,CCL26,HP,ORM1,SLC22A8,PROK2,F2RL3,CLEC18A,NXPE4,CXCL8,CKM,COL1A2,CD2,LCK,ALOX15B,H2AC12,LCN10,UBASH3A,SERPINH1,IL24,MMRN1,CST7,COL8A1,WNT6,HSPB1,ECM2,HSPA1A,CD177,TCN1,OIT3,NOTCH3,C6,LYZ,TGFB1I1,SCT,LCN6,NGFR,ANPEP,GDF15,GZMM,CR1,ANGPT2,MGAM,TRIP10,SLAMF6,LYG2,TNFSF14,CEACAM1,PRELP,DKKL1,CCL14,AEBP1,GPRC5A,VNN1,AOC1,AZGP1,COL1A1,IQG

					AP2,FOLR3,ADM2,H4C5,COL3A1,C11ORF52,IFNA2,COL8A2,COL27A1,ACAN,IGF2,PRLR,H2AC6,BTN1A1,TGM4,INS-IGF2,DNAJB1,CFHR3,MMP9,VNN2,TGFBI,H2AC7,IHH,SERPINF2,CNN2,C7,PTX4,COL4A4,APOC4,TLR9,ADAMTS2,OLFML1,KRT15,H2BC11,KRT19,SEMA3F,TMC8,CD163,FLT4,PLA2G12B,CCL15-CCL14,SELENOP,S100P,PGF,TOR4A,CEL,COL6A2,CD180,MYH11,SLC37A2,H2BC9,PCK1
GO:0038023	MF	signaling receptor activity	2.01E-14	13.6969021	80	GABRR2,CXCR6,CXCR1,CXCR2,OR7C1,SLAMF1,GPR174,GPR20,PIGR,OR2B11,FCRL1,IL1R2,P2RY10,CXCR4,CCR2,OR7A5,TREML4,IL7R,MRGPRF,INSR,CXCR3,F2RL3,GIPR,CD2,TNFRSF10D,GHRHR,FFAR2,HCAR3,OR2B6,GPR15,HRH4,PEAR1,OR2A7,LILRA4,NOTCH3,ITGA11,P2RX7,IL3RA,CD3E,NGFR,ANPEP,CR1,IL2RB,TLR8,GPRC5A,IL18RAP,P2RY14,LILRB5,OR51E1,GPR4,ADORA2A,ADGRG3,FOLR3,ADRA2B,FCRLA,CHRNG,FCRL3,GPER1,OR5K2,KLRB1,PRLR,BTN1A1,S1PR4,FCGR2B,TNFRSF10A,TLR5,IL18R1,IL2RG,TLR9,ADGRD1,EPHA2,GFRA3,C5AR1,FLT4,CYSLTR2,PTH1R,CEL,FZD9,LEF1,FPR2
GO:0004930	MF	G protein-coupled receptor activity	0.000859098	3.065957046	38	CXCR6,CXCR1,CXCR2,OR7C1,GPR174,GPR20,OR2B11,P2RY10,CXCR4,CCR2,OR7A5,MRGPRF,CXCR3,F2RL3,GIPR,GHRHR,FFAR2,HCAR3,OR2B6,GPR15,HRH4,OR2A7,GPRC5A,P2RY14,OR51E1,GPR4,ADORA2A,ADGRG3,ADRA2B,GPER1,OR5K2,S1PR4,ADGRD1,C5AR1,CYSLTR2,PTH1R,FZD9,FPR2

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

Pathway ID	Pathway Name	Adj.P.Val	Negative_log10_of_ adjusted_p_value	Gene Count	Gene
			Up regulated genes		
REAC:R-HSA-112316	Neuronal System	9.33E-20	19.03029601	47	GABRA6,GJD2,SLC32A1,IL1RAPL2,GAD2,CHRNA9,GAD1,GABRA1,KCNV1,GABRG2,CHRNB4,SLC5A7,KCNK18,NEFL,SNAP25,GABRB2,KCNG3,KCNS2,SYT1,HTR3B,GLRA3,GRIN2B,HCN1,KCNB2,DLGAP1,GABRA4,AKAP5,KCNC2,KCNH5,NCALD,GLRA2,SYT2,NS

					F,CHRNB3,SYT10,GRIN2A,KCNQ5,CAMK4,TUBB2A,SYN2,NRG1,PLCB1,CHRNA6,NRXN3,GABRG3,RAB3A,PPM1E
REAC:R-HSA-112314	Neurotransmitter receptors and postsynaptic signal transmission	1.54E-09	8.812159549	24	GABRA6,CHRNA9,GABRA1,GABRG2,CHRNB4,NEFL,GABRB2,HTR3B,GLRA3,GRIN2B,GABRA4,AKAP5,NCALD,GLRA2,NSF,CHRNB3,GRIN2A,CAMK4,TUBB2A,NRG1,PLCB1,CHRNA6,GABRG3,PPM1E
REAC:R-HSA-373076	Class A/1 (Rhodopsin-like receptors)	1.41E-07	6.850438507	28	TAC1,NMU,SST,PENK,NPSR1,PNOC,CXCL11,HTR2C,RXFP3,TACR1,MCHR1,ADRA1D,AVP,HTR2A,MCHR2,HCRTR2,ADRB3,NPBWR1,RXFP1,HTR1A,XK,PLPPR4,KISS1,F2RL2,RHO,PYY,CHRM4,TAC3
REAC:R-HSA-416476	G alpha (q) signalling events	5.35933E-05	4.270889165	19	TAC1,NMU,NPSR1,RGS4,HTR2C,TACR1,MCHR1,ADRA1D,AVP,DGKB,HTR2A,MCHR2,HCRTR2,PRKCE,TRPC7,PLCB1,KISS1,F2RL2,TAC3
REAC:R-HSA-372790	Signaling by GPCR	0.000127112	3.895813541	51	CRH,TAC1,NMU,SST,ADCYAP1,PENK,PPEF1,OR52N2,NPSR1,RGS4,PNOC,CXCL11,WNT8A,HTR2C,OR1N1,RXFP3,TACR1,MCHR1,OR2AE1,GLP2R,CALCB,ADRA1D,RGS7,AVP,DGKB,HTR2A,PAK1,GUCA1C,MCHR2,HCRTR2,ADRB3,NPBWR1,RXFP1,PRKCE,CAMK4,HTR1A,XK,WNT1,TRPC7,PTH2R,PLPPR4,PLCB1,KISS1,REEP1,OR13C5,F2RL2,CNGB1,RHO,PYY,CHRM4,TAC3
REAC:R-HSA-162582	Signal Transduction	0.533619768	0.272768091	78	CRH,TAC1,NMU,VGF,SST,ADCYAP1,PENK,PPEF1,OR52N2,EGR4,NPSR1,RGS4,EGR3,PNOC,CXCL11,GABRA1,EGR1,WNT8A,BDNF,GABRG2,FLT3,HTR2C,TERT,NEFL,OR1N1,RXFP3,GREM2,GABRB2,TACR1,MCHR1,OR2AE1,GLP2R,CALCB,GFRA4,GRIN2B,RHOV,ADRA1D,PTPN3,RGS7,AVP,DGKB,FGF9,HTR2A,PAK1,PAK3,GUCA1C,MCHR2,HCRTR2,ADRB3,NPBWR1,RSPO2,RXFP1,PRKCE,CAMK4,TUBB2A,HTR1A,XK,WNT1,TRPC7,NRG1,PTH2R,PLPPR4,PLCB1,SH3GL2,KISS1,REEP1,OR13C5,F2RL2,GABRG3,CNGB1,DYNC1I1,SDR16C5,RHO,MYB,PYY,CHRM4,IGF1,TAC3
Down regulated genes					
REAC:R-HSA-500792	GPCR ligand binding	2.77211E-06	5.557190041	32	PPBP,CXCR6,CXCR1,CXCR2,PF4,P2RY10,CXCR4,CCR2,CXCR3,PROK2,F2RL3,CXCL8,GIPR,GHRHR,FFAR2,HCAR3,WNT6,HRH4,SCT,P2RY14,GPR4,ADORA2A,ADM2,ADRA2B,GPER1,S1PR4,IHH,C5AR1,CYSLTR2,PTH1R,FZD9,FPR2
REAC:R-HSA-162582	Signal Transduction	0.000562416	3.249942189	92	MMP7,PPBP,CXCR6,TTR,CXCR1,CXCR2,OR7C1,GPR20,OR2B11,PF4,P2RY10,CXCR4,ETV4,SGO1,CCR2,OR7A5,CXCR3,PROK2,F2RL3,GATA3,CXCL8

					,COL1A2,GIPR,LCK,TNFRSF1 0D,RGS1,ARHGEF35,GHRHR, FFAR2,HCAR3,OR2B6,GPR15, WNT6,HSPB1,HRH4,OR2A7,N OTCH3,SCT,IL3RA,NGFR,RU NX3,IL2RB,TRIP10,RRAD,P2 RY14,OR51E1,GPR4,ADORA2 A,COL1A1,IQGAP2,ADM2,AD RA2B,COL3A1,RCVRN,COL2 7A1,GPER1,OR5K2,IGF2,H2A C6,S1PR4,DNAJB1,MMP9,PR KX,TNFRSF10A,SYDE1,H2AC 7,IHH,FOXO4,IL2RG,DLL4,C OL4A4,APOC4,TLR9,GFRA3, H2BC11,C5AR1,FLT4,CYSLT R2,PIK3R5,PGF,KIF5A,PTH1R ,COL6A2,FZD9,LEF1,MYH11, H2BC9,LATS2,MYL9,FPR2,C BX2,PCK1
REAC:R-HSA-168256	Immune System	0.005462988	2.262569739	74	MMP8,PPBP,CD40LG,TTR,NC R1,CXCR1,CXCR2,HSPA6,PIG R,IL1R2,MCEMP1,CCR2,NLR P4,TREML4,IL7R,S100A12,HP, ORM1,GATA3,CXCL8,COL1A 2,LCK,IL24,CLEC4D,HSPA1A, CD177,TCN1,LILRA4,C6,LYZ, P2RX7,IL3RA,CD3E,ANPEP,G ZMM,CR1,JAML,IL2RB,MGA M,SLAMF6,TNFSF14,CEACA M1,TLR8,IL18RAP,BLK,VNN1 ,LILRB5,AOC1,ADGRG3,COL 1A1,IQGAP2,FOLR3,COL3A1, IFNA2,KLRB1,PRLR,BTN1A1, FCGR2B,CFHR3,MMP9,TLR5, IL18R1,CNN2,C7,IL2RG,TNFR SF12A,TLR9,GFRA3,C5AR1,S 100P,KIF5A,CD180,TRIM63,F PR2
REAC:R-HSA-109582	Hemostasis	0.008164756	2.088056792	32	PPBP,SERPINA5,PF4,ORM1,IT GA10,F2RL3,GATA3,COL1A2, CD2,LCK,TNFRSF10D,MMRN 1,CD177,MAFF,P2RX7,ANGP T2,JAML,CEACAM1,ITGA5,C OL1A1,NFE2,ADRA2B,IFNA2, IGF2,TNFRSF10A,SERPINF2, DOK2,KIF1C,PIK3R5,SELENO P,KIF5A,TOR4A
REAC:R-HSA-418594	G alpha (i) signalling events	0.093256027	1.030323089	21	PPBP,CXCR6,TTR,CXCR1,CX CR2,PF4,CXCR4,CCR2,CXCR 3,CXCL8,RGS1,HCAR3,HRH4, P2RY14,ADRA2B,RCVRN,GP ER1,S1PR4,PRKX,C5AR1,FPR 2
REAC:R-HSA-202733	Cell surface interactions at the vascular wall	0.131182326	0.882124673	13	PF4,COL1A2,CD2,LCK,TNFRS F10D,CD177,ANGPT2,JAML,C EACAM1,ITGA5,COL1A1,TNF RSF10A,DOK2

Table 4 Topology table for up and down regulated genes

Category	Node	Degree	Betweenness	Stress	Closeness
Up	PAK1	173	0.028159	40928804	0.323514
Up	ELAVL2	123	0.017931	49416154	0.288766
Up	NSF	115	0.020114	23044990	0.326051
Up	HTR2C	114	0.018259	29134326	0.29829

Up	TERT	109	0.013862	12161812	0.330253
Up	KRT5	90	0.011287	14388756	0.327439
Up	GPRASP2	83	0.012488	16027128	0.299805
Up	CHRM4	83	0.013908	10442482	0.306192
Up	MYB	82	0.011101	11639612	0.302896
Up	PRKCE	82	0.010414	13383932	0.317181
Up	SH3GL2	81	0.015009	8602342	0.310041
Up	NEFL	80	0.011512	5837396	0.325809
Up	CD70	80	0.010479	24671164	0.281655
Up	DCLK1	80	0.009007	8668148	0.299411
Up	CHRNA9	74	0.012796	6636898	0.273363
Up	C6orf141	74	0.012519	22948968	0.282449
Up	NRG1	70	0.011734	13185638	0.286376
Up	UBE2U	69	0.0133	12297096	0.284087
Up	MAS1	68	0.011565	6079632	0.304668
Up	DSG1	66	0.006721	7395226	0.325361
Up	SYT1	62	0.008216	6702626	0.30212
Up	HPRT1	62	0.006281	10787838	0.300254
Up	NEFM	62	0.006421	5424570	0.308176
Up	PLK4	61	0.007071	9899496	0.283697
Up	DYNC1I1	58	0.008029	13075920	0.29282
Up	SERPINB2	57	0.007714	10923044	0.280615
Up	MDH1	57	0.005988	11576132	0.30161
Up	FATE1	57	0.012052	13973146	0.266928
Up	ATP12A	57	0.01499	6636836	0.285227
Up	VSIG1	57	0.007035	14538940	0.275447
Up	MOS	56	0.006895	5823686	0.298519
Up	RAB3A	54	0.00791	5354190	0.297217
Up	CADPS	54	0.008146	5092982	0.287011
Up	PTPN3	52	0.006799	3138966	0.310784
Up	PLK2	52	0.007488	8564946	0.288111
Up	PNMA2	52	0.007674	3911212	0.301569
Up	NEFH	52	0.005669	4367880	0.308983
Up	GRIN2B	50	0.005221	8685832	0.284393
Up	INA	50	0.005513	4826808	0.304052
Up	PPEF1	49	0.005028	3077816	0.297391
Up	TACR1	48	0.006838	4984298	0.266745
Up	EGR1	47	0.006124	6985264	0.290376
Up	SNAP25	46	0.005405	2840312	0.301281
Up	PTPRR	46	0.006717	3023620	0.297578
Up	AKAP5	46	0.00726	8846218	0.282063
Up	MYOG	45	0.007307	7976338	0.273781
Up	SYP	42	0.005295	6009614	0.280698
Up	CHGB	42	0.004402	1985544	0.301432
Up	GDA	41	0.006789	14090952	0.274293
Up	PRMT8	40	0.004426	2202906	0.290875
Up	NELL1	39	0.005924	5040984	0.294897
Up	FLT3	37	0.003048	2106224	0.298586
Up	NELL2	37	0.004661	2218788	0.266745
Up	RTN1	36	0.005687	5502506	0.260892
Up	ADCYAP1	35	0.005746	13075048	0.240147
Up	RAB3B	34	0.006122	2292976	0.294831
Up	STMN2	33	0.00397	1770596	0.296511
Up	SERPINB13	32	0.0045	5247158	0.256141
Up	GRIN2A	31	0.002348	3084160	0.283345
Up	NR1H4	31	0.002749	4098122	0.289043
Up	NAP1L5	31	0.003486	3520432	0.273046
Up	MAP7D2	31	0.002383	2903454	0.276669
Up	MYH13	31	0.003581	5127138	0.276183
Up	PLCB1	30	0.002985	6888848	0.268959
Up	ARL4D	30	0.003932	4739098	0.280901
Up	PDP1	30	0.005082	8507176	0.275573
Up	GLRA2	30	0.004682	2252842	0.270455
Up	DLGAP1	29	0.002937	3899192	0.280519
Up	CSN1S1	29	0.003814	5024846	0.269562
Up	PPM1E	29	0.003333	6353814	0.266648
Up	AVP	28	0.004318	4913378	0.254838
Up	CHML	27	0.003671	1670908	0.266111
Up	MAL2	27	0.004432	3827092	0.278851
Up	RFX6	27	0.002862	2398226	0.270123

Up	HSPB3	26	0.002435	1605440	0.270389
Up	P2RX2	26	0.004146	11179848	0.237584
Up	CAP2	25	0.002331	3475372	0.277761
Up	F7	25	0.00398	3619126	0.279736
Up	GAP43	25	0.002633	3213868	0.271098
Up	ROBO2	25	0.00361	1673720	0.270876
Up	HTR2A	24	0.002224	5272268	0.25469
Up	NLRP2	24	0.002474	3046242	0.281739
Up	GAD1	24	0.002699	1543090	0.296724
Up	ALOX12B	24	0.002911	1524586	0.284112
Up	RPH3A	23	0.00392	1274136	0.28917
Up	STAT4	23	0.00225	3186110	0.277109
Up	PAK3	22	7.45E-04	1359976	0.269826
Up	BDNF	22	0.002084	2214532	0.274065
Up	NRN1	22	0.002343	2904362	0.229884
Up	PAX5	21	0.001571	1209290	0.273747
Up	NCALD	21	0.002094	742050	0.290708
Up	NXPH2	21	0.001483	2282474	0.241383
Up	CAMK4	21	0.0013	2651870	0.265641
Up	RGS7	20	0.001629	2101340	0.281439
Up	TDO2	20	0.001135	1237716	0.254347
Up	CT55	20	0.003323	1125688	0.28481
Up	GABRG2	19	0.002225	2260632	0.244571
Up	ENC1	19	0.001288	2259178	0.27747
Up	MYPN	19	0.001796	2745936	0.267176
Up	FGF12	19	0.002205	2840438	0.275332
Up	SYN2	19	0.001259	1054996	0.279393
Up	RHO	19	0.002088	2186802	0.262102
Up	NAPB	19	0.001486	1681700	0.256091
Up	ADRA1D	19	0.001857	2080534	0.26814
Up	GABRD	19	0.002339	2055124	0.249105
Up	F2RL2	19	0.00182	2963726	0.265641
Up	RAB27B	18	0.002824	1258866	0.263093
Up	BEX1	18	0.001303	619184	0.271176
Up	HRG	18	0.001925	3325830	0.248993
Up	NMU	17	0.003046	950374	0.244237
Up	TAC1	17	0.00292	2083210	0.267014
Up	CDH8	17	8.86E-04	1263642	0.260368
Up	PIWIL1	17	0.001003	629764	0.284026
Up	KRT82	17	0.001168	1799040	0.2675
Up	MUCL1	17	0.003019	3086562	0.265513
Up	TRHDE	17	0.002298	3972136	0.256499
Up	DYDC1	16	8.21E-04	560938	0.253908
Up	NPSR1	16	0.001909	2186922	0.259774
Up	RGS4	15	0.001288	1683598	0.263533
Up	GAD2	3	2.36E-05	48934	0.245242
Up	RBFOX1	2	8.89E-05	107910	0.244662
Up	TAC3	2	1.02E-04	103622	0.238733
Up	SVOP	2	3.00E-05	59688	0.224049
Up	IL12RB2	1	0	0	0.216989
Up	RAB3C	1	0	0	0.224315
Up	CARTPT	1	0	0	0.218611
Up	SV2B	1	0	0	0.23203
Up	CACNB4	1	0	0	0.23203
Up	C1QL3	1	0	0	0.254641
Up	ANKRD7	1	0	0	0.263198
Up	B4GALT6	1	0	0	0.20309
Up	SYT2	1	0	0	0.23203
Up	VSNL1	1	0	0	0.232823
Up	KCNS2	1	0	0	0.210696
Up	CCDC185	1	0	0	0.246605
Up	PGM2L1	1	0	0	0.206214
Up	CDH18	1	0	0	0.214943
Up	ATP8A2	1	0	0	0.265332
Up	NRXN3	1	0	0	0.251972
Up	MLLT11	1	0	0	0.229796
Up	C11orf87	1	0	0	0.238415
Up	SYT4	1	0	0	0.23203
Up	ADRB3	1	0	0	0.236673
Up	RXFP1	1	0	0	0.220015

Up	KISS1	1	0	0	0.215237
Down	UBD	654	0.15112	2.24E+08	0.361138
Down	MKI67	484	0.110753	1.42E+08	0.352211
Down	HSPB1	483	0.110888	1.71E+08	0.357197
Down	PYHIN1	342	0.066113	58482622	0.336832
Down	TES	291	0.061653	61255336	0.354858
Down	RBPMS	227	0.048426	53178790	0.313036
Down	LATS2	216	0.040908	40957474	0.340177
Down	LCK	162	0.031545	30303362	0.331978
Down	EPHA2	154	0.028721	23266342	0.339461
Down	ANLN	153	0.024763	22039474	0.327845
Down	SERPINH1	150	0.024753	28138694	0.341618
Down	TP63	142	0.022498	24847586	0.324212
Down	KRT15	138	0.026351	14360242	0.32731
Down	DNAJB1	127	0.019403	22378202	0.325328
Down	HSPA6	121	0.016967	24899482	0.324642
Down	TEAD2	116	0.01537	10601488	0.31825
Down	SLAMF1	114	0.023056	23597596	0.297632
Down	IL7R	109	0.012174	23407182	0.301845
Down	TRIM63	104	0.021726	28194588	0.297659
Down	UHRF1	87	0.010293	9157378	0.31776
Down	KIF1C	87	0.010567	14165088	0.300691
Down	NOTCH3	80	0.014787	15201970	0.306249
Down	GFI1B	80	0.013113	10842648	0.303466
Down	DKKL1	78	0.014836	23803094	0.280092
Down	PCK1	77	0.007681	13743418	0.303577
Down	COL1A1	76	0.01344	7278036	0.313377
Down	KRT19	75	0.007277	9943438	0.311091
Down	FANCC	74	0.009764	8216824	0.309388
Down	FPR2	74	0.011769	13954910	0.261594
Down	MYH11	73	0.007581	17559364	0.295029
Down	S100A4	72	0.010394	5315164	0.320658
Down	ITGA5	66	0.011449	10345216	0.302093
Down	CBX2	66	0.008779	13925408	0.291941
Down	TTR	65	0.008634	7419964	0.302979
Down	SGO1	65	0.007788	13289692	0.278992
Down	KANK2	65	0.008311	4874830	0.323324
Down	NGFR	64	0.009393	8007396	0.313779
Down	TRIP10	64	0.008122	13028764	0.291426
Down	BLK	64	0.0107	17329554	0.297297
Down	SYDE1	64	0.003939	4450816	0.287948
Down	CXCR4	63	0.007485	10836722	0.289512
Down	LEF1	61	0.007391	6350706	0.298344
Down	TNFRSF10A	61	0.010834	8048490	0.288917
Down	GATA3	60	0.007917	5540288	0.311223
Down	LYZ	59	0.005302	10916132	0.302217
Down	PTH1R	53	0.009808	9310524	0.281487
Down	FOXA3	53	0.005544	3422360	0.298748
Down	CCR2	52	0.010443	11006662	0.27281
Down	MMP9	51	0.008978	3281478	0.274258
Down	HP	51	0.00693	5312024	0.304458
Down	ABCC2	49	0.00821	8016758	0.284026
Down	COL1A2	49	0.0058	4123054	0.298155
Down	KIF5A	48	0.008469	6093688	0.297712
Down	GEM	48	0.006291	5887716	0.289753
Down	TNFRSF10D	47	0.004006	4841196	0.275286
Down	TBX3	46	0.003966	6776878	0.304122
Down	TGFB1I1	45	0.005439	2236700	0.316467
Down	DOK2	44	0.004931	2719906	0.298519
Down	IL1R2	42	0.005083	7132876	0.270488
Down	RUNX3	42	0.003872	6891482	0.283017
Down	SERPINA5	41	0.006095	10451870	0.259174
Down	ADAM33	41	0.007471	2763720	0.275195
Down	FOXC2	40	0.00431	2542046	0.287848
Down	VNN2	40	0.006975	9163084	0.245333
Down	MAFF	39	0.006108	6202430	0.270333
Down	IL2RG	39	0.004818	3065952	0.286774
Down	HAL	39	0.005077	7921062	0.272686
Down	CACNG5	39	0.00689	10012096	0.258202
Down	CNN2	38	0.003478	3117688	0.308522

Down	CD3E	37	0.004444	1846130	0.285548
Down	HIC1	37	0.002325	4445664	0.280889
Down	MMP7	37	0.004334	4687842	0.261967
Down	PIGR	36	0.004518	3553372	0.286252
Down	COL6A2	36	0.006829	4592548	0.26563
Down	FLT4	34	0.00523	3858760	0.292406
Down	CRNN	34	0.003756	5529764	0.265822
Down	TNS1	33	0.002772	2522944	0.283211
Down	TLR9	33	0.004962	9237656	0.27208
Down	AZGP1	33	0.002456	4065630	0.283844
Down	PITX1	32	0.004421	2343672	0.289271
Down	SLC38A2	32	0.003422	3980992	0.276299
Down	S100P	31	0.002822	2548722	0.287835
Down	IL2RB	31	0.002118	1912550	0.299873
Down	SAP25	30	0.002022	3734230	0.269243
Down	IQGAP2	29	0.00233	3195168	0.279973
Down	FHL5	29	0.003089	4224230	0.259683
Down	LYG2	29	0.006032	1839648	0.2718
Down	E2F2	28	0.003259	4455944	0.277633
Down	AJUBA	28	0.002664	1325164	0.30422
Down	COL8A1	28	0.003201	4474880	0.263219
Down	CKM	28	0.003473	2628128	0.276264
Down	ZC3H12A	28	0.002855	3844038	0.279322
Down	SIK1	28	0.002844	5143526	0.282836
Down	NFE2	27	0.003585	2996958	0.257789
Down	CYSLTR2	27	0.003188	5442164	0.260419
Down	FOXO4	26	0.001596	2850706	0.282932
Down	ITPRIP	26	0.005136	1403128	0.289145
Down	CXCR2	25	0.002852	1512172	0.248282
Down	CXCL8	25	0.003976	2693066	0.27452
Down	ADORA2A	25	0.002427	3913074	0.258687
Down	PPBP	25	0.002728	5682784	0.254877
Down	MYL9	25	0.002755	1417230	0.312621
Down	FOXJ1	25	0.002844	3072104	0.269364
Down	TLR5	25	0.002706	3772068	0.209116
Down	UBASH3A	25	0.002111	2511872	0.286376
Down	IL24	25	0.001705	2208432	0.279878
Down	FNDC11	25	0.002638	1382328	0.273476
Down	CD2	24	0.002495	1138490	0.28421
Down	PRLR	24	0.00185	2555138	0.26921
Down	IGF2	24	0.004788	1590838	0.279028
Down	CEACAM1	24	0.002966	3423386	0.27976
Down	FCGR2B	24	0.002147	2868264	0.282533
Down	CCDC102A	24	0.00323	2192490	0.257849
Down	COL3A1	23	8.40E-04	861406	0.262445
Down	FOXD3	23	0.001402	1312200	0.263481
Down	GPRC5A	23	0.001394	2330634	0.276541
Down	SIX1	21	0.002036	1876960	0.246422
Down	SERPINF2	21	0.001831	3513870	0.243876
Down	NANOS2	21	0.002169	2656028	0.24217
Down	ACAN	20	0.002762	3879096	0.228202
Down	CXCR1	3	9.72E-06	13098	0.22333
Down	ALX4	2	1.13E-05	12912	0.239894
Down	TBX2	2	1.83E-05	28734	0.246275
Down	TGFBI	2	0	0	0.242499
Down	SLC12A7	2	2.60E-05	44798	0.221556
Down	MAGEA12	2	5.51E-05	31038	0.220742
Down	ADAMTS2	2	3.48E-05	69644	0.234841
Down	COL8A2	1	0	0	0.208378
Down	PRELP	1	0	0	0.238613
Down	ANGPT2	1	0	0	0.232014
Down	MS4A1	1	0	0	0.249246
Down	P2RY14	1	0	0	0.221935
Down	TBX6	1	0	0	0.238415
Down	SIT1	1	0	0	0.249246
Down	PF4	1	0	0	0.215398
Down	TLR8	1	0	0	0.213893
Down	VHLL	1	0	0	0.238415
Down	PIK3R5	1	0	0	0.232536
Down	FOXD1	1	0	0	0.208542

Down	CSNK1G2-AS1	1	0	0	0.238415
Down	MMRN1	1	0	0	0.237362
Down	ETV4	1	0	0	0.244843
Down	ONECUT1	1	0	0	0.203917
Down	CXCR3	1	0	0	0.210696
Down	RBPMS2	1	0	0	0.238415
Down	MARVELD2	1	0	0	0.213286
Down	CLEC18A	1	0	0	0.216046
Down	ALOX15B	1	0	0	0.224315
Down	BCL6B	1	0	0	0.238415
Down	ORM1	1	0	0	0.244843
Down	NCR1	1	0	0	0.222129
Down	HOXB6	1	0	0	0.246605
Down	SAMD4A	1	0	0	0.216046
Down	SLAMF6	1	0	0	0.249246
Down	CLDN15	1	0	0	0.224665
Down	PMAIP1	1	0	0	0.203115
Down	KCNE1	1	0	0	0.22263
Down	MMP8	1	0	0	0.185807
Down	ADRA2B	1	0	0	0.236673
Down	CD163	1	0	0	0.233406
Down	F2RL3	1	0	0	0.209893
Down	MMP10	1	0	0	0.215237
Down	COL4A4	1	0	0	0.215237

Table 5 miRNA - hub gene and TF – hub gene interaction

Regulation	Hub Genes	Degree	MicroRNA	Regulation	Hub Genes	Degree	TF
Up	NEFL	78	hsa-mir-378a-3p	Up	ELAVL2	15	NRF1
Up	NSF	45	hsa-mir-100-5p	Up	MYB	15	STAT1
Up	ELAVL2	43	hsa-mir-27a-3p	Up	DCLK1	14	YY1
Up	PRKCE	42	hsa-mir-513a-5p	Up	CD70	10	PPARG
Up	MYB	34	hsa-mir-15b-5p	Up	TERT	10	E2F6
Up	DCLK1	28	hsa-mir-365a-3p	Up	PRKCE	9	GATA2
Up	SH3GL2	23	hsa-mir-548o-5p	Up	PAK1	7	REL
Up	CD70	17	hsa-mir-374a-5p	Up	KRT5	7	SREBF1
Up	PAK1	15	hsa-mir-107	Up	NSF	7	SRF
Up	GPRASP2	15	hsa-mir-518c-5p	Up	HTR2C	6	JUND
Up	TERT	13	hsa-mir-498	Up	CHRM4	6	PAX2
Up	HTR2C	12	hsa-mir-339-5p	Up	CHRNA9	5	JUN
Up	KRT5	9	hsa-mir-125b-5p	Up	SH3GL2	5	EN1
Up	CHRNA9	6	hsa-mir-23b-3p	Up	NEFL	5	SREBF2
Up	CHRM4	4	hsa-mir-16-5p	Up	GPRASP2	2	HNF4A
Down	ANLN	126	hsa-mir-138-1-3p	Down	TP63	17	ZNF354C
Down	MKI67	124	hsa-mir-548d-5p	Down	TES	11	ARID3A
Down	SERPINH1	83	hsa-mir-4726-3p	Down	LCK	10	FOXL1
Down	LATS2	70	hsa-mir-320d	Down	HSPB1	9	RUNX2
Down	TES	57	hsa-mir-1202	Down	PYHIN1	8	TP53
Down	DNAJB1	42	hsa-mir-191-5p	Down	SERPINH1	8	FOS
Down	EPHA2	40	hsa-mir-450b-5p	Down	ANLN	8	TFAP2C
Down	HSPB1	22	hsa-mir-548f-3p	Down	MKI67	7	FOXC1
Down	RBPMS	19	hsa-mir-214-3p	Down	DNAJB1	7	EGR1
Down	TP63	9	hsa-mir-139-5p	Down	UBD	6	GATA1
Down	KRT15	9	hsa-mir-1343-3p	Down	HSPA6	5	MEF2A
Down	HSPA6	8	hsa-mir-204-3p	Down	LATS2	5	HOXA5
Down	LCK	6	hsa-mir-101-3p	Down	EPHA2	5	ELK1
Down	UBD	5	hsa-mir-21-3p	Down	RBPMS	4	SPIB
Down	PYHIN1	2	hsa-mir-375	Down	KRT15	3	SOX5